ORAL PRESENTATION

WOTA-01-1

Using whole-exome sequencing to identify novel pathogenic variants in a Chinese obese cohort

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Abstract: Objectives Whole-exome sequencing (WES) was used to detect monogenic obesity variants in Chinese obese cohort. **Methods** We collected 119 obese patients aged 17 to 65 with a BMI ≥ 28 kg/m^2 and who underwent weight loss surgery (gastric bypass or laparoscopic sleeve gastrectomy) from January 2011 to July 2019 at Shanghai Sixth People's Hospital. WES was carried out to detect the gene mutations related to the feeding center, and the pathogenic variants were screened by multiple bioinformatics methods, and the mutations with minor allele frequency (MAF) less than 0.01 in East Asian population were screened in oneKG, ExAC, and gnomAD databases. **Results** A total of 25 variants were detected in 24 patients, all of which were heterozygous mutations. The mutated genes are detected as follows: *SH2B1* in 7 cases (5.88%), *MCHR1* in 4 cases (3.36%), *PHIP* in 3 cases (2.52%), *ADCY3*, *LEPR* in 2 cases (1.68%), and *LEP*, *NTRK2*, *AGRP*, *KSR2, MC3R, MC4R, BDNF, PCSK1* in just 1 case (0.84%). Two variants were detected in two patients, separately, and a same novel pathogenic mutation in *LEPR* was detected in a pair of sister samples. Besides, 12 variants were not included in any of the public databases. **Conclusions** A total of 25 rare variants in feeding pathways were detected in whole-exome region, of which 12 were novel in East Asian populations. This study provides new insights into the pathogenesis of obesity.

WOTA-01-2

Defective branched-chain amino acids catabolism in the hypothalamus leads to adiposity

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Objective:

Impaired branched-chain amino acid (BCAA) catabolism in peripheral tissues contributes to metabolic abnormality. However, the role of hypothalamic BCAA catabolism in the maintenance of energy homeostasis remains elusive.

Methods:

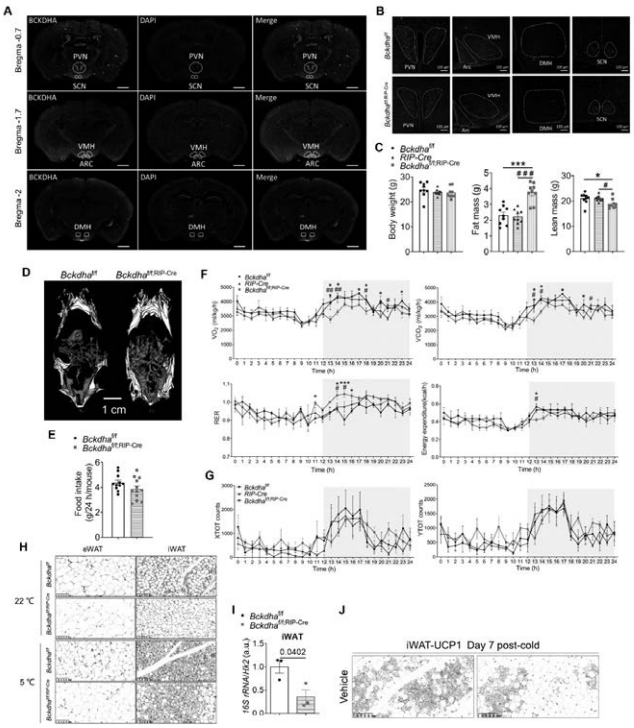
Branched-chain ketoacid dehydrogenase (BCKDH) is the rate-limiting enzyme for BCAA catabolism. To determine the role of hypothalamic BCAA catabolism in the regulation of energy homeostasis, we generated mice lacking the E1α subunit (BCKDHA) in the hypothalamus by conducting rat insulin-2 promoter-mediated deletion of branched-chain keto acid dehydrogenase E1α subunit (*Bckdha*$^{f/f;RIP\text{-}Cre}$ mice) and conducted metabolic phenotyping.

Results:

We found that BCKDHA was enriched in hypothalamic neurons, with the most abundant expression found in the paraventricular nucleus (PVN), followed by the arcuate nucleus (ARC) and ventromedial nucleus (VMH). We generated *Bckdha*$^{f/f;RIP\text{-}Cre}$ mice lacking BCKDHA selectively in the hypothalamic neurons. *Bckdha*$^{f/f;RIP\text{-}Cre}$ mice showed considerably higher fat mass and lower lean mass compared with their *Bckdha*$^{f/f}$ and *RIP-Cre* littermates, without significant change in body weight. The whole-body oxygen consumption (VO_2), carbon dioxide production (VCO_2), and energy expenditure in *Bckdha*$^{f/f;RIP\text{-}Cre}$ mice were decreased, while the respiratory exchange ratio (RER) was increased at the onset of the active period, suggesting a reduction in utilizing fat. Food intake and locomotor activity remained unchanged. Cold-induced inguinal white adipose tissue beiging was impaired in *Bckdha*$^{f/f;RIP\text{-}Cre}$ mice, with larger adipocyte size and fewer mitochondrial content, compared with *Bckdha*$^{f/f;RIP\text{-}Cre}$ mice.

Conclusion:

This is the first study to reveal the link of hypothalamic BCAA catabolism to adipose tissue homeostasis, which greatly expands our understanding of how amino acids regulate systemic lipid metabolism.



WOTA-01-3

Understanding the regulation of Mig-6 on Energy Homeostasis due to modulating thermogensis in brown adipose tissue

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Objective

Brown adipose tissue (BAT) governs thermogenic energy expenditure. Mitogen-inducible gene 6 (Mig-6) is a negative regulator of the epidermal growth factor receptor signal. In previous study, we demonstrated the association between EGFR signaling and metabolic disorder such as NAFLD. However, the roles of Mig-6 in BAT remain poorly understood. In the present study, we investigated the metabolic role of Mig-6 in BAT.

Methods

We down-regulated the expression of Mig-6, using lentivirus mediated shRNA by transducing immortalized brown adipocytes and 3T3-L1 adipocytes. We generated BAT specific Mig-6 knock-in and knock-out models using a genetic strategy. BKI and BKO mice were measure GTT, ITT, biochemical parameters and energy expenditure. Western blot and qPCR were performed to analyze related genes.

Results and Conclusion

The inhibition of Mig-6 declined adipogenesis and thermogenesis in the BAT cell. Mig-6 BKI mice were improved glucose metabolism, lipid levels and fasting glucose. Mig-6 BKO mice were impaired glucose metabolism, increased fasting glucose. We detected a reduction in the size of adipocyte and a relative increase of UCP1 expression in Mig-6 KI BAT. Of note, Mig-6 augmented the expression of thermogenesis relative genes , consistent with the increased UCP1 in the BAT of mice. In conclusion, Mig-6 is as potential factor improving obesity by regulating adipogenesis and thermogenesis in the BAT.

WOTA-01-4

SCAP-Activated Astrocyte Release 27-OHC Compromises Neuroplasticity Associated with Diabetic Cognitive Impairment

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Objective: SCAP may mediate the development of diabetes-associated cognitive impairment(DACD). We aim to explore the underlying mechanism of astrocyte SCAP-associated cholesterol metabolic homeostasis abnormal on neuroplasticity damage in DACD.
Methods: C57BL/6J WT and astrocyte SCAP-specific knockout mice (G-SCAPKO) were subjected to High Fat diet(HFD) feeding-induced diabetes model. Neuroplasticity damage and levels of cholesterol deposition in the hippocampus were evaluated. The SCAP/SREBP2 and CYP27A1, 27-hydroxycholesterol(27-OHC) levels were detected in vivo and in vitro, and the transcriptional activation of CYP27A1 by SREBP2 was detected by chromatin immunoprecipitation.
Results: The data revealed that lipid homeostasis between astrocytes and neurons is impaired due to astrocytic SCAP-mediated abnormal cholesterol metabolism. At the same time, we found that SCAP in hippocampal astrocytes of diabetic mice was abnormally elevated, and the SCAP in astrocytes was positively correlated with the latency time of the mouse water maze. Interestingly, G-SCAPKO mice attenuated hippocampal pyramidal neuron damage in diabetes by reducing SREBP2-CYP27A1 activation. In-depth molecular analysis showed that under the intervention of AGEs, SCAP recruited SREBP2 to the Golgi apparatus, mediated the increase of SREBP2 into the nucleus, and specifically activated CYP27A1 production in astrocytes at the transcriptional level, thereby promoting the release of 27-OHC in astrocytes. This process ultimately leads to the impairment of neuronal synapse density and dendritic morphology.
Conclusion: SCAP promotes CYP27A1 transcriptional activation to mediate increased 27-OHC production by transporting SREBP2 into the nucleus, serving as a novel regulator of DACD. Inhibition of astrocyte SCAP may be a new therapeutic strategy for the treatment of DACD.

WOTA-01-5

External validation of new non-laboratory-based pre-DM/DM risk prediction models for case finding in HK primary care

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Early detection of undiagnosed prediabetes (Pre-DM) is crucial in preventing type-2 diabetes mellitus (T2DM). Yet, Hong Kong primary care (HKPC)'s practice focuses on T2DM screening among ≥ 45 years old. We aimed to determine the external validity of two new non-laboratory-based risk prediction models, which were developed from HK population-based data using machine learning (ML) and logistic regression (LR), in pre-DM/DM case finding in HKPC.

A cross-sectional prospective study. 919 Chinese adults without DM from HK's public and private PC clinics completed a questionnaire on the models' non-laboratory clinical and lifestyle predictors and performed a pre-DM/DM diagnostic blood test. Pre-DM/DM were defined by oral glucose tolerance test and/or hemoglobin-A1c levels. Area under the receiver operating characteristic curve (AUC-ROC) assessed the discriminatory power of the models.

The prevalence of newly diagnosed pre-DM/DM was 53.4%. Both models offered good external discrimination in case finding (AUC-ROC: ML:0.744, LR:0.739). The sensitivity of detecting pre-DM/DM at optimal risk cutoffs were 0.70 and 0.72, respectively. The ML model had a better discrimination than existing models in the younger age subgroup (18-45 years old). Both models' predicted risks were significantly lower than the observed event rates in our sample (Hosmer-Lemeshow Test $p<0.001$). We converted the LR model into a risk scoring algorithm, with similar discriminatory power as original.

We confirmed the new models' validity in detecting individuals with high pre-DM/DM risks in an external PC Chinese population. The algorithm can be utilised at the point-of-care to facilitate opportunistic case finding of asymptomatic pre-DM patients in clinical practice.

WOTA-01-6

Identification of Liver-derived Brown adipocyte Activating Factor

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【Objective】
Activating brown adipose tissue (BAT), which is involved in energy expenditure, prevents metabolic diseases. We searched for the serum factor that regulates brown adipocyte activity.
【Methods】
A proteomics analysis of serum from the inducible adipocyte-specific IR and IGF1R knockout (Ai-DKO) mice was conducted to identify a Brown adipocyte Activating Factor (BAF). After adding the BAF recombinant protein to the brown adipocytes in the culture media, cells were examined by EDU, real-time PCR, and an extracellular flux analyzer for mitochondrial activity. We measured glucose metabolism and energy expenditure in BAF whole-body knockout mice (BAFKO) and liver-specific transgenic mice (BAFTg) *in vivo*. We investigated BAF receptors by immunoprecipitation and proteomics analysis using BAF-overexpressing brown preadipocytes.
【Results】
We searched molecules upregulated during brown adipose tissue regeneration in the serum of Ai-DKO mice. A liver-derived BAF induced the proliferation of brown preadipocytes and increased the expression of uncoupling protein 1 (UCP1) to promote mitochondrial activation in mature brown adipocytes. BAFKO mice showed decreased adipocyte mitochondrial function, impaired thermogenesis, obesity, and systemic insulin resistance. Reciprocally, BAFTg mice displayed increased adipose tissue browning, leading to higher energy expenditure and improved glucose tolerance. In adipocytes, BAF formed a complex with the protein that triggers the brown adipocyte signaling as the BAF receptor (BAFR).
【Conclusion】
We introduce BAF as a hepatokine that improves energy expenditure and glucose metabolism by activating brown adipocytes and a potentially powerful means for treating metabolic diseases.

WOTA-01-7

Prospective clinical study of Bariatric Surgery in the Treatment of Women with Obesity and Polycystic Ovary Syndrome

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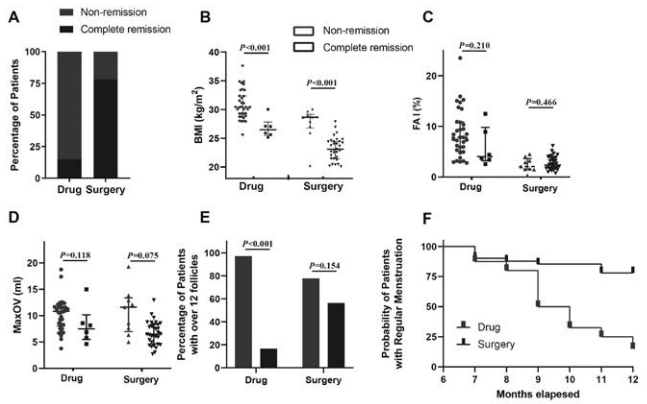
Objective: We aimed to compare the efficacy between medication and bariatric surgery therapy for women with obesity and PCOS.
Methods: Ninety women aged 18 to 40 years fulfilling the diagnostic criteria for PCOS with BMI over 27.5kg/m^2 were recruited and 81 subjects completed the study. The participants were divided into the drug or surgery group. In the drug group, patients were administered metformin and oral contraceptives containing ethinyl-estradiol and cyproterone acetate for the first 6 months, and metformin alone for the second 6 months. In the surgical group, patients underwent laparoscopic sleeve gastrectomies. The follow-up period was 12 months. The main outcome was the complete remission of PCOS, requiring 6 consecutive regular menstruation cycles or spontaneous pregnancy in the second 6 months.

Results: Median BMI at endpoint was 30.1 kg/m2 in the drug group and 23.7 kg/m2 in the surgical group; complete remission rate was 15% and 78%, respectively. Endpoint BMI was the only index with significant difference in

indexes including free androgen index, ovarian morphology and HOMA-IR. Logistic regression analyses revealed that the final BMI was the major factor influencing the remission of PCOS. The cutoff points for the final BMI were 27.5 kg/m^2 for the drug group and 26 kg/m^2 for the surgical group. Overall, nearly 95% of patients with an endpoint BMI below the cutoff values achieved complete remission.

Conclusion: Complete remission of PCOS in patients with obesity depends on the final BMI after weight loss. Thus, bariatric surgery should be prioritized for these patients.



WOTA-01-8

Immunological efficacy of SHED for pancreatic islet transplantation.

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Objective: It has been reported that IBMIR, immunoresponse after intraportal islet transplantation, induces activation of NK cells and damages the islet graft. In this study, we investigated whether stem cells from human exfoliated deciduous teeth (SHED) show the immunosuppressive effects.

Methods: SHED were stimulated with TNF-α, IL-1β and IFN-γ, which were increased by IBMIR in the liver. The cell-surface antigen of stimulated SHED was assessed by FACS analysis. The secretion of the anti-inflammatory factors, IDO, TGF-β and PGE2 from stimulated SHED was evaluated by ELISA. To assess the immunosuppressive effects of SHED, we co-cultured human peripheral blood mononuclear cells (PBMCs) with stimulated SHED, and evaluated the cell proliferation activity of PBMCs by CFSE staining. Non-radioactive cellular cytotoxicity assay was performed to assess the anti-cytotoxic effects of SHED on iPS cell-derived pancreatic β cells. Furthermore, we generated islet-like organoids by the fusion of dissociated pancreatic islet cells and SHED, and evaluated the insulin secretion from these organoids by ELISA.

Results: Stimulation with pro-inflammatory cytokines did not change the cell-surface antigen expression of SHED. Stimulated SHED secreted more anti-inflammatory factors compared to BM-MSCs. Furthermore, stimulated SHED inhibited the cell proliferation activity of PBMCs, and protected iPS cell-derived pancreatic β cells from cytotoxicity by PBMCs. These data indicated that SHED had the potential to suppress the immunoactivity. Finally, islet-like organoids mixed with SHED increased the insulin secretion compared to the organoids without SHED.

Conclusion: These results suggest that SHED have the immunosuppressive effects and protect the transplanted islets from immunoresponse.

WOTA-01-9

The Legacy Effect of Early Intensive Glycaemic Control on Cancer Risk in People with Newly Diagnosed Type 2 Diabetes

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Background

Diabetes is a known risk factor for developing cancer. We examined whether earlier intensive glycaemic control versus intensive glycaemic control achieved later in diabetes continuum lowers cancer risk.

Methods

We conducted a retrospective analysis of people with newly diagnosed type 2 diabetes attending Hong Kong Hospital Authority between 2000-2019 followed for incident all-site cancer until 2019. We used Cox regression to test the association between time-weighted mean HbA1c (mHbA1c) achieved during different periods after diabetes diagnosis and incident cancer. Fine-Gray model was used to account for competing risk of death.

Results

Among 103,236 people with newly diagnosed type 2 diabetes, 3,811 developed all-site cancer during a median follow-up of 7.1 (inter-quartile range 5.0, 9.4) years. Weighted mean HbA1c levels in the first year after diabetes diagnosis were positively associated with risk of cancer. The respective fully-adjusted hazard ratios (95% confidence interval) versus mHbA1c<5.7% (reference) were 1.5 (1.0, 2.3) for 5.7%≤mHbA1c<6.5%, 1.9 (1.3, 2.9) for 6.5%≤mHbA1c<7%, and 2.0 (1.3, 3.1) for mHbA1c≥7% for incident cancer. In the subgroup who achieved adequate glycaemic control (mHbA1c<7%) during the entire follow-up period, the associations between glycaemic control within one year of diabetes diagnosis and cancer persisted, with corresponding hazard ratios 1.6 (1.0, 2.4) for 5.7%≤mHbA1c<6.5%, 2.0 (1.3, 3.0) for 6.5%≤mHbA1c<7%, and 1.9 (1.3, 3.0) for mHbA1c≥7% versus mHbA1c<5.7% (reference), respectively.

Conclusion

Failure to achieve good glycaemic control at early stages of type 2 diabetes is associated with higher cancer incidence, even among individuals who maintain adequate glycaemic control in the long run.

WOBS-01-1

Suppression of glucagon signaling promotes α-to-β reprogramming

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Objective: As diabetes results from the absolute or relative deficiency of insulin secretion from pancreatic β cells, the generation of surrogate β cells has attracted a lot of attention for the cure of diabetes. Insulin-producing cells have been generated from various cell types. However, it still remains unclear as to how surrogate β cells can be efficiently generated toward establishing future regenerative therapies for diabetes. We have revealed that glucagon antibody induces α-cell neogenesis in adult mice (Himuro M. et al. under revision), suggesting that the suppression of glucagon signaling could play a role in cellular plasticity in α-cell lineage. Therefore, we hypothesized that inhibiting glucagon signaling may affect the efficiency of α-to-β reprogramming.

Methods: We generated transgenic mice that exogenously and inducibly express Pdx1 specifically in α cells, and treated the mice with glucagon receptor antagonist. It is noted that Flag-tagged sequence is attached to *Pdx1*, so that the exogenous expression of *Pdx1* can be distinguished from the endogenous *Pdx1* gene. FLAG-tag/insulin double-positive cells was defined as α-cell-derived insulin-producing cells and α-to-β reprogramming ratio was calculated by dividing FLAG-tag/insulin double-positive cells by FLAG-tag

positive cells.
Results: Immunohistological analysis demonstrated that the administration of glucagon receptor antagonist significantly increased the number of α-cell-derived insulin-producing cells in the transgenic mice, compared with vehicle (27.2 ± 1.3 vs 12.9 ± 1.8%, p<0.0001, n=8-9).
Conclusions: The suppression of glucagon signaling with glucagon receptor antagonist promotes α-to-β reprogramming in mice, which could lead to establishing efficient methods for generating surrogate β cells.

WOBS-01-2
Impact of fructose on β-cell metabolism and insulin secretion
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Objective

Increasing evidence suggests that fructose is detrimental to glycemic control, possibly leading to type 2 diabetes. However, how circulating fructose impacts pancreatic β-cell function remains elusive. We aimed to elucidate the effect of fructose on glucose-induced insulin secretion (GIIS) and intracellular metabolism of β cells.

Methods

MIN6-K8 clonal mouse β-cell line or C57BL/6J mouse pancreatic islets were stimulated with 0.1-12.5 mM fructose in the presence of 2.8 (2.8G) or 8.8 mM glucose (8.8G). Insulin secretion was measured by static incubation. Intracellular Ca^{2+} (Ca^{2+}_i) levels were visualized by Fura-2. Metabolic flux of glucose and fructose were analyzed by stimulating MIN6-K8 with [U-^{13}C]-glucose or [U-^{13}C]-fructose and quantifying ^{13}C incorporation in intracellular metabolites.

Results

Fructose dose-dependently increased insulin secretion at 8.8G but not 2.8G. The lowest fructose concentration to elicit significant increase in GIIS was 0.3 and 2.5 mM in MIN6-K8 and mouse islets, respectively. Fructose dose-dependently augmented 8.8G-induced Ca^{2+}_i increase. The amplifying effect of fructose on GIIS was suppressed by treatment with nifedipine, an inhibitor of voltage-dependent Ca^{2+} channels (VDCC), or in the β-cell line deficient for Kir6.2, a pore-forming subunit of the K_{ATP} channel. Metabolic flux analysis indicated that fructose is able to enter later glycolytic steps while limiting the glycolytic flux from coexistent glucose.

Conclusion
Our results suggest that fructose-amplified insulin secretion is dependent on K_{ATP} channel closure and subsequent Ca^{2+} influx through VDCC. We also reveal that fructose is metabolized in β cells. Further investigation is warranted to clarify whether fructose metabolism contributes to insulin secretion.

WOBS-01-3
Chronic exposure of imeglimin exerts pleiotropic effects on pancreatic α-cells
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Objective: It has been unknown whether imeglimin, anti-diabetes drug, affects pancreatic α-cell function. In this study, we investigated the effects of chronic exposure of imeglimin on α-cells.

Methods: Single-cell RNA sequencing (scRNA-seq) for mouse islets after treatment with imeglimin for 24 hours was conducted. Mouse islets, human islets, or hPSC-derived glucagon producing spheroids were treated with imeglimin. α-cell-specific analysis was also performed by sorted α-cells from mouse islets using flow cytometer and single-cell western blotting (scWB) to assess the impact of imeglimin.

Results: α-cell-specific analysis of scRNA-seq showed imeglimin upregulated 59 genes and downregulated 111 genes. Pathway analysis revealed that “ER stress response” and “protein translation” for upregulated genes and “secretion” and “endocrine development” for downregulated genes were suggested in imeglimin-treated α-cells. Imeglimin reduced glucagon gene expression by 71%, glucagon secretion by 62%, and the proportion of glucagon-producing cells in islets by 26% in mouse islets (p<0.05). Those effects of imeglimin on α-cells were also observed in both human islets and hPSC-derived glucagon-producing spheroids. The imeglimin-induced reduction in α-cells in mouse islets was validated by flow cytometry. In sorted mouse α-cells, the expression of Mafb and Arx were downregulated and the expression of Ddit3 and Mafa were upregulated by imeglimin. The scWB demonstrated that imeglimin augmented protein levels of insulin (1.55-fold) and Ddit3 (2.57-fold) in α-cells (p< 0.05).

Conclusion: Treatment of islets with imeglimin decreased glucagon secretion, reduced α-cell mass, altered α-cell identity gene expression. Thus, imeglimin might affect glucose metabolism by inducing dedifferentiation of α-cells and suppressing glucagon secretion.

WOBS-01-4
PDPN-knockdown alleviate islet fibrosis in T2DM mice
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Objective: Through RNA-sequencing, we found that the *Pdpn* gene was significantly overexpressed in islet stellate cell (ISC) of fibrotic islet. Combined with validations in multiple T2DM animals, we hypothesized that the *Pdpn* may be the key gene for the activation of ISC. The role of *Pdpn* in the fibrotic islet needs to be further verified.
Methods: A GFAP-specific promoter adeno-associated virus was constructed to knock-down the *Pdpn* in stellate cells (GFAP-AAV-Pdpn-). C57 mice were randomly selected for tail vein injection of GFAP-AAV-Pdpn-virus ($3*10^{11}$ v.g). After 3 weeks, low-dose STZ and high-fat diet were used to establish T2DM. Intraperitoneal glucose tolerance test (IPGTT) was used to evaluate the glucose metabolism. Masson and immunofluorescence were used to evaluate the islet morphology, insulin and fibrosis in islets.
Results: 1. The expression of PDPN in the pancreas of T2DM was significantly higher than control, and the PDPN expression of T2DM+AAV-pdpn- group was significantly lower than T2DM. 2. The fasting blood glucose of T2DM+AAV-pdpn- group was significantly lower than T2DM. 3. The IPGTT experiment found that the AUC curve of T2DM+AAV-pdpn- group had a decreasing trend than T2DM and the blood glucose was significantly decreased at 180 minutes. 4. Immunofluorescence showed that the insulin in T2DM+AAV-pdpn- group was significantly higher than T2DM. 5. Masson staining showed that T2DM+AAV-pdpn- group had significantly less fibrotic areas in islets.
Conclusion: Specific knockdown of the *Pdpn* gene in stellate cells suppressed the occurrence and development of islet fibrosis, and improved the function of β cells in mice.

WOBS-01-5
Irisin inhibited islet stellate cells activation
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Objective: Pancreatic islet stellate cells (ISC) have a strong fibrogenic ability, and ISC activation may be an important biological event leading to islet fibrosis in type 2 diabetes mellitus (T2DM). However, the mechanism of ISC activation is still unclear. In this study, we will investigate the effect of irisin on ISC activation and explore its molecular mechanism.

Method: 1. The ISCs from GK and Wistar rat islets were extracted and simulated by Transforming Growth Factor-β(TGF-β). These cell models were divided into the control group and the irisin intervention group. 2. Cell viability Migration rates and the disappearance rate of lipid droplets of the ISCs were detected by the CCK8, Wound Healing, and Oil red O staining. 3. RT-PCR, Western Blotting, and immunofluorescence experiments were applied to observe ISC activation marker α-SMA and ECM components, and the phosphorylation levels of TGF-β/Smad pathway-related proteins.
Results: 1. Irisin intervention reduce the activity, migration rate, and lipid droplet disappearance rate of ISC. 2. Irisin inhibits the increase of the Wistar-ISC migration rate induced by TGF-β intervention and reduces the expression levels of α-SMA and Col-I at the mRNA and protein levels. 3. Irisin inhibits the phosphorylation level of Smad2/3 protein in a concentration-dependent manner.
Conclusion: Irisin inhibits the cell viability, migration, and lipid droplet disappearance rate of activated ISCs. It also prevents the AGEs/TGF-β-induced activation of ISCs. Irisin suppresses the activation of ISC by inhibiting the phosphorylation of Smad2/3 proteins.

WOBS-01-6
A pharmacological dose of imeglimin activates mitochondrial function and glucose-induced insulin secretion.

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The underlying pathology of diabetes mellitus is inadequate insulin secretion and resistance. The resulting hyperglycemia leads to complications, decreased quality of life and shortened life span. Imeglimin is a derivative of the hypoglycemic agent metformin, an oral hypoglycemic agent with a tetrahydrotriazin structure. There are several reports that imeglimin promotes glucose-induced insulin secretion in diabetic mouse models and protects pancreatic beta cells from inflammation and ROS-induced apoptosis, but whether imeglimin promotes insulin secretion in mice with normal glucose tolerance, and if so, the mechanism is not known. Therefore, to clarify the mechanism by which imeglimin promotes insulin secretion, we examined the effect of imeglimin on glucose-stimulated insulin secretion (GSIS) in islets isolated from C57Bl/6, ICR and DBA/2. The results showed that in islets isolated from C57Bl/6 mice, exposure to imeglimin 10 μM, which is equivalent to the human pharmacological dose, for 24 hours stimulated insulin secretion with 16.7 mM glucose but not with 2.8 mM glucose. Under the same conditions, mitochondrial function was evaluated by flux analyzer and immunoblotting. we found that imeglimin stimulation at this 10 μM increased oxygen consumption rate and mitochondrial complex V. Although it has been reported that the imeglimin-induced increase in GSIS in streptozotocin-treated mice is attributed to an increase in NAD^+ and enhanced calcium influx by activating NAMPT expression, no change in NAD^+ levels by imeglimin was observed under the conditions described above. These results suggest that imeglimin promotes glucose-dependent insulin secretion by activating mitochondrial function in mice with normal glucose tolerance.

WOBS-02-1
Functional analysis of genes expressed differentially in MIN6 sublines with high versus reduced glucose-responsiveness

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Object. Molecular mechanisms of glucose-stimulated insulin secretion (GSIS) from pancreatic β-cells are not fully understood. Since GSIS deteriorations are believed to underlie the pathogenesis of type 2 diabetes mellitus, precise understandings of GSIS mechanisms are of essential importance. By comparing transcript levels of 3 insulin secreting MIN6 cell sublines with strong glucose-responsiveness and 3 with mildly reduced responsiveness, we identified 630 differentially expressed genes. In order to clarify causal relationships of these genes in GSIS alterations, we conducted large-scale generation of stable clones overexpressing the genes.
Methods. For this purpose, we used our recently developed system based on recombinase-mediated cassette exchange with the tetracycline-inducible system. We attempted to generate stable transformants of 100 genes, but failed to clone cDNAs of 8 genes. In addition, during the course of this study, 9 genes have been reported to be important for GSIS. Therefore, the results of overexpressions of 83 genes are reported.
Results. We identified 18 genes as GSIS regulators, 15 positive and 3 negative regulators. Then, *Sox11* ((sex determining region Y)-box 11) was selected to confirm its roles in regulating insulin secretion, and the gene was subjected to shRNA-mediated suppression. While *Sox11* overexpression decreased GSIS, its suppression increased GSIS, confirming the role of *Sox11* as a negative regulator of insulin secretion. Furthermore, metabolic experiments using radiolabelled glucose showed *Sox11* to participate in regulating glucose metabolism.
Conclusion. Our data suggested that overexpression screening is a feasible option for systemic functional testing to identify important genes in GSIS.

WOBS-02-2
Hispidulin is an insulin secretagogue targeting the AKAP9-mediated PKA signaling pathway.

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Background and objective: Inadequate insulin secretory impairment in response to high glucose is considered predominant in Asian non-obese type 2 diabetic subjects. Hispidulin, a natural flavone, was identified as a new insulin secretagogue that enhances insulin secretion in response to high glucose and seems a better drug candidate than synthetic marketed drugs. Here, we explored the insulinotropic mechanism(s) of hispidulin. **Materials and methods:** Secreted insulin and intracellular cAMP contents from batch-incubated C57BL/6 J mice islets and INS-1 832/13 cells were measured using an AlphaLISA kit. Preparation of hispidulin-immobilized beads and affinity purification with hispidulin-immobilized beads were performed. INS-1 832/13 β-cells were transfected with the AKAP-9 siRNA or scrambled siRNA using Lipofectamine RNAiMAX reagent. AKAP-9 knockdown was confirmed by western blotting. **Results:** Hispidulin showed insulin secretory potential in INS1832-13 cells and isolated mice islets in response to high-glucose. Hispidulin showed no effect on intracellular cAMP concentration; however, showed an additive effect in both forskolin and IBMX-induced insulin secretion. Among the inhibitors of major signaling pathways, H89, a PKA inhibitor, completely inhibited hispidulin-induced insulin secretion. Hispidulin showed a strong binding affinity with A-kinase anchoring protein 9 (AKAP-9). Interestingly, in AKAP-9 knock down β-cells, hispidulin-mediated glucose-induced insulin secretion was further amplified. Furthermore, it was also observed that the intracellular PKA signaling was further increased using hispidulin alone and AKAP-9 knockdown β-cells. **Conclusion:** Hispidulin increases intracellular PKA concentration and inhibits the negative regulation of AKAP-9-cAMP-PKA signalosome, enhancing glucose-induced insulin secretion. The promising glucose-dependent insulin-releasing mechanism makes hispidulin a potential anti-diabetic drug candidate.

WOBS-02-3
Apigenin stimulates insulin secretion through PKA-MEK kinase signaling cascade-independent of K-ATP channels

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Background and objectives: Claims and counter-claims exist about pathophysiology in Asian type 2 diabetic subjects; however, recent reports suggest that insulin secretory impairment is predominant in Asians. Apigenin, a

natural bioflavonoid, was identified as a new insulin secretagogue enhances glucose-stimulated insulin secretion and seems better candidate than sulfonylureas. Here, we explored the insulinotropic mechanism(s) of apigenin. **Materials and methods:** Secreted insulin from batch incubated islets was measured by ELISA. Intracellular cAMP contents were measured using an acetylation enzyme immunoassay. K+ and Ca2+ channels currents were recorded in MIN6 cells with whole-cell and perforated whole-cell patch-clamp technique. The effect of apigenin on glucose tolerance and plasma insulin was evaluated in diabetic mice. **Results:** Apigenin, unlike sulfonylurea, enhanced insulin secretion in mice islets at stimulatory glucose with no effect at basal glucose concentrations. Apigenin exhibited no effects on inward rectifying K+ or Ca2+ currents. Furthermore, apigenin amplified glucose-induced insulin secretion in depolarized and glibenclamide-treated islets. Subsequently, apigenin showed no effect on intracellular cAMP concentration; however, exerted additive effect in forskolin and IBMX-induced insulin secretion. Among the inhibitors of major signaling pathways, H89, a PKA inhibitor, and U0126, a MEK kinase inhibitor, significantly inhibited apigenin-induced insulin secretion. Apigenin improved glucose tolerance, enhanced glucose-stimulated plasma insulin, and improved insulinogenic index (β-cell function) in non-obese type 2 diabetic mice. **Conclusion:** Apigenin exerts glucose-stimulated insulin secretion by modulating the PKA-MEK kinase signaling cascade independent of K-ATP channels. These findings have significant implications for understanding apigenin's promising glucose-lowering mechanism and its potential as an anti-diabetic drug candidate.

WOBS-02-5
Regulation of Pancreatic Beta-Cell Function by Salt-Inducible Kinases.

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A prerequisite for the development of hyperglycaemia in diabetes is when the beta cells are unable to secrete sufficient insulin to maintain glucose homeostasis. Current efforts to enhance beta-cell function focus mostly on the pathways that stimulate insulin release, but very little is known about the intracellular inhibitory mechanisms that terminate insulin secretion. Salt inducible kinase 3 (SIK3) is a serine/threonine protein kinase that regulates multiple signalling pathways involved in metabolic regulation in response to changes in hormonal and nutrient status. SIK3 is highly expressed in mouse pancreatic beta cells and is highly conserved in humans. However, the role of SIK3 in regulating insulin secretion and beta-cell biology has never been studied. In this talk, I will provide a detailed overview of the physiological roles of salt-inducible kinases in glycaemic control and disease development, with a focus on the regulation of pancreatic beta-cell biology and glucose metabolism by SIK3.

WOBS-02-6
Microelectrode array (MEA) based recording of glucose responsiveness in pancreatic islets

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Pancreatic islet cells are known to depolarize synchronously. However, depolarization characteristics between species and electrical properties by insulin secretagogues are still largely unknown. Here we investigated the electrophysiological properties of islets.
Mouse islets, human islets, and human pluripotent stem cell (hPSC)-derived islets, and the effects of imeglimin, an anti-diabetes drug, were analyzed by combining microelectrode array (MEA) recording with suction, glucose-induced insulin secretion (GSIS), perifusion analysis, and imaging of membrane potentials with Plasma Membrane Potential Indicator (PMPI), in the context of response to glucose.
MEA recording revealed a significant increase in mean spike counts, burst count, and fraction of plateau phase (FOPP) in response to glucose in mouse, human, and iPSC-derived islets ($p<0.05$). Meanwhile, human islets showed individual variation and poorly responsive to glucose.
Treatment of mouse islets with imeglimin augmented firing frequency (1.4-fold), burst counts (2.0-fold), total burst duration (2.1-fold), and FOPP (2.1-fold) in MEA recording under high-glucose., predominantly in first half time of glucose stimulation. Imeglimin also enhanced GSIS (1.5-fold) in mouse islets mainly during early phase of high glucose. Mouse islet perifusion exhibited shortening of insulin peak time and upregulation of secreted insulin (1.3-fold) in the presence of imeglimin. Imaging membrane potential with PMPI demonstrated that imeglimin showed an earlier depolarization tendency compared to vehicle in INS-1 β-cells.
MEA has a potential to delineate the differences in electrophysiological characteristics of islet between species. Alteration of the electrophysiological properties in islets could be captured when insulin secretion was facilitated by imeglimin.

WOBS-02-7
Regulation of SIRT1 in enteroendocrine cells

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The longevity gene Sirtuin is one of the most important molecules involved in the regulation of aging. Although there are many studies on Sirt1 (Sirtuin1) related to the intestine, there are no reports on Sirt1 function in enteroendocrine cells. We aimed to investigate glucose metabolism-related phenotypes in intestine-specific SIRT1 knockout (iKO) and endocrine cell-specific SIRT1 knockout (NgnKO) mice and to clarify the function of SIRT1 in enteroendocrine cells. When iKO mice were subjected to a high-fat diet, suppression of body weight gain and improvement of glucose metabolism were observed compared to the wild-type mice. The immunohistochemistry of these mice revealed an increase in the number of enteroendocrine cells in the iKO and an increase in GLP-1 secretion. Furthermore, RNA expression analysis of isolated enteroendocrine cells using FACS showed that Neurogenin3, a transcription factor involved in intestinal differentiation, was upregulated in these cells. We also analyzed the downstream mechanism using intestinal organoids. Analysis of SIRT1 regulation in the intestine may provide a new therapeutic target in glucose metabolism and obesity.

WOBS-03-1
Betaine–homocysteine methyltransferase promotes adipocyte commitment and insulin resistance via p38 MAPK/Smad signaling

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Objective: Betaine homocysteine methyltransferase (Bhmt) belongs to the family of methyltransferases and is involved in the one-carbon metabolic cycle, which is associated with the risk of diabetes and adiposity. This study aimed to explore whether Bhmt participated in the development of obesity or its associated diabetes, as well as the mechanism involved.
Methods: The expression levels of Bhmt were examined in stromal vascular fraction cells (SVCs) and mature adipocytes, non-obese and obese status. Knockdown and overexpression of Bhmt in C3H10T1/2 cells were used to investigate Bhmt's function in adipogenesis. Bhmt's role *in vivo* was analyzed using an adenovirus expressing system and a high-fat diet-induced obesity (DIO) mouse model.
Results: Bhmt was highly expressed in SVCs rather than mature adipocytes of adipose tissue and upregulated in adipose tissue of obesity and C3H10T1/2-commited preadipocyte. Overexpression of Bhmt promoted adipocyte commitment and differentiation *in vitro* and exacerbated adipose tissue expansion *in vivo*, with a concomitant increase in insulin resistance, while Bhmt silencing exhibited opposite effects. Mechanistically, Bhmt-induced adipose expansion was mediated by stimulating the p38 MAPK/Smad pathway.
Conclusions: Our findings highlight a novel and distinct role of Bhmt in adipocyte and propose Bhmt as a promising therapeutic target for obesity and obesity-related diabetes.

WOBS-03-2

Molecular signature of insulin resistance in visceral adipose tissue in obesity

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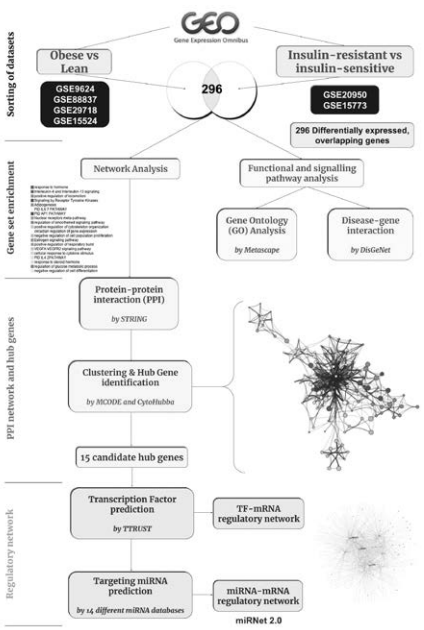
Objective: We adopted an interactomics approach to identify the gene expression patterns, functions, and regulatory molecular networks responsible for insulin resistance (IR) in visceral adipose tissue (VAT) of obese individuals.
Methods: We identified six microarray datasets for differentially-expressed genes (DEGs) in VAT (Selection criteria: $p \leq 0.05$, |Log(fold change)|≥1.0) in obesity (GSE9624, GSE88837, GSE29718, and GSE15524; 60 samples-34 obese, 26 lean) and obesity-related IR (GSE20950, GSE15773; 30 samples-15 insulin-resistant, 15 insulin-sensitive). The DEGs were further analysed for protein–protein interaction (PPI) (in STRING), functional enrichment, and hub gene identification to detect genetic clusters, targeting transcription factors (TFs), microRNA (miRNA), and molecular networks (in Cytoscape).
Results: The PPI interaction network ($p<0.001$), constituting 296 DEGs with 11 significant clusters (analysed through MCODE plug-in) was functionally enriched for 225 biological processes, 10 molecular functions, two cellular components, and 40 KEGG pathways, portraying an underlying immune-inflammatory network. The 15 candidate hub genes (through cytoHubba app) (JUN, EGR1, FOS, IL6, PIK3R1, NR3C1, SOCS3, STAT1, IRS1, DUSP1, JUNB, ZFP36, CXCL10, MMP9, and HSP90AB1) were regulated by TFs (top 5 TFs: RELA, STAT3, NFKB1, SP1, TP53) and miRNA (top five miRNA: miR-16-5p, miR-20a-5p, miR-124-3p, miR-155-5p, and miR-1-3p), according to highest degree and betweenness in the miRNA-mRNA network (through miRNet). The network was significantly enriched (FDR <0.01) for TLR signaling pathway, pathways in cancer, type 2 diabetes mellitus, colorectal cancer, B cell receptor signaling pathway, among others.
Conclusion: The results dictate an immuno-modulatory network and crosstalk in VAT of obese individuals, suggesting potential theranostic targets and regulatory mechanisms of IR pathogenesis.



WOBS-03-3

Eepd1 promotes PKA-mediated adipose tissue lipolysis and ameliorates obesity

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Objective: Protein kinase A (PKA) plays a key role in promoting lipolysis and thermogenesis in adipocytes to combat obesity. However, how PKA activity is spatiotemporally controlled during adipose tissue lipolysis and thermogenesis remains elusive.
Methods: *Eepd1* global knock-out, adipose tissue-specific knockout and virus-mediated Eepd1-overexpression mice were constructed and challenged with high-fat diet to study the function of Eepd1 *in vivo*. Overexpression or knock-down of Eepd1 in C3H10T1/2-derived mature adipocyte or human primary adipocytes were used to investigate the Eepd1's function on lipolysis and thermogenesis *in vitro*. Molecular inhibitors, site mutations, coimmunoprecipitation and click chemistry were used to explore the Eepd1's regulation on PKA activation.
Results: Here, we demonstrate that a DNA damage response protein, endonuclease–exonuclease–phosphatase family domain containing 1 (Eepd1), plays a key role in the spatiotemporal regulation of PKA in adipocytes. Myristoylation on the Gly2 residue of Eepd1 tethers it to the plasma membrane, where it further sequesters the catalytic and regulatory subunits of PKA and its downstream substrates, including HSL and p38 MAPK. PKA is spatiotemporally regulated in the polyphyletic complex, in which it phosphorylates and activates downstream targets, thereby effectively initiating thermogenesis in adipose tissues. Functionally, Eepd1 ablation inhibits PKA activation and lipolysis in adipose tissue, which exacerbates the obesity development; in contrast, virus-mediated overexpression of Eepd1 in mouse adipose tissue or human adipocytes efficiently enhances thermogenesis and hence inhibits the obesity onset.
Conclusion: Thus, we uncover an unanticipated and important role of Eepd1 in regulating adipose lipolysis.

WOBS-03-4

Phosphorylation-dependent adipose circadian reprogramming induces a window for enhanced fat burning

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Circadian rhythm of animals could be changed by environmental temperature with elusive mechanism. In the present work, we applied multi-omics approaches to quantify the circadian transcripts, proteins and phosphorylation of mouse brown adipose tissue (BAT) under mild cold treatment (16°C) and room temperature (22°C). The results showed that the extents and amplitudes of cold-responsive rhythmic phosphorylation exceeded those of RNA and protein abundances. The enhanced cold-response rhythmic phosphorylation mainly distributed in metabolic pathways on energy consuming, particularly beta-oxidation pathway, whereas the decreased rhythmic molecules located in the lipogenesis, implying dominant role of phosphorylation in metabolic circadian reprogramming. We found that cold-induced phosphorylation enhancement focused on specific time phase (around ZT12). Interestingly, high-fat food could result in lower body weight if eating during specific time period (ZT11-ZT18) at lower temperature, indicating a new cold-induced window for fat burning created through phosphorylation-dependent circadian reprogramming.

WOBS-03-6

Dysfunction in pacemaker activity of sinoatrial nodal cells in a mouse model of myocardial steatosis

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Higher prevalence of sinus node disfunction (SND) has been reported in patients with diabetes mellitus and obesity, and they often exhibit accumulation of lipid droplet (LD) in cardiomyocytes, cardiac steatosis. However, the causal association between SND and cardiac steatosis has not been elucidated. Transgenic (Tg) mice with cardiac-specific overexpression of perilipin 2 (PLIN2), a mouse model of myocardial steatosis, exhibited accumulation of LD around mitochondria in atrial myocytes (Sato et al. 2019). We hypothesized that such accumulation of LD in sinoatrial nodal cells (SNCs) may affect pacemaker function based on our previous findings that Ca^{2+}-mediated interplay between mitochondria, sarcoplasmic reticulum (SR), and channels/transporters at the plasma membrane is associated to automaticity of SNCs.

Objective: To investigate cardiac pacemaker function in PLIN2-Tg mice.

Methods: Electron micrographs (EM), electrocardiogram, reactive oxygen species (ROS), local calcium release (LCR) from SR and Ca^{2+} transient were compared between wild-type (WT) and PLIN2-Tg SA node.

Results: EM exhibited accumulation of LD, especially around mitochondria, and partial swelling of SR in SNCs. Electrocardiogram revealed increased R-R variability in PLIN2-Tg compared to WT mice, suggesting SND. Cytosolic and mitochondrial ROS levels were increased in PLIN2-Tg SNCs. The amplitude and size of LCR were reduced and the occurrence of early LCR tended to increase in PLIN2-Tg SNCs. The duration of Ca^{2+} transient was reduced whereas the variability of Ca^{2+} transient interval was increased in PLIN2-Tg SNCs.

Conclusion: Our findings suggest that myocardial steatosis induces sinoatrial node dysfunction, which is associated with increased ROS levels and impaired SR Ca^{2+} handling.

WOBS-03-7

Neuregulin4 Acts on Hypothalamic ErBb4 to Excite Oxytocin Neurons and Preserve Metabolic Homeostasis

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Neuregulin 4 (Nrg4) is an adipose tissue-enriched secreted factor that modulates glucose and lipid metabolism. Nrg4 is closely associated with obesity and preserves diet-induced metabolic disorders. However, the specific mechanisms via which Nrg4 regulates metabolic homeostasis remain incompletely understood. Here, we find that the Nrg4 receptor, ErbB4, is highly expressed in the hypothalamus, and the phosphorylation of hypothalamic ErbB4 is reduced in diet-induced obesity (DIO) mice. Peripheral Nrg4 can act on ErbB4 via blood circulation and excite neurons in the paraventricular nucleus of hypothalamus (PVN). Central administration of recombinant Nrg4 (rNrg4) reduces obesity and related metabolic disorders by influencing energy expenditure and intake. Overexpression of ErbB4 in the PVN protects against obesity, whereas its knock down in oxytocin (Oxt) neuron accelerates obesity. Furthermore, Nrg4-ErbB4 signaling excites Oxt release, and ablation of Oxt neuron considerably attenuates the effect of Nrg4 on energy balance. These data suggest that the hypothalamus is a key target of Nrg4, which partially explains the multifaceted roles of Nrg4 in metabolism.

WOBS-03-8

Calcitonin Acts on Hypothalamic CALCR to Preserve Metabolic Homeostasis

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Data from genome wide association study (GWAS) showed that multiple single nucleotide polymorphisms on calcitonin receptor (CALCR) were closely related with body mass index (BMI). CALCR was highly expressed in the hypothalamus of both human and mouse. Mouse hypothalamus single cell sequencing data showed that the mRNA expression of CALCR was decreased in fasting state and increased in fed state. Calcitonin is a natural ligand of CALCR, which can improve the glucose and lipid metabolism homeostasis, suggesting that calcitonin may play a vital role in regulating energy homeostasis by binding to CALCR in the hypothalamus. Further study demonstrated that the food intake and body weight of mice were significantly decreased, while the energy consumption were significantly increased after injecting calcitonin into the ventricles. Immunofluorescence staining showed that calcitonin inhibited the activity of AgRP, an appetite promoting neuron in the hypothalamus, which may contribute to metabolic homeostasis.

WOBS-03-9

Follistatin-like 3 is a biomarker and mediator of human adipose tissue inflammation

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Objective: This study aimed to investigate the association of adipose tissue follistatin-like 3 (FSTL3) expression and serum FSTL3 levels with overweight/obese state, as well as to explore the role of FSTL3 in human adipose tissue.

Methods: A total of 236 participates (65 normal weight and 171 overweight/obesity) aged 18-67 years were included. Subcutaneous and visceral adipose tissues of all participates were collected and performed transcriptome sequencing. The role of FSTL3 was explored in human primary adipocyte. Serum FSTL3 levels were measured using enzyme-linked immunosorbent assay. Body fat distribution was assessed by magnetic resonance imaging.

Results: The adipose tissue FSTL3 expression was higher in overweight/obesity than in normal-weight individuals ($P < 0.001$). Gene co-expression analysis showed that FSTL3 was positively correlated with inflammatory pathways, including tumor necrosis factor (TNF), nuclear factor-Kappa B and toll-like receptor signaling. Cell experiments found that recombinant FSTL3 protein promoted, while FSTL3 knockdown inhibited, inflammatory response. Besides, serum FSTL3 levels were higher in overweight/obesity than in normal-weight individuals (4104.96 [3137.20-5129.47] pg/mL versus 3413.94 [1850.84-5555.89] pg/mL, $P<0.05$). Serum FSTL3 levels were positively correlated with adipose tissue expression levels, obesity-related and inflammatory indicators (all $P<0.05$). Multivariate linear regression analysis showed that serum FSTL3 levels were independently associated with visceral fat area (standardized $\beta= 0.364$, $P < 0.001$) and serum TNF-α levels (standardized $\beta= 0.65$, $P < 0.05$).

Conclusion: FSTL3 in adipose tissue was involved in regulating adipocyte inflammatory response, and serum FSTL3 levels might be a biomarker of visceral obesity and inflammation.

WOCS-01-1

Supervised machine learning-based prediction for insulin related lipohypertrophy using electronic health records

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Objective: The purpose of this study was to construct a predictive model for insulin-related lipohypertrophy which included feature variables that can be collected on the first day of hospitalization by nurses who routinely input the data to electronic health records.

Methods: The outcome measure was insulin-related lipohypertrophy which detected by

Ultrasound. We utilized four major classifiers: logistic regression, random forest, linear support vector machine, and extreme gradient boosting (XGBoost) with 5-fold cross-validation technique. The area under the receiver operating characteristic curve (AUC) was used for evaluating predictive performance.

Results: The proportion of insulin-related lipohypertrophy was 86.7%. The

receiver operating characteristic curves revealed the best predictive performance for the XGBoost model, achieving the highest sensitivity of 0.89 ±0.03 and AUC of 0.82 ±0.02 amongst four types of classifiers. Variables related to the duration of insulin treatment, rotation of injection sites, frequency of needle reuse, and number of insulin injections per day were extracted as important features.
Conclusions: We successfully developed a supervised machine learning predictive model for insulin-related lipohypertrophy in patients with diabetes. This model has the potential to aid clinical physicians in identifying high-risk patients earlier, thereby allowing for timely intervention and prevention of insulin-related lipohypertrophy, ultimately improving patient outcomes.

WOCS-01-2

Effects of switching from insulin glargine (Gla)-100 to Gla-300 on glycemic control and treatment satisfaction

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Aims: To investigate effects of switching from insulin glargine U100 (Gla-100) to insulin glargine U-300 (Gla-300) on glycemic control and treatment satisfaction in people with type 1 and 2 diabetes.
Methods: We studied152 outpatients with diabetes (type 1/type 2 diabetes/ others = 29/119/4) who were treated with basal-bolus therapy (BBT; n=95) or basal only (n=57) using Gla-100 as a basal insulin. At switching from Gla-100 to Gla-300, the initial dose of Gla-300 was the same as that of Gla-100 at regular outpatient visits. We investigated changes in HbA1c, body weight, insulin dose of glargine, and Diabetes Treatment Satisfaction Questionnaire scores for 3 months.
Results: HbA1c level and body weight did not change significantly at three months after switching to U-300. In a total of 152, basal insulin dose with Gla-300 significantly increased compared with that of Gla-100. When analyzing separately, basal insulin dose with Gla-300 increased significantly in the BBT group, but not the Basal only group. We found no significant changes in the treatment satisfaction score before and after switching to Gla-300. In the BBT group, hypoglycemia was less frequent after switching to Gla-300.
Conclusions: Insulin Gla-100 and Gla-300 had similar efficacy (HbA1c), body weight changes, and treatment satisfaction. In only people treated with BBT, Gla-300 may be associated with less frequent hypoglycemic episodes than Gla-100.

WOCS-01-3

Effect of Once-Weekly Insulin for Diabetes Population: A Systematic Review and Meta Analysis of Randomized Trial

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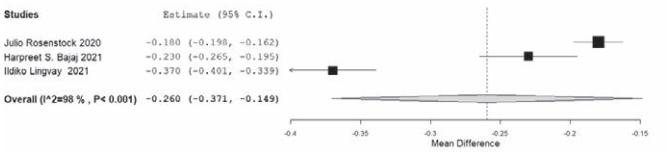
Objective: This study aims to determine the effectiveness of once weekly basal insulin on glycemic parameters in T2DM patients compared to once daily basal insulin.
Method Articles obtained from several databases; PubMed, CENTRAL, Science direct dan clinical trial.gov with keywords ((Once Weekly Basal Insulin) AND ((Diabetes Mellitus) OR (T1DM) (T2DM))) The included studies were randomized controlled trials (RCTs) and studies are assessed by critical review using the CEBM critical review, then the data adjusted according to the PRISMA and GRADE approach. The analysis was carried using the Hartung-Knapp-Sidik-Jonkman method.
Result
There were six studies that were included in review consisting of 1204 subjects with the once weekly insulin [Icodec;basal insulin Fc/BIF] compare to once daily basal insulin. From the analysis using random effects found in the mean difference between the Icodec group and the Glargine U100 among T2DM on the variable time in range [TIR] (MD 6.43 [95%IK 3.65 - 9.204]; p < 0.001; I2 :96%); HbA1C (%) (MD -0.26 [-0.37 – -0.14]; p< 0.001; I2 : 97%); and total insulin weekly dosage (IU) (MD -21.16 [-54.2 - 12.11]; p = 0.213; I2 : 97%). Two study basal insulin once weekly fc vs Degludec was significant statically difference HbA1C (%) (MD 0.074 [0.045– 0.103]; p <0.01; I^2 : 76%) in T2DM. While TIR for T1DM population was similar between BIF (56.1%) vs degludec (58.9%) p-value= 0.112.
Conclusion
Insulin Icodec and BIF had similar efficacy with once-daily insulin among Type II and I diabetes.
Keyword once weekly insulin basal, Meta-analysis



WOCS-01-4

The mice treated with imeglimin show increased energy expenditure and are protected from weight gain.

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Objective: imeglimin, a novel antidiabetic drug, was originally identified and developed as a drug enhancing mitochondrial functions. Clinically, many studies show that imeglimin enhances glucose-stimulated insulin secretion, while there has been controversy regarding the effects of imeglimin on insulin sensitivity. Importantly, the mechanism of imeglimin actions or its actual molecular targets have not been systematically investigated. Our study here is to clarify by extensive metabolic assessments whether imeglimin has insulin-sensitizing effects in peripheral insulin target organs. We also systematically assess the changes in transcriptomes of insulin target tissues upon imeglimin treatment and unbiasedly characterize the tissue responses to imeglimin at molecular levels.
Methods: we administered imeglimin to high fat diet (HFD)-fed obese mice for 6 weeks and assessed their metabolic profiles. After 6 weeks of treatment, we analyzed the molecular signature of insulin target organs by transcriptomic analyses.
Results: With imeglimin administration for 6 weeks, the mice were protected from HFD-induced body weight gain compared to the control treatment. This reduced weight gain was associated with higher energy expenditure and enhanced insulin sensitivity. Of note, the brown adipose tissue (BAT) of imeglimin treated mice was significantly smaller than the controls, histologically indicating that it was protection from whitening upon HFD feeding. The transcriptomic analyses revealed upregulation of mitochondria-related genes in BAT of imeglimin-administered mice on HFD.
Conclusion: We propose BAT as a previously uncharacterized, potential target tissue of imeglimin. Our results suggest the possibility that imeglimin treatment could modify BAT function, thereby increasing energy expenditure and insulin sensitivity under obesity.

WOCS-01-5

Evaluation of efficacy and safety of glucokinase activators——a systematic review and meta-analysis

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Peking University People's Hospital

Aims: Glucokinase activators (GKAs) promote the activity of glucokinase (GK) and is under development for the treatment of diabetes. The efficacy and safety of GKAs require evaluation.
Methods: This meta-analysis included randomized controlled trials (RCTs)

with a duration of at least 12 weeks conducted in patients with diabetes. The primary objective of this meta-analysis was the difference of hemoglobin A1c (HbA1c) change from baseline to study end between GKA groups and placebo groups. Risk of hypoglycemia and laboratory indicators were also evaluated. Weighted mean differences (WMDs) and 95% confidence intervals (CIs) were calculated for the continuous outcomes, odd ratios (ORs) and 95% CI were calculated for the risk of hypoglycemia.

Results: Data from 13 RCTs with 2,748 participants treated with GKAs and 2,681 control participants were analyzed. Overall, the level of HbA1c decreased significantly in patients with GKA treatment compared with placebo (WMD=-0.316%, 95% CI -0.426 to -0.206%, P<0.001). The OR comparing GKA versus placebo was 1.88 for risk of hypoglycemia (95% CI 1.51 to 2.33, P<0.001). The WMD comparing GKA versus placebo was 0.308mmol/L for triglyceride (TG) levels (95% CI 0.153 to 0.464mmol/L, P<0.001). When stratified by drug type, selectivity, and study duration, significant difference was found between groups.

Conclusions: In patients with diabetes, GKA treatment was associated with a better glycemic control, but a significant increased risk of hypoglycemia and elevation in TG concentration in general. The efficacy and safety varied with drug type and selectivity.

WOCS-01-6

Efficacy of Imeglimin in The Real-world Clinical Practice for Diabetes in Japan

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[Purpose] This study was designed to investigate the efficacy and safety of imeglimin in the real-world clinical practice for diabetes in Japan.

[Methods] We examined changes in biochemical data such as HbA1c levels, body weight, and renal functions in 125 out-patients with type 2 diabetes mellitus treated with imeglimin.

[Results] HbA1c levels significantly decreased from 7.20 ± 0.92% to 6.97 ± 0.90% after 3 months, 6.92 ± 0.82% after 6 months, and 6.62 ± 0.79% after 12 months (p = 0.003, p = 0.001, p < 0.001, respectively).

No significant changes in the other data were observed as following: body weight (61.4±14.7 kg to 61.2±14.7 kg (p=0.464)), systolic and diastolic blood pressure, ALT, AST, LDL cholesterol, HDL cholesterol, triglycerides, eGFR, and uric acid level. Adverse events included nausea in 25 subjects; diarrhea in 22 subjects; decreased appetite in 7 subjects; constipation and headache in 5 subjects each; loose stools and malaise in 2 subjects each; and vomiting, abdominal fullness, eczema, and hypoglycemia in 1 subject each. Although no serious adverse events were observed, treatment was discontinued in 21 subjects at their request.

[Conclusion] In the real-world clinical practice, Imeglimin administration lowered HbA1c levels, and its safety was confirmed to be the same as in previous clinical trials.

WOCS-02-1

The effect of haptoglobin genotype on the association of ADMA and *DDAH 1* polymorphism with diabetic macroangiopathy

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Objective: Dimethylarginine dimethylaminohydrolase (DDAH) 1 maintains the bioavailability of nitric oxide by degrading asymmetric dimethylarginine (ADMA). We aimed to investigate the effect of haptoglobin (Hp) genotype on the association of ADMA and *DDAH 1* polymorphism with diabetic macroangiopathy. **Methods:** In stage 1, 90 Chinese participants with type 2 diabetes were enrolled to measure a panel of targeted metabolites, including ADMA, using tandem mass spectrometry. In stage 2, an independent cohort of 2,965 Chinese patients with type 2 diabetes was recruited to analyze the effect of Hp genotype on the association between *DDAH 1* rs233109 and diabetic macroangiopathy. Hp genotypes were detected by the TaqMan method. *DDAH 1* rs233109 was genotyped using the MassARRAY platform. **Results:** In stage 1, serum ADMA levels correlated with common Hp genotypes (β ± SE = −0.049 ± 0.023, *P* = 0.035). In stage 2, the distribution of *DDAH 1* rs233109 genotype frequencies was 15% (CC), 47% (TC), and 38% (TT). A significant Hp genotype by rs 233109 genotype interaction effect on diabetic macroangiopathy was found (*P* = 0.017). After adjusting for confounders, patients homozygous for rs233109 CC were more likely to develop diabetic macroangiopathy than those carrying TT homozygotes in the Hp 2-2 subgroup [OR = 1.750 (95% CI, 1.101–2.783), *P* = 0.018]. **Conclusions:** Hp genotype affects the association between *DDAH 1* rs233109 and diabetic macroangiopathy in Chinese patients with type 2 diabetes.

WOCS-02-2

Machine Learning-based Approach to Diagnose Type 2 Diabetes and Predict Cardiovascular Complications in 5 years

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Objective

To establish effective artificial intelligence-based models to identify type 2 diabetes mellitus (T2DM) patients and predict cardiovascular complications in 5 years among patients with T2DM.

Methods

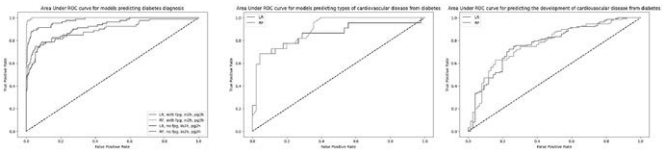
The study enrolled 3241 individuals from two middle-income communities in Shanghai. Anthropometric and clinical characteristics were used. Two machine learning models known as linear regression (LR) and random forest (RF) were applied to predict T2DM in participants, and then the occurrence of cardiovascular complications after 5 years in the participants without cardiovascular complications at baseline was predicted. The performance of two models was validated and important predictors were assessed.

Results

When the predictive factors of T2DM included fasting plasma glucose, two-hour postprandial insulin level and two-hour postprandial glucose level, the AUC of LR and RF could reach 0.95 and 1.00, respectively, with fasting plasma glucose being the most contributing feature in both LR and RF. When the models were trained again by excluding the above-mentioned features, the AUC of LR and RF reached 0.91 and 0.92, respectively, and HOMA-IR was the most contributing feature in both predictions. LR and RF reached AUC of 0.72 and 0.77, respectively, when predicting cardiovascular complications within 5 years, and age was the most valuable feature in both models

Conclusion

This retrospective study shows that artificial intelligence is more effective to identify T2DM and in timely prediction of cardiovascular complications in diabetic patients after 5 years.



WOCS-02-3

Two-year diabetic foot ulcer incidence and risk factors: Second phase report of Ahvaz diabetic foot cohort study (ADFC)

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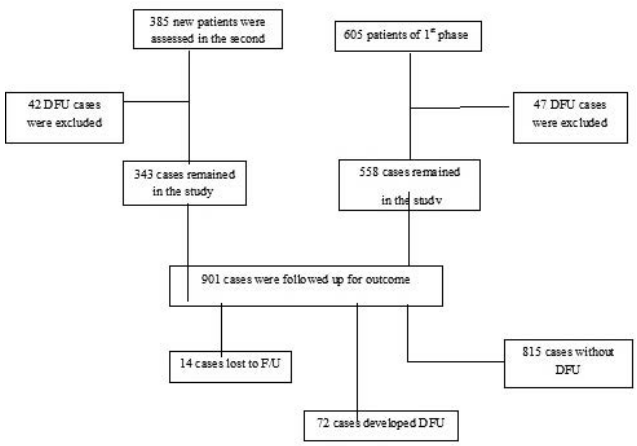
Objectives: This study was designed as the second phase of a prospective cohort study to evaluate diabetic foot ulcers (DFU).

Methods: In a university hospital in Iran, each participant was examined and followed up for two years in terms of developing newfound DFU as ultimate outcome.**Results:** The mean age of participants was 53.24± 11.46 years. Based on backward elimination multiple logistic regression, the following variables were the main risk factors for DFU incidence: former history of DFU or amputation [OR=76.5, 95% CI(33.45,174.97), P value<0.001], ill-fitting footwear [OR=10.38, 95% CI(4.47,24.12), P value <0.001], smoking [OR=3.87,95%CI(1.28, 11.71),P value=0.016], preventive foot care [OR=2.91%CI(1.02,8.29),P value=0.045], and physical activity[OR=2.25,95% CI(0.95,5.35),P value=0.066].

Conclusion: Overall, the two-year cumulative incidence of diabetic foot ulcer was 8%; [Incidence rate: 49.9 /1000 person-years] however, the second-year incidence was higher than the first-year incidence which was coincident with the COVID-19 pandemic (4.18 % and 1.8%, respectively). Independent risk factors of DFU occurrence were prior history of DFU or amputation, ill-fitting footwear, smoking, preventive foot care and physical activity.



WOCS-02-4

The association between blood pressure reduction by antihypertensive agents and the risk of peripheral arterial disease

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Objective: To assess the association between the blood pressure reduction mediated by antihypertensive agents and the risk of peripheral arterial disease (PAD) in patients with diabetes.

Methods: PubMed, EMBASE, the Cochrane Center Register of Controlled Trials for Studies and Clinicaltrial.gov were searched from January 1980 to October 2022. Randomized controlled trials (RCTs) with statistically significant differences in blood pressure reduction between intensive antihypertensive agent treatment and control treatment arms, and reports of PAD, amputation, or diabetic foot were included. Subgroup analyses and meta-regression analyses were performed to address potential influencing indicators.

Results: 18 RCTs involving 108,901 participants were included. Profound blood pressure reduction achieved by antihypertensive agents was associated with a slightly increased risk of PAD (RR=1.07, 95%CI, 1.00 to 1.14, P=0.04,). Meta-regression analyses suggested that difference in systolic blood pressure (SBP) reduction was positively associated with risk of PAD (β=-0.1107, 95%CI, -0.219 to -0.002, P=0.047). The risk of PAD was increased in subgroup with higher percentage of smokers (RR=1.07, 95%CI, 1.00 to 1.14) when compared with the subgroup with lower percentage of smokers (RR=0.68, 95%CI, 0.45 to 1.01, P for subgroup difference=0.03). Moreover, the risk of PAD was lower in patients with CCB when compared with RAASi (P=0.03), ARNI (P=0.01) and β-blockers(P=0.01).

Conclusion: Th intensive blood pressure reduction mediated by antihypertensive medications was associated with the increased risk of PAD in patients with diabetes. CCB might be indicated in patients in need of improved blood pressure control by medications but with high risk of PAD.

WOCS-02-5

HUC-MSCs combined with platelet lysate treat diabetic chronic cutaneous ulcers in Bama miniature pig

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Objective: To observe the efficacy of PL-induced HUC-MSCs on diabetic chronic wound in miniature pigs firstly.

Methods: High glucose induced HaCat, HDF-n, HUVEC and RAW264.7 were mimicked diabetic wound related cells. Five diabetic and 2 control pigs were created chronic cutaneous skin wounds (DCU). Control pigs were set as the normal saline treatment and the PL treatment. Diabetic pigs were set as saline group, PL group, HUC-MSCs group and PL+HUC-MSCs treatment groups (6×10^6/mL/ cm^2). Inflammatory factors, wound healing factors and TGFβ/Smad signal pathway expression were detected in both cells and pigs' study.

Results: HUC-MSCs supernatant (MSC-Sp) promoted proliferation of diabetic wound related cells, inhibited TGFβ1, Smad2/3/4, and up-regulated Smad7 and TGFβ3, promoted the secretion of VEGF-α and PDGF-BB by keratinocytes and fibroblasts. Besides, MSC-Sp significantly down-regulated the expression of CD86, IL-6, and TNF-α in macrophage cells. In vivo experiments, the HUC-MSCs combined with the PL had the highest wound healing rate, with the best effect of epidermal hyperplasia, neo-epidermal thickness, dermal maturity, collagen formation, and microvessel density. It regulated the balance of IL-6/TGFβ1 and IL-6/Arg-1, and up-regulated the expression of VEGF-α and TGFβ1. In contrast, HUC-MSCs treatment mainly down-regulated IL-6, α-SMA, and Col1 up-regulated the expression of TGFβ3.

Conclusion: MSC-Sp might promote the healing of diabetic wound by secreting VEGF-α and PDGF-BB from keratinocytes and fibroblasts; inhibiting TGFβ1, Smad2/3/4, and up-regulated Smad7 and TGFβ3. PL+HUC-MSCs improved DCU better than HUC-MSCs therapy alone by regulating the balance of IL-6/Arg-1, and IL-6/TGFβ1, up-regulating TGFβ1, α-SMA, Col1 and VEGF-α.

WOCS-02-6

Skin invisible damage and Wnt/β-catenin signaling pathways changes induced by diabetes

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Objective: This work aimed to compare morphological differences and changes in Wnt/β-catenin signaling pathways of non-injured skin and granulation tissues between non-diabetic and diabetic pigs.

Methods: The tissue used for this study was extracted from diabetic pigs induced by streptozotocin and non-diabetic pigs. After establishing the diabetic

status, circular full-thickness skin samples from buttocks, and granulation tissues in the wound center 12 days after trauma were harvested for subsequent analysis of alterations (thickness of epidermis and dermis, collagen expression, microvascular density, and expression of Wnt/β-catenin signaling pathways) caused by diabetes.

Results: Our results demonstrated that diabetes could lead to a thinner epidermis and dermis and less collagen expression in non-injured skin compared to non-diabetic pigs, but there was no significant difference in microvascular density between the two groups. In addition, collagen expression and vascular density in granulation tissues were lower in diabetic pigs. In the non-injured skin and granulation tissues of diabetic pigs, the relative mRNA or protein levels of Wnt3a, β-catenin, Fzd6, DVL1, CyclinD1, and c-Myc were significantly lower than those in non-diabetic pigs, except for higher Axin2.

Conclusion: Changes in non-injured skin and granulation tissues caused by diabetes might be related to suppressed Wnt/β-catenin signaling pathways in diabetic pigs.

WOCS-03-1

The clinical characteristics of severe SARS-CoV-2 among patients with type 2 diabetes mellitus

Xiaomin Xie, Guirong Bai, Rui Ping, Yanting He, Li Zhang, Haiyan Zhou, Ling Li, Dan Qiang, Renda Li

The First People's Hospital of Yinchuan

Objective To analyze the clinical data of severe novel coronavirus (SARS-CoV-2) infection and explore the clinical characteristics of severe SARS-CoV-2 in patients with type 2 diabetes. **Methods** Compare and analyze the clinical data of 61 patients with severe SARS CoV-2, including 31 patients with diabetes (DM) and 30 patients with non diabetes (NGT).

Results (1)The arterial blood oxygen partial pressure (PO2) and carbon dioxide partial pressure (PCO2) of the two groups were significantly lower than those of the normal people. (2)The LA of arterial blood in DM group was significantly higher than it in NGT group($p<0.05$);(3)There was no significant difference between two groups in blood K^+, Na^+, Cl^-, $Ca^{2+}$and P^{3+}, but blood K^+, $Na^+$and P^{3+}were at the lower limit of normal, and blood Cl - was at the upper limit of normal; Ca^{2+}between the two groups is lower than the normal level;(4)PH value was positively correlated with SB and BD independently ($P<0.05$~0.01), and negatively correlated with PCO2 and K^+independently ($P<0.05$); PO2 was positively correlated with Cl^- independently ($P<0.05$), and negatively correlated with FBG independently ($P<0.05$).**Conclusion** Hyperglycemia in patients with type 2 diabetes is an independent risk factor leading to the critical condition of SARS CoV-2.Severe hypoxemia, mixed acid-base balance disorder, mainly respiratory alkalosis and metabolic alkalosis, may occur.The imbalance of water and electrolyte may be related to the increased secretion of aldosterone and antidiuretic hormone.**[Key words]** Type 2 diabetes; Novel coronavirus;Hhypoxemia; Disorder of acid-base balance; Water and electricity balance disorder

WOCS-03-2

Efficacy of imeglimin in Japanese patients with type 2 diabetes mellitus with poor glycemic control

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Objective: Imeglimin is a novel medicine for diabetes mellitus that acts by improving mitochondrial function. In this study, we evaluated the effects of imeglimin on parameters related to diabetes mellitus with poor glycemia control despite treatment with multiple antidiabetic drugs and/or had difficulty in following therapeutic modifications of diet and exercise.

Methods: A total of 16 patients with poor glycemic control who received imeglimin at the dose of 2000 mg/day for 5 months, and the following parameters were measured before and after the treatment: plasma HbA1c, lipid profile and other relevant blood parameters.

Results: HbA1c levels decreased significantly after imeglimin treatment. The patients were divided into 2 groups according to the degree of body weight loss after the treatment: ≥1 kg body weight loss /no significant weight loss. HbA1c decreased from 8.83 ± 0.7% to 6.84 ± 0.7% ($P<0.01$) in the weight loss group, and from 9.81 ± 1.5% to 8.79 ± 1.0% ($P<0.01$) in the no significant weight loss group; thus, significant decrease of the HbA1c after treatment was observed in both the groups, although the degree of decrease was greater in the weight loss group.

Conclusions: Imeglimin significantly lowered the HbA1c levels in all the patients with poor glycemic control. Furthermore, the degree of decrease of the HbA1c was greater in the patients who showed significant body weight loss after treatment with imeglimin than in those who did not. Imeglimin appears to be a beneficial agent for diabetic patients showing poor glycemic control.

WOCS-03-3

Serial Cases of Hyperglycemic Crises and Other Critical Illness in Old Patients

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Background

Diabetic Ketoacidosis (DKA) and hyperglycemic hyperosmolar state are the most common acute complication of diabetes mellitus. The incidence is estimated about 9.5 per 1000 persons with diabetes. DKA is characterized by uncontrolled hyperglycemia, metabolic acidosis, and increased total body ketone concentration. While HHS is characterized by severe hyperglycemia (>600 mg/dL), hyperosmolarity dehydration, and the absence of significant ketoacidosis. The treatments of DKA and HHS is based on the correction of dehydration, hyperglycemia, electrolyte imbalances, improving mental status, and avoiding complications. The better understanding of pathophysiology, prevention and management of hyperglycemic crises has sharply declining death rates in the US.

Case Presentation

We present two cases of hyperglycemic crisis. The first patient was a male patient with hyperglycemic hyperosmolar state and uremic syndrome. His initial blood glucose level was 1078 mg/dL. The second patient was a female patient presenting with ketoacidosis diabetic and hypertensive emergency. Her initial blood glucose level was 1031 mg/dL. Both patients were treated with initial fluid resuscitation and insulin pump. Other Medication was given based on their other conditions. Both of them had a good response to the treatments and was able to discharged from the Intensive Care Unit.

Conclusions

DKA and HHS are life threatening hyperglycemic crisis. The incidences of these case are increasing lately, including in younger age. Early Recognition and organized treatment of DKA and HHS will improve the outcome.

WOCS-03-4

Enabling automatic meal bolus decision using artificial-pancreas-like closed-loop control in adults with type 2 diabetes

Wei Liu, Linong Ji

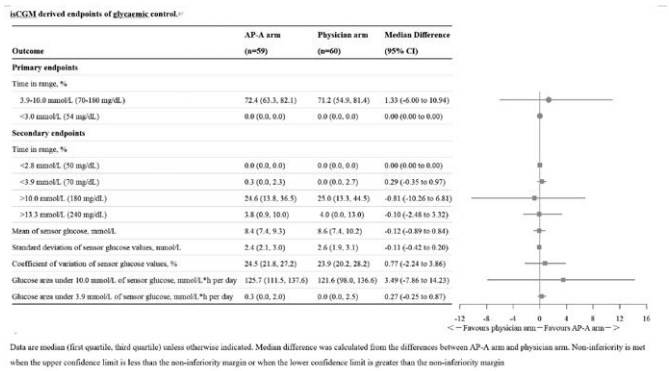
Peking University People's Hospital

Proper dosage titration is still the most effective way to mitigate intra- and inter-subject variations in insulin requirements and achieve euglycemic control in insulin therapy. We proposed an artificial-pancreas-like algorithm (AP-A) which could automatically determine the appropriate pre-prandial insulin dose based on intermittently scanned continuous glucose monitoring (isCGM) data trajectories in multiple dose injection (MDI) therapy.

We performed a randomized, single-blind, clinical trial at a tertiary, referral hospital in Beijing, China. Eligible participants were randomly assigned (1:1) to the AP-A arm supervised by physician and the conventional physician treatment arm. The study is registered with Chictr.org number, ChiCTR2200055328.

Between Nov 6, 2021 and July 26, 2022, 140 participants were screened, of whom 119 were randomly assigned to AP-A arm (n = 59) or physician arm (n = 60). The TIR achieved by the AP-A arm was statistically non-inferior compared with the control arm (72.4% (63.3-82.1) vs. 71.2% (54.9-81.4)), with a median

difference of 1.33% (95% CI, -6.00 to 10.94, non-inferiority margin -7.5%). TBR was also statistically non-inferior between the APA and control arms (0.0% (0.0-0.0) vs. 0.0% (0.0-0.0), respectively; median difference (95% CI, 0.00% (0.00 to 0.00), non-inferiority margin 2.0%).
The AP-A supported physician titration of pre-prandial insulin dosage offers non-inferior glycemic control compared with optimal physician care in type 2 diabetes.



isCGM derived endpoints of glycaemic control.[a]

Outcome	AP-A arm (n=59)	Physician arm (n=60)	Median Difference (95% CI)
Primary endpoints			
Time in range, %			
3.9-10.0 mmol/L (70-180 mg/dL)	72.4 (63.3, 82.1)	71.2 (54.9, 81.4)	1.33 (-6.00 to 10.94)
<3.0 mmol/L (54 mg/dL)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.00 (0.00 to 0.00)
Secondary endpoints			
Time in range, %			
<2.8 mmol/L (50 mg/dL)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.00 (0.00 to 0.00)
<3.9 mmol/L (70 mg/dL)	0.3 (0.0, 2.3)	0.0 (0.0, 2.7)	0.29 (-0.35 to 0.97)
>10.0 mmol/L (180 mg/dL)	24.6 (13.8, 36.5)	25.0 (13.3, 44.5)	-0.81 (-10.26 to 6.81)
>13.3 mmol/L (240 mg/dL)	3.8 (0.9, 10.0)	4.0 (0.0, 13.0)	-0.10 (-2.48 to 3.32)
Mean of sensor glucose, mmol/L	8.4 (7.4, 9.3)	8.6 (7.4, 10.2)	-0.12 (-0.89 to 0.84)
Standard deviation of sensor glucose values, mmol/L	2.4 (2.1, 3.0)	2.6 (1.9, 3.1)	-0.11 (-0.42 to 0.20)
Coefficient of variation of sensor glucose values, %	24.5 (21.8, 27.2)	23.9 (20.2, 28.2)	0.77 (-2.24 to 3.86)
Glucose area under 10.0 mmol/L of sensor glucose, mmol/L*h per day	125.7 (111.5, 137.6)	121.6 (98.0, 136.6)	3.49 (-7.86 to 14.23)
Glucose area under 3.9 mmol/L of sensor glucose, mmol/L*h per day	0.3 (0.0, 2.0)	0.0 (0.0, 2.5)	0.27 (-0.25 to 0.87)

Data are median (first quartile, third quartile) unless otherwise indicated. Median difference was calculated from the differences between AP-A arm and physician arm. Non-inferiority is met when the upper confidence limit is less than the non-inferiority margin or when the lower confidence limit is greater than the non-inferiority margin

WOCS-03-5

Efficacy and Safety of Semaglutide, Oral Glucagon-like peptide 1 (GLP-1) receptor agonist, in Japanese Type 2 Diabetes

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Objective: The efficacy and safety of Semaglutide (SG), oral glucagon–like peptide-1 (GLP-1) receptor agonist were assessed in Japanese type 2 diabetes over 32 weeks. Study Design : We started the treatment of 3mg of SG in 42 patients who were treated on dipeptidyl peptidase-4 (DPP-4) inhibitor or dulaglutide (DG) at least for 8 months with inadequate glycemic or body weight control. 28 patients were on DPP-4 inhibitor, 12 were on DG 0.75mg weekly and 38 subjects were on Sodium Glucose co Transporters 2 Inhibitor with metformin treatment. SG was titrated according to glycemic control. After 32 weeks, the change in glycated haemoglobin (HbA1c) level, body weight and the incidence of adverse events were accessed in retrospective way. Results: The patients were 66.6±10.6 years of mean age, and 25.9 of BMI with average duration of 15.5 years in Diabetes. The mean HbA1c in baseline was 8.0% and decreased to 6.8% however the mean BMI was not decreased and stayed at 25.8 at 32 weeks later. The mean dose of SG at 32 weeks were 6.4mg, however 50% of all were on 3mg, 25% of all required 7mg and 20% needed 14mg. Average dose in obese group were 7.5mg and 5.4mg in non-obese. The adverse events were few in gastrointestinal-related events.
Conclusions: SG were effective for the subjects both in obese or non-obese with inadequate glycemic or body weight control on DPP-4 inhibitor or DG; in lowering HbA1c with few adverse event, and no weight loss in lean subjects.

WOCS-03-6

Plantar pressure distributions of the diabetic patients in Sichuan province, southwest China

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Objective: To explore the characteristics of plantar pressure distributions of diabetic patients in Sichuan province, southwest China.
Methods: We recruited 106 diabetic patients without chronic diabetic complication(DM), 117 diabetic patients with peripheral neuropathy(DPN) and 57 normal volunteers(control) for static and dynamic analysis using the Footscan® platform system. The peak pressure, force and impulse were investigated in 10 areas of the foot, which was divided into medial heel (MH), lateral heel (LH), midfoot(MF), first to fifth metatarsals(M1-M5), hallux (T1), and toes 2-5 (T2-5).
Results: Compared with the control group, the DPN group had significantly lower peak force in the 1st toe (P=0.017), the 2nd (P=0.016) and 3rd (P=0.020) metatarsal regions of the left foot and the right 1st toe (P=0.053), and lower force pressure in the left 2nd metatarsal region (P=0.047), while the peak force in the right 5th metatarsal region (P=0.04) statistically increased. The impulses of the left MF (P=0.05) and right MH (P=0.006) regions were significantly increased in the DPN group. The peak force, peak pressure and impulses were not statistically different between the DM and control groups.
Conclusion: The DPN patients had different plantar pressure distribution with pressure transferring to the 5th metatarsal region, the middle foot and the heel during walking.
Key words: diabetes mellitus, diabetic peripheral neuropathy, plantar pressure distribution, peak force, impulse

WOCS-04-1

Use of Sensor Augmented Pump with predictive low glucose suspend system in Japanese pregnant women with type 1 diabetes

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It is a challenging task in pregnant women with type 1 diabetes to maintain the target glucose level to attain good neonatal outcomes. In this study, we retrospectively studied pregnant women with type 1 diabetes, who delivered between 2011 and 2021 in the two medical institutions in Japan, to evaluate the efficacy of sensor-augmented pump (SAP) with predictive low glucose suspend (PLGS) system in the real-world use. SAP with PLGS was used in 11 women, and multiple daily injection (MDI) or insulin pump was used in 11 women. HbA1c level was under 6.5% throughout the pregnancy period in cases using SAP with PLGS, and the time in range (TIR, 63-140mg/dl) was over 70 % in the second and third trimester. The target glucose level could not be attained in cases without SAP. PLGS was safely used without causing ketoacidosis. Positive correlation was observed between insulin suspension time (IST) and TIR (r=0.62, p<0.01). Weak but negative correlation was observed between IST and TBR (r=0.40, p=0.02). Total daily insulin dose was adequately increased without increasing the time below range (TBR, <63 mg/dl). Heavy for date (HFD) infants were less observed in cases using SAP (1 in 11) compared to cases without SAP (5 in 11).
Our study showed that SAP with PLGS can be safely and effectively used in pregnant women with type 1 diabetes to achieve the target glucose level without increasing the risk of hypoglycemia, and this may lead to a good neonatal outcome.

WOCS-04-2

Time in range as a potential marker for diabetes remission after Roux-en-Y gastric bypass surgery

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Objective: The current definition of diabetes remission after metabolic surgery was largely based on glycated hemoglobin A1c (HbA1c). This study aimed to examine the role of time in range (TIR), an emerging glycemic marker, as a potential new marker for diabetes remission after Roux-en-Y gastric bypass (RYGB).
Methods: 175 individuals with type 2 diabetes and obesity who underwent RYGB were retrospectively analyzed. Subjects were classified as remission/non-remission according to the current HbA1c-based standard (<6.0%). Each participant underwent continuous glucose monitoring both before and 1 year after RYGB. Glycemic variability was measured by glucose coefficient of variation (CV), and hypoglycemia was assessed by time below range (TBR).
Results: Complete remission was achieved in 88 of the 175 participants following RYGB. In the remission group, hypoglycemia including both TBR (<3.9mmol/L) and TBR (<3.0mmol/L) was significantly increased (both P<0.05). Glucose CV was significantly correlated with TBRs (both P<0.001), and a glucose CV >32.2% was associated with an abrupt increase in the risk of

hypoglycemia. After excluding patients with glucose CV >32.2% from the remission group, the 5th percentile of TIR of the resultant participants was 84%, which was set as the threshold of TIR for defining diabetes remission. Compared with patients who met the TIR criteria but not HbA1c criteria (n=32), those achieving the HbA1c criteria but not TIR criteria (n=18) had significantly greater worsening in TBRs and glucose CV, and less improvement in TIR (all P<0.05).

Conclusions: TIR may serve as a new metric for defining diabetes remission after bariatric surgery.

WOCS-04-3

Dawn Phenomenon and All-Cause Mortality Risk in Patients with Type 2 Diabetes Mellitus: A Prospective Cohort Study

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Objective:

The dawn phenomenon (DP) is a spontaneous blood sugar rise in the early morning without nocturnal hypoglycemia, which can be precisely assessed by continuous glucose monitoring (CGM). To date, the relationship between DP and clinical outcomes of diabetes remains unknown. We aimed to investigate the association between DP, based on CGM, and all-cause mortality risk among patients with type 2 diabetes mellitus (T2DM) in a prospective cohort study.

Methods:

A total of 4,778 inpatients with T2DM from January 2005 to December 2021 in a single center were analyzed. The magnitude of DP (ΔG) was defined as the increase in CGM-determined glucose value from nocturnal nadir (after 24:00) to prebreakfast, and DP was defined as ΔG > 1.11 mmol/L without nocturnal hypoglycemia. Participants were stratified into four groups by ΔG: ≤ 1.11, 1.11-3.00, 3.00-5.00, and > 5.00 mmol/L. Cox proportional hazards regression models were used to evaluate the impact of DP on all-cause mortality risk.

Results:

During a median follow-up of 9.4 years, 928 deaths were identified. The frequency of DP was 71.8%. Multivariate Cox regression showed that ΔG ≥ 5.00 was associated with 29% (95% *CI* 1.00-1.67) higher risk of all-cause mortality as compared with ΔG 1.11-3.00. The restricted cubic spline revealed a nonlinear (*P* for nonlinearity = 0.008) relationship between ΔG and all-cause mortality risk after multivariate adjustment.

Conclusion:

Higher ΔG is significantly related to a higher risk of all-cause mortality in T2DM, suggesting that severe DP should be avoided to reduce the risk of long-term adverse outcomes.

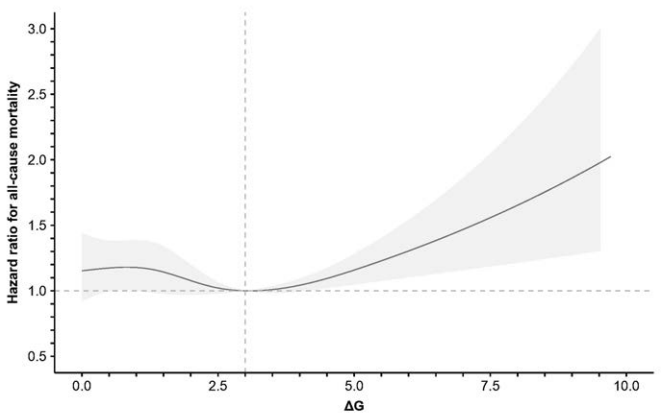

Fig. HRs of all-cause mortality by different levels of magnitude of dawn phenomenon (ΔG)

WOCS-04-4

Application effect of remote digital platform for diabetes case management based on rtCGM

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Objective:To evaluate the application effect of remote digital platform for diabetes case management based on real-time continuous glucose monitoring(rtCGM).in patients with type 2 diabetes(T2D).

Methods:A remote digital platform for diabetes case management based on rtCGM was developed, which including patient-side, doctor-side and case manager-side, realizing remote sharing of patients' Rt-CGM data,visual lifestyle coaching, continuous glucose profile analysis and regular health reports. 200 outpatient patients with T2D were selected and randomly divided into intervention and control group, the control group was given routine outpatient case management, the intervention group was given remote digital case management based on rtCGM for 3 months. Both groups wore CGM for 14 days before and after intervention. The differences of diabetes self-management behavior, TIR, TBR and HbA1c before and after intervention were evaluated. The satisfaction of patients with remote digital management in the intervention group was investigated.

Results:The baseline of the two groups was comparable, and after intervention, the diabetes self-management behavior, TIR, TBR and HbA1c of the two groups were improved compared with the baseline, and the intervention group was better than the control group(P<0.05). Patients' satisfaction with remote digital case management based on rtCGM reached 91%.

Conclusion:The remote digital platform for diabetes case management based on rtCGM has the potential to support the case management of T2D patients between outpatient visits.

WOCS-04-5

Haptoglobin Genotype Modifies the Effect of Glycemic Variability on Risk of Diabetic Macroangiopathy

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Objective: Haptoglobin (Hp) is a hemoglobin-binding protein that functions as an antioxidant in human plasma. Here we aim to investigate whether the effect of glycemic variability (GV) on the risk of diabetic macroangiopathy depends on *Hp* genotype in type 2 diabetes. **Methods:** A number of 860 Chinese patients with type 2 diabetes was genotyped and assigned to two *Hp* subgroups, *Hp* 2-2 and *Hp* 1 carriers (*Hp*1-1 and *Hp* 2-1). GV was measured by the glucose coefficient of variation (%CV) obtained from continuous glucose monitoring. To determine whether the association between %CV and risk of diabetic macroangiopathy was differed between the two *Hp* subgroups, we tested the interaction effect between %CV and *Hp* subgroups in univariable analysis. Furthermore, serum concentration of 8-hydroxy-2'-deoxyguanosine (8-OHdG) was measured as a biomarker of oxidative stress. **Results:** Serum 8-OHdG levels were positively correlated with %CV in *Hp* 1 carriers (r = 0.117; *p* = 0.021). Patients within the highest %CV tertile were more likely to develop diabetic macroangiopathy than those in the lowest tertile in *Hp* 1 carriers (OR = 2.461 [95% CI, 1.183–5.121], *p* = 0.016), but not in those with *Hp* 2-2 genotype (OR = 0.540 [95% CI, 0.245–1.191], *p* = 0.127). A significant interactive effect of *Hp* genotypes and %CV on risk of diabetic macroangiopathy was found (*p* interaction = 0.008). **Conclusions:** *Hp* genotype modifies the effect of GV on risk of diabetic macroangiopathy in Chinese patients with type 2 diabetes.

WOCS-04-6

Lesson Learned from Patient Support Program for Insulin Initiation and Intensification in Type 2 Diabetes in Indonesia

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Objective: To learn the characteristics of patient involving in the patient support program for insulin initiation and intensification in Indonesia, named Incontrol Program, the challenge and future hope.

Methods:

Type 2 diabetes patient who start basal insulin enrolled in this program to intensify insulin dose based on blood glucose monitoring. Each subject received a diabetes and insulin education tool kit and join education session conducted by diabetes nurse educator virtually for 12 months.

Results:

Incontrol Program enrolled 1,630 patient, female:male 61%:39%, mean age 55.98±13.76 years, most were 50-59 years (32.5%) followed by 60-69 (24.6%) years age group, diabetes duration mostly more than 10 years. About 68.71% were overweight/obese, which may relate with high carbohydrate snacking between meals and less physical activities. Only 31.84% reported HbA1c level at early program. Basal insulin starting dose were vary, trend increased with peak mostly on month 6, the highest was 55 unit, and had little change after month 7. Average morning fasting blood glucose decreased from baseline 189.75 mg/dL to 110.36 mg/dL, as well as HbA1c level: 9.61% to 7.09%. Technology barrier were found including digital informed concerned signing, self-monitoring blood sugar, and engaging online education meeting.

Conclusions: InControl patient support program help type 2 diabetes to initiate and intensify the insulin dose to achieve fasting blood glucose and HbA1c target. Understanding technology is still a challenge to run this program among seniors and need further effort to encourage patient to actively participate in diabetes self-management education program.

WOCS-04-7

Osteocalcin and its trajectories with mortality among patients with type 2 diabetes

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Objective This study aimed to investigate the association between serum osteocalcin (OCN) and its trajectories and the risks of all-cause and cardiovascular disease (CVD) mortality among patients with type 2 diabetes. **Methods** We performed a prospective cohort study of 9,413 type 2 diabetic patients with at least 3 OCN measurements. Baseline, mean values of osteocalcin levels and its trajectories were used as exposures. Multivariable adjusted Cox proportional hazards model was used to estimate the association of osteocalcin levels and its trajectories with mortality. **Results** During a mean follow up of 4.76 years, 1,638 patients died, of whom 588 were due to CV events. Multivariable-adjusted hazard ratios (HRs) across quintiles of baseline OCN levels were 2.88 (95% confidence interval (CI) 2.42-3.42), 1.65 (95%CI 1.37-1.99), 1.17 (95%CI 0.96-1.42), 1.00, and 1.92 (95%CI 1.60-2.30) for all-cause mortality, and 3.52 (95%CI 2.63-4.71), 2.00 (95%CI 1.46-2.73), 1.03 (95%CI 0.72-1.47), 1.00, 1.67 (95%CI 1.21-2.31) for CVD mortality, respectively. These U-shaped associations were consistent among patients of different baseline characteristics. Patients with a stable or even increasing trajectory of OCN may have a lower risk of mortality. **Conclusions** A U-shape association between OCN and mortality was observed among patients with type 2 diabetes. Additional trajectory analyses showed a potential protective effect of osteocalcin maintenance or increase on life span.

WOCS-05-1

Efficacy of antihyperglycemic therapies on cardiovascular and heart failure events: A meta-analysis and meta-regression

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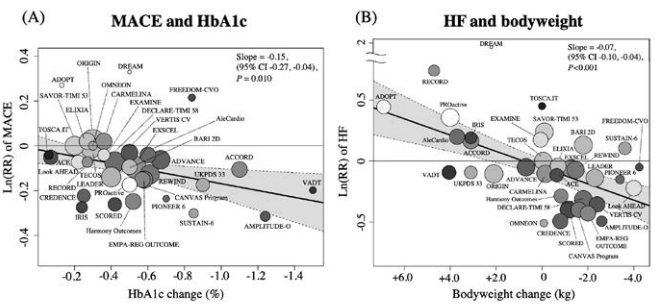
Objective: To evaluate the efficacy of antihyperglycemic therapies on major adverse cardiovascular events (MACE) and heart failure (HF) in all cardiovascular outcome trials (CVOTs), thereby robustly determining the relationships between glycated hemoglobin (HbA1c) or bodyweight changes and these outcomes.

Methods: We searched PubMed and EMBASE up to 25 January 2023 for all randomized controlled CVOTs of antihyperglycemic therapies reporting both MACE and HF outcomes in patients with type 2 diabetes or prediabetes. We performed meta-regression analyses following random-effects meta-analyses to evaluate the effects of HbA1c or bodyweight reductions on each outcome.

Results: Thirty-five trials with 256,524 patients were included. Overall, antihyperglycemic therapies reduced MACE by 9% (risk ratio [RR]: 0.91; 95% confidence interval [CI]: 0.88–0.94; P<0.001; I^2=36.5%). In meta-regression, every 1% greater reduction in HbA1c was associated with a 14% reduction in the RR of MACE (95% CI: 4–24; P=0.010), whereas bodyweight change was not associated with the RR of MACE. On the other hand, antihyperglycemic therapies showed no overall significant effect on HF (RR: 0.95; 95% CI: 0.87–1.04; P=0.28; I^2=75.9%), while every 1 kg bodyweight reduction, but not HbA1c reduction, was found to reduce the RR of HF by 7% (95% CI: 4–10; P<0.001). However, significant residual heterogeneity (P<0.001) was observed, and sodium-glucose cotransporter-2 inhibitors(SGLT2i) reduced HF more than could be explained by HbA1c or bodyweight reductions.

Conclusion: Antihyperglycemic therapies reduce MACE in an HbA1c-dependent manner, while HF is reduced in a bodyweight-dependent manner. Notably, SGLT2i have shown class-specific benefits for HF beyond HbA1c or bodyweight reductions.

Figure. Association between (A) the risk of major adverse cardiovascular events (MACE) and HbA1c reduction, or (B) the risk of heart failure (HF) and bodyweight change



WOCS-05-2

Anti-inflammatory therapies in patients with established cardiovascular disease or high cardiovascular risks

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Objective: To evaluate the association between anti-inflammatory therapies and the incidence of cardiovascular events in patients with established cardiovascular disease (CVD) or high cardiovascular risks.

Methods: Literature retrieval was conducted in Pubmed, Medline, Embase, the Cochrane Central Register of Controlled Trials and Clinicaltrial.gov website from the inception to July 2022. Randomized controlled trials compared anti-inflammatory therapies with placebo in patients with established CVD or high

cardiovascular risks were included. The results of the meta-analysis were computed as the risk ratio (RR) with 95% confidence interval (CI).

Results: Compared with placebo, anti-inflammatory therapies were associated with decreased incidence of myocardial infarction (MI) (RR=0.93, 95%CI, 0.88 to 0.98), which was mainly driven by therapies targeting central IL-6 signaling pathway (RR=0.83, 95%CI, 0.74 to 0.93). IL-1 inhibitors treatment was associated with reduced risks of heart failure (RR=0.38, 95%CI, 0.18 to 0.80) while lower incidence of stroke was observed in patients with colchicine treatment (RR=0.47, 95%CI, 0.28 to 0.77). MI events were less frequent in patients over 65 years old (RR=0.90, 95%CI, 0.83 to 0.98) or with follow-up duration over 1 year (RR=0.90, 95%CI, 0.85 to 0.96) when comparing anti-inflammatory therapies with placebo.

Conclusion: Anti-inflammatory therapies, especially those targeting central IL-6 signaling pathway may serve as promising treating strategies to ameliorate the risk of MI. Meanwhile, IL-1 inhibitor and colchicine were associated with decreased risks of heart failure and stroke respectively. MI risk reductions by anti-inflammatory therapies seem to be more prominent in patients who were older and with long follow-up duration.

WOCS-05-3

Analysis of Mean Platelet Volume and Platelet Distribution Width in AMI Patient With and Without Diabetes Mellitus

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Objective: Trombocyte activity increases in Diabetes Mellitus (DM). This increase indicates vascular disorders or increased inflammation. Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) are specific parameters of the activity. Acute myocardial infarction (AMI) is one of the microvascular complications that many patients suffer from DM. The aim of this study is to analyze the relationship between MPV and PDW with acute myocardial infarction in patients with DM.

Methods: This study is an explanatory, observational, cross-sectional study of AMI patients treated in the Chest Pain Unit (CPU), dr. Ramelan Central Naval Hospital, Surabaya, Indonesia, from January 2022 to February 2023.

Results: A total of 201 subjects consisted of 151 men (75.1%) and 50 women (24.9%). Acute Myocardial Infarction with Diabetes Mellitus in 146 subjects (72.6%) and Acute Myocardial Infarction non-Diabetic in 55 subjects (27.3%); average levels of MPV and PDW were 10.441.10 fL and 10.761.76 fL, respectively. There is a significant relationship between MPV (p 0,000, OR = 201.739, 95% CI: 26.274-1548.995) and PDW (p = 0.021, OR = 3.75, 95% CI: 2.981-4.729) with AMI at DM.

Conclusions: MPV and PDW are related to AMI events with DM

WOCS-05-4

Correlation Hba1c levels and Ejection Fraction in Type-2 Diabetes Mellituspatients at Central Naval Hospital Surabaya

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Objective: Type-2 Diabetes Mellitus (T2DM) is a chronic metabolic disease or disorder with multiple etiologies characterized by high blood sugar levels that can increase the risk of atherosclerosis and other cardiovascular diseases, one of the main causes of death among Type 2 DM patients is Heart Failure. This study aims to analyze the Correlation between Hba1c values and Heart Failure events based on ejection fraction. This type of analytic research with a case control approach using medical record data.

Methods: This type of analytic research with a case control approach using medical record data. The research sample consisted of 47 samples using simple random sampling. Univariate and bivariate data analysis with chi-square test.

Results: Comparing HbA1C with EF results with mild criteria 22 respondents with details of 5 respondents (10.6%) experiencing HFrEF<40%,3respondents(6.4%) experiencing HFrEF<41-49%,and 14 respondents(29.8%) experiencing HFrEF >50 %. Moderate criteria included 19 respondents with details of 7 respondents (14.9%) experiencing HFrEF<40%,7 respondents (14.9%) experiencing HFrEF<41-49%, and 5 respondents (10.6%) experiencing HFrEF >50%. respondents with details of 0 respondents (0%) experienced HFrEF<40%, 0 respondents (0%) experienced HFrEF<41-49%, and 6 respondents (12.8%) experienced HFrEF >50%. Because there are cells with an expected value < 5, then testing the hypothesis using fisher, the test results obtained by the hypothesis a significance value of 0.018, the value is < 0.05, then H0 is rejected and H1 is accepted, which means there is a relationship between HbA1C and EF.

Conclusions: Statistical results that Hba1C levels had a Relationship with the Ejection Fraction

WOCS-05-5

The atherogenic index of plasma as a predictor of arterial stiffness measured by ba-PWV in type 2 diabetic patients

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Objectives: Early detection of arterial stiffness in Type 2 diabetes mellitus (T2DM) patients before the clinical manifestation of atherosclerosis is substantial. This study aimed to explore the correlation of the atherogenic index of plasma (AIP) with arterial stiffness and construct a predictive model for arterial stiffness in T2DM patients using it.

Methods: A total of 184 adult T2DM patients in the diabetes outpatient clinic at the Dr. Soetomo general academic hospital, in 2015 & 2019 were enrolled in this cross-sectional study. Sociodemographic, glycosylated hemoglobin (HbA1c), lipid profiles, and brachial-ankle pulse wave velocity (ba-PWV) data were collected. The AIP was calculated from log(triglycerides/HDL-cholesterol). Arterial stiffness was defined by ba-PWV > 18 m/sec. The association was estimated using a correlation test, and receiver operator characteristics (ROC) curves analysis was used to determine the cut-off value of AIP for arterial stiffness. Bivariate logistic regression analysis was used to calculate the risk analysis model.

Results: The lipid profiles and AIP were higher in the group with arterial stiffness. The AIP was correlated significantly with ba-PWV. The AIP can be used as a predictor of arterial stiffness with a cut-off value of 0.65 (sensitivity 74.2% & specificity 81.0%). An elevated AIP demonstrated a higher risk (OR = 11.31; 95% CI: 4.619 – 27.715; $p < 0.001$) of having arterial stiffness even after adjusting for age, hypertension, and obesity.

Conclusion: The AIP is a potential biochemical marker for arterial stiffness in T2DM patients.

Keywords: dyslipidemia, arterial stiffness, cardiovascular disease, risk, type 2 diabetes mellitus

WOCS-05-6

Low Cardiometabolic Indexes Associated with Diastolic Dysfunction in Type 2 Diabetes Mellitus Patient with HFpEF

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Objective

To investigate association between cardiometabolic indexes (TG/FBG, TG/HDL-C, and LDL-C/HDL-C) and diastolic dysfunction in T2DM patients with HFpEF.

Methods

Data from this cross-sectional study were obtained from the electronic medical

record database on October 2021 to January 2022. In total 66 patients with T2DM and HFpEF without coronary artery disease or valvular heart disease were enrolled. Baseline characteristics, clinical and laboratory variables, medication, and echocardiography data were obtained. Cardiometabolic indexes (TG/FBG, TG/HDL-C, and LDL-C/HDL-C) are presented as numeric data (median with IQR). Meanwhile, the diastolic function is presented as categorical data based on the echocardiographic parameters. Mann-Whitney analysis was performed to determine the association between cardiometabolic index with diastolic dysfunction. P-value <0.05 represent significant associations.

Results

The mean concentration of FBG, TG, HDL, and LDL were 135.73 ± 54.34, 145.96 ± 75.85, 47.21 ± 13.22, and 112.20 ± 37.53, respectively. The echocardiography study found there were 55 patients (83%) had normal diastolic function, 4 patients with indeterminate diastolic function results, and 7 patients had diastolic dysfunction grade I. The data analysis present that there were significant associations between lower TG/FBG, TG/HDL-C, and LDL-C/HDL-C with diastolic dysfunction (p-value <0.05). The p-values were 0.015, 0.003, and 0.044, respectively.

Conclusion

Low TG/FBG, TG/HDL-C, and LDL-C/HDL-C was significantly associated with diastolic dysfunction. Optimal dyslipidemia control represented by high TG/FBG, TG/HDL-C, and LDL-C/HDL-C may become an appealing approach to prevent HFpEF progression in T2DM patients.

WOCS-05-7

Analysis of the influencing factors of stress hyperglycemia in patients after cardiac bypass transplantation

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Objective To understand the blood glucose after cardiac bypass transplantation and explore the influencing factors of stress hyperglycemia in patients after cardiac bypass transplantation

Methods The clinical data of 186 patients undergoing cardiac bypass transplantation at the Cardiovascular Center of Tsinghua Changgeng Hospital in Beijing from January 2021 to November 2022 were retrospectively analyzed. The patients were divided into normal group and hyperglycemia group (blood glucose value>10.0 mmol/L) according to the blood glucose results of the first arterial blood gas, and the factors affecting postoperative stress hyperglycemia were analyzed.

Results According to age, history of diabetes, course of diabetes, glycosylated hemoglobin, body mass index, extracorporeal circulation, start time and duration of surgery, and glucose control program, the difference between the normal group and the hyperglycemic group was statistically significant (P<0.05).

Conclusion The stress hyperglycemia factors after heart bypass transplantation include age, history of diabetes, course of diabetes, glycosylated hemoglobin, body mass index, cardiopulmonary bypass, operation start time and duration, and sugar control program; Nursing staff should take corresponding measures in the clinical process to avoid the harm of hyperglycemia to patients.

WOCS-06-1

Comparison of therapeutic efficacy and safety of adding sitagliptin, dapagliflozin or lobeglitazone in T2DM patients.

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OBJECTIVE

To compare the efficacy and safety of sitagliptin, a dipeptidyl peptidase-4 inhibitor, dapagliflozin, a sodium glucose co-transporter-2 inhibitor, and lobeglitazone, a thiazolidinedione in patients with type 2 diabetes uncontrolled with metformin and sulfonylurea therapy.

RESEARCH DESIGN AND METHODS

In this two year, randomized, clinical trial, 78 patients were enrolled and randomized to receive sitagliptin 100 mg, dapagliflozin 10 mg, or lobeglitazone 0.5 mg daily (n = 26 each). The primary and secondary efficacy endpoints were changes in HbA1c at 6 months and 24 months, respectively. The proportion of patients who achieved HbA1c £7% without hypoglycemia was also examined. Other biomedical parameters and body composition changes were also investigated for 2 years.

RESULTS: The adjusted mean change (± standard error) in HbA1c in the sitagliptin, dapagliflozin, and lobeglitazone groups was –1.06 ± 0.63%, –1.35 ± 0.74%, –1.27 ± 1.13%, after 6 months, and –0.81 ± 1.06%, –1.05 ± 0.70%, –1.09 ± 0.98%, after 24 months, respectively, without between-group difference. Dapagliflozin and lobeglitazone treatment reduced proteinuria significantly, but sitagliptin did not. Between-group comparisons showed a significantly greater reduction in body fat% (–1.18% ± 2.28%) with maintaining muscle% (1.03% ± 2.12%) in the dapagliflozin group. Safety profiles were comparable between three groups.

CONCLUSIONS All three drugs showed good glucose-lowering efficacy and safety profiles in patients with type 2 diabetes for 2 years. Compared to sitagliptin and lobeglitazone, dapagliflozin showed improvement in lipid profiles and proteinuria and decreased body weight and fat (NCT02338921).

WOCS-06-2

The Effect of Diabetes Management Shared Care Clinic on HbA1c Compliance and Self-management Abilities in Patients

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Objective: We aim to evaluate the impact of diabetes management shared care clinic (DMSCC) on glycated hemoglobin A1c (HbA1c) compliance and self-management abilities in patients with type 2 diabetes mellitus (T2DM).

Methods: This study was a prospective cohort study of patients with T2DM participating in the DMSCC. At baseline and after management, the HbA1c levels were measured, the HbA1c compliance rate were calculated, and the Summary of Diabetes Self-Care Activities-6 (SDSCA-6), Diabetes Empowerment Scale-DAWN Short Form (DES-DSF), and Problem Areas in Diabetes Scale — Five-item Short Form (PAID-5) were completed. These pre- and post-management data were compared.

Results: A total of 124 eligible patients were enrolled. After the diabetes management of DMSCC, the average HbA1c decreased and the HbA1c compliance rate increased significantly ($P < 0.01$). SDSCA-6 showed significant improvement in physical activity, glycemic monitoring, smoking ($P<0.01$), and taking medication ($P<0.05$). DES-DSF suggested a greater willingness to try to effectively treat diabetes ($P<0.05$). PAID-5 indicated significant improvement in diabetes-related emotional distress.

Conclusion: DMSCC can help patients with T2DM reduce HbA1c, increase HbA1c compliance, improve diabetes self-management behaviors, empowerment, and diabetes-related emotional distress and serve as an effective exploration and practice of diabetes self-management education and support.

WOCS-06-3

Effect of the increasing intensity exercise therapy in linoleic acid metabolism of type 2 diabetic patients

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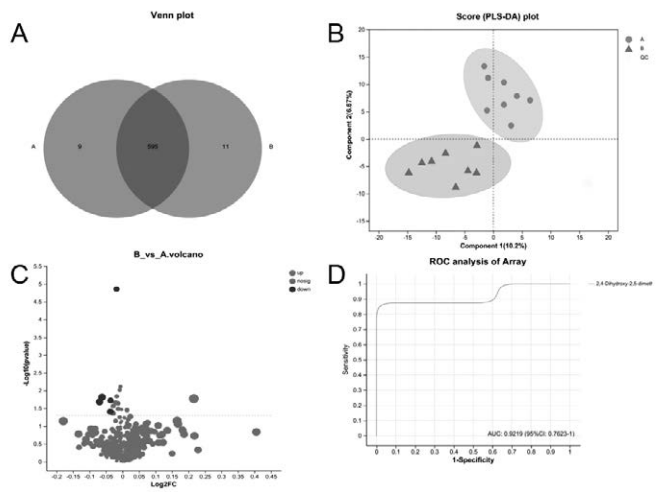
Objective: To observe the effects of the increasing intensity exercise therapy, which was used to gradually increase the VO2max of patients and improve their metabolic capacity, on the adaptations in multi-tissue metabolome of men with T2DM.

Methods: Men fitting the inclusion (T2DM, age 52.75±4.36 years) and exclusion criteria (concurrent systemic disease, and regular exercise training) were included in this study (n = 8). After comprehensive evaluation of physical activity level, patients completed a three-months increasing intensity exercise therapy. Blood was obtained before and after the training period. Metabolomic analysis was performed on all samples. Differential content was assessed by Students' t-test and PLS-DA. KEGG pathway enrichment analysis was performed. Meaningful metabolites were identified by the criteria (VIP>1.5 and P<0.05). ROC curves for differential metabolites were plotted by SPSS.

Results: All subjects tolerated the study well. FBG, HbA1C, UA and body fat percentage were improved to some extent after the exercise therapy, but the differences were not significant(p>0.05). However, changes in relevant metabolic pathway were identified. The increasing intensity exercise therapy increased plasma tyrosyl-proline, and decreased triphenylphosphine oxide, Gly Phe, 7-hydroxyolanzapine, (S)9-Hydroxy-10-undecenoic acid, which mainly related to lipid metabolism. Besides, the AUC of the (S)9-Hydroxy-10-undecenoic acid reached 0.9219, which could effectively distinguish between before and after the increasing intensity exercise therapy.

Conclusion: (S)9-Hydroxy-10-undecenoic acid, which related to the linoleic acid metabolism could effectively distinguish between before and after the exercise therapy. The intensity exercise therapy could improve lipid metabolism of T2DM patients to some extent, but the differences were not significant.



WOCS-06-4

Comparison of the therapeutic effects of oral semaglutide and SGLT2i.

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Objective: Various oral antidiabetic agents are used clinically, but there is scant comparison of oral semaglutide and SGLT2i. We compared the efficacy of semaglutide and SGLT2i in patients with type 2 diabetes. Methods: Patients who began oral semaglutide or SGLT2i between February 2021 and October 2022 were included in the study. Changes in HbA1c, body weight, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and creatinine before and 6 months after initiation were analyzed. Results: 51 of the 68 patients in the semaglutide group and 209 of the 229 patients in the SGLT2i group continued treatment for 6 months. HbA1c and body weight were significantly decreased in both groups. While AST and ALT were significantly decreased in the SGLT2i group, in the semaglutide group there was a tendency to reduction, but it did not reach statistical significance. Creatinine was significantly increased in the SGLT2 group but not in the semaglutide group. Conclusion: Both oral semaglutide and SGLT2i significantly improve glycemic control and reduce body weight. However, the effects on liver enzymes and renal function differed somewhat in the two groups, reflecting differences in the mechanisms of action.

WOCS-06-5

DIABETIC KETOACIDOSIS WITH ACUTE PANCREATITIS IN PRE-ECLAMPSIA PATIENT

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Abstract

Background. Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes that requires immediate treatment. Diabetic ketoacidosis in pregnancy is an emergency that significantly causes maternal and fetal morbidity and mortality.

Case. A 33-year-old woman, was admitted at 32 weeks of gestation to the emergency department with shortness of breath, two-day history of nausea and vomiting. She had a history of diabetes mellitus four years earlier. She missed her medication one day due to traveling for greeting her family. She also presented with abdominal tenderness, hypertension, elevated heart rate, increased respiratory rate, and fatigue. The presenting blood sugar level was 713 mg/dl. Ketone testing done using her urine sample showed ketonuria of 3^{+}. Amylase and Lipase enzymes increased at 1004,8 and 899,4. CT Abdominal revealed acute pancreatitis. Her breath odor revealed acetone-smelling breathing. Upon admission, she was treated with insulin infusion for 48 hours and antibiotics for her pancreatitis. Her serum glucose and pancreatic enzyme level decreased to normal range. The patient and her baby recovered and was discharged in stable condition.

Objective. To know how to manage type 2 diabetes with complex complication.

Methods. This is a case report using one sample patient.

Results. With correct management, the patient and her baby recovered and was discharged in stable condition

Conclusions. This case report describes the correlation between diabetes mellitus and acute pancreatitis. With proper treatment, the mortality rate of pregnant women with diabetes mellitus and its complications can be reduced.

Keywords: diabetic ketoacidosis, acute pancreatitis, pregnancy

WOCS-06-6

Exercise-induced improvement of glycemic fluctuation and its relationship with fat and muscle distribution in T2DM

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Objective: Management of glycemic fluctuation is essential for diabetes. Exercise is an important therapeutic strategy for diabetes patients, while little is known about determinants of glycemic response to exercise. We aimed to investigate the effect of acute combined aerobic and resistance exercise training on glycemic fluctuation of type 2 diabetes patients, and explore the influence factors of exercise-induced glycemic response.

Methods: The study randomized 50 sedentary patients with type 2 diabetes 1:1

to maintain sedentary lifestyle or receive combined exercise training for two weeks. All participants received diet administration during the study. Blood glucose fluctuation was evaluated by flash continuous glucose monitoring. Baseline fat and muscle distribution were accurately quantified through magnetic resonance imaging (MRI).

Results: Combined exercise training decreased standard deviations of sensor glucose (SDSG: pre *vs.* post, mean 1.35 *vs.* 1.10 mmol/l, $P = 0.006$) and coefficient of variation (CV: mean 20.25 *vs.* 17.20 %, $P = 0.027$). No significant change was observed in the control group. Multiple stepwise linear regression showed that baseline MRI-quantified fat and muscle distribution, including visceral fat area ($\beta = -0.761$, $P = 0.001$) and mid-thigh muscle area ($\beta = 0.450$, $P = 0.027$), were independent influence factors of changes of SDSG and CV in the exercise group.

Conclusion: Acute combined exercise training improved glycemic fluctuation of diabetes patients. Baseline body composition was important influence factors of changes of glycemic variability, providing new insights into personalized exercise intervention for diabetes.

WOCS-07-1

Prevalence, clinical characteristics and HLA-DR genotypes of idiopathic type 1 diabetes: a cross-sectional study

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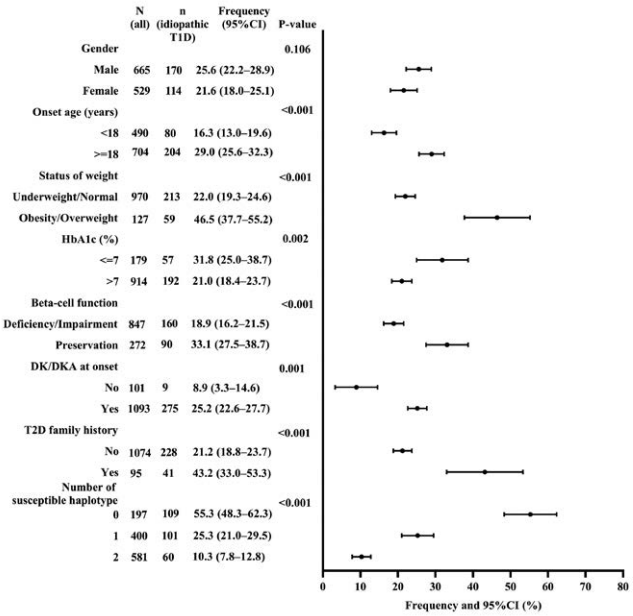
Objective: Idiopathic type 1 diabetes (T1D) is a neglected subtype of T1D, the frequency, clinical characteristics, human leukocyte antigen (HLA) genotypes of idiopathic T1D were unknown.

Methods: A total of 1205 newly diagnosed T1D patients were included for analysis. A custom monogenic diabetes gene panel were used to exclude monogenic diabetes in autoantibody-negative patients. Individuals with negative autoantibodies and subsequently excluding monogenic diabetes were diagnosed as idiopathic T1D. Clinical characteristics, islet autoantibodies measured by radioligand assay, and HLA DR-DQ were collected.

Results: After excluding 11 monogenic diabetes patients, 284 cases were diagnosed with idiopathic T1D, accounting for 23.8% (284/1194) of all newly diagnosed T1D. When compared with autoimmune T1D, idiopathic T1D patients showed older onset age, higher body mass index in adults, lower hemoglobin A1c, higher levels of fasting C-peptide and 2-hour postprandial C-peptide, and more often of type 2 diabetes family history and 0 susceptible HLA haplotype (all P<0.01). Lower proportions of carrying 2 susceptible HLA haplotypes in idiopathic T1D were observed in the adult-onset subgroup (15.7% vs. 38.0% in child-onset subgroup, P<0.001) and in subgroup who had preserved beta-cell function (11.0% vs. 30.1% in subgroup with poor beta-cell function, P<0.001). Multivariable correlation analyses showed that overweight, positive type 2 diabetes family history and without susceptible HLA haplotypes were positively related with negative autoantibodies.

Conclusion: Idiopathic T1D accounts for approximately 1/4 among newly diagnosed T1D, and individuals who are adult-onset and had preserved beta-cell function tend to have lower HLA susceptibility and more insulin resistance.



WOCS-07-3

Subtype identification by data-driven methods for patients with type 1 diabetes

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Background

The heterogeneity of patients with type 1 diabetes mellitus (T1DM) has been noticed, but it remains to be fully understood. This study aims to identify subtypes of T1DM patients using machine learning algorithms.

Methods

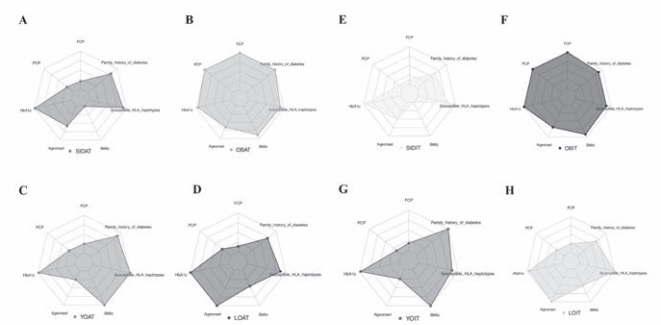
Patients with autoimmune and idiopathic T1DM were subcategorized separately. Clustering methods were utilized with onset age of diabetes, fasting C peptide (FCP), and body mass index (BMI) z score as variables. To investigate the distribution of β cell function for the patients, they were further subclassified by a classification and regression tree (CART) model. And the outcome of β cell function failure was compared among clusters during the five-year follow-up.

Results

The clustering methods sub-classified patients with autoimmune T1DM (AT) and idiopathic T1DM (IT) into four clusters with distinctive characteristics, and were named severe insulin-deficient clusters (SIDAT[29.2%] and SIDIT[33.9%]), optimal β cell function clusters (OBAT[17.1%] and OBIT[18.7%]), young onset clusters (YOAT[33.2%] and YOIT[27.6%]), and late onset clusters (LOAT[20.5%] and LOIT[19.8%]). The CART model subcategorized patients with AT into four subgroups and IT into two subgroups. Notably, the four subgroups distributed almost evenly in YOAT cluster, and the majority (99.2%) of SIDIT cluster were from CN1 subgroup. Additionally, individuals in the OBAT cluster were less likely to occur b cell function failure (p=0.019), and the OBIT cluster had the smallest percentage (9.1%) of the outcome occurrence during the follow-up.

Conclusion

The methods stratified patients with T1DM into subgroups with different characteristics of demography, b cell function, autoimmune and genetics, and with prognostic values for T1DM management.



WOCS-07-4

Insulin resistance related metabolic disorders are associated with cognitive decline in type 1 diabetes

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Aims: To investigate the association between insulin resistance (IR) related metabolic disorders and cognitive function in adult patients with type 1 diabetes (T1D).

Materials and methods: A total of 117 adult patients with T1D were recruited in this study. IR related metabolic disorders were defined when patients had overweight/ obesity/ central obesity, hypertension, atherogenic dyslipidemia, or estimated glucose disposal rate (eGDR)<9 mg/kg/min. The Wechsler Memory Scale-Chinese Revision (WMS-RC), Wisconsin Card Sorting Test (WCST), and Sustained Attention to Response Task (SART) was applied to assess memory, executive function and sustained attention, respectively. Cognitive differences were measured between T1D patients with and without IR related metabolic disorders, and between patients with different levels of IR related metabolic components. Multivariate regression analysis was performed to further examine relationships between IR-related metabolic components and cognitive function.

Results: IR related metabolic disorders were observed in 39.3% of the T1D patients. Patients with IR related metabolic disorders performed worse on executive function and immediate visual memory task, but did not show any difference regarding the sustained attention compared to patients without disorders. Among the IR-related metabolic components, higher waist-to-hip ratio (WHR) was independently correlated with lower executive function, and higher log (triglyceride [TG]/ high-density lipoprotein-cholesterol [HDL -C]) was correlated with lower memory scores.

Conclusions: We have provided evidence of an association between IR related metabolic disorders and deteriorated memory and executive function in adult patients with T1D**.** WHR and log (TG/ HDL -C) showed negative correlation with executive function and memory, respectively.

Table 1. WHR and Log TG/ HDL -C in association with cognitive function in linear regression model.

Components	Verbal memory-immediate		Verbal memory-delayed		Visual memory-immediate		Visual memory-delayed		Preservative errors		Completed categories	
	R^2 = 0.239, P = 0.004		R^2 = 0.286, P = 0.001		R^2 = 0.448, P<0.001		R^2 = 0.267, P<0.001		R^2 = 0.129, P=0.038		R^2 = 0.191, P=0.002	
	β	P	β	P	β	P	β	P	β	P	β	P
Age (years)	-0.108	<0.001	-0.127	<0.001	-0.109	<0.001	-0.090	0.003	-0.153	0.153	0.004	0.742
Male	-0.520	0.293	-0.462	0.377	0.287	0.507	-0.193	0.707	2.695	0.150	0.074	0.747
Education (years)	0.073	0.417	0.132	0.172	0.180	0.025	0.205	0.032	-0.170	0.640	0.111	0.014
Disease duration (years)	0.068	0.211	0.038	0.510	-0.018	0.700	0.008	0.890	-0.175	0.419	-0.031	0.244
WHR	2.088	0.656	-1.320	0.790	-4.236	0.302	-2.433	0.616	-52.211	0.005	-7.185	0.002
Log (TG/ HDL -C)	-1.678	0.091	-2.261	0.034	-4.804	<0.001	-2.982	0.005	-4.061	0.262	-0.329	0.457
Hyperglycemia exposure score	-0.336	0.131	-0.210	0.370	0.193	0.319	0.046	0.835	0.131	0.879	0.068	0.525

WHR: waist-to-hip ratio; TG: triglyceride; HDL -C: high-density lipoprotein-cholesterol.

WOCS-07-5

Circular RNA profile identifies circSAMD8 as a novel potential biomarker for fulminant type 1 diabetes

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Objective: Circular RNAs (circRNAs) are associated with diabetes, but their role in fulminant type 1 diabetes (FT1D) is completely unknown. This study is to identify the circRNA expression profiles in the peripheral blood mononuclear cells (PBMCs) of patients with FT1D and characterized the role of circRNAs.

Methods: CircRNA expression profiles were detected in the exploratory cohort including five FT1D patients and five controls using a circRNA microarray. An independent validation cohort comprised of 40 FT1D cases, 75 type 1 diabetes (T1D) cases, and 115 controls was used to verify the circRNAs using quantitative real-time polymerase chain reaction (qRT-PCR). Spearman's correlation analysis and receiver operating characteristic (ROC) curve analysis were performed to determine the clinical diagnostic capability of circRNAs. Bioinformatics was used to identify potential biological functions and circRNA–miRNA–mRNA interactions.

Results: There were 13 upregulated and 13 downregulated circRNAs in PBMCs of patients with FT1D. Five circRNAs were further verified in the second validation cohort. circSAMD8 was significantly upregulated in the FT1D and T1D groups. CircSAMD8 was differentiated between patients with FT1D and controls [area under the curve (AUC) 0.846; 95% CI 0.776-0.916; P<0.0001] as well as between patients with FT1D and patients with T1D (AUC 0.726; 95% CI 0.633-0.820; P<0.0001). Bioinformatics analysis showed that circSAMD8 may be involved in 47 circRNA-miRNA-mRNA signaling pathways associated with diabetes.

Conclusion: CircRNAs were aberrantly expressed in PBMCs of patients with FT1D, and circSAMD8 may be a novel potential biomarker for FT1D.

WOCS-07-6

Insulin resistance is more frequent in type 1 diabetes patients with long diabetes duration

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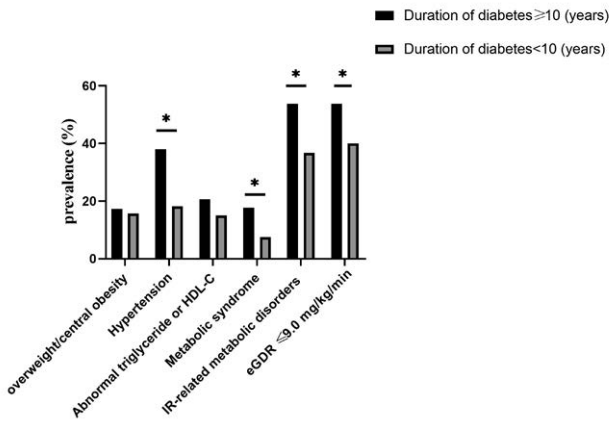
Aims: To investigate the clinical status of insulin resistance (IR) and its correlation with disease duration in patients with type 1 diabetes (T1D).

Materials and methods: Cross-sectional data from a T1D cohort were obtained (n=923). IR-related metabolic disorders including hypertension, obesity, and dyslipidemia were used as outcome variable to explore the cut-off point for estimated glucose disposal rate (eGDR) by restricted cubic spline (RCS) curve. Regression models were used for multivariate analysis on the clinical factors associated with IR. The correlation between the status of IR and diabetes duration was depicted with RCS curve.

Results: IR-related metabolic disorders were observed in 39.4% of patients, with 9.1% met the criteria for metabolic syndrome. Specifically, patients with ≥10 years of T1D were more likely to have IR-related metabolic disorders (53.8% vs. 36.7%, p<0.05). The presence of IR, defined as an eGDR ≤ 9.0 mg/kg/min, were observed in 42.2% of patients. Patients with IR had longer diabetes duration (3.5 vs. 2.7, years, p=0.003) and higher insulin dose (0.5 vs. 0.4, units per kg per day, p<0.001). Moreover, the presence of IR showed a gradual increase during 10 years' disease duration and further analysis showed diabetes duration ≥10 years was a key element behind the development of IR and IR-related metabolic disorders.

Conclusions: The status of IR is common in T1D, especially in those with ≥10 years of disease duration. Therapies targeting at balancing glycemic control and IR will be needed to decrease the future risks of cardiovascular diseases in T1D.



WOCS-07-7

Clinical and HLA Genotype Analysis of Immune Checkpoint Inhibitor-Associated Diabetes Mellitus

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Objective: To investigate the clinical characteristics and HLA genotypes of patients with immune checkpoint inhibitor-associated diabetes mellitus (ICI-DM) in China.

Methods: We enrolled 23 patients with ICI-DM and 51 patients with type 1 diabetes (T1D). HLA genotyping was conducted via next-generation sequencing.

Results: Most (78.3%) ICI-DM patients presented with diabetic ketoacidosis, and all received insulin injections. Compared to T1D patients, ICI-DM patients were significantly older and had higher blood glucose but lower HbA1c levels (P<0.05). Only two (8.7%) ICI-DM patients were positive for islet autoantibodies, which was lower than that in T1D patients (66.7%, P<0.001). A total of 59.1% (13/22) of ICI-DM patients were heterozygous for an HLA T1D risk haplotype, and DRB1*0901-DQA1*03-DQB1*0303 and DRB1*0405-DQA1*03-DQB1*0401 were the major susceptible haplotypes. Compared to T1D, the susceptible DR3 and DR9 haplotypes were less frequent (17.7% vs 2.3% and 34.4% vs 15.9%; P<0.05), whereas the protective haplotypes (DRB1*1101-DQA1*05-DQB1*0301 and DRB1*1202-DQA1*0601-DQB1*0301) were more frequent in ICI-DM patients (2.1% vs 13.6% and 4.2% vs 15.9%; P<0.05). Among the 23 ICI-DM patients, 7 presented with ICI-associated fulminant type 1 diabetes (IFD), and 16 presented with ICI-associated type 1 diabetes (IT1D). Compared to IT1D patients, IFD patients exhibited marked hyperglycemia, low C-peptide and HbA1c levels (P<0.05). Up to 66.7% (4/6) of IFD patients were heterozygous for reported fulminant type 1 diabetes susceptibility HLA haplotypes (DRB1*0405-DQB1*0401 or DRB1*0901-DQB1*0303).

Conclusion: The lack of islet autoantibodies, the low frequencies of T1D susceptibility and high frequencies of protective HLA haplotypes indicate that ICI-DM represents a new model distinct from classical T1D.

WOCS-07-8

Clinical analysis of 17 patients with adult fulminant type 1 diabetes in China

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Objective: To explore the clinical characteristics of patients with fulminant type 1 diabetes mellitus (FT1DM).

Methods The clinical records of the FT1DM patients and type 1 diabetes mellitus (T1DM) patients with onset of diabetic ketoacidosis (DKA) admitted in West China Hospital from Jan 1, 2010 to Dec 31, 2019 were collected, and the FT1DM patients were followed up.

Results There were 70 T1DM patients with onset of DKA, and FT1DM accounted for 24.3% of them. The mean ages of 17 FT1DM patients and 53 T1DM patients with onset of DKA were 33.2±12.8 years and 27.5±11.2 years, respectively. 13 patients in the FT1DM group had flu-like or gastrointestinal symptoms before onset of the disease, and 4 cases were related to pregnancy. The maximum blood glucose levels (39.9±11.4 mmol/L) of the FT1DM patients were significantly higher than those of the T1DM patients (28.9±9.2mmol/L), but HbA1c (6.6±0.6%) and glycosylated serum albumin (GA) (21.4±3.0%) of the FT1DM patients were significantly lower than those of the T1DM group (HbA1c: 12.8±2.7%; GA: 44.8±15.0%). The mean daily insulin dose of the FT1DM patients was 0.73±0.19 IU/kg after about 6.5 years of follow-up, which was similar to the insulin dosage on discharge (0.67±0.22 IU/kg).

Conclusion Compared with T1DM with onset of DKA, FT1DM patients have fewer typical diabetic symptoms, lower fasting C-peptide levels, higher serum amylase levels, an increased incidence of gastrointestinal infections such as vomiting, and are more likely to be misdiagnosed.Therefore, it is of great importance for clinicians to identify FT1DM correctly and administer insulin early.

Table 1 Comparison of clinical characteristics between FT1DM group and T1DM group with onset of DKA

	FT1DM group (n=17)	T1DM group (n=53)	P
Male: female	6:11	27:26	0.261
Age (years)	33.2±12.8	27.5±11.2	0.057
BMI (kg/m^2)	22.6±2.9	19.2±2.9	0.001
Duration (days)*	2(1-4)	30(17-78)	<0.001
Family history of diabetes	1(5.9%)	2(3.8%)	1.000&
Diabetes symptoms #	13(76.5%)	51(96.2%)	0.042
Flu-like symptoms	6(35.3%)	13(24.5%)	0.579
Gastrointestinal symptoms	13(76.5%)	25(47.2%)	0.035
Consciousness disorder	6(35.3%)	8(15.1%)	0.143

*, Duration from onset to occurrence of DKA; #, polyuria, thirst, body weight loss and hyperphagia; &, Fisher's exact test.

WOCS-07-9

High incidence of end-stage renal disease in slowly progressive childhood-onset type 1 diabetes: a cohort study in Japan

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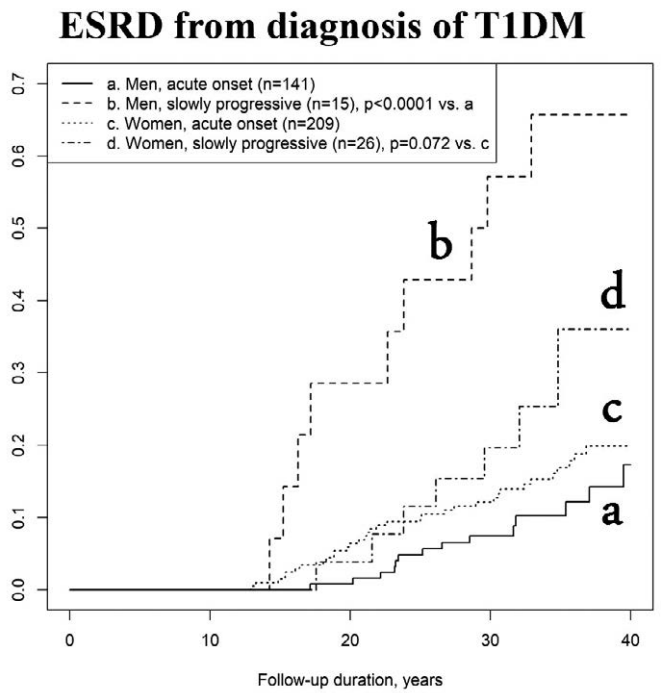
Objective: To examine factors associated with the incidence of end-stage renal disease (ESRD) in childhood-onset type 1 diabetes in a cohort with long-term follow-up.

Methods: A questionnaire was mailed to the attending physicians of 521 all patients who developed type 1 diabetes at age <15 years between 1959 and 1996. Among 391 valid responses received by March 2022, 66 patients developed ESRD. A Kaplan—Meier curve was drawn to assess potential risk factors.

Results: Mean follow-up duration was 32.2 (SD: 9.7) years, and the mean age at diagnosis of ESRD was 35.7 (SD: 7.8) years. The rate of ESRD was 525 per

100,000 person-years. Just over 20% of patients developed ESRD 40 years after onset; there were no differences in ESRD rates between men and women. For both sexes, onset before puberty reduced the ESRD rate. Having the slowly progressive type significantly increased the ESRD rate compared with the acute-onset type (also significant in multivariable analysis). Compared with cases diagnosed before 1979, those diagnosed after 1980 had a significantly lower ESRD rate. After ESRD, approximately 20% of patients had died by 10 years and 70% had died after 25 years.

Conclusion: The incidence rate of ESRD in type 1 diabetes has decreased chronologically. This may reflect the introduction of insulin self-injection and self-monitoring of plasma glucose. The complication of ESRD is less common with pre-pubertal onset, as previously reported. A novel finding is that childhood-onset slowly progressive type 1 diabetes has a higher rate of ESRD than the acute-onset type.



WOCS-08-1

Insulin, Glucagon & Incretin response to OGTT & Diet Pattern in patients with newly diagnosed T2DM & Non DM persons

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Objective: To study insulin, glucagon & incretin response to OGTT & diet pattern in T2DM & non DM persons.

Methods: The study was a hospital based comparative cross sectional study. An OGTT was conducted. Newly diagnosed T2DM (n=20) & non DM persons (n=20) were included. The responses of insulin, glucagon, GIP & GLP1 were examined before (0 minutes) and (30, 60, 120 minutes) after ingestion of glucose. To assess the diet pattern, questionnaires including food frequency & amount were asked by using FFQ.

Results: During OGTT, T2DM group showed statistically significant rise in glucagon & reduced insulin at 30, 60 minutes respectively. There was lower GLP1, GIP in T2DM group than in non DM group although statistically not significant. Regarding diet pattern, in T2DM group, there were associations of lower insulin and higher glucagon with poor diet score. And higher GIP and lower GLP1 were associated with poor diet score.

Conclusion: Impaired early phase insulin, glucagon secretions & lower GLP1, GIP secretions were observed in newly diagnosed T2DM group than those in non diabetic group. In Diabetic group, poor adherence to healthy diet pattern was associated with unfavorable level of insulin & glucagon and also unhealthy diet pattern enhanced GIP secretion & suppressed GLP1 secretion.

WOCS-08-2

Trapα deficiency impairs early events of insulin biosynthesis causing age- and diet-related impaired glucose tolerance

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Objective: Translocon-associated protein alpha (TRAPα) is critical for insulin biosynthesis. However, its role in PPI folding and ER homeostasis is unknown. Here, we aimed to reveal the function of TRAPα in the early events of insulin biosynthesis and pathological consequences of TRAPα deficiency in b-cells. An association of TRAPα expression with amount of PI and insulin in T2D was also examined.

Materials and Methods: b-cell specific TRAPα knockout (TRAPα-bKO) mice were monitored BW, FBG, IPGTT. PPI translocation and PPI folding were examined by WB. The transcriptome changes were analyzed by RNA-seq. Intracellular localization of PI were observed by confocal immunofluorescence microscopy.

Results: Although TRAPα-bKO resulted in a decrease of plasma insulin starting from 1 month of age, it did not cause impaired glucose tolerance (IGT) until 5 months of age. However, TRAPα-bKO mice developed IGT as early as 1 month after fed with HFD.To determine whether UPR activation is consequence or cause of PI misfolding, we knocked out both alleles of insulin genes (*Ins1 and Ins2*) in INS1 b-cell line, and found that UPR activation associated with TRAPα deficiency was significantly alleviated in INS1 cells without expression of PPI/PI.

Conclusion: These data demonstrate that TRAPα deficiency in islet b-cells impairs PPI translocation and PI folding, leading to decreased insulin content and age-/diet related IGT. Given the fact that TRAPα is a T2D associated gene and the expression of TRAPα is decreased in islets of T2D, This study suggest that TRAPα deficiency may play an important role in pathogenesis of T2D.

WOCS-08-3

Waist Circumference is More Strongly Associated with Diabetes than BMI in Taiwanese Adults, Especially in Women

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Objective: Our aim is to assess whether waist circumference (WC) or BMI is more associated with the risk of type 2 diabetes in Taiwanese population and even in different gender.

Methods: This cross-sectional study were obtained from MJ Health Screening Center in Taiwan from 2009 to 2017. Basic patient characteristics were obtained including age, gender, BMI, WC, HDL, TG, FBS and BP. Type 2 DM defined both as fasting plasma glucose ≥126 mg/dl and HbA1c ≥6.5% according to the American Diabetes Association criteria. The logistic regression model was applied for analyze the relationship between WC, BMI and with or without diabetes after adjusting for age, HDL,TG and BP. Two-sided $p < 0.05$ indicated statistical significance.

Results: Total 5,915 participants were recruited in this study, including 5,422 participants without diabetes and 493 participants with diabetes. The distribution of all parameters was significantly different between participants with and without diabetes ($p<0.001$). In logistic regression model, we found abnormal WC parameters was crucial risk factor for diabetes (OR: 3.59; 95% CI, 2.66-4.84, $p<0.001$) better than BMI (OR: 1.99; 95% CI, 1.44-2.76, $p<0.001$) after adjusting for age, sex, TG, HDL, FBS and BP. Finally, we also found that abnormal WC of Taiwanese women have the most crucial risk factor for diabetes (OR: 6.20 ; 95% CI, 3.35-11.47, $p<0.001$).

Conclusion: WC is more strongly associated with type 2 diabetes than BMI in Taiwanese adults, especially in Taiwanese women. Thus, weight reduction especially in abdominal adiposity reduction are important way to prevent type 2 diabetes.

WOCS-08-4

Mediating Effects of ionic elements on the association between tea drinking and dysglycaemia

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Objective: Evidence have revealed that ionic elements are involved in the development of dysglycaemia. Our previous study also showed that tea drinking was negatively associated with diabetes. However, the role of ionic elements in the relationship between tea drinking and dysglycaemia is still unclear. The present study aimed to address this gap.

Methods: We conducted a cross-sectional study to examine the associations of urinary concentrations of 27 elements and serum concentrations of 19 elements with prediabetes and diabetes among 2649 community-dwelling adults. Mediation analysis was used to assess whether the association between tea drinking and dysglycaemia is mediated by ionic elements.

Results: A total of 1548 with normoglycaemia, 503 with prediabetes and 598 with diabetes were enrolled in this study. Serum arsenic, lead, strontium, lanthanum, iron, antimony and selenium were positively associated with prediabetes and diabetes (P<0.05); serum cobalt was also positively associated with diabetes (P=0.02). Urinary molybdenum, nickel and titanium were negatively associated with prediabetes; urinary nickel, lithium, titanium, vanadium and magnesium were negatively associated with diabetes (P<0.05), while urinary arsenic, selenium, zinc, phosphorus were positively associated with diabetes (P<0.05). Mediation effect analyses showed that serum arsenic, selenium had a partial mediation effect between tea drinking habits, drinking tea daily, drinking dark tea and dysglycaemia (including prediabetes and diabetes).

Conclusions: Our results suggest that multiple elements in serum and urine are associated with dysglycaemia. Serum arsenic and serum selenium play a mediating role in the relationship between tea drinking and dysglycaemia.

WOCS-08-5

Impact of Hypoglycemia on Heat Shock Protein Concentration in Kidney Tissue: A Study in Type-2 Diabetes Rat Models

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Objective: Hypoglycemia can cause oxidative stress in kidney tissue, which is characterized by increased concentrations of Heat Shock Protein 70 (HSP70). However, there has been limited research investigating this topic. To determine whether hypoglycemia can increase HSP-70 concentrations in kidney tissue, we performed a randomized experimental study using 24 male rats (*Rattus norvegicus*).

Method: The rats were divided into four groups: control group (K1), streptozocin-induced diabetic and no hypoglycemia (K2), streptozocin-induced diabetic and stimulated to have mild hypoglycemia (K3), and streptozocin-induced diabetic and stimulated to have severe hypoglycemia (K4). Aspart Insulin was intraperitoneally injected into K3 and K4 groups to reach mild and severe hypoglycemia, and the blood glucose level was checked every 15 minutes. The rats were euthanized at least 30 minutes after being confirmed to have hypoglycemia to remove kidney organs. ELISA method was performed to determine the various of HSP-70 concentration in kidney tissue.

Result: We found that the experimental group (K2, K3, and K4) has higher concentrations of HSP-70 concentration than the control group (K1). Moreover, there was a significant increase in HSP-70 concentrations in the diabetic rat group with episodes of mild hypoglycemia (K3) than rat group without hypoglycemia (K2) (p=0,03). However, there was no statistically significant difference between rats with mild hypoglycemia compared to the group with severe hypoglycemia (p =0,902).

Conclusion: Therefore, these results indicate that hypoglycemia, even mild hypoglycemia, can cause a significant increase in HSP-70 concentrations in kidney tissue.

Keywords: Hypoglycemia, heat stroke protein 70, kidney tissue, type-2 diabetes rat models

WOCS-08-6

The Association of Bone Metabolism with Glycemic Traits and the Risk of Diabetes: A Mendelian Randomization Study

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Objective: Diabetes is associated with an increased bone mineral density (BMD) and fracture risk. However, whether BMD is associated with glycemic traits and the risk of diabetes remains largely unknown. This study aims to evaluate the genetic causal association of BMD with glycemic traits and the risk of diabetes.

Methods: Using two-sample Mendelian randomization, the causal relationship of estimated BMD (eBMD) with 2-hour glucose level after an oral glucose challenge test (2hGlu), fasting glucose, HbA1c, fasting insulin, and incidence of T2DM were evaluated by inverse-variance weighted (IVW) method and multiple sensitivity analyses. Relevant genetic data were obtained from the largest possible publicly available genome-wide association studies.

Results: A significant genetic causal relationship of genetically determined eBMD with 2hGlu was observed in the IVW (estimate: 0.038, 95% CI 0.011 to 0.066), and a similar significant association was observed in the weighted median and ConMix analyses. The genetically increased eBMD was also shown to be associated with an increased risk of T2DM in the IVW (OR: 1.050; 95% CI: 1.022 to 1.078), and a similar association was observed in the ConMix analysis. No pleiotropy was detected in the MR-Egger intercept test in all analyses.

Conclusion: This study provided evidence that higher BMD might be causally associated with a higher 2hGlu and risk of diabetes. Further studies evaluating the crosstalk between bone and glucose metabolism are warranted.

WOCS-08-7

The association between exposure to famine in early life and risk of diabetic complications for type 2 diabetes in China

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Objective: The historical origin for the T2D pandemic in China may lie in the 1959-1961 Chinese famine. This study is aimed to exam the associations between exposure to famine in early life and risks of diabetic complications for T2D in China.

Methods: The participants were selected from China National HbA1c Surveillance System (2009-2013), and further stratified according to the birth year. The participants born in 1959-1961 were classified as fetal exposed group (70852 participants). The participants born in 1956-1959 were classified as infant/toddler exposed group (93616 participants). The participants born in 1962-1964 were classified as unexposed group (72723 participants). By using the logistic regression approach, we analyzed the association between exposure to famine in early life and risks of diabetic complications.

Results: As for diabetic complications, the adjusted model indicated that, compared with T2D without exposure to famine, the risks of coronary heart disease (fetal exposed: OR=1.254, 95%CI: 1.196-1.315; infant/toddler exposed: OR=1.343, 95%CI: 1.286-1.403), cerebrovascular disease (fetal exposed:

OR=1.290, 95%CI: 1.200-1.388; infant/toddler: OR=1.342, 95%CI: 1.254-1.436) and diabetic retinopathy (fetal exposed: OR=1.083,95%CI: 1.036-1.132) were significantly increased while the reduced risk of diabetic kidney disease (infant/toddler exposed:OR=0.885, 95%CI: 0.841-0.932) was observed in adult T2D patients with early-life exposure to famine.

Conclusions: Early-life exposure to famine in patients with T2D was associated with increased risks of coronary heart disease, cerebrovascular disease, diabetic retinopathy but reduced risks of diabetic kidney disease in adulthood. Improving early-life nutritional status may promote better risk prevention and management of diabetic complications and comorbidities in patients with T2D.

WOCS-08-8

Association between skinfold thickness and the risk of type 2 diabetes independent of body mass index

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Objective

Which skinfold thickness is associated with the development of type 2 diabetes has not been fully investigated. We prospectively examined the association between triceps, subscapular, and abdominal skinfold thicknesses and the risk of type 2 diabetes.

Methods

Study participants were 6,024 non-diabetic Japanese men aged 35 to 57 years at baseline. Skinfold thickness was measured at triceps, subscapular, and abdomen sites. Type 2 diabetes was defined as a fasting plasma glucose ≥126 mg/dL or taking glucose-lowering medications.

Results

During the 61,918 person-years follow-up period, 824 men developed type 2 diabetes. Participants were classified into quartiles of skinfold thickness levels. In the Cox proportional hazards models, higher subscapular and abdominal skinfold thicknesses were associated with an increased risk of type 2 diabetes, whereas triceps skinfold thickness was not. As for subscapular skinfold thickness, multiple-adjusted hazard ratios (HRs) of incident type 2 diabetes for quartile 2, quartile 3, and quartile 4 (highest) were 1.24 (95% CI, 0.96-1.61), 1.53 (1.19-1.97), and 2.07 (1.59-2.71), respectively, compared with quartile 1 (lowest). As for abdominal skinfold thickness, multiple-adjusted HRs for quartile 2, quartile 3, and quartile 4 (highest) were 1.28 (1.00-1.65), 1.53 (1.19-1.96), and 1.78 (1.38-2.31), respectively, compared with quartile 1 (lowest). These associations were independent of body mass index (BMI), age, fasting plasma glucose, smoking habits, daily alcohol consumption, regular physical exercise, and family history of diabetes.

Conclusion

In Japanese men, both higher subscapular and abdominal skinfold thicknesses were associated with an increased risk of type 2 diabetes. These associations were independent of BMI.

WOCS-08-9

GPSM1 impairs metabolic homeostasis by controlling a pro-inflammatory pathway in macrophages

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G-protein-signaling modulator 1 (*GPSM1*) exhibits strong genetic association with Type 2 diabetes (T2D) and Body Mass Index in population studies. However, how GPSM1 carries out such control and in which types of cells are poorly understood. Here, we demonstrate that myeloid GPSM1 promotes metabolic inflammation to accelerate T2D and obesity development. Mice with myeloid-specific GPSM1 ablation are protected against high fat diet-induced insulin resistance, glucose dysregulation, and liver steatosis via repression of adipose tissue pro-inflammatory states. Mechanistically, GPSM1 deficiency mainly promotes TNFAIP3 transcription via the $G\alpha_{i3}$/cAMP/PKA/CREB axis, thus inhibiting TLR4-induced NF-κB signaling in macrophages. In addition, we identify a small-molecule compound, AN-465/42243987, which suppresses the pro-inflammatory phenotype by inhibiting GPSM1 function, which could make it a candidate for metabolic therapy. Furthermore, GPSM1 expression is upregulated in visceral fat of individuals with obesity and was correlated with clinical metabolic traits. Overall, our findings identify macrophage GPSM1 as a link between metabolic inflammation and systemic homeostasis.

WOCS-09-1

Relationship between thyroid stimulating hormone, time in range and diabetic retinopathy in euthyroid type 2 diabetes

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Objective: Diabetic retinopathy (DR) can occur even in well-controlled type 2 diabetes, suggesting residual risks of DR in this population. In particularly, we investigated the combined effect of thyroid function and glycemic control assessed by an emerging continuous glucose monitoring (CGM)-derived metric, time in range (TIR), with DR.

Methods: We analyzed cross-sectional data from 2,740 euthyroid patients with type 2 diabetes. Thyroid indicators, including thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TGAb), were measured. TIR was measured from CGM data.

Results: Even in well-controlled participants who achieved a TIR target of > 70% (n = 1449), the prevalence of DR was 23.8%, which was significantly related to TSH (*OR* = 1.54, 95%*CI* 1.12-2.12, highest vs. lowest TSH tertile). The relationship between FT3 and DR was influenced by glycemic control, and there were no associations of FT4, TPOAb positive or TGAb positive with DR. Participants (n = 2,740) were then classified into 6 groups by the joint categories of TIR (> 70%, ≤ 70%) and TSH (tertiles), and the multivariable-adjusted *ORs* for DR were highest in the TIR ≤ 70% and the highest TSH tertile group (*OR* = 1.96, 95%*CI* 1.41-2.71) when compared with the TIR > 70% and the lowest TSH tertile group.

Conclusions: In type 2 diabetes patients with well-controlled glycemic status, higher TSH within the normal range was associated with increased risk of DR. The combination of suboptimal TSH and TIR further increased the risk for DR.

WOCS-09-2

Independent risk factors of rapid renal function decline in patients with type 2 diabetes with preserved kidney function

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Objective: It is known that rapid decliners, in whom renal function declines rapidly, exist among patients with type 2 diabetes mellitus. Research on the incidence and underlying mechanisms of rapid renal function decline in patients with type 2 diabetes with preserved kidney function and normoalbuminuria is limited. This study aimed to investigate risk factors for rapid decliners in patients with type 2 diabetes with preserved kidney function and normoalbuminuria.

Methods: This was a retrospective observational study of 242 patients with type 2 diabetes with a baseline estimated glomerular filtration rate of ≥60 mL/min/1.73 m^2 and normoalbuminuria (<30 mg/gCr), followed up for ≥1 year. The annual rate of estimated glomerular filtration rate decline during the

follow-up was calculated using least square regression analysis; rapid decliners defined at ≥3.3%/year. Risk factors associated with rapid decliners were identified using a logistic regression analysis of variables previously identified as risk factors of rapid decliners.

Results: The mean follow-up period was 6.7 years, and 34 patients showed rapid decliners. On multivariate analysis, lower baseline hemoglobin level was a risk factor of rapid decliners (odds ratio, 0.69; 95% confidence interval, 0.47–0.99; $P = 0.046$). Furthermore, baseline hemoglobin levels were correlated positively with iron and ferritin levels and negatively with erythropoietin levels.

Conclusions: In patients with type 2 diabetes with preserved renal function and normoalbuminuria, lower hemoglobin levels were a risk factor for rapid decliners, where impaired iron metabolism may precede the development of diabetic kidney disease.

WOCS-09-3

Determinants of Hand Function in Patients with Type-2 Diabetes Mellitus (T2DM)

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Objectives: the study aimed to investigate the differences in hand function among patients with T2DM with DPN, without DPN and healthy controls. This study also aimed to identify the determinants of hand function among patients with T2DM. **Methods:** A cross-sectional study was conducted at one of the hospitals in Klang Valley Malaysia involving patients with T2DM with DPN (n=84) and without DPN (84) and healthy controls (n=84). Patients were recruited in the outpatient DM clinic, while the healthy controls were recruited among the visitors in the hospital by using the purposive sampling technique. Hand function was assessed using the Jebsen-Taylor Hand Function Test. In addition, the individual's hand measurements such as grip strength, pinch strength, hand disability, dexterity and total active motion (TAM) were assessed using the JAMAR handheld dynamometer, pinch gauge, disability of arm, shoulder and hand (DASH), Purdue pegboard dexterity test and goniometer, respectively. **Results:** One-way ANOVA results showed significant differences in hand function among the patients with T2DM with DPN and without DPN and healthy control (p=0.00). Post hoc Tukey analysis revealed there were significant differences (p=0.00) between the three groups. Multiple linear regression results indicate that the dexterity of both hands and pinch strength explained 59.2% of the variability in dominant hand function. Meanwhile, dexterity of both hands, TAM and grip strength explained 58.1% of the variability in non-dominant hand function. **Conclusion: T**his study highlights the need for hand rehabilitation to improve dexterity, strength and TAM of patients with T2DM for independent living.

WOCS-09-4

Metformin reverses high fructose-induced renal tubular injury by targeting ChREBP-β/TXNIP

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Objective: High fructose intake is an important risk factor for renal injury. However, the specific mechanism and the treatment of high fructose-induced renal injury are still unclear. In addition to lower blood sugar, metformin is also capable of protecting the kidneys. This study aims to explore the novel mechanism underlying the protective role of metformin in high fructose-induced renal tubular injury.

Methods: C57BL/6J mice aged 5-6 weeks were fed with a high-fructose diet and intervened by metformin and ferroptosis inhibitor Fer-1. A ChREBP-β-specific overexpression mouse model (ChREBP-β-KT) was constructed, followed by 12-weeks of Fer-1 intervention. General conditions, urine proteins and renal pathological changes of mice were detected. In addition, high fructose-induced HK-2 cells were induced with metformin and Fer-1. The ferroptosis-related proteins, iron content and ROS levels in cells and mice were analyzed.

Results: Metformin treatment significantly reduced UAE and NAG levels in high-fructose-fed mice, relieved renal pathological changes, and inhibited ferroptosis in renal tubular epithelial cells, which effectively attenuated high fructose-induced renal damages. Carbohydrate response element-binding protein (ChREBP) is a key transcriptional activator that regulates fructose metabolism. Ferroptosis was detected in primary renal tubular epithelial cells of ChREBP-β-KT mice. ChREBP-β promotes the gene transcription of thioredoxin-interacting protein (TXNIP) and thereby increases its expression level. TXNIP is associated with activation of ferroptosis. Through down-regulating ChREBP-β, metformin can inhibit gene transcription of TXNIP, attenuate high fructose-induced ferroptosis in renal tubular epithelial cells, and alleviate kidney injury.

Conclusion: Metformin contributes to protect high fructose-induced renal tubular injury by targeting ChREBP-β/TXNIP.

WOCS-09-5

Mediating effects of metabolism profile on the relationship 25(OH) D with cognitive function in diabetic patients

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Background: We aim to determine the role of 25(OH)D, the active vitamin D, in diabetes-associated cognitive dysfunction (DACD).

Methods: This present cross-sectional study was preliminary conducted from 103 patients with type 2 diabetes (aged 40–75years), focusing on cognitive function, which was evaluated by comprehensive neuropsychological tests. The partial correlation analysis were used to estimate the relationship between plasma 25(OH)D level and multiple neuropsychological scare and metabolism profile after adjustment for age, gender and education level. The mediating effects of metabolism profile on the relationship 25(OH)D with cognitive function were were performed by mediation analysis.

Results: These participants were finally divided into two groups basing on MoCA: MoCA score < 26 was MCI group (n=31) and MoCA score > 26 was control group with healthy cognition (n=72). Participants in MCI group showed a lower 25(OH)D levels, and had unfavorable metabolic profiles characterized by higher levels of HbA1c and LPa, but lower levels of INR and FT3 than in group group (all $p<0.05$). Plasma 25 (OH) D level was significantly negatively correlated with cognitive function, including patients' execution, attention function and memory. Additionally, there was a positive correlation between 25(OH)D level and FT3 and 25(OH)D level were negatively related to HbAc1, LPa and FDP. The association between 25(OH)D and MoCA was found to be mediated by HbAc1, LPa and FDP, with the mediation effect calculated to be 21.74%, 17.95% and 16.69%, respectively.

Conclusion: Decreased 25(OH)D increased the risk of incident DACD, and their relationship was may mediated by HbAc1, LPa and FDP.

Figure1. The association between 25(OH)D and MoCA was found to be mediated by HbA1c, LPa and FDP.

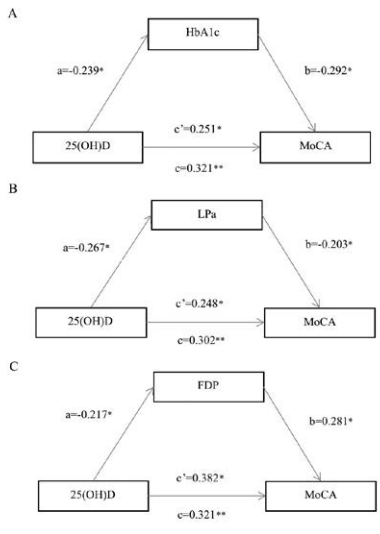

Fig.1 After adjusting the age and gender, mediation effect of HbA1c, LPa and FDP on the relationship between 25 (OH)D and MoCA in diabetic participants were analyzed.

(A) In diabetic participants, inclusion of HbA1c in the model reduced the strength of the direct relationship between 25(OH)D and MoCA by 21.74% [(-0.239×-0.292) /0.321] (a×b = 0.070, bootstrap 95%CI: 0.004–0.162).

(B) In diabetic participants, inclusion of LPa in the model reduced the strength of the direct relationship between 25(OH)D and MoCA by 17.95% [(-0.267×-0.203) /0.302] (a×b = 0.054, bootstrap 95%CI: 0.004–0.162).

(C) In diabetic participants, inclusion of FDP in the model reduced the strength of the direct relationship between 25(OH)D and MoCA by 18.20% [(-0.217×0.281) /0.321] (a×b = 0.054, bootstrap 95%CI: -0.137 –0.085).

*p<0.05; **p<0 .001; a×b, indirect effect; c, total effect; c', direct effect.

WOCS-09-6

Application of antibiotic bone cement in the treatment of moderate and severe diabetic foot infection

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Objective To explore the clinical efficacy of antibiotic loaded bone cement in the treatment of moderate to severe diabetic foot infection (DFI) patients, and analyze the distribution characteristics of pathogenic bacteria.

Methods 167 patients with moderate to severe DFI were collected. After admission, the tissue at the base of the wound was taken for bacterial culture to determine the pathogenic bacteria. 63 patients in the traditional group were treated with conventional therapy, while 104 patients in the study group were treated with antibiotic loaded bone cement. The healing rate, healing time, length of hospital stay, number of debridements, hospitalization costs, pain numerical rating scale (NRS)score, patient health questionnaire-9 (PHQ-9) score, generalized anxiety disorder-7 (GAD-7) score and ulcer recurrence rate were compared between the two groups.

Results The most common pathogenic bacteria in the two groups were Staphylococcus aureus and Escherichia coli, which were mainly gram-negative bacteria. The healing rate of the study group was higher than that of the traditional group, and the wound healing time, length of hospital stay, number of debridements, hospitalization cost, NRS score, PHQ-9 score, GAD-7 score of the study group were lower than those of the traditional group (P<0.05). There was no significant difference in ulcer recurrence rate between the two groups (P>0.05).

Conclusion Antibiotic loaded bone cement can treat wounds of DFI patients, shorten hospital length of stay, reduce medical costs and relieve patients' burden.

WOCS-09-7

Etiological characteristics of diabetes foot with different degrees of renal damage

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Objective To explore the pathogenic distribution characteristics of diabetes foot patients with different degrees of renal damage. Grouped by CKD classification and CKD risk stratification, we compare the difference between the two methods in studying the impact of kidney damage on diabetes feet.

Methods 368 patients diagnosed as diabetes foot in this study. The patients were divided into groups according to CKD risk stratification and CKD classification. The wound secretions or tissues of patients were collected for pathogenic culture and analyzed.

Results According to CKD classification, the patients were divided into 6 group. The detection rates of bacteria were 44.94%, 44.21%, 44.64%, 48.48%, 60% and 0% respectively. The proportion of gram-positive bacteria was 55%, 54.75%, 56%, 43.75%, 33.33% and 0% respectively. The proportion of gram-negative bacteria was 50%, 52.37%, 52%, 81.25%, 66.67% and 0% respectively. Multiple infections were 5.05%, 11.57%, 8.92%, 15.15%, 20% and 0% respectively. According to CKD risk stratification, the patients were divided into 5 groups. The detection rates of bacteria were 44.94%, 100%, 42.31%, 42.37% and 50%. The proportion of gram-positive bacteria was 55%, 0%, 61.36%, 52% and 30.76% respectively. The proportion of gram-negative bacteria was 50%, 1, 50%, 56% and 84.61% respectively. Multiple infections were 5.05%, 100%, 11.54%, 8.47% and 15.38% respectively. **Conclusions** The two grouping methods showed that with the aggravation of kidney damage, there was no significant difference in the detection rate of bacteria, the risk of multiple bacterial infections increased, the proportion of gram-negative bacteria increased, and the proportion of gram-positive bacteria decreased.

WOCS-09-8

Clinical characteristics and risk factors of lower extremity amputation in the diabetic inpatients with foot ulcers

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Objective: To analyze clinical characteristics of the diabetic inpatients with foot ulcers and explore the risk factors of lower extremity amputation (LEA). Methods: A retrospective analysis was performed based on the patients with diabetic foot ulcer (DFU) hospitalized in West China Hospital of Sichuan University from January, 2012 to December, 2020. The ordinal logistic regression analysis was used to identify the risk factors for LEA. Results: 992 diabetic patients with DFU were hospitalized in the Diabetic Foot Care Center of Sichuan University, and 72 (7.3%) (55 minor and 17 major amputations) cases experienced amputation. Excluding 21(2.1%) patients who refused amputation, the mean age and duration of diabetes of and HbA1c the 971 patients with DFU, were 65.1±12.3 years old, 11.1±7.6 years, and 8.6±2.3% respectively. Compared with the non-amputation patients (55.1%), more patients with amputation (minor (63.5%) and major amputation (88.2%)) suffered from peripheral arterial disease. The amputated patients had statistically lower hemoglobin, serum albumin and ankle brachial index (ABI), but higher white blood cell, platelet counts, fibrinogen and C-reactive protein levels. The patients with amputation had a higher incidence of osteomyelitis, foot gangrene, and a history of prior amputations than those without amputation. Furthermore, a history of prior amputation, foot gangrene and ABI were significantly associated with LEAs. Conclusion: The DFU inpatients with amputation were older with long duration of diabetes, poorly glycemic control, malnutrition, PAD, severe foot ulcers with infection. A history of prior amputation, foot gangrene and low ABI level were the independent predictors of LEA.

Table 1 – Baseline demographic and laboratory data among the non-amputation, minor amputation and major amputation groups.

Factor	Non-amputation (N=899)	Minor Amputation (N=55)	Major Amputation (N=17)	*P* value
Demographics				
Age, yr	65.1±12.3	62.9±12.4	69.4±9.9	0.146
Sex				0.086
Male	563	33	15	
Female	336	22	2	
BMI, kg/m^2	23.3±3.4†(*n*=780)	23.2±3.3†(*n*=45)	23.3±3.4	0.118
Smoking (current or ever)	462	27	13	0.113
Drinking (current or ever)	346	18	10	0.155
Hospital stays (day)	31(18-56)	57(38-95)	47(37-63)	<0.001
Diabetes-related characteristics				
Duration of diabetes, yr	11.1±7.6	10.9±7.3	8.5±4.7	0.416*
ABI	0.97±0.28†(*n*=539)	0.85±0.33†(*n*=23)	0.76±0.31†(*n*=9)	0.012
Ulcer area, cm^2	4.0(1.3-12.0)†(*n*=710)	10.0(3.0-32.4)†(*n*=45)[a]	10.3(3.3-30.0)†(*n*=13)	0.005*
Laboratory results				
FBG, mmol/L	9.0±4.1†(*n*=680)	9.2±3.8†(*n*=37)	9.9±4.1†(*n*=13)	0.666
HbA1c, %	8.6±2.3†(*n*=803)	8.8±2.4†(*n*=50)	8.7±1.9†(*n*=16)	0.897
Hb, g/L	114±22†(*n*=854)	104±25[a]	109±23	0.004
PLT, ×10^9/L	232±108†(*n*=851)	266±104	304±143[a]	0.001
FIB, g/L	4.4±1.5†(*n*=827)	4.9±1.7 (*n*=54)	5.0±1.8 (*n*=16)	0.019
WBC count, ×10^9/L	7.8±3.7†(*n*=853)	9.6±5.1† (*n*=54)	11.6±6.1	0.001*
NEUT, %	68.5±12.5†(*n*=806)	71.4±16.8	81.0±9.3†(*n*=15)[a]	<0.001*
Albumin, g/L	36.4±6.1†(*n*=892)	33.1±7.3[a]	32.8±6.1[a]	<0.001
TG, mmol/L	2.1±1.5†(*n*=887)	2.2±1.6	1.6±1.0	0.315
TC, mmol/L	3.5±1.4†(*n*=888)	3.0±1.4[a]	3.0±1.2	0.016
LDL-C, mmol/L	2.2±1.0†(*n*=888)	1.9±0.9†(*n*=54)	1.9±1.0	0.148
HDL-C, mmol/L	1.09(0.87-1.42)†(*n*=888)	1.03(0.67-1.48)	0.93(0.69-1.29)	0.308*
UA, μmol/L	322±110†(*n*=888)	276±123†(*n*=54)[a]	255±133[a]	0.001
Creatinine, μmol/L	81.0(63.5-108.0)†(*n*=892)	68.5(55.5-91.8)†(*n*=54)	70.6(53.5-103.5)	0.152
eGFR, mL/mL.1.73m^2	76.4±31.4†(*n*=864)	86.3±32.7†(*n*=53)	85.5±36.2†	0.047
CRP, mg/L	10.0 (3.3-30.2)†(*n*=547)	24.3(4.9-105.9)†(*n*=28)	74.6(9.7-146.5)†(*n*=13)[a]	0.002*

Values are presented as number, median (IQR), or mean±standard deviation. BMI, body mass index. ABI, ankle-brachial index, FBG, fasting blood glucose. HbA1c, glycosylated hemoglobin. Hb, hemoglobin. PLT, platelet. PT, prothrombin time. FIB, fibrinogen. WBC, white blood cell, NEUT, neutrophil granulocyte percentage. TG, triglyceride. TC, total cholesterol. LDL-C, low-density lipoprotein cholesterol. HDL-C, high-density lipoprotein cholesterol. UA, uric acid. eGFR, estimated glomerular filtration rate. CRP, C-reactive protein. †Some cases are lacking data and the number of patients was shown in brackets. *, Kruskal–Wallis test. a, statistical significance compared with non-amputation group with Bonferroni post-test.

WOCS-09-9

Clinical characteristics and risk factors for mortality in patients with diabetic foot ulcers

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Objectives

This study reviews the mortality of patients with diabetic foot ulcers (DFU) in West China Hospital of Sichuan University and analyzes clinical characteristics and the risk factors associated with mortality.

Methods

All patients with DFU presenting for the first time to the diabetic foot care center of West China Hospital of Sichuan University for DFU between 2012 and 2020 were analyzed. These patients were followed until 01 March 2022 or death. Kaplan-Meier survival curves were developed. The association between various risk factors and mortality was analyzed using Cox regression.

Results: The cohort included 992 patients with DFU, with a mean age of 65.1±12.2 years and diabetes duration 11.1±7.6 years, and 657(66.2%) patients with DFU were male. They had inadequate glycemic control and high prevalence of chronic complications. There were 772 patients followed up, of which 251 (32.5%) died, with a 1-, 3-, 5- and 7-year-mortality rate of 18.6%, 30.3% and 44.1% respectively, with a median survival time of 90.3 months. In a multivariate analysis, age, hypertension, chronic kidney disease (CKD) (stage 4-5), foot gangrene and elevated CRP were significantly associated with mortality in DFU patients.

Conclusions: In hospitalized patients with DFU, age is an independent risk factor for death, and patients with foot gangrene, hypertension and CKD have a significantly increased risk of death. A high CRP levels is a potential risk factor for death in patients with DFU. Cardiovascular disease is the leading cause of death in patients with DFU, and falls cannot be ignored.

Table 1 Baseline clinical and biochemical characteristics of 992 participants.

	DFU(N=992)
Hospital stays/d, median	41.8±33.3
Age/yr	65.1±12.2
Male	657(66.2)
BMI/(kg/m^2)	23.3±3.4 (*n*=857)
Duration of diabetes/years	11.1±7.6
HbA1c(%)	8.6±2.3
Whether to monitor blood glucose regularly	
Frequently	113(11.4)
Occasion	351(35.4)
Unmonitored	475(47.9)
Newly diagnosed diabetes	53(5.3)
Insulin therapy before admission	680(68.5%)
Smoking (current or ever)	511(51.5%)
Drinking (current or ever)	378(38.1%)
Prior ulcer	294(29.6%)
Prior amputation	78(7.9%)
Diabetic retinopathy	388(39.1%)
PAD	587(59.2%)
Diabetic peripheral neuropathy	940(94.8%)
Cardiac autonomic neuropathy	673(67.8%)
Gastrointestinal autonomic neuropathy	253(25.5%)
Bladder autonomic neuropathy	478(48.2%)
Hypertension	691(69.7%)
Coronary heart disease	235(23.7%)
Hyperlipidemia	254(25.6%)
Hyperuricemia	123(12.4%)
CKD	653(65.8%)
FBG	9.0±4.0
HbA1c(%)	8.6±2.3
TG(mmol/L)	2.1 ± 1.6
LDL-C(mmol/L)	2.1 ± 1.0
HDL-C(mmol/L)	1.2 ± 0.7
Hb(g/L)	113.3±22.7
ALB(g/L)	36.1±6.2
WBC(×10^9/L)	8.02±3.9
eGFR(mL/min/1.73m^2)	76.8±32.0
CRP(mg/L)	0.06(0.04-0.12)
PCT(ng/L)	10.40(3.41-39.10)

Values are presented as number, median (IQR), or mean±standard deviation. BMI. Body mass index. PAD, peripheral arterial disease. CKD, chronic kidney disease. FBG, fasting blood glucose. HbA1c, glycosylated hemoglobin. Hb, hemoglobin. ALB, serum albumin. WBC, white blood cell, NEUT, neutrophil granulocyte percentage. TG, triglyceride. LDL-C, low density lipoprotein. HDL-C, high-density lipoprotein cholesterol. UA, uric acid. eGFR,

WOCS-10-1

Decreased Abundance of *Akkermansia muciniphila* leads to the Impairment of Insulin Secretion in Type 2 Diabetes

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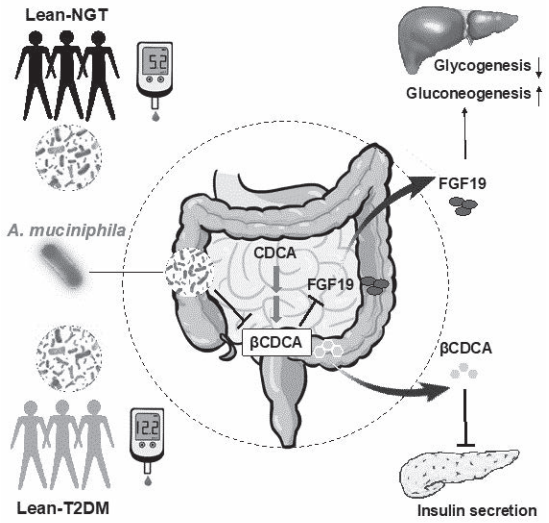
Although obesity occurs in most of the patients with type 2 diabetes (T2D), a fraction of patients with T2D are underweight or have normal weight. Several studies have linked the gut microbiome to obesity and T2D, but the role of gut microbiota in T2D with normal body weight having unique clinical characteristics remains unclear. A metagenomic and targeted metabolomic analysis is conducted in 182 lean and abdominally obese individuals with and without newly diagnosed T2D. The abundance of *Akkermansia muciniphila* (*A. muciniphila*) significantly decreases in lean individuals with T2D than without T2D, but not in the comparison of obese individuals with and without T2D. Its abundance correlates inversely with serum 3β-chenodeoxycholic acid (βCDCA) levels and positively with insulin secretion and fibroblast growth factor 15/19 (FGF15/19) concentrations. The supplementation with *A. muciniphila* is sufficient to protect mice against high sucrose-induced impairment of glucose intolerance by decreasing βCDCA and increasing

insulin secretion and FGF15/19. Furthermore, βCDCA inhibits insulin secretion and FGF15/19 expression. These findings suggest that decreased abundance of *A. muciniphila* is linked to the impairment of insulin secretion and glucose homeostasis in lean T2D, paving the way for new therapeutic options for the prevention or treatment of diabetes.



WOCS-10-2

Clinical characteristics of DKA in Chengdu over the past 20 years

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The Department of Endocrinology and Metabolism West China Hospital

Objective

To investigate changes in the precipitants,clinical characteristics and outcomes of diabetic ketoacidosis (DKA) in Chinese diabetic patients over the last two decades.

Methods

A retrospective medical record review of all DKA episodes in diabetic patients was performed in Wset China Hospital,a university teaching hospital in Chengdu from Jan 1,2000 to Dec 31, 2020. Clinical and laboratory data were collected respectively. Patients were classified as having type 1 or type 2 diabetes or atypical diabetes mellitus(ADM) based on clinical history and autoimmune condition.

Results

Detailed and accurate information was obtained in a chort of 1710 patients with diabetes accounted for the 1925 DKA episodes, of whom 325 patients had type 1 diabetes (19.01%) meanwhile 1020 patients were diagnosis as T2DM (59.65%) and 302 patients could not be "typed" were classified as ADM (17.66%). In addition,there were 9(0.53%)gestational diabetes mellitus(GDM) and 54(3.16%) patients with other specific types. The most common contributing factor for DKA was infection, followed by noncompliance with anti-diabetes treatment including omission of insulin, unknown causes and other medical conditions. Strikingly, these middle-age obese male patients often lapse into ketoacidosis without identifiable triggers. A total of 54 patients died in hospital (3.15% of all episodes). Older age and infection appeared to influence mortality.

Conclusions

There is a rapidly increasing episodes of DKA in Chengdu, continue to be associated with significant mortality in pitients with diabetes. DKA could occur not only in T1DM but also in patients with T2DM under infection or stress condition, further more without any identifiable precipitants.

WOCS-10-3

Risk Factor Exploration of Pre-Diabetes/T2DM Under 40 Years : Multivariate Cross-Sectional Retrospective Study

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Introduction: The rising number of young people with T2DM is a more recent and particular concern. The prevalence Diabetes under 45 years in Indonesia were 1,4% and steadily increasing over years. The various factor involved in the onset of T2DM of the young. The aim of this study was to explore numerous risk factor for the occurrence of Pre-DM or T2DM in subject age £ 40 years.

Methods : The cross-sectional retrospective study was conducted at Sumber Waras Hospital, Jakarta at February 2023. The main inclusion criteria: age £ 40 years and diagnosed with pre-DM or T2DM. For the comparison, we including normal subjects with same demographic characteristics. Data extracted including demographic, lifestyle, anthropometric, psychosocial and family history. Multivariate analysis using biner logistic regression model. The further analysis conducted for only significance variable using MANOVA.

Result and Analysis : The number of subjects was 53 subjects (observation group) and 50 subject (control group). There were 84.91% female with the mean age 32.58. There no difference in demographic variable between two groups. The independent variables with significant result are smoking (p=0.038), hypertension (p=0.000), obesity (p=0.000), excessive calorie intake (p=0.000), poor stress management (p=0,04), depression (p=0.001), short sleep duration (p=0,003), physical inactivity (p=0,002), family history of Diabetes (p=0.000). The overall statistic shows significant result (p=0.000). The further analysis and sub-analysis show same results.

Conclusion : Significant independent risk factor for occurrence of pre-DM or T2DM before age 40 years are **multifactorial**, include poor lifestyle, obesity, hypertension, psychosocial factor, and strong family history.

Table 2. Multivariate Analysis

Variable	p value	Odds Ratio (CI 95%)
Sex	0.691	0.647 (0.091-4.593)
History of Living	0.064	0.265 (0.064-1.096)
Education	0.997	0.792 (0.192-3.270)
Economic Status	0.337	0.351 (0.044-2.787)
Smoking History	0.038*	2.972 (0.708-12.469)
Alcohol History	0.524	1.072 (0.029-38.999)
High Blood Pressure (>140mmHg)	0.000*	1.475 (0.346-6.283)
High Body Mass Index (> 25kg/m2)	0.000*	13.205 (1.428-122.115)
High Waist Circumference (>80cm)	0.002*	1.270 (0.038-1.908)
Obese History	0.886	0.805 (0.189-3.423)
Excessive Calorie Intake History	0.000*	3.399 (0.537-21.527)
Poor Health Perception	0.108	2.968 (0.284-30.991)
Poor Stress Management	0.04*	6.728 (1.840-13.882)
Depression History	0.001*	2.170 (0.632-18.360)
Shorter sleep duration (<6 hours)	0.003*	5.728 (1.153-28.454)
Infertility Problem	0.101	0.890 (0.152-5.201)
Physical inactivity	0.002*	8.139 (1.403-47.218)
Family History of Obesity	0.251	0.113 (0.014-0.898)
Family History of Diabetes Mellitus	0.000*	3.288 (1.661-16.367)
Family History of Hypertension	0.000*	5.159 (1.280-20.803)
Family History of Dyslipidemia	0.036*	2.027 (0.414-9.929)
Overall Statistic p=0.000*		

WOCS-10-4

Decipher the role of B-cell-activating factor (BAFF) in metabolism

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Objective

B-cell-activating factor (BAFF) belongs to the TNF ligand family and has been shown to promote expansion and differentiation of B cell population. It is

mainly expressed in immune cells and adipocytes. It is up-regulated in visceral adipose tissue of dietary-induced-obese mice, which drove attention to its role in metabolic regulation. Interestingly, its function on metabolic response varied in different studies. Here we generated a recombinant BAFF protein and applied it to mouse models, aiming to decipher the role of BAFF on glucose metabolism.

Method

The recombinant BAFF protein was produced in E. Coli expression system with pET-28a vector carrying the sequence of the secret form of BAFF with a 6XHis-tag. The protein was purified with immobilized metal ion affinity chromatography. C57BL/6J mice were fed with a high-fat diet for 12 weeks, then treated by recombinant BAFF protein for 5 consecutive days. Glucose tolerance was assessed by the intraperitoneal glucose tolerance test (IPGTT).

Results

Glucose tolerance test revealed that recombinant BAFF protein improved glucose tolerance. Blood chemistry analysis revealed that there was no difference in lipid profile between the mice treated with PBS and recombinant BAFF protein. In addition, no apparent effect on liver injury markers after recombinant BAFF protein treatment was found, supporting its tolerability and safety.

Conclusion

Recombinant proteins are commonly used to produce pharmaceutical products for disease treatment. Our in-house recombinant BAFF protein displayed the effect of improving glucose metabolism, which can be considered as a potential anti-diabetic medicine.

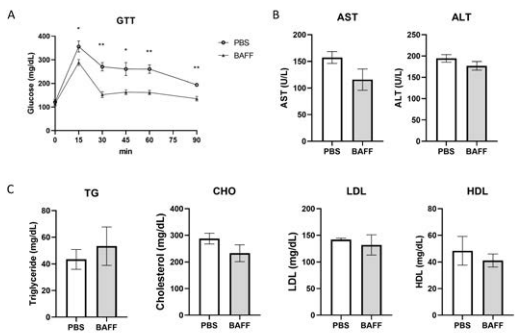

Figure 1. (A) Glucose tolerance test; (B) Level of enzymes aspartate transaminase (AST) and alanine transaminase (ALT); (C) Levels of lipids triglyceride (TG), cholesterol (CHO), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) after 5 days BAFF injection.

WOCS-10-5

Maximum weight loss shows better predictivity in reporting weight regain after bariatric surgery

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Objective: weight regain (WR), which may have deleterious effects on weight-related comorbidities, is a concern following surgical treatment of obesity. However, there is no consensus on the definition of WR. Therefore, we aimed to compare measures of WR and their association with glucose metabolism deterioration.

Methods: This retrospective study included patients with obesity and T2DM who underwent bariatric surgery and were followed up from baseline to 3 years after surgery. WR was assessed by weight changes (Δkg), BMI changes (ΔBMI), percentage presurgery weight (%PSW), percentage nadir weight (%NW), and percentage maximum weight lost (%MWL). Glucose metabolism deterioration was defined as a change from an absence of antidiabetic medication use to use, or absence of insulin use to use, or an increase in HbA_{1c} by at least 0.5% to 5.7% or greater.

Results: Among the 249 participants (59% women), the mean age was 45 ± 13 years and BMI was 34.7 ± 5.5 kg/m^2. In the discrimination of glucose metabolism deterioration 3-year postoperative, %MWL had an AUC of 0.769 (95% *CI*: 0.707-0.831), significantly better than Δkg (P = 0.009), ΔBMI (P = 0.002), %PSW (P = 0.000), or %NW (P = 0.000). The optimal %MWL cutoff point to screen glucose metabolism deterioration was 20%, with a sensitivity of 67.7% (56.5%-79.0%) and specificity of 70.1% (63.6%-76.5%).

Conclusion: Among Chinese patients with obesity and T2DM who underwent bariatric surgery, WR quantified as %MWL predicted glucose metabolism deterioration 3-year postoperative better than the alternatives; 20% %MWL was the optimal cutoff point.

WOCS-10-6

Population attributable fractions of modifiable risk factors for microvascular complications of type 2 diabetes in China

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Objective: To assess the population attributable fractions (PAFs) for modifiable risk factors for microvascular complications of type 2 diabetes (T2D) in China.

Methods: The data collected from the China National HbA1c Surveillance System between 2009 and 2013 were used. The PAFs of four predefined risk factors, including HbA1c ≥ 7%, blood pressure (BP) ≥ 130/80mmHg, low-density lipoprotein-cholesterol (LDL-C) ≥1.8mmol/L and BMI ≥ 24kg/m^2 were calculated for diabetic microvascular complications, including diabetic retinopathy (DR), diabetic kidney disease (DKD), and distal symmetric polyneuropathy (DSPN).

Results: In total, there were 998,379 participants with T2D from nationwide mainland China included in this analysis. As for DR, HbA1c ≥ 7%, BP ≥ 130/80mmHg, LDL-C ≥ 1.8mmol/L and BMI ≥ 24kg/m^2 conferred PAFs of 16.2%, 15.2%, 5.8% and 2.8%. In the case of DKD, BP ≥ 130/80mmHg provided a PAF of 25.2%, followed by HbA1c ≥ 7% (13.9%), BMI ≥ 24kg/m^2 (8.0%) and LDL-C ≥ 1.8mmol/L (5.6%). As for DSPN, HbA1c ≥ 7%, BP ≥ 130/80mmHg, LDL-C ≥ 1.8mmol/L and BMI ≥ 24kg/m^2 contributed to PAFs of 14.2%, 11.7%, 5.9% and 5.8% respectively.

Conclusions: The suboptimal glycemic and BP control were the main contributors for diabetic microvascular complications while the PAFs of unmet LDL-C and BMI control targets were quite limited for diabetic microvascular complications. In addition to glycemic control, BP control should be especially prioritized in the management of diabetic microvascular complications to further reduce the disease burden.

WOCS-10-7

Effect of Bashan tea drink on function of beta cells in type 2 diabetic patients

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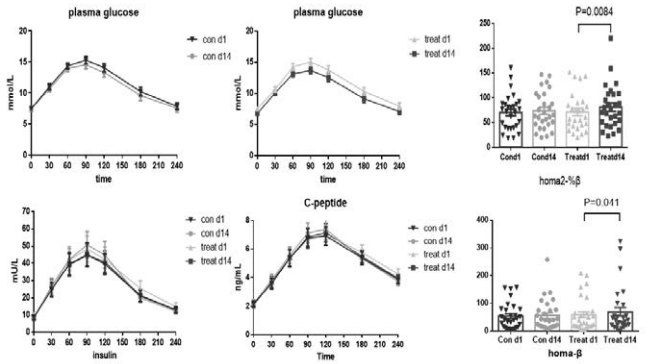
Objective: To observe the effects of Bashan, which was a combination of several pure plant ingredients drink, on the blood glucose (BG) in T2DM patients by a standardized mashed potato meal.

Methods: 25 patients (23 males, age 49.64±1.71years; HbA1C 8.49±0.42 %) with T2DM were included in this study. Patients were randomized to receive two interventions (7 days apart):1) Water as control, the subjects keep their daily diet, taking 180ml water immediately after meals; 2)Bashan, the subjects keep their daily diet, taking 180ml Bashan immediately after meals. Each

intervention last for 2 weeks and switched after the 7-day wash-out period. Before and after the intervention, subjects underwent measurements of BG for 240 min after a standardized meal (368.5 kcal). Data are mean ± SEM. $P < 0.05$ was considered statistically significant.

Results: All subjects tolerated the study well. Though there is no significant difference between the two groups, a tendency shows that the Homa2-IR decreased after drinking Bashan.(Bashan day 14:1.80±0.17 & Bashan day 1:1.97±0.19 vs control day 14:1.83±0.15 & control day 1:1.80±0.18 ,P>0.05). Homa2-%β also showed a tendency to increase after drinking Bashan.(Bashan day 14:86.26±9.02 & Bashan day 1:73.40±8.24 vs control day 14:74.29±7.46 & control day 1:71.42±7.27 ,P>0.05)

Conclusion: Drink Bashan continuously could improve the insulin resistance and the function of beta cells.



WOCS-10-8

Efficacy of Probiotics on the Modulation of Gut Microbiota in the treatment of Type-2 Diabetes Mellitus: A Meta-analysis

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Objective

Dysbiosis, an imbalance in gut microbial community, contributes to the pathogenesis of type-2 diabetes mellitus (T2DM). As an effective means of regulating gut microbiota, probiotics are believed to positively modulate the glucose metabolism of the host. Whilst meta-analyses on the effects of probiotics on T2DM evidenced some beneficial changes in the metabolic profiles, the regulatory role of probiotics on gut microbiota after treatment of T2DM has not been addressed. The aim of the study is to explore any effect of probiotic supplementation on gut microbiota of T2DM.

Methods

MEDLINE, EMBASE and the Cochrane Library were searched for randomized controlled trials with a diagnosis of T2DM that used a specified probiotic in the treatment. Changes in microbial diversity were expressed as mean difference with 95% confidence interval between treatment and placebo groups, as computed using Review Manager 5.2.

Results

After removing duplicates and ineligible studies, 87 studies were extracted for review of titles and abstracts. The number was reduced to 7 articles for the analysis. Our meta-analysis revealed non-significantly higher Firmicutes ($p=0.33$) and lower Bacteroidetes ($p=0.10$). At the genus level, significantly higher proportions of Bifidobacterium ($p<0.001$), and relatively lower proportion of Lactobacillus, Fusobacterium, Streptococcus, and Clostridium were found in T2DM adults after probiotic treatment. Subgroup analyses show that the probiotic treatment comparatively increased microbial diversity across all probiotic species, single vs. multiple species, and treatment lengths.

Conclusion

This meta-analysis demonstrated supplementation of multi-species probiotic supplementation for at least 12 weeks, associated with positive microbiome effects on T2DM.

WOCS-10-9

Obesity impairs pancreatic β-cell integrity through targeted degradation of CtBP2

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The adaptive increase in insulin secretion in the early stages of obesity serves as a safeguard mechanism to maintain systemic glucose homeostasis. However, this adaptive response cannot be sustained for a prolonged period of time and the eventual decompensation of β-cells is a key event in the pathogenesis of diabetes. Here we describe a novel transcriptional system orchestrated by a transcriptional cofactor C-terminal binding protein 2 (CtBP2) that plays a crucial role in this context. In cultured pancreatic β-cells, insulin gene expression is reduced by CtBP2 knockdown and increased by CtBP2 overexpression, respectively, suggesting a coactivating role of CtBP2 in insulin gene transcription. Global mapping of CtBP2 binding sites through our ChIP-seq analysis identifies a key interaction between CtBP2 and NEUROD1 through which CtBP2 decompacts repressive chromatin in the insulin gene promoter. Intriguingly, CtBP2 expression is markedly diminished in the pancreatic islets in multiple preclinical mouse models of obesity as well as human obesity. Consistent with the in vitro findings, the pancreatic β-cell-specific CtBP2-deficient mouse models manifest glucose intolerance with impaired insulin secretion. Our comprehensive transcriptome analysis reveals an essential role of CtBP2 in the maintenance of β-cell integrity. This novel transcriptional system provides clues to the molecular basis underlying the β-cell decompensation in obesity and may be targetable to develop new therapeutic approaches.

WOCS-11-1

National screening of non-communicable disease in Mongolia

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Objective

To determine prevalence an early detection of the non-communicable disease (NCD) in

Mongolian adults.

Methods

In this cross-sectional study, we used the data of NCD screening campaign which took place

in 2022 from primary health centers in rural and urban areas of Mongolia. In total of 116856

Mongolians aged above 18 years were involved in this study. Study questionnaire included

lifestyle including diet, physical activity, smoking and alcohol use. In physical measurements,

body weight, height and waist circumference were measured. We also collected some lab

data including fasting blood glucose and lipids. MetS was diagnosed when the presence of

central obesity, in addition to two or more of the other four factors for the IDF definition of MetS. Diabetes risk score was calculated based on ADA standards.

Results

Out of 116856 patients recruited in our study, 47211 (66.1%) were female. The mean age

was 51.2 ± 14.8. Regard to lifestyle-related risk factors, the prevalence of physical inactivity

(51%), lower daily consumption of fruits and vegetables (31.0%) and smoking (27.0%) was

greater among Mongolian people. The prevalence of obesity and increased blood pressure

was 56.0% and 44.0% respectively. The prevalence of diabetes and impaired fasting glucose
in general population was 6.7% and 17.1% respectively. MetS was present in 28.6% subjects;
prevalence was 26.8% in men and 30.4% in women (p<0.05).

Conclusion

The prevalence of non-communicable risk factors is higher in Mongolian population.

Keywords

Lifestyle, obesity, diabetes, hypertension

WOCS-11-2

Detecting the tipping points of type 2 diabetes by dynamic network biomarkers

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Detecting the tipping points of type 2 diabetes or predicting the diabetes is a key to achieving preventive medicine. By exploiting rich information of high-throughput data, a novel model-free method has been developed to detect early warning signals of diseases, i.e. dynamic network biomarker (DNB), which is composed of a number of interconnected molecules. In this work, we applied the new method to the analysis of type 2 diabetes mellitus (T2DM). Specifically, based on the gene expression data of T2DM, we identified DNBs corresponding to the critical transitions occurring in liver, adipose and muscle during T2DM development and progression or prediabetes stage. Actually, we found that there are two different critical states during T2DM development characterized as responses to insulin resistance and serious inflammation, respectively. Interestingly, a new T2DM-associated function, i.e. steroid hormone biosynthesis, was discovered, and those related genes were significantly dysregulated in liver and adipose at the first critical transition during T2DM deterioration. Moreover, the dysfunction of genes related to responding hormone was also detected in muscle at the similar period. Based on the functional and network analysis on pathogenic molecular mechanism of T2DM, we showed that most of DNB genes tended to be located at the upstream of biological pathways, which implied that DNB genes act as the causal factors rather than the consequence to drive the downstream molecules to change their transcriptional activities.

WOCS-11-3

Preoperative NAFLD status could be a predictor of improvement in beta-cell function in bariatric and metabolic surgery

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Objective:

Bariatric and metabolic surgery (BMS) is a beneficial treatment for type 2 diabetes (T2D) and non-alcoholic fatty liver diseases (NAFLD). BMS could induce diabetes remission in part due to improved beta-cell function. Here, we investigated the efficacy of BMS on NAFLD and beta-cell function, and examined preoperative factors associated with amelioration of beta-cell function.

Methods:

We conducted a prospective observational study of Japanese obese subjects with T2D and NAFLD for 1 year. Subjects were evaluated for the change of liver steatosis and fibrosis before and after BMS by MRI; steatosis, by MRI-estimated proton density fat fraction (MRI-PDFF), fibrosis, by MR elastography (MRE). Beta-cell function was evaluated by Insulin secretion-sensitivity index-2 (ISSI-2) and Disposition index (DI) in oral glucose tolerance test, and we examined the preoperative factors associated with these changes.

Results:

In 18 eligible subjects, NAFLD improved significantly (ΔMRI-PDFF; -11.3 [-18.8, -2.6] %, P<0.05, ΔMRE -0.2 [-0.4, 0.1] kPa, P<0.01), and beta-cell function improved (ΔISSI-2; 0.5±0.6, P<0.01, ΔDI; 0.1 [-0.1, 0.3], P=0.08) after BMS. ΔISSI-2 correlated with preoperative MRE (r=-0.56, P<0.05). In 16 subjects without severe fibrosis in MRE, ΔDI correlated with preoperative MRI-PDFF (r=-0.52, P<0.05).

Conclusion:

BMS demonstrated the improvement of NAFLD and beta-cell function. Preoperative NAFLD status could be a predictor of improvement in beta-cell function in BMS.

WOCS-11-4

Bariatric Surgery as Management for Young Obese Patient with Pre-T2DM : Prospective Observational Study in Sumber Waras

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Introduction : Obesity is projecting to become major public health concern worldwide, and being the main cause of Diabetes Mellitus Type 2 (T2DM) in young adult. Studies showed bariatric surgery may improve glucose metabolism. The aim of this study was to investigate prospectively role of bariatric surgery for young obese patient with Pre-T2DM.

Methods : This prospective observational study carried to compare pre-bariatric and post-bariatric outcome in young obese patients (<40 years) with Pre-T2DM, from January 2021 to August 2022 in Sumber Waras Hospital, West Jakarta. Types of bariatric surgery were Sleeve Gastrectomy or Roux-en-Y Gastric bypass (RYGB). Follow-up was done 3 months post-operatively. The main outcomes were changes in HbA1c, BMI, metabolic syndrome status, and re-hospitalization events. Bivariate analysis was carried out with paired student t-test.

Results and Analysis : Total 48 young obese patients with Pre-T2DM had done bariatric surgery included in the analysis, and drop-out rate were 0%. Mean age was 37.1 ± 8.1 years and 60.4% subject done Sleeve Gastrectomy. Post-bariatric group show significantly reduction in HbA1c (reduce 1.4 mg/dL [95% CI 1.0-1.7], p=0.000) and BMI (reduce 3.9 kg/m^2 [95% CI 2.7-5.3], p=0.000). Metabolic syndrome status reduce significantly after 3 months post bariatric surgery (reduce 43.7%, p=0.000). Only 6 re-hospitalization events observe (12.5%, p>0.05). Bariatric surgery could enhanced GLP-1, incretin, and PYY levels, inducing metabolic improvement and glycaemic control

Conclusion : This study shows bariatric surgery could improve T2DM, obesity, and metabolic syndrome. Bariatric surgery may be effective treatment for severe obesity and related condition.

Variable	Pre Bariatric (n=48)	Post Bariatric (n=48)	Difference (95% CI)	p value
HbA1c (%)	6.44 ± 1.45	5.04 ± 0.69	1.4 (1.0-1.7),	p = 0.000
BMI (kg/m²)	44.55 ± 14.75	40.32 ± 14.11	4.23 (2.7-5.3)	p=0.000
Metabolic syndrome diagnosis; n(%)	48 (100)	27 (56.25)	43.7	p=0.000
Systolic Blood Pressure (mmHg)	137.63 ± 24.64	127.16 ± 22.04	10.46 (5.27-15.64)	p=0.000
Diastolic Blood Pressure (mmHg)	81.75 ± 15.85	77.06 ± 13.67	4.69 (0.0-9.37)	p=0.004
Total Cholesterol (mg/dL)	199.25 ± 38.41	183.33 ± 18.77	15.92 (7.82-22.56)	p=0.04
HDL (mg/dL)	45.07 ± 12.98	52.33 ± 9.02	7.26 (3.63-10.89)	p =0.03
Triglyceride (mg/dL)	159.03 ± 66.32	134.67 ± 43.51	24.36 (12.08-36.54)	p=0.04
Fasting Blood Glucose (mg/dL)	119.61 ± 51.27	96.97 ± 21.20	22.63 (10.29-34.98),	p=0.000
Re-hospitalization event (%)		6 (12.5%)	p>0.05	

WOCS-11-5

Can postprandial glucose and triglyceride excursions be normalized in morbidly obese patients after metabolic surgery?

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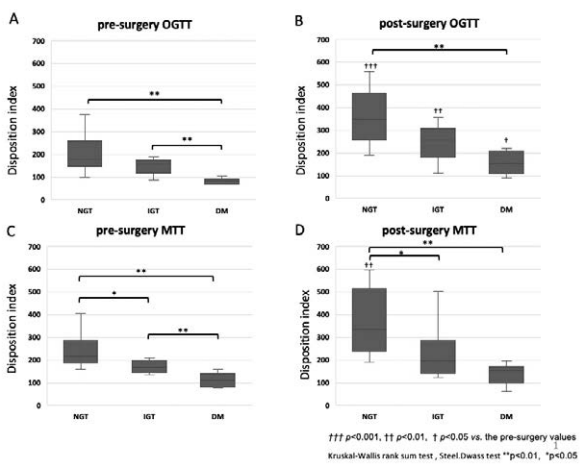
【Objective and Methods】To confirm whether postprandial blood glucose and triglyceride (TG) excursions in 30 morbidly obese patients with or without diabetes were normalized 1-year after laparoscopic sleeve gastrectomy (LSG) *vs.* before surgery, we performed a 75-g oral glucose tolerance test (OGTT) and a meal tolerance test (MTT) using a 75g glucose and fat-containing meal. **【Results】**The following findings were obtained. (1) Diabetes remission and significant cardiometabolic risk reductions were obtained after LSG. (2) Glucose intolerance detected in the OGTT was significantly improved postoperatively in relation to dumping syndrome, whereas the MTT without hypoglycemia showed only weak improvements after LSG. (3) Insulin sensitivity index (ISI) calculated from both tests significantly increased in association with weight loss and improved hyperinsulinemia without changes in glucose-stimulated insulin secretion (GIS) after LSG. Disposition index (DI), a product of [ISI] x [GIS] calculated from both tests was progressively decreased from normal glucose tolerance (NGT) to diabetes, where the diabetes patient's values were significantly lower than NGT patient's values, postoperatively. Thus, an insufficient increase in DI in diabetes patients was a good indicator for impaired normalization of glucose tolerance curves. Conversely, postprandial hypoglycemia after OGTT was significantly associated with high DI after surgery. (4) Both baseline and postprandial TG levels after MTT were negatively correlated with ISI and DI and were improved after LSG.

【Conclusion】DI measurements are essential to assess whether glucose tolerance is normalized after LSG and MTT is an appropriate method to accurately assess improvements in postprandial glucose and lipid metabolism postoperatively.



WOCS-11-6

D-Allulose directly activates satiety neurons and inhibits appetite neurons in the arcuate nucleus and inhibits feeding

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A rare sugar D-Allulose decreases blood glucose and food intake, thereby ameliorating type 2 diabetes and obesity. These effects of D-Allulose are substantially mediated by secretion of glucagon liken peptide-1 (GLP-1) from the intestine and its activation of vagal afferent nerves. It was reported that D-Allulose does not enter the brain through the blood-brain-barrier.

Recently, a new peripheral-central pathway represented by Tanycytes in the 3rd ventricle was found. Tanycytes transport the relatively large molecules from the circulation to the brain. This prompted us to investigate the direct action of D-Allulose on the neurons in the hypothalamic arcuate nucleus (ARC) that regulate feeding and metabolism, and the effect of intracerebroventricular injection of D-Allulose on feeding.

Centrally administered D-Allulose decreased cumulative food intake for 1~4 hours after injection in mice. D-Allulose (1.68~5.6 mM) increased $[Ca^{2+}]_i$ in the satiety neurons isolated from ARC: the pro-opiomelanocortin (POMC) neurons and the neurons that responded to GLP-1. Notably, D-Allulose decreased $[Ca^{2+}]_i$ in the appetite neurons in ARC: the neuropeptide Y (NPY) neurons and the neurons that respond to ghrelin and low glucose.

The results show that D-Allulose directly activates anorexigenic and inhibits orexigenic neurons in ARC. This reciprocal regulation of satiety and appetite neurons can efficiently regulate feeding, glucose and energy metabolism. The property of D-Allulose to evoke both the tanycyte- ARC pathway and GLP-1-vagal afferent pathway represents D-Allulose as a promising compound to regulate metabolism/feeding and ameliorate diabetes/obesity in human.

WOCS-12-1

Importance of early stage of immune response in COVID 19 vaccination in diabetes with renal complication (KDDS11)

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[Aim]
To evaluate efficacy of COVID19 vaccine, we measured anti-SARS-CoV-2 antibodies in both normal and diabetes subjects.
[Method]
Diabetes subjects were recruited in this antibody study. Total participants were 248 subjects in this study. The number of diabetic patients were 182, the number of normal subjects were 66.
More than 95% of Pfizer vaccine (Comirnaty) were applied, the rest of vaccine were Moderna.
COVID 19 vaccination has been applied 5 times at maximum in Japan.
Serum specimen was examined by Abbott Kit in the BML laboratory (Saitama Prefecture).
Laboratory examination has been done by the use of anti-Sars Cov2 antibody. Furthermore, examination including anti-Nucleocapsid IgG antibody, anti-spike IgM antibody and anti-Spike IgG antibody. Performing of these three examination sets were very useful.
[Results]
Titer of serum antibody showed mean values of 1094±1282 (Mean±SD) AU/ml in diabetic subject (N=70), and 350±261 AU/ml in patients with renal insufficiency on hemodialysis (N=6). There were significant differences between these patients in the period before the third inoculation of COVID 19

vaccine.
After third inoculation there were no significant differences in the titer between the two groups.
This suggests that in early stage of immune establishment diabetic patients with renal insufficiency on hemodialysis is lower than diabetic patient without renal complication.
[Conclusion] 1) early and frequent COVID 19 vaccine inoculation is recommended in diabetic patient with renal insufficiency. 2) both anti-Nucleocapsid IgG Ab and anti-Spike IgG Ab were useful in estimating the effectiveness in the diabetes subjects.

WOCS-12-2
Diabetes Care during the Covid-19 Pandemic in China

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Objective:Analyze the blood glucose control, severity of Covid-19 infection, anti-diabetic drugs and other treatment therapy of diabetic patients combined with Covid-19 infection in Hunan Provincial People's Hospital during the Covid-19 pandemic from October 2022 to January 2023 in Hunan China after Chinese Open Policy.Methods: Data of 1131 cases with Covid-19 infection were collected, 387 patients with diabetes were among them. Time in Range(TIR), usage of anti-diaetic drugs, complications of diabetes, severity of Covid-19 infection and parameters of inflammation were studied in those patients. Results:1.Nearly 40% diabetic patients with Covid-19 infection didn't own good control of the blood glucose, TIR were below target. 2.Diabetic patients had higher rate of severe infection of Covid-19, longer time for hospitalization and more to enter ICU. 3.There were high rate of diabetic complications in patients combined with Covid-19 infection, including Myocardial infarction, stroke and diabetic foot.4.Inflammation makers were significantly elevated in diabetic patients with Covid-19 infection. 5.Bad blood glucose control was correlated with types of anti-diabetic drugs, use of glucocorticoid, severity of Covid-19 infection, diabetic complications and other combined diseases.Conclusion: Covid-19 infection had worsen the blood glucose control and diabetic complications in diabetic patients, more diabetes care procedures still need to be done to help the patient.

WOCS-12-3
RELATIONSHIP OF NUTRITIONAL STATUS AND VITAMIN D LEVELS WITH ANTI-SARS-COV-2 ANTIBODIES IN HEALTH CARE WORKERS

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Objective: To determine the relationship of nutritional status and vitamin D levels with anti-SARS-CoV2 antibodies in healthcare workers at Prof. I.G.N.G. Ngoerah Hospital Denpasar.

Methods: This was an analytical cross-sectional study. The sample consisted of 96 healthcare workers at Prof. I.G.N.G. Ngoerah Hospital with age is 18-59 years old and has undergone a 4-dose COVID-19 vaccination program (twice booster and the last booster vaccine using the mRNA-1273 or Moderna vaccine).

Results: There was no significant relationship between nutritional status and anti-SARS-CoV2 (p=0.983; RP=0.995; 95%CI 0.638-1.552). Vitamin D levels were significantly associated with anti-SARSCOV-2 level (p=0.032; RP=1.963, 95%CI 1-2.864), where vitamin D levels below 20 ng/ml (deficient) were at risk for the formation of anti-SARS-CoV-2 lower than 40,000 AU/ml by 1.693 times compared to those with vitamin D levels above 20 ng/ml. Systolic and diastolic blood pressure correlated with anti-SARS-CoV-2 level (r=0.265, p=0.009 and r=0.245, p=0.016), while age did not correlate with anti-SARS-CoV-2 (r=- 0.010; p=0.921) and gender did not have a significant relationship with anti-SARS-CoV-2 (p=0.562; RP=0,867; 95%CI=0,529-1,420). In the obese group, systolic and diastolic blood pressure were positively and significantly correlated with anti-SARSCOV-2 levels (r=0.373; p=0.011 and r=0.351; p=0.017).

Conclusion: There is no significant relationship between nutritional status and anti-SARS-CoV2, and there is a relationship between vitamin D levels and anti-SARS-CoV2 in health workers at Prof. I.G.N.G. Ngoerah. Systolic and diastolic blood pressure was positively and significantly correlated with anti-SARS-C0V-2 levels, especially in the obese group.

Keywords: nutritional status, body mass index, obesity, vitamin D, anti-SARS-CoV-2

WOCS-12-4
Clinical characteristics of the hospitalized patients with diabetic foot ulcers during COVID-19 pandemic

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Objectives: To explore the clinical characteristics of the hospitalized patients with diabetic foot ulcers(DFU) during COVID-19 pandemic.
Methods: We recruited 344 DFU patients(COVID group) with age of 63.4±13.2yr and 379 DFU(NON-COVID group) patients with age of 65.2±11.9yr, admitted from January 24, 2020 to December 31, 2023 and from January 1, 2017 to January 23, 2020, respectively. The clinical data during hospitalization were collected.
Results: The diabetic course(13.1±8.5yrs vs. 12.5±8.0yrs, p=0.281) and HbA1c(8.6%±2.2% vs. 8.5%±2.1%, p=0.799) were not significantly different between two groups. The COVID group had lower hemoglobin(108.8±24.4g/L vs. 113.2±23.8g/L, p=0.017) and albumin(36.3±6.3g/L vs. 37.4±5.9g/L, p=0.009) than the NON-COVID group. Compared with the DFU patients in the NON-COVID group, the patients in the COVID group had higher prevalence of osteomyelitis and gangrene with higher WBC counts, procalcitonin, ESR and CRP levels($p < 0.05$). The median hospital stay were 30 and 28 days before and during pandemic (p=0.098), respectively. The healing rates of the foot ulcers in hospital before and during pandemic were 33.5% and 13.1%, respectively($p<0.001$). The median healing time in the COVID group was shorter than that in the NON-COVID group(19 days vs. 35 days, p=0.003). Compared with the NON-COVID group, the amputation rate in the COVID group was statistically higher(7.8% vs. 3.4%, $p<0.001$). The death rates during hospitalization were 0.8% and 1.2% in the NON-COVID and COVID groups, respectively.
Conclusion: During the COVID-19 pandemic, the hospitalized patients with DFU had higher incidence of malnutrition osteomyelitis, gangrene, and amputation with a greater severity of foot ulcers.

WOCS-12-5
Issues with sick day guidance and self-care that have become apparent during the COVID-19 pandemic

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Introduction: During the COVID-19 pandemic, we experienced two cases of type 1 diabetes mellitus with DKA due to difficulties with self-care during home isolation. In this report, we present the problems and prevention strategies for recurrence. Case 1: A 53-year-old man. Treated with MDI and isCGM for type 1 diabetes mellitus. On August 15, he was diagnosed with mild COVID-19 and began self-isolation at home. On the 20th, his cohabiting family discovered that he had a decreased level of consciousness. He was diagnosed with DKA from PG 1240 mg/dL, pH of 7.073, HCO3-3.0 mmHg, and urine ketones (2+). Case 2: 61-year-old female. Treated with MDI for type 1 diabetes mellitus. Symptoms such as vomiting and anorexia appeared on August 31. She visited the hospital on September 2 and had mild COVID-19, but was diagnosed with DKA from PG 657 mg/dL, pH 7.098, HCO3-5.1 mmol/L, and urine ketones (4+).Discussion: Diabetes carries a high risk of DKA during illness. Although sick day rules have been established self-care has been primarily emphasized. However, in the above two cases where isolation at

home or family cooperation could not be obtained due to COVID-19, insufficient safety net measures led to the development of DKA when self-care became difficult. Family education on sick day rules is important not only for elderly or cognitively impaired patients but also for independent adult patients. Safety net measures using devices via cloud technology are also important.

WOCS-12-6
Incidence of diabetes following COVID-19 vaccination and SARS-CoV-2 infection: a population-based cohort study

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Objective: We evaluated incidence of diabetes following mRNA(BNT162b2), inactivated(CoronaVac) COVID-19 vaccines, and after SARS-CoV-2 infection.
Methods: Two separate COVID-19 vaccination and infection cohorts were extracted from the population-based electronic health database in Hong Kong. Vaccination cohort included people who received COVID-19 vaccine during February–September2021, matched with those who did not receive any COVID-19 vaccines up to September2021. Infection cohort included confirmed COVID-19 patients during January2020–March2022, and people who were never infected up to March2022. Both cohorts were followed until August2022. COVID-19 vaccine recipients and COVID-19 patients were 1:1 matched to their respective controls using propensity score. Hazard ratios(HRs) for incident diabetes were estimated using Cox regression models.
Results: Vaccination cohort comprised 167337 CoronaVac and 158378 BNT162b2 recipients with their respective 1:1 matched control. Upon 13-month follow-up(FU), neither vaccination was associated with increased risks of incident diabetes. Infection cohort comprised 145199 COVID-19 patients and 145199 matched controls. Among COVID-19 survivors, 60348(41.6%) were fully vaccinated and 25792(17.8%) did not receive any COVID-19 vaccines. Upon 5-month FU, 2109 COVID-19 patients(all type 2 diabetes) and 1775 non-COVID-19 people(one case of type 1 diabetes) were diagnosed with diabetes. SARS-CoV-2 infection was associated with higher risk of incident diabetes(HR=1.23[95%CI:1.15–1.31]) regardless of the predominant circulating variants, albeit lower with Omicron(p-interaction=0.009). Fully vaccinated COVID-19 survivors did not have increased risk of incident diabetes.
Conclusion: Risk of incident diabetes was increased following SARS-CoV-2 infection, but not COVID-19 vaccination. The excess risk was lower for Omicron variants. Fully vaccinated individuals might be protected from risk of post-COVID incident diabetes.

WOCS-13-1
eGFR and CKD progression in late-stage elderly people with type 2 diabetes and normoalbuminuria

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Aim: To clarify the association between estimated glomerular filtration (eGFR) and the risk of progression of chronic kidney diaese (CKD) in late-stage elderly poeple with type 2 diabetes and normoalbuminuria.

Methods: Japanese people ≥ 75 years of age with type 2 diabetes and normoalbuminuria were classified into four groups based on the baseline eGFR : ≥ 60, 45 - 59, 30 - 44, and < 30 ml/min/1.73m^2. The endpoint was sustained reduction in eGFR (≥ 30% from baseline) or initiation of kidney replacement therapy. A competing risk model was employed treating death as a competing risk. Missing values of covariates were imputed using the multiple imputation method, assuming missing at random.

Results: Eligible 454 people with type 2 diabetes and normoalbuminuria were studied (mean age, 80 ± 4 years; 186 women and 268 men). During a median follow-up of 6.1 years, 83 people reached the endpoint. The multivariable-adjusted cumultive incidence of the endpoint was significantly increased in those with eGFR of 30 to 44 and <30, respectively, but not in those with eGFR of 45-59, compared to those with eGFR ≥ 60 mL/min/1.73 m^2.

Conclusion: Among elderly people with type 2 diabetes and normoalbuminuria, those with eGFR < 45 mL/min/1.73 m^2 was associated with future risk of progression of kidney disease.

WOCS-13-2
Efficacy and safety of empagliflozin administration for 52 weeks in Japanese elderly with T2D: The EMPA-ELDERLY trial

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Objective: To evaluate the effect of empagliflozin 10 mg for 52 weeks on glycemic control, body composition, and physical performance in Japanese elderly adults with type 2 diabetes (T2D).
Methods: Adults with T2D aged ≥65 years with HbA1c between 7% and 10% on diet and exercise alone or on oral hypoglycemic agents with a BMI of 22 kg/m^2 or higher were randomized and administered empagliflozin 10 mg or placebo orally once daily for 52 weeks in a double-blind fashion. The change from baseline at 52 weeks in HbA1c, body composition measured by bioelectrical impedance analysis, grip strength, and time of 5-time chair stand test were evaluated.
Results: 129 patients were randomized and127 were included in the efficacy analysis (64 for empagliflozin group, 63 for placebo group, 74.1 ± 5.0 years old (mean ± SD), 72.4% male). For the primary outcome, HbA1c was significantly lower after 52 weeks of the treatment in empagliflozin group than placebo group. (-0.57 ± 0.11% (mean ± SE), p<0.0001). The body weight, fat mass, and total body water content were significantly lower in empagliflozin group than placebo group. No significant difference was observed in muscle mass, grip strength, or time of 5-time chair stand test between both groups. The incidence of adverse events was similar between the two groups.
Conclusion: Administration of 10 mg empagliflozin to Japanese elderly adults with T2D improved glycemic control and lowered body weight, mainly by reducing fat mass and body water content without impact on muscle mass and physical performances.

WOCS-13-3
The correlation between health risk factors and diabesity and lipid profile indicators: the role mediator of TSH

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Introduction: Obesity in adults is a problem, particularly when paired with other metabolic abnormalities. Previous research have linked various screening approaches to diabetes, but additional evidence points to the relevance of combining diabetes screening methods with obesity and its effects. **Methods:** From March to July 2022, the Hefei Community Health Service Center connected with the First Affiliated Hospital of Anhui Medical University was chosen, and the multi-stage cluster sample approach was utilized to test adults aged 21-90 in each community. Latent category analysis(LCA) was performed to investigate the clustering patterns of HRFs. A one-way ANOVA was used to examine waist circumference(WC), biochemical markers, and general data. Furthermore, multivariate logistic regression analysis was utilized to investigate the relationship between health risk variables and WC. **Results:** A total of 708 samples were included in the study with an effective rate of 94.4%. The average WC was(90.0±10.33)cm, the prevalence in the >P_{75}, P_{50}~P_{75}, P_{25}~P_{50},

and ≤P_{25} groups were 24.7%, 18.9%, 28.7% and 27.7%, respectively. The average TSH was(2.76±2.0) μIU/mL. Male(β=1.91), HOMA-IR(β=0.06), TyG(β=2.41), SBP(β=0.08), TG(β=0.94) and UA(β=0.03) were more likely to have a higher prevalence of WC level. The analyses revealed significant correlations between HRFs, TSH, age, other metabolic indexes and WC(P < 0.05). **Discussion:** Our findings suggest that the quality of metabolic-related indicators used to successfully decrease diabetes in Chinese individuals with high HRFs levels should be prioritized.

WOCS-13-4

Association between high muscle mass and carotid atherosclerosis in a community-based population cohort

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Aims: Although low muscle mass may make an under-appreciated contribution to increasing the risk of cardiovascular diseases, no prospective studies have explored the association between low muscle mass and carotid atherosclerosis. We investigated whether muscle mass is related to a higher carotid intima-media thickness (C-IMT) and carotid artery plaque in a community-based population.**Methods:** The study included 1,253 asymptomatic participants without known cardiovascular disease, who underwent carotid ultrasonography at baseline in 2013-2014 and received a re-examination in 2015-2016. The skeletal muscle mass index was estimated using a bioelectrical impedance analyzer. We assessed the relationship between the skeletal muscle mass index and the development of C-IMT and carotid plaque, both, using multivariate-adjusted logistic regression models.**Results:** During the follow up, 400 (51.0%) subjects with normal C-IMT at baseline developed elevated C-IMT and 215 (17.2%) subjects developed carotid plaque. The risk of elevated C-IMT occurrence linearly decreased with an increase in skeletal muscle mass index quintiles or its continuous data, after multivariate-adjustment in men and women, respectively (both $P_{\text{for trend}}$ < 0.05; both P < 0.05). Subgroup analyses showed that this association was BMI-dependent. Besides, there was an inverse association between a high skeletal muscle mass index and carotid artery plaque in women, but the association disappeared after multivariate adjustment. In men, the skeletal muscle mass index was not associated with the incidence of carotid plaque.**Conclusion:** Skeletal muscle mass was inversely associated with the incidence of carotid atherosclerosis, suggesting muscle mass maintenance may play a role in modifying atherosclerosis.

WOCS-13-5

Elderly women with type 2 diabetes are at high-risk for bone complications

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Background and aims: Type 2 diabetes mellitus (T2DM) is a major cause of secondary osteoporosis. However, the surveillance for bone lesions in patients with T2DM is impractical from a health economics perspective. Therefore, we should identify diabetic patients at a high risk of developing bone complications by measuring the bone mineral density (BMD) and the trabecular bone score (TBS).

Methods: We retrospectively included patients with T2DM ≥40 years without acute disorders or treatment history of osteoporosis. Lumber spine and femoral neck BMD were measured, and TBS was calculated.

Results: A total of 137 (male/female = 85/52) patients with T2DM were included in this study with the following characteristics: Age: 65 [53, 75] (median [interquartile range]) years, body mass index: 24.6 [22.8, 27.8] kg/m^2, and glycated hemoglobin: 10.1 [9.0, 11.7] %. Approximately, 13% of the participants manifested with bone quality loss, 38% manifested with bone mass loss, and 48% manifested with losses in both bone quality and mass. The overall frequency of bone complications was 65%. The prevalence of bone complications was higher in ≥65 years women than in <65 years men, with odds ratios of 12.7 (95% confidence interval [CI]: 4.2–34.9, p<0.01) for bone quality loss, 30.5 (CI 7.8–120, p<0.01) for femur mass loss, and 3.5 (CI 1.4–9.3, p<0.01) for lumbar spine mass loss.

Conclusion: The risk of bone complications was markedly higher in elderly women than other groups. Therefore, early surveillance and treatment of bone complications for elderly women in T2DM are highly recommended.

WOCS-13-6

Clinical Profile and Identification of Osteoporosis Risk Factors in Patients with Diabetes Mellitus

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Diabetes Melitus (DM) has an adverse effect on decreasing Bone Mineral Density (BMD), thereby increasing the risk of fracture through pathophysiological mechanisms. We conducted a cross-sectional approach of 51 DM patients who met the criteria and were examined for BMD. The analysis was carried out univariate and bivariate using the Chi Square Test (X^2) to analyze the correlation of risk factors with the incidence of osteoporosis in DM patients. The clinical profiles of the subjects were 60.8% had decreased bone density, 66.7% women, 86.2% were over 50 years old, 15% had a risky BMI, 17% smoked, 39.2% had diabetes onset <48 years, 58.8% had DM duration >5 years, 82.4% had HbA1c levels ³7, 5.9% had TZD consumption, 43.9% had eGFR <60, 54.1% had TC levels ³200mg/dL, 67.7% had low HDL levels, 91.9% had LDL levels ³70mg/dL, 44.7% had TG levels ³150mg/dL. There was no statistically significant corellation between the onset of DM diagnosis (p = 0.119), duration of DM (p = 0.187), BMI (p = 0.697), HbA1c (p = 1,000), TZD use (p = 0.410), eGFR (p = 0.218), total cholesterol (p = 0.309), HDL (p = 0.835), LDL (p = 0.278), and triglycerides (p = 1,000) with decreased bone density. Onset of DM diagnosis, duration of DM, glycemic control, BMI, use of TZD drugs, kidney function, total cholesterol, HDL, LDL, and triglycerides were not risk factors for osteoporosis in DM patients at Dr. Kariadi Hospital.

WOCS-14-1

Identification of pathogenic mutations for a Wolfram syndrome pedigree by whole exome sequencing

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Objective: The aim of this study was to identify the causative gene and mutations and describe the clinical traits in a Chinese diabetes pedigree. Methods: Whole exome of the proband and his family members were screened using Whole Exome Sequencing and subsequently validated by PCR-DNA direct sequencing. Effects of the mutations on the structure and function of the indicated protein were evaluated by bioinformatics. Results: Two mutations, a rare mutation R558H, and a novel mutation S411Cfs*131, both in the *WFS1* gene were identified. The proband and his sister were both compound heterozygous of the two mutations and their parents carried one mutation, separately. Bioinformatics predicted that the R558H mutation located in the α-helical structure of the protein, Woframine, was a serious damage mutation and the mutation region is highly conservative among different species. Conclusions: This study identified two causative mutations of *WFS1* gene in a Chinese diabetes pedigree by Whole Exome Sequencing.

WOCS-14-2

Sensitivity to thyroid hormone and risk of components of metabolic syndrome in a Chinese euthyroid population

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Objective: To evaluate the association of sensitivity to thyroid hormone with MetS and its components in a Chinese euthyroid population.

Method: A total of 3,573 subjects from Pinggu Metabolic Disease Study were analyzed. Serum free thyroxine (FT4), and thyrotropin (TSH), total adipose tissue (TAT), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) area of abdominal, and lumbar skeletal muscle area (SMA) were measured. Central thyroid hormone resistance was calculated by the Thyroid Feedback Quantile-based Index (TFQI) and Chinese-referenced Parametric TFQI (PTFQI), Thyrotroph T4 Resistance Index (TT4RI) and TSH Index (TSHI). Peripheral thyroid hormone resistance was assessed by FT3/FT4 ratio.

Results: Higher values of TSHI (OR=1.167, 95% CI: 1.079, 1.262, p<0.001), TT4RI (OR=1.115, 95% CI: 1.031, 1.206, p=0.006), TFQI (OR=1.196, 95% CI: 1.106, 1.294, p<0.001), PTFQI (OR=1.194, 95% CI: 1.104, 1.292, p<0.001), and lower values of FT3/FT4 ratio (OR=0.914, 95% CI: 0.845, 0.990, p=0.026) were associated with MetS after adjusting for age, gender, and homeostasis model assessment of insulin resistance. Increased levels of TFQI and PTFQI were associated with abdominal obesity, hypertriglyceridemia, and hypertension. Increased levels of TSHI and TT4RI were associated with abdominal obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C). Reduced levels of FT3/FT4 ratio were associated with hyperglycemia, hypertension and hypertriglyceridemia. The levels of TSHI, TFQI and PTFQI were negatively associated with SMA and positively associated with VAT, SAT and TAT (all p<0.05).

Conclusions: Reduced thyroid hormone sensitivity was associated with MetS and its components. Impaired thyroid hormone sensitivity might affect the distribution of adipose tissue and muscle.

WOCS-14-3

Deficiency of FAM172A in Oxytocin neurons confers no influence on dietary dysglycolipid metabolism

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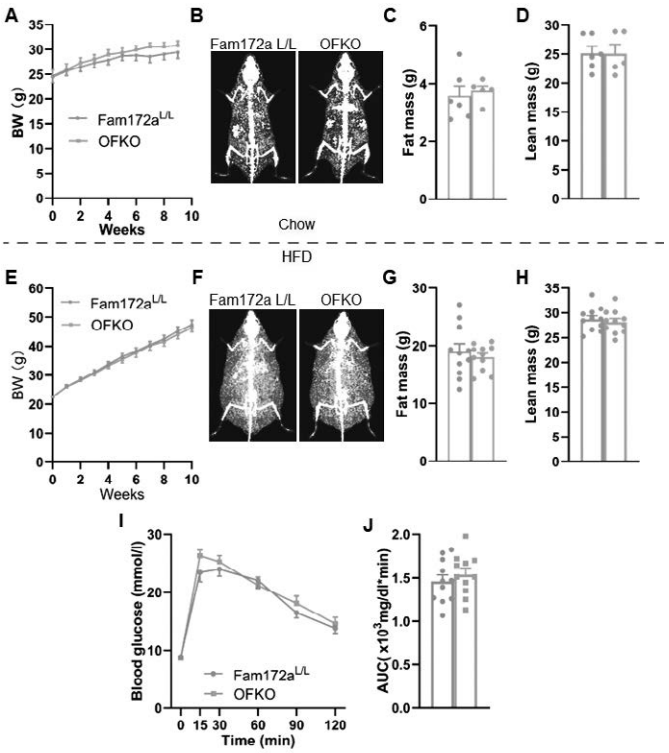
Objective: Diabetes has become a serious public health problem, and the incidence of chronic diseases related to diabetes has also increased significantly. Therefore, it is urgent to find new and effective interventions or therapeutic targets. In this study, we investigated the role of FAM172A in oxytocin neurons of hypothalamus PVN in the development of nutritional dysglycolipid metabolism.

Methods: Oxytocin neuron-specific FAM172A knockout (OFKO) mice were generated by crossing the *FAM172A*$^{loxP/loxP}$ mice with the *OxT-Cre* mice. The *FAM172A*$^{loxP/loxP}$ mice and *OFKO* mice were fed a chow diet or high-fat-diet (HFD), and the body weight, fat mass, lean mass and glucose metabolism were then monitored.

Results: In both chow diet and HFD fed mice, there was no difference between *OFKO* mice and their control group in the body weight, fat mass, lean mass and glucose metabolism.

Conclusion: FAM172A expressed in Oxytocin neurons of hypothalamus has no effect on the glycolipid metabolism balance in mice which were fed with whether a chow diet or a high-fat diet.



WOCS-14-5

ASSESSING FINNISH DIABETES RISK SCORE (FINDRISC) AMONG MEDICAL STUDENTS IN BALI, INDONESIA, 2023

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Objective

Medical students have busy schedules and tend to ignore healthy lifestyle. This study aim to evaluate the type 2 diabetes mellitus (T2DM) risk score using FINDRISC among medical students in Denpasar Bali, Indonesia.

Methods

A cross-sectional study was conducted in January 2023, based on validated questionnaires of FINDRISC.

Results

A hundred undergraduates were involved in this study; female:male 62%:38%, mean age 22.813±0.93. Diabetes risk scores were between 2-15, average 6.51±3.40; classify as low risk 57%, slightly elevated 34%, moderate 5%, high 4%, and none were very high. Almost half (43%) of the students were moderate-high risk of T2DM. Based on body mass index (BMI) values (≥25 kg/m^2), 20% of students were obese. While average BMI was within normal: 22.71±3.88 kg/m^2, high waist circumference (WC) >80 cm in female were found in 9 out of 65 (13.84%) and >90 cm in male were 12 out of 35 (34.28%). Interestingly, the most common contributing risk factor was unhealthy dietary habit (59.4%), and lack of physical activity 25.7%. First degree relative family history was only found 11.9%, second degree relative family history was quite high 45.5%.

Conclusion

Almost half of the participants were at risk of T2DM and the modified risk factors including unhealthy dietary habit and lack of physical activity were

highly contributed. Awareness of diabetes risk and lifestyle changes should advocate among young adult to prevent diabetes in the future.

WOCS-14-6

Association between early weaning-inducible fatty liver and phosphatidylcholine molecule decreases in mouse liver

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Objective

Early weaning (EW) induces the development in rodents and pigs, and that deficiency of choline, which composes phospholipids as phosphatidylcholines (PC), induces severe fatty liver in rodents. In this study, we examined whether phospholipid composition changes including PC induced by EW is associated with the fatty liver development and expression of genes related to lipid droplet (LD) formation.

Methods

The male pups were divided into two groups, which were weaned from their mothers at 17 (EW) and another 21 (normal weaning) days old. All pups and mothers were given an AIN93G diet and the pups were killed by decapitation and livers were collected at ○○ weeks-old. The mRNA expression of genes related to LD formation, the number and diameter of LDs and phospholipid composition in livers were assessed by RT-qPCR, HE staining, and UHPLC-MS, respectively. Associations were assessed by student's *t*-test and multiple liner regression (MLR).

Results

Early weaned mice showed higher LD diameter and higher expression of genes related to LD formation including *Plin4* in liver. The MLR showed an strong-positive association between LD diameter and a decrease of PC(38:8) level. The levels of PC(38:6), PC(38:8), PC(40:2), PC(40:3) were lower in the early weaned mice than that in the normally ones.

Conclusion

The development of fatty liver induced by EW is positively associated with decreases of several phosphatidylcholine levels and mRNA increases of genes related to LD formation.

Table. Multiple linear regression analysis for diameter of lipid droplets as a depende

	Independent variables	β	SE	*P*	
Model 1 (n=20),	Phospholopid				
R^2=0.67	LPC (20:3)	-0.098	0.000	0.643	
	PC (38:6)	-2.596	0.000	0.020	*
	PC (38:8)	1.141	0.000	0.156	
	PE (38:4)	0.226	0.000	0.383	
	PI (40:4)	0.998	0.002	0.011	*
	PS (34:1)	-0.069	0.001	0.720	
	Intercept	0	92.92	0.003	**
Model 2 (n=20),	LPC (20:3)	-0.012	0.000	0.962	
R^2=0.50	PC (38:8)	-0.775	0.000	0.015	*
	PE (38:4)	-0.112	0.000	0.672	
	PI (40:4)	0.323	0.000	0.237	
	PS (34:1)	-0.089	0.000	0.701	
	Intercept	0	43.55	0.027	*

*$P < 0.05$, **$P < 0.01$

WOCS-14-7

Age-adjusted diabetes prevalence –an investigation from IDF Diabetes Atlas 2021–

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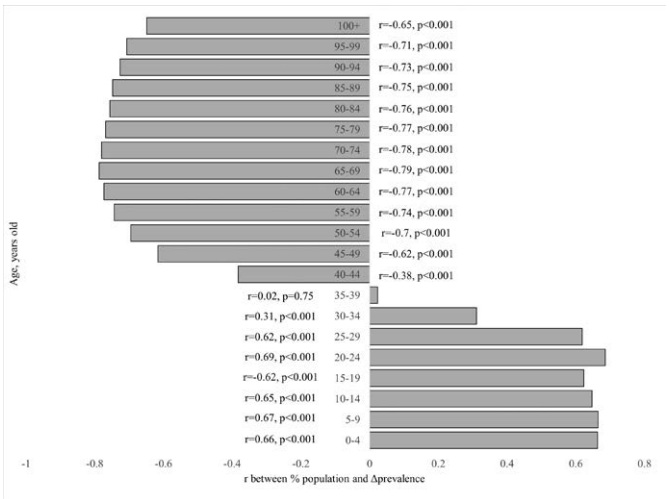
Objective: We examined the impact of population distribution on age-adjusted diabetes prevalence using data from the IDF Diabetes Atlas 2021.

Methods: We proposed and calculated the metric named "% population", according to the following formula: population for each 5-year age group ÷ total population × 100 (%), using the most recent United Nations World Population Prospects data for each country or territory. The age-adjusted diabetes prevalence (20–79 years) was taken from the IDF Diabetes Atlas 2021 data. Diabetes prevalence (20–79 years) was calculated using the IDF Diabetes Atlas 2021 data, according to the following formula: the number of people with diabetes (20–79 years) ÷ total population (20–79 years) × 100 (%). Countries or territories for which both population data and age-adjusted diabetes prevalence could not be obtained were excluded.

Results: This study included 189 countries or territories. The figure shows the r between "% population" and "age-adjusted diabetes prevalence – diabetes prevalence" ("Δprevalence"). For any 5-year age group aged less than 35 years, the "% population" positively correlated with the Δprevalence (r = 0.31-0.69). For any 5-year age group older than 40 years, the "% population" negatively correlated with Δprevalence (r = –0.38-–0.79).

Conclusion: In our world, relatively larger population older than 40 years old may result in an underestimation of age-adjusted diabetes prevalence compared to diabetes prevalence.



WOCS-15-1

Prevalence and associated factors of hyperuricemia among patients with diabetes: a cross-sectional study

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Objective: The objective of the present study was to investigate the prevalence of hyperuricemia among patients with diabetes and identify associated factors.

Methods: Herein, we included patients with diabetes managed at nine healthcare centers in Chenghua District, Chengdu, from February 2021 to November 2021. Clinical data, lifestyle habits, and laboratory data were collected to determine the prevalence and factors associated with hyperuricemia.

Results: In total, we included 1577 patients with diabetes (males, 50.35%; females, 49.65%). The mean serum uric acid level was 347.1±91.7 μmol/L, and the prevalence of hyperuricemia in patients with diabetes was 21.24%. The prevalence of hyperuricemia in male patients was significantly higher than in females (29.35% in males *vs*. 13.03% in females, $P<0.001$). Male patients with obesity ($P=0.006$) or triglyceride (TG) ≥1.7 mmol/L ($P<0.001$) had a high risk of developing hyperuricemia, and hyperuricemia was negatively associated with estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m^2 ($P<0.001$), glycosylated hemoglobin (HbA1c) ≥7% ($P<0.001$), fenofibrate ($P=0.010$), and sodium-glucose cotransporter 2 (SGLT-2) inhibitors ($P=0.035$). Considering females, overweight ($P=0.004$), alanine transaminase (ALT) >40 U/L ($P<0.001$) and TG ≥1.7 mmol/L ($P=0.015$) showed a significant positive correlation with hyperuricemia, while eGFR ≥60 mL/min/1.73 m^2 ($P<0.001$)

was negatively associated with the risk of hyperuricemia.
Conclusion: Hyperuricemia is highly prevalent in patients with diabetes, especially in males. In addition to traditionally associated factors, such as eGFR, TG, overweight, and obesity, ALT, HbA1c, fenofibrate, and SGLT-2 inhibitors were associated with the risk of hyperuricemia.

WOCS-15-2

Associations of serum uric acid to HDL-cholesterol ratio with trunk fat mass and visceral fat accumulation

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Objective: It was reported that the ratio of uric acid to HDL-cholesterol (UHR) was a strong predictor of metabolic syndrome. The present study aimed to investigate the relationship between UHR and body fat distribution.
Methods: A total of 300 individuals (58 men and 242 women, aged from 18 to 64 years) were enrolled. The levels of serum uric acid and HDL-cholesterol were measured using fasting venous blood samples by standard enzymatic methods. A body mass index (BMI) of 28kg/m^2 or over was considered obese. A bioelectrical impedance analyzer was used to measure total, trunk, and leg fat mass (FM). The visceral fat area (VFA) and subcutaneous fat area (SFA) were obtained using magnetic resonance imaging.
Results: In the total population, compared with BMI, waist circumference was more closely associated with UHR (standardized $\beta = 0.427$, $P < 0.001$) after adjusting for several metabolic and cardiovascular risk factors. Additionally, total FM (standardized $\beta = 0.225$, $P = 0.002$) and trunk FM (standardized $\beta = 0.296$, $P = 0.036$) were more closely linked to UHR than total fat-free mass and leg FM, respectively. In the population with obesity, VFA was independently correlated with UHR (standardized $\beta = 0.188$, $P = 0.008$), but no such relationship existed between UHR and SFA.
Conclusion: UHR was closely associated with trunk FM and visceral fat accumulation. Attention should be paid to the role of excessive trunk FM in the relationship between UHR and metabolic disorders.

WOCS-15-3

Higher body mass index and waist to hip ratio are associated with fatty liver regardless of skeletal muscle index status

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Objective: Weight loss is important in the treatment of fatty liver (FL); however, setting body composition goals clinically is difficult due to the possibility of increased sarcopenia risk. We have investigated indices of body composition associated with FL in T2DM patients.
Methods: Medical records of the patients hospitalized with T2DM from April 2020 to March 2021 were reviewed. Information on medical history, dietary habits, body composition, and test results was collected retrospectively. FL was diagnosed by abdominal ultrasonography or CT scan. Skeletal muscle loss was quantified as the skeletal muscle index (SMI) measured by BIA method. Patients were divided into normal and low SMI groups according to AWGS criteria; logistic regression analysis was performed in each group with the presence of FL as the objective variable and age, sex, and body composition as explanatory variables (Model 1, body mass index (BMI); Model 2, waist to hip ratio (WHR)).

Results: Among the 121 patients included, 53.7% were male, median age was 68 years, HbA1c 9.7%, and BMI 25.7 kg/m^2; FL was observed in 62.1%. In the normal SMI group (n= 75), BMI and WHR were both associated with FL in each model (Odds ratio: BMI, 1.37, $p < 0.01$; WHR, 11.30, $p < 0.01$, respectively). Similar results were observed in the low SMI group (n= 38; odds ratio: BMI, 1.47, $p= 0.02$; WHR, 6.15, $p= 0.03$, respectively).

Conclusion: Caution for FL is appropriate in T2DM patients when weight gain or increased WHR occurs regardless of the degree of SMI.

WOCS-15-4

Risk assessment with gut microbiome and metabolite markers inNAFLD development

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Objective A growing body of evidence suggests interplay between the gut microbiota and the pathogenesis of nonalcoholic fatty liver disease (NAFLD). However, the role of the gut microbiome in early detection of NAFLD is unclear. Prospective studies are necessary for identifying reliable, microbiome markers for early NAFLD.
Methods We evaluated 2487 individuals in a community-based cohort who were followed up 4.6 years after initial clinical examination and biospecimen sampling. Metagenomic and metabolomic characterizations using stool and serum samples taken at baseline were performed for 90 participants who progressed to NAFLD and 90 controls who remained NAFLD free at the follow-up visit. Cases and controls were matched for gender, age, body mass index (BMI) at baseline and follow-up, and 4-year BMI change.
Results Machine learning models integrating baseline microbial signatures (14 features) correctly classified participants (auROCs of 0.72 to 0.80) based on their NAFLD status and liver fat accumulation at the 4-year follow up, outperforming other prognostic clinical models (auROCs of 0.58 to 0.60). We confirmed the biological relevance of the microbiome features by testing their diagnostic ability in four external NAFLD case-control cohorts examined by biopsy or magnetic resonance spectroscopy, from Asia, Europe, and the United States.
Conclusion Our findings raise the possibility of using gut microbiota for early clinical warning of NAFLD development

WOCS-15-5

Impact of fat accumulation and serum triglyceride levels on MAFLD and NAFLD in Japanese non-obese male young adults

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Objective: With the rising prevalence of diabetes mellitus, metabolic dysfunction-associated fatty liver disease (MAFLD) and nonalcoholic fatty liver disease (NAFLD) are global concerns. The study aim was to reveal the pathophysiologic role of body composition and metabolic parameters on NAFLD and MAFLD in nonobese male young adults.

Methods: We included 305 nonobese (body mass index < 25 kg/m^2) male graduate students who underwent a health checkup in April 2022. The diagnosis of MAFLD and NAFLD was based on health checkup data and ultrasonography. Muscle and fat mass were evaluated using bioelectrical impedance analysis and demonstrated as skeletal muscle mass index (SMI) and fat mass index (FMI), respectively. Factors associated with NAFLD and MAFLD using the logistic regression, decision tree, and random forest analyses.

Results: The median age of the participants was 22 years, and 3% had MAFLD, and 6% had MAFLD. In the multivariate logistic regression analysis included age, SMI, FMI, and handgrip strength, FMI was independently associated with MAFLD (odds ratio [OR], 1.58; 95% confidence interval [CI], 1.12–2.24; *P* = 0.010) and NAFLD (OR, 1.35; 95% CI, 1.09–1.68; *P* = 0.006). In addition, the random forest analyses included all the variables revealed that serum triglyceride levels are the strongest classifier for nonobese MAFLD and NAFLD.

Conclusion: Our study showed that fat accumulation is important in the development of NAFLD and MAFLD in nonobese male young adults. Comprehensive assessment of body composition and metabolic parameters may provide individualized care for MAFLD and NAFLD among nonobese young individuals.

WOCS-15-6

Sodium-glucose cotransporter-2 inhibitors reduce liver fibrosis in people with type 2 diabetes: An interim analysis

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Background and objective: Emerging data suggest sodium-glucose cotransporter-2 inhibitors (SGLT-2i) may have beneficial effects in people with non-alcoholic steatohepatitis. We aimed to investigate the effects of SGLT-2i on the changes of liver fibrosis in Chinese with type 2 diabetes (T2D).

Methods: T2D patients from the Hong Kong Diabetes Register completed transient elastography examinations at baseline (2013-2014) and were prospectively followed-up (2021-2023). All participants were naïve to SGLT2i at baseline. Clinical evaluation including drug history was captured during follow-up. The primary endpoint was ≥30% liver stiffness measurement (LSM) reduction from baseline.

Results: This was an interim analysis of an ongoing study with 46% of the total cohort (883 out of 1918) contacted for follow-up. Among them, 341 died and 71 met exclusion criteria including non-Chinese ethnicity. A total of 471 subjects were included in this present analysis [56% men, mean age ± standard deviation: 65.5±10.1 years, T2D duration 19.5±8.2 years, body mass index (BMI): 25.6±4.2 kg/m^2, glycated hemoglobin (HbA_{1c}): 7.5±1.2 %]. After a mean follow-up of 8.6 ± 0.5 years, there were 273 participants (58%) treated with SGLT-2i, and 112 participants (24%) had ≥30% LSM reduction which was associated with BMI reduction from baseline [adjusted odds ratio (aOR): 1.139, 95% confidence interval (C.I.): 1.034-1.253, p=0.008], high-density lipoprotein–cholesterol (HDL-C) increment from baseline [aOR: 0.346, CI: 0.127-0.947, p=0.039] and SGLT-2i use [aOR: 0.571, CI: 0.338-0.964, p=0.036].

Conclusion: SGLT-2i user, increase in HDL-C and BMI reduction were independently associated with reduced liver fibrosis in Chinese with T2D.

WOCS-15-7

Pemafibrate improves liver complications in patients with AGHD and hypertriglyceridemia

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Objective: Adult growth hormone deficiency (AGHD) causes dyslipidemia and non-alcoholic fatty liver disease (NAFLD), which are often comorbid. Pemafibrate, a novel selective peroxisome proliferator-activated receptor modulator, can be safely used in combination with statins, and it is also expected to be effective against NAFLD. However, its efficacy has not been demonstrated in real-world clinical practice in patients with AGHD.

Methods: As a multicenter, prospective, observational study of the use of pemafibrate in patients with AGHD and hypertriglyceridemia, this analysis focused on the changes from baseline in NAFLD-associated biomarkers and scoring systems at 24 weeks for patients with or at risk for liver complications. Wilcoxon's signed-rank sum test was used for the comparisons. The significance level was set at 0.05, and two-sided tests were performed.

Results: Fifteen patients who started on pemafibrate were analyzed. Eleven patients received growth hormone replacement, and five were on a statin prior to baseline. γ-GTP (−10.0 [interquartile range, −14.5, −4.0] U/L, $p < 0.0001$) and ALP levels (−23.0 [interquartile range, −39.7, −16.0] U/L, $p < 0.0001$) were significantly decreased, whereas AST and ALT levels did not change. The hepatic steatosis index (−1.5 [interquartile range, −2.7, −0.6], $p < 0.01$) and NAFLD fibrosis score (−0.373 [interquartile range, −0.638, 0.271], $p < 0.05$) also improved significantly. IGF-1 and glycemic parameters were not changed or correlated with the changes in liver parameters.

Conclusions: In patients with AGHD and hypertriglyceridemia, pemafibrate appears to have some beneficial effects on liver complications.

WOCS-16-1

DPP-4 Inhibitors and the risk of infection: A Meta analysis and trial sequential analysis of CVOTs

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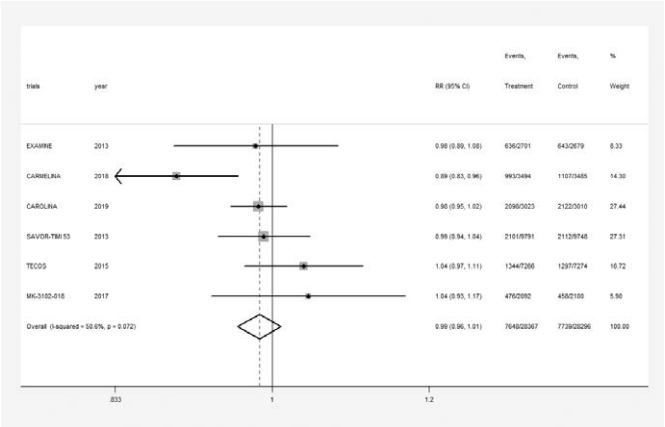
Objective: To evaluate the risk of infections in the treatment of type 2 diabetes patients with dipeptidyl-peptidase 4 (DPP-4) inhibitors in Cardiovascular Outcome Trials.

Methods: A literature search was conducted through electronic databases. The inclusion criteria included randomized controlled, cardiovascular outcome trials which made direct comparisons of DPP-4 inhibitors with placebo or active antidiabetic drugs. 6 Trials with 53,616 patients were finally included. Pooled relative risks (RRs) were calculated using random or fixed-effects models, as appropriate.

Results: The use of DPP-4 inhibitors was not associated with the risk of developing an overall infection (RR = 0.98, 95% CI,0.95 to 1.02), a serious infection (RR = 0.96, 95% CI, 0.85 to 1.08), an opportunity infection (RR = 0.73, 95% CI, 0.49 to 1.09), respiratory infection(RR =0.99, 95% CI, 0.95 to 1.03), urinary tract infection(RR = 1.02, 95% CI, 0.95 to 1.11), soft tissue infection(RR = 0.81, 95% CI, 0.60 to 1.08), abdominal and gastrointestinal infections(RR =1.02, 95% CI, 0.83 to 1.25), bone and joint infections(RR =0.96, 95% CI, 0.68 to 1.36), and bloodstream infection(RR = 0.96, 95% CI, 0.79 to 1.18). The cumulative Z curve crossed neither the conventional nor the TSA boundary for benefit or harm but did cross the boundary for futility having exceeded the required information size (RIS) for the above analysis.

Conclusions: The risk of infections of DPP-4 inhibitor was not increased compared with control groups.



WOCS-16-2

Effect of tryptophan-selective lipidated GLP-1 peptide on GLP-1 receptor in vitro and in vivo

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[Aim] GLP-1 receptor agonists, such as liraglutide (L), have a structure with fatty acid acylation. We synthesized new lipidated GLP-1 peptide in which palmitic acid (C16) and 8-amino-3,6-dioxaoctanoic acid (PEG) are attached to 31st tryptophan. We evaluated the effect of the peptide on GLP-1 receptor (GLP-1R). [Method] PBS, L, Peptide A [C16+PEG×1] (A), and Peptide B [C16+PEG×3] (B) were used. Intracellular cAMP production and insulin secretion were measured using GLP-1R-expressing COS-7 and MIN6, respectively. Insulin and blood glucose (BG) levels during OGTT, gastrointestinal (GI) transit, food intake, and c-Fos-positive cell number in arcuate nucleus (ARC) were evaluated after acute injection of PBS, L, A, or B in wild-type mice. PBS, L, A, or B was injected in high-fat diet fed mice for 2 weeks and body weight was measured. [Results] A and B had similar cAMP production and insulin secretion with L. Insulin levels were greater and BG levels and GI transit were lower in L, A, and B group compared to those in PBS group. L and A but not PBS and B reduced food intake. L, A, and B increased c-Fos-positive cell number but the number was significantly higher in L and A group than that in B group. Body weight was lower in L and A group compared to that in PBS and B group. [Conclusion] Tryptophan-selective lipidated GLP-1 had similar insulin secretion and GI transit inhibition with liraglutide, while the number of PEG which is attached to the lipidated GLP-1 affected food intake and body weight.

WOCS-16-3

Comparison of the oral and injectable semaglutide use in patients with type 2 diabetes: a survey from medical records

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Objective: To provide useful data for the formular selection of semaglutide.
Methods: A comparative observational survey was performed on medical records. A total of 230 outpatients with type 2 diabetes (T2D) were administered with oral semaglutide (OS, n=135) or injectable semaglutide (IS, n=95) between June 2021 and October 2022. Differences in the clinical background at baseline, 24-week course, and characteristics of patients who discontinued treatment were investigated between the two drugs.
Results: Median age, BMI, and HbA1c at baseline were 62 vs 56 years (P<0.05), 27.5 vs 27.4 kg/m^2 (P=0.60), and 7.7 vs 8.5% (P<0.05), OS vs IS respectively. The percentages of pre-treatment injection, DPP-4 inhibitor, metformin, and SGLT2 inhibitor use were 17.1 vs 60.9% (P<0.05), 55.6 vs 12.7% (P<0.05), 86.3 vs 76.2% (P=0.09), and 84.6 vs 76.2% (P=0.16), OS vs IS respectively. After 24-week treatment, both OS and IS significantly reduced body weight and HbA1c with no between-drugs differences. There were no between-drugs differences in the discontinuation ratio (25.6 vs 38.1%) and the duration from baseline to discontinuation (10.5 vs 18.0 weeks, OS vs IS respectively). However, significant reductions in body weight and HbA1c from baseline to discontinuation were observed only in IS but not in OS. Gastrointestinal symptoms that caused discontinuation were observed in 40.0% for OS and 20.8% for IS (P=0.16).
Conclusion: Compared to IS, OS could be used in older patients with the earlier stage of T2D, but gastrointestinal symptoms should be noted and otherwise OS would be discontinued before glucose or weight loss is achieved.

WOCS-16-4

Effects of combination therapy with GLP-1RA and SGLT2i on hepatic steatosis and atherosclerosis in diabetic mice.

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Objective
Glucagon-like peptide-1 receptor agonists (GLP-1RAs) and sodium-glucose cotransporter 2 inhibitors (SGLT2is) have multiple effects on the heart, kidneys, and liver, in addition to their glucose-lowering effects. However, effects of combining these drugs have not been adequately examined. Thus, we have studied the effects of single or combined use of liraglutide (GLP-1RA) and ipragliflozin (SGLT2i) on hepatic steatosis and atherosclerosis in murine diabetes models.

Methods
Using diet-induced obese (DIO) and db/db mice as models of the early and advanced stages of type 2 diabetes, we evaluated the histological changes in the liver and expressions of several genes important for hepatic lipid metabolism after treatment with single or combination therapies of liraglutide and/or ipragliflozin. Furthermore, ApoE-deficient mice made diabetic with nicotinamide and streptozotocin have been subjected to studies of histological atherosclerotic changes in the aortic sinus and expressions of atherosclerotic genes after similar treatments.

Results
The combination therapy with liraglutide and ipragliflozin for 4 weeks in both DIO and db/db mice significantly reduced hepatic lipid accumulation and improved expressions of genes associated with lipid metabolism. Significant changes of some parameters were observed in mice treated with the combination therapy but not monotherapies. Similarly, the combination therapy but not monotherapies for 8 weeks reduced intraplaque lipid deposition at the aortic sinus and improved MCP-1 expression in the aorta of diabetic ApoE-deficient mice.

Conclusion
Our data suggest that the combination therapy with liraglutide and ipragliflozin is better choice for the treatment of type 2 diabetes with hepatic and cardiovascular complications.

WOCS-16-5

The association between the use of GLP-1 RAs and the incidence of asthma in patients with T2DM and/or obesity

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Objective: Recent studies have indicated potential anti-inflammatory effects of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in asthma, which is often comorbid with type 2 diabetes mellitus (T2DM) and obesity. Therefore, we conducted a meta-analysis to evaluate the association between the use of

GLP-1RAs and the incidence of asthma in patients with T2DM and/or obesity.

Methods: PubMed, MEDLINE, Embase, the Cochrane Central Register of Controlled Trials and *Clinicaltrial.gov*, were systematically searched from the inception to October 2022. Randomized controlled trials of GLP-1RAs, as well as dual and triple receptor agonist, with reports of asthma events were included. The outcomes were computed as risk ratios (RR) in fixed-effect model.

Results: Thirty-six RCTs with 77,026 participants were included. Compared with non-GLP-1RAs users, a trend of reduced risk of asthma were observed in patients with GLP-1RAs treatment, although a statistical significance was not reached (RR=0.90, 95%CI 0.64 to 1.25). Similar trends were also unveiled in patients with nondiabetic obesity (RR=0.49, 95%CI 0.12 to 1.96), in patients with duration of diabetes over 10 years (RR=0.82, 95%CI 0.51 to 1.31), in the female predominant trials (RR=0.73, 95%CI 0.29 to 1.82), in patients with light-molecular-weight GLP-1RAs (RR=0.67, 95%CI 0.43 to 1.06), and in patients with short-acting GLP-1RAs (RR=0.56, 95%CI 0.20 to 1.53).

Conclusion: In general, compared with non-users, a trend of modest risk reduction was indicated in the patient with GLP-1RAs treatments, but the statistical significance was not reached. More investigations are warranted to further evaluate the association between GLP-1RAs and the risk of asthma.

WOCS-16-6
Evaluation of physical activity level, calorie intake, quality of life and cognitive function in EMPA-ELDERLY trial

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Objective: To evaluate the effect of empagliflozin 10 mg for 52 weeks on physical activity level, calorie intake, quality of life, and cognitive function in Japanese elderly adults with type 2 diabetes (T2D).

Methods: Adults with T2D aged 65 years or older with HbA1c between 7% and 10% on diet and exercise alone or on oral hypoglycemic agents with a BMI of 22 kg/m^2 or higher were randomized and administered empagliflozin 10 mg or placebo orally once daily for 52 weeks in a double-blind fashion (Total 129 patients). The change in HbA1c from baseline was evaluated as the primary outcome. The change in free-living physical activity from baseline was evaluated by accelerometer. The change in energy, protein and carbohydrates intake from baseline were computed by food frequency questionnaire. Quality of life (EQ-5D-5L) and cognitive function (MMSE-J) were descriptively estimated.

Results: The HbA1c was significantly lower in empagliflozin group after 52 weeks of treatment (-0.57 ± 0.11%, p<0.0001). There was no statistical difference in physical activity (placebo -2.058 ± 3.072 (mean ± SE) and empagliflozin -5.647 ± 2.475 min), energy intake (placebo -24.7 ± 53.2 and empagliflozin 43.0 ± 46.7 kcal), protein and carbohydrates intake between groups. Descriptive results of quality of life and cognitive function indicated similar score between groups.

Conclusion: Administration of 10 mg empagliflozin did not impact physical activity level, energy, protein, and carbohydrates intake after 52 weeks. Moreover, it did not change the quality of life and cognitive function in Japanese elderly adults with T2D.

WOEC-01-1
Awareness of hyperuricemia and gout among patients with diabetes and community health workers: a community survey

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Objective: Hyperuricemia has a high incidence in patients with diabetes.This study aimed to assess awareness of hyperuricemia and gout among community health workers and patients with diabetes.

Methods: Two questionnaires were designed to investigate awareness of hyperuricemia and gout among community health workers and patients with diabetes in Chenghua District, Chengdu.

Results: The average score of community health workers was 17.74/30 (59.13%). Approximately half of general practitioners (GPs) knew the target serum uric acid level of hyperuricemia and gout. Only 11.15% of GPs were fully aware of the preferred medicine for acute gout. Most general practitioners had no idea about the contraindication of colchicine (86.69%) and the types of drugs inhibiting uric acid synthesis (65.11%). Approximately 32.28% of patients with diabetes knew about hyperuricemia, and 60.83% knew about gout. Most patients with diabetes (87.42%) declared that hyperuricemia would certainly develop gout. Almost 66% agreed that massage or a hot compress could be used when gout acute arthritis attacks.

Conclusions: The awareness of hyperuricemia and gout among community health workers and patients with diabetes was low.

WOEC-01-2
Development of Diabetic Ketoacidosis Extraction Algorithm for a Large-scale Clinical Database

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Objectives

We created an outcome definition(def) to identify DKA cases requiring hospitalization (DKA-def) from MID-NET, a large-scale infrastructure database of Data-driven medical studies established for drug safety by PMDA.

Methods

We create ①a def to include all possible cases(APC-def), ②DKA-defs by combining the APC-def with the items of diagnoses, clinical tests and drug information(inf), ③refined DKA-defs by including or excluding important variables obtained by machine learning using integrated data from multiple institutions.

Results

① The APC-def is "There are ketoacidosis(KA) or KA-related diagnoses in the 6 items
of DPC inf and the EHR." The PPV and sensitivity was 47.9 and 100%.

② 11 DKA-defs were created by combining the APC-def with items related to the diagnoses,
drug inf such as insulin and glucose infusion, and pH and HCO3- results recorded in EHR. The def of "There are KA or KA-related diagnoses in 3 items of DPC inf(main, triggering hospitalization and needed the most medical resources) and EHR" resulted in PPV of 59.5% and sensitivity of 95.7%, resulting in a practical DKA-def.

③ 2 defs were obtained using variables obtained by machine learning of 1971 data items on
EHR as explanatory variables: one focused on the higher PPV and the other higher sensitivity. The PPV and sensitivity were 88.1, 75.6%, and 80.0, 81.9%, respectively, resulting in a universal improved DKA-defs.

Conclusion

The usefulness and practicality of utilizing medical inf databases in the evaluation of drug efficacy and safety in the field of diabetes were demonstrated.

WOEC-01-3

Medications and medical expenditures for diabetic patients with osteoporosis

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Objective: This study aimed to clarify the changes in treatment regimens and medical expenditures in diabetic patients with osteoporosis.

Methods: We recruited 2,853,036 diabetic patients from the Beijing medical insurance database between 2016 and 2018. Among them, 406,221 patients also had osteoporosis. Clinical characteristics, treatment regimens, and medical costs were investigated in diabetic patients with and without osteoporosis.

Results: Diabetes and osteoporosis were most prevalent in participants aged 45−84 years (89.00% and 92.32% in 2018, respectively). Compared with men, women had a higher prevalence of osteoporosis. Diabetic patients with osteoporosis were prone to developing comorbidities and diabetic complications. They often required multiple glucose-lowering drugs(74.52% vs. 63.64%, 2018) and had a higher rate of insulin use(27.96% vs. 25.39%, 2018). Similarly, osteoporosis leads to an increased number of medications for non-hypoglycemia(2.65 ± 1.89 vs. 2.07 ± 1.86, 2018, $P < 0.01$) as well as higher healthcare costs(12312.88 ± 10634.09 vs. 9862.77 ± 9259.74, 2018, $P < 0.01$). These medications and costs increased with the number of complications and comorbidities. From 2016 to 2018, although diabetic patients with osteoporosis took more drugs, medical costs were lower year by year.

Conclusions: Osteoporosis might contribute to a worse condition in diabetic patients, and this population often requires more medications with higher medical costs.

WOEC-01-4

Temporal cardiorenal complications and health-related quality of life in Chinese patients with type 2 diabetes

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Background

Type-2 diabetes (T2D) is associated with increased risk of cardiorenal complications and co-morbidities over lifetime with impaired health-related quality of life (HRQoL) being an independent predictor of mortality. Despite the epidemic of diabetes in Asia, there is a paucity on data pertaining to HRQoL in these populations.

Objective

Explore immediate and residual impacts of cardiorenal events on HRQoL in year of occurrence and subsequent years thereafter respectively.

Methods

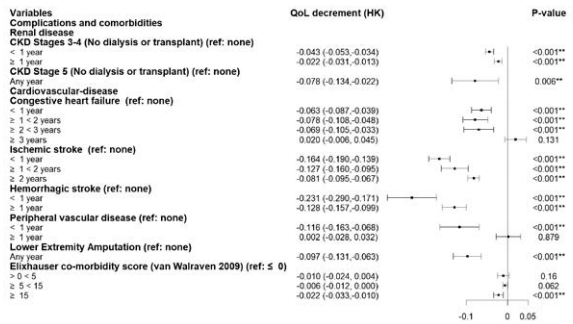
19,322 participants from two public and a private hospital diabetes centre (2007 to 2018) in Hong Kong enrolled in the Joint Asia Diabetes Evaluation (JADE) Register completed EQ5D-3L for assessment HRQoL had documentation of risk factors and clinical outcomes. We estimated HRQoL decrements associated with time-updated cardiorenal complications categorized by ICD-9 codes and Elixhauser co-morbidity score (ECI) (Van-Walvaren weights) using generalized-linear model, adjusted for baseline characteristics. HRQoL utility scores were mapped to Hong Kong tariff and stepwise covariate selection (p-value <0.01) was used to determine the final model.

Results

In descending order, large and long-term decrements were observed in patients who experienced hemorrhagic stroke, ischemic stroke, peripheral vascular disease, lower extremity amputation, congestive heart-failure, CKD stage-5 and stage-3 (both without dialysis or transplant) (Figure 1). Coronary heart disease and CKD stage-5 with renal-replacement therapy were not associated with HRQoL decrements. Higher ECI scores were associated with larger HRQoL decrements.

Conclusion

These regression models considering immediate and residual HRQoL decrements associated with cardiorenal events will provide accurate assessments of long-term net effects and cost-effectiveness of interventions for preventing T2D-related cardiorenal complications.



WOEC-01-5

Effective diabetes self-management education on the sustainability of metabolic control in persons with type 2 diabetes.

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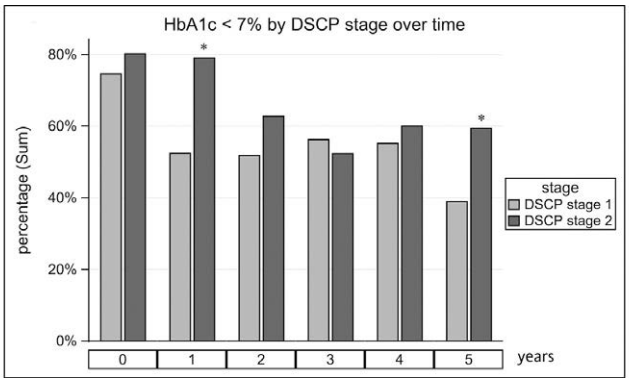
Objective: To study the frequency and sustainability of DSME for improving metabolic control.

Methods: The Diabetes Share Care Program (DSCP) stage 1 provided DSME every three months. If participants entered DSCP stage 1≥ 2 years and HbA1c < 7%, they could be transferred to stage 2, in which DSME frequency was decreased to once a year. We identified propensity score-matched 311 type 2 diabetes in DSCP stage 1 and 86 in DSCP stage 2 and evaluated their metabolic control and healthy behaviors annually for 5 years.

Results: The mean HbA1c was 6.7% ± 0.6%. In the first year, the HbA1c in the DSCP stage 2 group was lower than that in the DSCP stage 1 group. In the first and the fifth years, the percentage of patients achieving HbA1c < 7% was higher in the DSCP stage 2 group than in the DSCP stage 1 group. There was no difference in blood pressure and low-density lipoprotein cholesterol between these two groups during the 5-year follow-up. Among behaviors, self-monitoring of blood glucose (SMBG) frequency was associated with a reduced HbA1c after 5 years.

Conclusion: We demonstrated the sustainable effects of at least 2-year DSME on achieving better glycemic control for at least 1 year. SMBG contributed to improved glycemic control. The results may be applied to the reimbursement strategy in diabetes education.



WOEC-01-6

Diabetes Complications in Primary Health Care:Determinants, Metabolic Profile, Psychocological Aspect and Family Support

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Objective

To study comprehensively about diabetes complications in PHC in Jakarta as Indonesian capital city.

Methods

This is a cross-sectional study that recruited 200 adult T2D patients in 10 Jakarta PHC. Data collection was carried out through interviews, food record, questionnaires and health examinations.

Results

We found that prevalence of DM complication is 76,6%. The most prevalent was albuminuria (48,7%), followed by diabetic retinopathy (36%), cardiac complications (18%), neuropathy (17,5%) and PAD (10%). Majority of patients were female and long-standing diabetes. The mean HbA1C was 8,5% and BMI was 27 kg/m^2. High HbA1C ³ 7% (OR 2,381 95% CI 1,429-3,466) and uncontrolled blood pressure (RR 1,641 95%CI 1,011-2,83) were the associated risk factors. Compared to group without complications, there were more subjects with T2D complication who were obese, central obesity, hypertension, and poor lipid profile (high LDL-cholesterol, fasting triglyceride and non-HDL cholesterol). Majority of subjects showed high fat and low protein intake, low physical activity, and poor medication adherence. Most of subjects (88,3%) only consumed OAD, while Insulin was only used by 2% of patients. Only 40% of patients treated with Statin. As much as 30% of patients were depressive, complaining about family support, and 60% of patients did not satisfy on their conditions.

Conclusion

This study demonstrates high burden of diabetes complications in primary health care in Jakarta. Determinants of complications are uncontrolled blood glucose, hypertension, obesity, and poor lipid profile. The subjects showed poor nutritional intake, physical activity, medication coverage and adherence, psychological wellbeing and family support.

WOEC-02-1

Endocrinology healthcare workers' knowledge, attitudes, and practice of screening pre-ulcerative diabetic foot lesions

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Objective: To investigate knowledge, attitude and practice of screening pre-ulcerative lesions among endocrinology healthcare workers.

Methods: Questionnaires were developed and distributed online and 1004 valid questionnaires were returned.

Results: Knowledge, attitude, and practice of screening for pre-ulcerative lesions were 45.46±16.26, 92.11±10.50, and 72.27±17.63. Most participants had been trained to screen for pre-ulcerative lesions, but 39.8% still had not been trained. And 31.8% hospitals did not offer relevant screening projects. Positive relationships were between knowledge and practice, and attitude. Multiple linear regression analysis showed that: level II hospital and tertiary hospital were the main factors influencing knowledge scores; Undergraduate and participating in relevant training were the main factors influencing attitude scores; participating in relevant training, hospital conducts relevant project, and patient cooperation, and working hours were the main factors influencing practice scores.

Conclusion: Endocrinology healthcare workers need more knowledge about pre-ulcerative lesions, and screening practices need to be strengthened. Enhanced education and training of screening pre-ulcerative lesion should be implemented in endocrinology departments.

WOEC-02-2

Effectiveness of self-help interventions for psychological outcomes among people with diabetes: A meta-analysis

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Objectives: This study aimed to evaluate the pooled effects of self-help interventions (SHI) on psychological outcomes among people with diabetes (PWD).

Methods: Five databases were investigated by recruiting studies for adult PWD, implemented SHI, and reported interested outcomes were included. Studies that reported SHI on diabetes gestational/pregnant women were excluded. The endpoint was psychological outcomes, including diabetes distress, depression, and anxiety. The Hedge's g and 95% confidence interval (CI) were reported in immediate-term, mid-term, and long-term as pool estimates of effect size using random effect model. To explore the heterogeneity, I^2 and Q value were used.

Results: Of 1,438 identified studies, only 11 provided data for meta-analysis. Total of 2,275 PWD included in the study with mostly female (64.97%) and age was 54.98 years. This meta-analysis showed significant immediate-term effects of SHI on diabetes distress (Hedges' g = -0.363, 95%CI = -0.554;-0.173), depression (Hedges' g = -0.465, 95%CI = -0.773;-0.156), and anxiety (Hedges' g = -0.295, 95%CI = -0.523;-0.068) for PWD. The significant pooled effects were also recorded at the mid-term effect on diabetes distress (Hedges' g = -0.195, 95%CI = -0.374;-0.016), but it did not work for long-term effect.

Conclusion: This study indicates that SHI could immediately decrease diabetes distress, depression, and anxiety for PWD. In the mid-term effect, the interventions also help to reduce diabetes distress.

WOEC-02-3

Continuous subcutaneous insulin infusion versus multiple daily injection therapy in pregnant women with type 1 diabetes

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Objective

To compare glycemic control and pregnancy outcomes of women with type 1 diabetes using continuous subcutaneous insulin infusion (CSII) and multiple daily injection therapy (MDI) in pregnancy.

Methods

We conducted a prospective cohort involving pregnant women from 11 centers in China. Out of the 121 women, 65 were treated with MDI and 56 were using CSII therapy. The primary outcome was a composite pregnancy outcome including one or more of cesarean section, preeclampsia, pregnancy-induced hypertension, pregnancy loss in the second trimester, congenital malformations, preterm birth, macrosomia, large for gestational age, small for gestational age,

and neonatal hypoglycemia. Secondary outcomes included glycosylated hemoglobin (HbA1c) in pregnancy, components of the composite, and suboptimal outcomes (progression in microvascular complications, neonatal jaundice, and admission to the neonatal intensive care unit [NICU]).

Results At baseline, CSII users were more well-educated (P=0.044), had longer duration of diabetes(P=0.009), and were more likely to receive preconception counseling (P=0.004). CSII and MDI users had comparable HbA1c at first-trimester glycemia (P=0.807) and second-trimester glycemia (P=0.281). At 34 weeks, CSII users had a greater decline in HbA1c (6.02±0.62 vs. 6.25±0.88, P=0.017) and higher HbA1c on-target rate (71.43% vs. 65.63%, P=0.03). The incidence of composite pregnancy outcome did not differ between the groups (80.36% in CSII group vs. 76.92% in MDI group, P=0.291). CSII users had higher rates of neonatal jaundice (adjusted OR 2.69 95%CI1.45-5.00) and NICU (adjusted OR 2.00 95%CI1.13-3.54).

Conclusion CSII may better than MDI for glycemic control, while did not substantially affect the risk of optimal pregnancy outcome.

WOEC-02-4

Community based collaboration and peer support for diabetes care in China

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Objective: The Shanghai Integration Model (SIM) has started to improve diabetes care in China.

Methods: From 2019-2021, the SIM included a general model of cross-sector collaboration and peer support in 12 Peer Leader communities (PLCs), with 4 comparison communities (CCs). Implementation assessment documented community adaptation of standardized intervention components: public education, neighborhood activities, diabetes education classes, diabetes management meetings, follow-up with individuals and families, and online communication.

Results: Among those with baseline and follow-up data (n=1066), reductions of HbA1c favored the PLCs (-0.06±1.27 vs 0.22±1.56, p<0.001) with controlling for confounders and baseline HbA1c. Parallel analyses showed significant reductions favoring PLCs for FPG (-0.04±2.50 vs 0.76±2.84, p<0.001), diabetes distress (-0.07±0.41 vs 0.06±0.37, p=0.004), and depressive symptoms (PHQ-8) (-0.49±3.21 vs 0.54±2.73, p=0.002). Among those with elevated baseline levels, greater reductions for PLC vs CC were observed for those with baseline HbA1c ≥ 8% and FPG > 7 mmol/L. Significant differences were not observed for SBP, DPB, or general quality of life (EQ5D). A slight difference favoring CCs was observed among those with baseline LDLc ≥2.6 mmol/L (-0.28±0.90 vs -0.38±0.86, p=0.042). To assess consistency among the significant PLC vs CC differences for HbA1c, FPG, diabetes distress, and depressive symptoms, we examined gender differences, examining interactions between treatment (PLC vs CC) and gender. No significant interactions were found.

Conclusion: Community organization of PL for diabetes management implemented through community groups and community health centers showed greater changes in glucose control, diabetes distress, and depressive symptoms. These changes were generally consistent across gender differences.

WOEC-02-5

Study on the effect of diabetes digital management APP for self-management in patients with type 2 diabetes

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Objective To investigate the effect of digital diabetes management APP on self-management in patients with T2DM. **Methods** A total of 273 T2DM patients were randomly divided into 4 groups: blank group (C1 group, 68 patients), telephone follow-up group (C2 group, 67 patients), APP group (I1 group, 68 patients) and APP + telephone follow-up group (I2 group, 70 patients). The HbA_{1c}, blood pressure, and BMI of patients were collected at baseline and 3 and 6 months after intervention, and the frequency of self-blood glucose monitoring was measured after intervention. **Results** After intervention, the compliance rate of HbA_{1c} in I1 and I2 groups was higher than that in C1 and C2, with no difference between groups (44.0%, 45.5% vs 34.7%, 33.0%, $P > 0.05$). There were differences in systolic blood pressure which was lower in groups I1 and I2 than C1 (123.62, 124.78 vs 131.94, $P < 0.05$), and also lower in group I1 than C2 (123.62 vs130.61, $P < 0.05$) . Factorial analysis showed that APP reduced systolic blood pressure ($P < 0.05$). The proportion of patients with self-glucose monitoring in groups C2 and I2 was higher than that in C1 and I1, but there was no difference between groups (77.2%, 72.7% vs 69.4%, 58.0%, $P > 0.05$). **Conclusion** The use of digital diabetes management APP can improve the standard of HbA_{1c} and reduce systolic blood pressure in T2DM patients. There is no difference between digital diabetes management APP and telephone follow-up for self-glucose monitoring in T2DM patients.

WOEC-02-6

Exploring an online training program on motivational interviewing and diabetes for health care providers

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【Objective】People with Diabetes are required to make decisions daily. As per the ADA and EASD guidelines, motivational interviewing(MI) is a key skill that medical professionals need to communicate with patients. Although the awareness of MI is expanding in Japan, very few healthcare providers canappropriately use it. MI trainees usually have to attend several workshops or training courses. However, in the last 3 years, in- person meetings or training sessions have been canceled because of the COVID-19 pandemic.We aimed to determine the needs of healthcare providers with regards to MI training.

【Methods】In December 2020, we established the Diabetes Mellitus Motivational Interviewing

(DMMI) -study group, which provided free online training an monthly 2-hour long sessions.The

participants joined the group voluntarily of though referrals. We investigated the growth in the membership of various healthcare professionals since the group's inception.

【Results】As of February 2023, membership has grown rapidly to 122 members. The professional breakdown the group members is as follows : physicians, 37%; nurses,28%; dietitins,23%; pharmacists, 7%; psychologist,1%; and other professionals,4%. A wide range of professions indicate a need

for MI. Within the healthcare institutions, the propotion of dietitians is much smaller than that of physicians and nurses, but the proportions of them in the DMMI-study group were similar as nurses.Therefore, dietitians are more interested in MI training than other healthcare providers specializing in diabetes care.

【Conclusion】The need for web-based MI learning oppotunities is high among healthcare providers.

WOEC-02-7

Investigation and analysis of the status of insulin injection management in hospitals at all levels inChina

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Objective:To investigate the status of insulin injection management in hospitals at all levels in 31 provinces and autonomous regions, so as to provide

references for promoting standardized and homogenized management of insulin injection in hospitals.
Methods:Nursing managers in 1075 hospitals in 31 provinces, municipalities and autonomous regions were surveyed by stratified random cluster sampling from January to February 2019 with a self-designed questionnaire.
Results:A total of 1075 valid questionnaires for nursing managers from nursing departments, and 1 5794 valid questionnaires for nursing managers from clinical departments were collected.976 (90.79%) surveyed hospitals manage insulin as a high-risk drug. More than 80% surveyed hospitals formulated insulin injection specifications at the hospital level or department level, provided regular training and assessment, and organized insulin injection training for new nurses.828 hospitals (77.02%) regularly carried out insulin management quality control. Insulin management institution and insulin management status of departments in different levels of hospitals, and insulin management status in different departments showed statistically significant differences (P<0.001).Insulin management was more standardized in hospitals with regular quality control of insulin management (P<0.001).
Conclusion:Insulin management institution in hospitals at different levels in China needs to be improved, and the quality of insulin management in departments needs to be improved. Insulin management in different hospitals and departments needs to be homogenized.It is necessary to strengthen the insulin injection management in primary hospitals and non-endocrinology departments.

WOEC-03-1

Evaluation of Nursing Educational Material on Oral Health Behavior of Persons with Diabetes: Part 3—Physicians' Survey

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Objective: To examine physicians' evaluation of nursing educational material, as a team, to educate persons with diabetes on improving oral health behavior.
Methods: An anonymous self-reported questionnaire survey (five-point Likert scale) was conducted to evaluate appropriateness of the educational material (developed in previous studies). It targeted physicians involved in diabetes care in prefecture A. The educational material contained 32 items: oral health conditions (four items), oral hygiene behaviors (eight items), perceptions and knowledge of oral health behaviors (four items), health record sharing (four items), third molar (three items), tooth extraction (one item), dentures (six items), and oral problems (two items). The survey also included physicians' perceptions about oral health of persons with diabetes and expectations of nurses in oral health. Descriptive statistics and content analysis were performed for numerical values and free response items, respectively.
Results: Seventeen physicians (age 41±11 years), including five (29%) diabetologists, participated. All items were evaluated as appropriate/somewhat appropriate by 15 physicians (88%). Four items (including related to dry mouth) were evaluated as inappropriate/slightly inappropriate by only one physician each. The physicians believed it was necessary to inform persons with diabetes about "dental visits," "relationship between diabetes and oral diseases," and "method of oral care"; they expected nurses to "provide knowledge," "encourage and motivate oral care and dental visits," and "collect information on oral health and provide it to physicians."
Conclusion: Most physicians evaluated the educational material items as adequate. They expected nurses to provide specific support, suggesting the need for using educational material.

WOEC-03-2

Potential of role-playing in training medical staff who care for patients with diabetes

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Objective:
To provide medical staff the opportunity to develop their communication skills with patients with diabetes using training seminars that incorporate the role-playing method and evaluating the potential of such seminars.

Methods:
Before the COVID-19 pandemic, this seminar was conducted with participants working in small groups and playing the roles of patient, medical staff (diabetes educator), and observer in-person. Realistic simulated scenarios based on common clinical situations of patient-medical staff interactions were performed. During the pandemic, however, the seminars were conducted online as an alternative to in-person style. Participants were asked to answer a questionnaire which self-assessed their individual roles and impressions of the online seminar compared to that of in-person.

Results: As of March 2023, 74 seminars have been conducted and 2200 medical staff have participated in the seminars. Participants' impressions about the seminars were mostly positive. The representative answers were: "By playing the role of patient, I could understand patients' experience when they engage with medical staff," "Playing the role of an educator helped me recognize that my knowledge is insufficient," and "By observing other role player's conversations, I learned new interview skills." The positive aspects of online seminars were reduction in time and travel costs and removal of geographical obstacles. The negative aspects mostly regarded technology-related concerns.

Conclusion: The role-playing method used in the training seminars were generally evaluated as helpful for medical staff to improve their communication skills. Although online seminars have both advantages and disadvantages, they can be an effective tool for conducting seminars.

WOEC-03-3

The Research of Experiential Learning Family Empowerment Education in Insulin Injection Education for diabetes Patients

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Objective: To explore the application effect of experience learning combined with family empowerment education model in insulin injection skills education for elderly patients with diabetes. Methods: Type 2 diabetes patients over 60 years old who received insulin therapy for the first time were selected as the study subjects. According to the time of admission, 100 patients in each group were given routine education in the control group. On this basis, the intervention group conducted experiential learning in combination with family empowerment education. The HbAlc, insulin pen injection skill score and insulin injection site pain score were compared between the two groups at

discharge and 3 months after discharge. To analyze the effect of experiential learning combined with family empowerment education model on insulin pen injection skills and behaviors of elderly patients with diabetes. Results: Before the experiment, there was no significant difference between the two groups in HbAlc, insulin pen injection skill score, and pain score of insulin injection site (P>0.05); After the experiment, the control of HbAlc and the score of insulin injection skill in the two groups were significantly higher than those in the control group (P. Conclusion: Experiential learning combined with family empowerment education model can improve the elderly patients with diabetes to master the skills of insulin pen injection and insulin injection related knowledge, improve the compliance behavior, reduce the pain of insulin injection, and effectively reduce the level of HbAlc, which is worth popularizing in clinical education.

WOEC-03-4
Effect of training for Diabetes Specialist Nurse teachers based on core competency framwork

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Objective: To construct a training program for diabetes specialist nurse teachers based on core competence framework, and to evaluate the training effect.
Methods: The training program includes 3 weeks of theoretical course and 2 weeks of clinical practice. The theoretical course covers six modules: diabetes professional knowledge, diabetes-related knowledge, communication skills and health education ability, specialized skills, clinical judgment and specialty development capacity. At the same time, foreign experts in diabetes care and education were invited to introduce structured diabetes education program, diabetes educator certification system, diabetes health education strategies, etc. In the theoretical course, interactive and participatory teaching methods such as world coffee and workshop were used to discuss urgent problems in the field of diabetes care The clinical practice includes clinical teaching, patient education, skill operation, and case report.
Results: The six core competence of the teachers were significantly improved after the training program,and the course satisfaction reached 100%.
Conclusion: The training of diabetes specialist nurse teachers based on the core competence framework has a good effect and is worth promoting.

WOEC-03-5
Molecular network regulated by dietary resistant starch

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Dietary resistant starch (RS) is an effective intervention for metabolic dysfunction, however, the related pathways remain elusive. In order to reveal the molecular network regulated by dietary resistant starch, we collected the plasma proteome and lipidome data in individuals with non-alcoholic fatty liver disease (NAFLD) before and after RS intervention for 4 months. We found that the RS could significantly modulate certain lipids and proteins as early as the first month after intervention, especially the short-chain fatty acids and TGs with saturated fatty acids, while long-chain polyunsatureated fatty acids remained unchanged. The changes of most TGs obviously correlated with changes of BMI, fatty-liver index and HOMA-IR. The proteins related with oxidative stress and inflammation status were also regulated significantly by RS. Based on systems analysis, the molecular network integrating proteins and lipids further uncovered the treatment trajectory as a result of RS intervention. All the results show that the RS could alleviate NAFLD and insulin resistance through pathways dependent or independent on body-weight loss, revealing new insights and targets for metabolic intervention.

WOEC-03-6
The actual use of the online meal management application named "Oishi-Kenko" at home by people with diabetes

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Objective: "Oishi-Kenko" App can help people with diabetes cook their meals at home. In this study, we aimed to clarify the actual App use.

Methods: Study participants of multi-center, multi-purpose cohort study, Kamogawa-DM cohort study(RBMR-E-466), were invited to use the app free of charge for one year. In this study, we observed the actual conditions of app use by analyzing app log information on app users through the end of February 2023 (ERB-C-2421).

Results:Among 52 subjects, the average number of app usage days per week was 0.77. The average usage frequency during the first week was the highest (2.7 days) and decreased from the second week. The search log analysis suggested that male users had a poorer vocabulary for food-related search keywords than female users. In the recipe search log, tags such as "concerned about salt intake (16.2%)" and "want to take dietary fiber (14.7%)" were frequently selected by users.

Conclusion: There were individual differences in the usage rate of the app, and we need to develop strategies to encourage continued use from the second week onward. Additionally, we aim to conduct further analysis of the utilization of app's function to reveal users' choice behavior when people with diabetes cook their meals at home.

WOEC-03-7
Physical activity is associated with increased urine glucose excretion in Chinese adults: a population-based study

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Background: Increased physical activity (PA) is important in the prevention and control of diabetes. However, its effect on urine glucose excretion (UGE), an emerging treatment target for diabetes, remains unknown. This study aimed to evaluate the association between PA and UGE in Chinese adults.

Methods: This was a population-based, multicenter cross-sectional study conducted in 8 cities in China. A total of 10774 community-dwelling adults without previous history of diabetes were included. Participants were given a 75g oral glucose tolerance test, where 2-hour UGE was quantitively measured. Glycemic status was ascertained according to the American Diabetes Association criteria. PA levels were obtained using self-reported questionnaires and categorized into no, low, and high PA groups. Linear and logistic regression models were used to assess associations between PA and UGE.

Results: The mean age of participants was 49.8±13.0 years, and 68.6% were women. UGE was highest in the high PA group in the overall population and in different glycemic status groups compared with no PA or low PA group. After adjustment for age, sex, ethnicity, and HbA1c, PA was positively associated with UGE (standardized β=0.47, $p<0.001$). Multivariable logistic regression showed that high PA was associated with an increased odd of high UGE (defined as UGE exceeding the 75th percentile in different glycemic status) (OR 3.30, 95% CI 2.96-3.68), and this association remained comparable in participants stratified with different glycemic status.

Conclusion: PA was associated with increased UGE in Chinese adults, which may provide a new explanation for reduced glucose related to increased PA.

WOEC-03-8

The Impacts of 90 Minutes a Week in Four Weeks of Moderate-Intensity Exercise on Leptin in Type 2 Diabetes Mellitus

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Objective: Leptin resistance is common amongst patients with type 2 diabetes mellitus (T2DM) and could be improved by physical exercise. However, most T2DM patients do not adhere to the recommended 150 minutes per week of moderate- to high-intensity exercise. Only a few studies have evaluated the effects of short duration and short periods of exercise on leptin levels. Therefore, we aimed to investigate the impact of 90 minutes per week in four-week moderate-intensity treadmill exercise on leptin levels in Asian males with T2DM.

Methods: Twenty-two males with type 2 diabetes mellitus were divided into exercise and control groups. The exercise group was assigned 30 minutes of moderate-intensity treadmill exercise for four weeks, three sessions per week. The control group exercised independently. At the four-week intervention's beginning and end, weight, height, body mass index (BMI), insulin, fasting plasma glucose (FPG), and leptin levels were measured and analyzed.

Results: The exercise group showed increasing leptin levels (6.52 ± 3.56 to 6.81 ± 4.28 ng/mL, p=0.792) and the control group showed decreasing leptin levels (12.34 ± 15.15 to 6.31 ± 3.86 ng/mL, p=0.285). Both changes in leptin compared exhibited no significant alteration in leptin levels (p=0.145).

Conclusion: The 90-minutes per week moderate-intensity treadmill exercise in four weeks has no impact on leptin levels in males with type 2 diabetes mellitus. However, this finding should be interpreted with caution.

Keywords: Leptin, treadmill, moderate-intensity exercise, type 2 diabetes mellitus

WOEC-03-9

High prescription rate of nasal glucagon for hypoglycemia by pediatricians and physicians in Japan

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Objective

Hypoglycemia is one of the most common and life-threatening problem for people with type 1 diabetes mellitus (T1DM). Recently, nasal glucagon (NG) device, which is portable, ready-to-use, and easy-to-use, was approved for hypoglycemia in Japan. The prescription rate of intramuscular glucagon has been reported to be low. However, to the best of our knowledge, there are no reports on the prescription rate of NG. Therefore, we investigated the prescription rate of NG and identified the reasons not to prescribe NG.

Methods

A self-administered questionnaire was mailed to 430 pediatricians and 262 physicians working at large facilities in Hyogo prefecture. The following variables were investigated: department, whether or not to be treating people with T1DM, NG prescription rate, and reasons not to prescribe glucagon.

Results

After the exclusion of eight doctors due to their retirement, 684 doctors were enrolled. 306 (45%) doctors answered the questionnaire. 176 (39 pediatricians and 137 physicians) treated people with T1DM. 25 (64%) pediatricians and 92(67%) physicians prescribed NG. The most common reasons for not prescribing NG were patients'/caregivers' rejection and doctor's unfamiliarity with NG among pediatricians, and uncooperative caregivers among physicians.

Conclusion

As high as approximately two-thirds of both pediatricians and physicians prescribed NG. This study revealed challenges to be resolved for the further increase of NG prescription rates.

POSTER PRESENTATION

WPBS-01-1

Tetrahydrobiopterin in brown adipose tissue differentiation: its therapeutic implications for obesity and diabetes

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Objective

Brown adipose tissue (BAT) is a pivotal organ for energy dissipation that could be therapeutically relevant for diabetes and obesity. Tetrahydrobiopterin (BH4) is an essential co-factor of biosynthesis of norepinephrine and nitric oxide, and both products are known factors for BAT differentiation. However, the contribution of BH4 itself remains unclear.

Methods

We investigated the impact of BH4 on BAT differentiation using Hph-1 mice, a model of BH4 deficiency. We compared BAT phenotype and gene expression between hph-1 and control mice during the neonatal period using RNA-seq. We also evaluated the effect of BH4 supplementation in pregnant hph-1 mice and its impact on BAT differentiation in their offspring. Finally, we assessed the lasting effects of BH4 supplementation during embryonic development on BAT function after growth.

Results

BAT from hph-1 mice in the neonatal period showed impaired BAT differentiation, including reduced weight and decreased thermogenesis-related genes expression. RNA-seq analysis revealed hph-1 mice had a typical gene expression pattern of impaired differentiation. However, BH4 supplementation restored the genetic pattern of normal differentiation. Additionally, offspring born to BH4-supplemented hph-1 mothers demonstrated better BAT function and improved resistance to high-fat diet-induced obesity and glucose intolerance than non-supplemented offspring.

Conclusion

Our study highlights the critical role of BH4 in fetal BAT differentiation, indicating that BH4 deficiency during gestation hampers BAT differentiation. Conversely, maternal BH4 supplementation improves fetal BAT differentiation and subsequently affects postnatal energy metabolism in the offspring. Our findings suggest that regulating BH4 levels could be a promising strategy for preventing obesity and diabetes.

WPBS-01-2

Insulin dependent FoxK1/K2 pathway in regulation of mitochondrial metabolism in adipose tissue.

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【Objective】We previously identified a Forkhead transcription factor K1 (FoxK1) in the complex of insulin receptorβ chain, that translocates from the cytoplasm into the nucleus after insulin stimulation. FoxK1 has a paralog FoxK2 with very high homology. We aimed to elucidate the role of FoxK1 and Foxk2 in the regulation of metabolism in adipose tissue.

【Methods】We prepared FoxK1/K2 single-knockout and FoxK1/K2-overexpressed brown preadipocytes, and adipose-specific FoxK1 and FoxK2 transgenic (FoxK1-Tg, FoxK2-Tg) mice, and assessed their gene expression, mitochondrial activity, and metabolic function.

【Results】FoxK1 and FoxK2 regulate mitochondrial activity of brown adipocytes in the seahorse analysis *in vitro*. Created transgenic mice (FoxK1-Tg and FoxK2-Tg) improved glucose tolerance, insulin resistance, and sensitivity to cold exposure. Notably, we observed that these mice improved metabolism even after HFD feeding. To define the target genes of FoxK1/K2, we performed RNA-seq analysis of inguinal white adipose tissue (iWAT). FoxK1 regulates genes of oxidative phosphorylation, and FoxK2 regulates those of fatty acid metabolism associated with mitochondria. Using Chip-qPCR, we determined a target molecule of FoxK1 in response to insulin signaling.

【Conclusion】Insulin signaling promotes activation of mitochondrial function in adipocytes via FoxK1/K2. FoxK1 and FoxK2 are both involved in regulating adipose tissue function and provide an essential platform for treating obesity and metabolic diseases.

WPBS-01-3

Survivin is essential for adipose tissue thermogenic program and metabolic homeostasis

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Objective: Survivin belongs to the inhibitor of apoptosis protein family. Our previous work first revealed that Survivin promoted adipocyte maintenance in response to inflammatory stimuli. In the current study, we aim to further investigate the regulation of survivin expression in adipocytes under nutritional stress, and its function on adipose tissue energy metabolism in vivo and in vitro.

Methods: The thermogenic function of survivin was obeserved in brown and beige primary mature adipocytes. Meanwhile, the control and adipocyte-specific survivin knockout (SKO) mice were metabolically phenotyped under chow diet (CD) and high-fat diet (HFD) feeding, followed by assessment of energy and glucose metabolism. Additionally, the thermogenic function further was detected under cold exposure.

Results: The expression of survivin was regulated by short-term nutritional stress in adipose tissue and adipocytes. In brown and beige adipocytes, Survivin knockdown caused down-regulation of thermogenic programs, while overexpression led to up-regulation of it. The postnatal brown adipose tissue(BAT) development was impaired in SKO mice, resulting in reduced BAT mass and Ucp1 expression. After HFD feeding, SKO mice presented increased hepatic lipid ectopic deposition, insulin resistance and glucose intolerance. Upon cold exposure, the expression of thermogenic genes and proteins was reduced in BAT and inguinal white adipose tissue(iWAT) of SKO mice, accompanied by abnormal mitochondrial structure and induced autophagy.

Conclusions: Our research showed that survivin could be regulated by nutritional stress in adipocytes, and revealed a novel role of survivin in positively regulating the thermogenic program and maintaining normal BAT mass.

WPBS-01-4

Humans with Metabolically Active Brown Fat Demonstrate Higher Capacity to Catabolize Branched Chain Amino Acids

Mueez U-Din[1], Juho Raiko[1], Vanessa De Mello Laaksonen[2], Kati Hanhineva[2], John Newman[3], Karsten Kristiansen[4], Martin Klingenspor[5], Tobias Fromme[5], Tarja Niemi[6], Markku Taittonen[6], Teemu Saari[1], Nina Savisto[1], Merja Haaparanta-Solin[1], Pirjo Nuutila[1], Kirsi A. Virtanen[1]

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Objectives: Branched-chain amino acids (BCAA: valine, leucine, isoleucine) may synergize with circulatory lipids to induce insulin resistance. Metabolically active brown adipose tissue (BAT) may be a potent site for BCAA catabolism that participates in the systemic clearance of BCAA. The study aimed to investigate the systemic and BAT-specific metabolism of BCAA in healthy human adults.

Methods: Seventy-nine (25M/54F) humans participated in the study. Serum BCAA were determined using non-targeted metabolomics. Tissue BCAA were determined using non-targeted metabolomics, and tissue transcriptomics were determined with RNA-sequencing on human supraclavicular BAT samples.

BAT substrate metabolism was determined with PET imaging to classify subjects as either to be High-BAT or Low-BAT.
Results: High-BAT subjects demonstrated lower levels of circulatory BCAA compared to Low-BAT. In BAT, the relative levels of BCAA were lower in High-BAT compared to Low-BAT ($p < 0.05$). The mRNA expression of the genes in BAT regulating BCAA catabolism *BCKDHA, ACADSB,* and *HIBADH,* was higher in High-BAT in comparison to Low-BAT (all $p<0.05$).
Conclusion: Humans with metabolically active BAT have a greater capacity for systemic clearance of BCAA in comparison to those with lower metabolically active BAT. An enhancement of BAT metabolism may prove to be a useful target for combating systemic BCAA-induced metabolic disruptions in insulin resistance.

WPBS-02-1

Thiazolidinediones (TZDs) protect ß-cell's function from glucotoxic and lipotoxic conditions through GIP receptor.

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Objective: Thiazolidinediones (TZDs) are synthetic PPARγ ligands that enhance insulin sensitivity, resulting in increased insulin secretion from pancreatic ß-cells. We previously reported that TZDs could stimulate glucose-stimulated insulin secretion (GSIS) via PPARγ-dependent mechanisms by treating Troglitazone at INS-1 cell line. Troglitazone treatment also led to increased gastric inhibitory polypeptide receptor (GIPR) gene expression, however, the mechanisms and relationship with the incretin effects have not been investigated yet.

Results: TZDs significantly enhanced GSIS and GIPR expression, but not GLP-1R in INS-1 cells, and these effects were not detected in cells transfected with PPARγ shRNA. GIPR mRNA and protein levels were increased by 80 and 60%, respectively. The expressions of CHOP, pPERK, peIF2R, Cox4, and Nrf2 were reduced by TZD treatment in lipotoxicity and glucotoxicity conditions, and the number of TUNEL-positive cells was also significantly reduced when treated with TZDs. These effects were reversed in cells transfected with GIPR shRNA or PPARγ shRNA presented. The increase of GIPR expression by TZDs was associated with the increased incretin hormone sensitivity of INS-1 cells.

Conclusions: TZDs significantly increased the incretin sensitivity and protected ER stress and apoptosis in glucolipotoxic conditions through the increased expression of GIPR in pancreatic ß-cell.

Keywords:
Lobeglitazone; Insulin secretion; Glucolipotoxicity; GIPR, ER stress

WPBS-02-2

Mitochondrial Involvement in β-Cell Mass Preservation by Imeglimin in Db/db Mice

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Objective
Progressive loss of β-cell mass (BCM) is a hallmark of type 2 diabetes mellitus (T2DM) and strongly related with impaired insulin secretion. Therefore, BCM protection is a desirable trait of T2DM treatment. Imeglimin, a novel antidiabetic agent, has been reported to increase insulin secretion by optimizing mitochondria, which lowers the blood glucose. However, the effect of imeglimin on BCM preservation has not been fully understood.

Methods
The Lepr$^{db/db}$ (db/db) mouse is a diabetic mouse model with obesity, diminished mitochondrial number in β-cells and rapidly decreased BCM. Five-week-old male db/db mice were administered with 150 mg/kg imeglimin or vehicle orally B.I.D. for five weeks. Bodyweight and non-fasting blood glucose were recorded. Oral glucose tolerance tests (OGTTs) were performed at 4 (baseline), 7, and 10 weeks. Histological slides and electron micrographs from pancreases were generated.

Results
The non-fasting blood glucose and OGTTs results showed that imeglimin attenuated T2DM progression. By age of 10 weeks, imeglimin group had higher BCM and lower apoptosis rate. Furthermore, imeglimin also protected mitochondrial structure in β-cells. In separate experiment with 1-week in vivo intervention, imeglimin prevented cytochrome c release and preserved mitochondrial membrane potential (MMP) in islets. Imeglimin also partly restored MMP of isolated islet incubated in high glucose medium indicating a partial independent action from glucose concentration.

Conclusion
Imeglimin preserved BCM by inhibiting β-cells apoptosis in db/db mice, which was also supported by lower cytochrome c release and preserved βcells mitochondria structure. Furthermore, imeglimin restored islet MMP which was partially independent from glucose concentration.

WPBS-02-3

Protective effect of Recombinant Human Thrombomodulin on Streptozotocin-induced diabetes.

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Diabetes is one of the diseases that threaten our daily lives, and the number of the patients is increasing worldwide. Pancreatic β cell dysfunction and the cell mass reduction in diabetic patients cause impaired insulin secretion and β cell apoptosis is involved with the progression of diabetes. Thrombomodulin is a glycoprotein on the surface of endothelial cells, and it is noticed that thrombomodulin has inhibitory effect on cell apoptosis. In this study, we evaluated the effect of thrombomodulin on diabetic mice by induced by streptozotocin, that has toxicity to β cells. Administration of thrombomodulin attenuated hyperglycemia caused by STZ and ameliorated insulin secretion reduced by STZ. Moreover, thrombomodulin treatment increased islet area and β/α cell ratio in islet cells and reduced the number of apoptotic cells in islets. These results indicate that thrombomodulin has antidiabetic effect and point out the new possibility of the existing drug for diabetic therapy.

WPBS-02-4

Effects of combination therapy of imeglimin and metformin on pancreatic β-cells in db/db mice

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Objective: The impact of early combination therapy of imeglimin and metformin on β-cells has been unclear. Here, we investigated those combinatorial effects in db/db mice.

Methods: 6-week-old db/db mice were treated with imeglimin (400 mg/kg/day), metformin (250 mg/kg/day), or their combination (Imeg+Met) for 5-7 weeks.

Results: Imeglimin, metformin, or Imeg+Met treatment had no significant effects on glucose tolerance and insulin resistance in db/db mice. Insulin

secretion in response to glucose was recovered by 1.3-fold in Imeg+Met db/db mice. Imeg+Met, but not imeglimin or metformin monotherapy, showed significant increase in β-cell mass by enhancing β-cell proliferation (2.7-fold vs. control, $p<0.05$) and ameliorating β-cell apoptosis (50% vs. control, $p<0.05$) in db/db mice. Hepatic steatosis, the morphology of adipocytes, adiposity assessed by computed tomography, and the expression of genes related to glucose or lipid metabolism and inflammation in the liver and fat tissues showed no remarkable differences in all groups of db/db mice. RNA-Seq and pathway analysis suggested an association of "cell proliferation" and "negative regulation of cell death" in Imeg+Met db/db islets. Treatment of isolated db/db islets with Imeg+Met ameliorated β-cell apoptosis by 25%. The expression of above-mentioned genes related to apoptosis including Snai1, Tnfrsf18, Pdcd1, Mmp9, Ccr7, Egr3, and Cxcl12 in db/db islets was reduced by Imeg+Met. Imeg+Met also improved both hydrogen peroxide- and palmitate-induced cell apoptosis in β-cell line.

Conclusion: Imeg+Met treatment is beneficial for the maintenance of β-cell mass in db/db mice probably through direct action on β-cells, suggesting a potential of their early combination therapy to protect β-cells.

WPBS-02-5

Noninvasive evaluation of islet grafts BCM following intraportal transplantation using ^{111}In-exendin-4 SPECT/CT

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Objective. Islet transplantation (IT) is an effective treatment for individuals with type 1 diabetes who require β-cell replacement therapy. However, the lack of techniques for identifying islet grafts and measuring their β-cell mass (BCM) has challenged the advancement of IT protocols. As a result, noninvasive β-cell imaging is necessary. Our study investigated the effectiveness of the ^{111}Indium-labeled exendin-4 probe {[Lys12(111In-BnDTPA-Ahx)] exendin-4} (^{111}In exendin-4) single-photon emission computed tomography/computed tomography (SPECT/CT) in assessing the BCM of islet grafts after intraportal IT.

Methods. Streptozotocin-induced diabetic mice were intraportally transplanted with 150 or 400 syngeneic islets. After a six-week observation following IT, the *ex-vivo* liver graft uptake of ^{111}In-exendin-4 was compared with the liver insulin content. Furthermore, the *in-vivo* liver graft uptake of ^{111}In exendin-4 using SPECT/CT was compared with the histological liver graft BCM.

Results. The *ex-vivo* liver graft uptake in the 400-islet-transplanted group was significantly higher than that in the control and the 150-islet-transplanted groups, consistent with glycemic control and liver insulin content. *In-vivo* ^{111}In-exendin-4 SPECT/CT visualized liver islet grafts and distinguished the graft BCM of control, 150 IT, and 400 IT mice.

Conclusion. *In-vivo* SPECT/CT detected liver islet grafts from the control, 150 IT, and 400 IT mice. ^{111}In-exendin-4 SPECT/CT can be useful for noninvasive evaluation of the liver islet grafts after intraportal IT.

WPBS-02-6

Elucidation of HHEX in pancreatic endoderm differentiation using a human iPSC differentiation model

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Objective

For pluripotent stem cell-based regenerative therapy against diabetes, the differentiation efficiency to pancreatic lineage cells needs to be improved based on the mechanistic understanding of pancreatic differentiation. Here, we aimed to elucidate the molecular mechanisms underlying pancreatic endoderm differentiation by searching for factors that regulate a crucial pancreatic endoderm marker gene, NKX6.1.

Methods

We developed a screening system for regulators of NKX6.1 expression in pancreatic endoderm cells differentiated from human induced pluripotent stem cells (iPSCs) using siRNA-mediated gene knockdown. After the candidate gene was extracted by screening, subsequent analyses were performed to clarify its role in pancreatic endoderm.

Results

Unbiasedly screening an siRNA knockdown library, we identified a candidate transcription factor, HHEX. *HHEX* knockdown suppressed the expression of another pancreatic endoderm marker gene, *PTF1A*, as well as *NKX6.1*, independently of *PDX1*, a known regulator of *NKX6.1* expression. In contrast, the overexpression of *HHEX* upregulated the expressions of *NKX6.1* and *PTF1A*. RNA-seq analysis showed decreased expressions of several genes related to pancreatic development, such as *NKX6.1*, *PTF1A*, *ONECUT1* and *ONECUT3*, in *HHEX* knockdown pancreatic endoderm. When *HHEX*-knockdown pancreatic endoderm cells were differentiated into C-peptide$^+$NKX6.1$^+$ pancreatic β cells, the differentiation efficiency was lower than that of controls.

Conclusion

These results suggest that HHEX is essential for the differentiation of mature pancreatic endoderm cells that show the differentiation potential into β cells.

WPBS-02-7

Output clock gene DBP regulates diurnal variation in skeletal muscle insulin sensitivity

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Abnormalities in clock genes are thought to play a role in the development of diabetes. We have focused on E4BP4, a transcriptional repressor of D-box, and have studied using an overexpression model. In the present study, we analyzed systemic *Dbp* deficient (KO) mice to clarify the role of DBP, a transcriptional activator of D-box, in glucose metabolism. Oral glucose tolerance test at Zeitgeber Time (ZT)1 at 12 weeks of age showed that serum insulin at 30 minutes after glucose loading was significantly lower in KO mice than in wild-type (WT) mice, although there was no significant difference in blood glucose levels. At 13 weeks of age, insulin tolerance tests were performed. At ZT1, blood glucose levels 120 min after loading were significantly lower in KO mice (WT vs KO = 215 vs 123 mg/dL, $p \leq 0.01$). However, there was no difference at ZT13. 2-deoxy glucose (2DG) content in liver and gastrocnemius muscle after simultaneous administration of 2DG and insulin at ZT1 showed no difference in liver, but an approximately 4.5-fold increase in gastrocnemius muscle in KO mice. Akt phosphorylation at 60 min after insulin administration at ZT1 also showed no difference in the liver, but in the gastrocnemius muscle, phosphorylation was about 3-fold higher in KO mice than in WT mice. KO mice did not show impaired glucose tolerance despite the defeated insulin secretion, which was attributed to increased muscle insulin sensitivity. These findings suggest that DBP plays an important role in the regulation of muscle insulin sensitivity.

WPBS-02-8

Calorie Restriction induced physiological insulin resistance to maintain the superstability of blood glucose

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Objective: This study aimed to investigate the metabolic phenotype and mechanism of calorie restriction (CR) in mice.

Methods: The mice were randomly assigned to fed with chow diet, CR (chow diet with 40% calorie restriction) and high-fat diet for 8 weeks. The energy expenditure and behaviors of animals were determined in metabolic cages. Various tolerance tests were performed to evaluate the glucose and ketone metabolism.

Results: CR mice exhibited super-stable blood glucose, as evidenced by increased fasting blood glucose (FBG), decreased postprandial blood glucose, and reduced glucose fluctuations. Additionally, both fasting plasma insulin and the homeostasis model assessment of insulin resistance increased significantly in CR mice. Compared with control, the phosphorylation of insulin receptor substrates-1 and serine/threonine kinase decreased in liver and fat but increased in muscle of CR mice after insulin administration, indicating hepatic and adipose insulin resistance, and muscle insulin sensitization. CR reduced visceral fat much more than subcutaneous fat. The elevated FBG was negatively correlated with low-level fasting β-hydroxybutyrate, which may result from insufficient free fatty acids and diminished ketogenic ability in CR mice. Furthermore, liver glycogen increased dramatically in CR mice. Analysis of glycogen metabolism related proteins indicated active glycogen synthesis and decomposition. Additionally, CR elevated plasma corticosterone and hypothalamic orexigenic gene expression.

Conclusion: CR induced lipid insufficiency and stress, resulting in global physiological insulin resistance except muscle and enhanced glycogen metabolism, culminating in the stability of blood glucose manifested in increased FBG, which compensated for insufficient blood ketones.

WPBS-02-9

Hepatocyte to endothelial cell crosstalk via extracellular vesicles in non-alcoholic fatty liver disease

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Objective: Non-alcoholic fatty liver disease (NAFLD) is an independent risk factor for cardiovascular disease (CVD), although the mechanism of association is still unclear. Extracellular vesicle (EV) is a biological nanoparticle that plays critical roles in inter-organ crosstalk. We aimed to investigate the role of hepatocyte-derived EVs on endothelial cells in NAFLD condition.

Methods: Hepatocytes isolated from C57BL6 mice were exposed to palmitic acid (PA). Mice were fed a choline deficient+high fat diet (CD/HFD) for NAFLD model. Human umbilical vein endothelial cells (HUVEC) and human aortic endothelial cells (HAEC) were treated with EVs released from hepatocytes.

Results: The amount of EVs derived from PA-treated hepatocytes was greater than the EVs from control hepatocytes. Fluorescence-labeled hepatic EVs uptake were detected in endothelial cells. Treatment of EVs derived from PA- or CD/HFD-exposed hepatocytes induced endothelial dysfunction with subsequent upregulation of inflammatory cytokines, adhesion molecules, and oxidative stress markers in HUVEC/HAEC. Small RNA profiling of miRNA isolated from hepatic EVs identified 23 upregulated and 4 downregulated miRNAs in PA-treated hepatocytes. miR-30b-5p was identified as a possible candidate cargo and its elevation was confirmed by qPCR in EVs from PA-treated hepatocytes and CD/HFD-induced fatty liver. We identified *Elovl5* as a direct target of miR-30b-5p, a key enzyme in fatty acid elongation. Suppression of *Elovl5* resulted in endothelial dysfunction which was rescued by supplementation of polyunsaturated fatty acids.

Conclusion: Our findings suggest a novel role of hepatic EVs that regulate crosstalk between hepatocytes and endothelial cells. This may explain the independent relationship between NAFLD and CVD.

WPBS-03-1

Glucolipotoxicity inhibits proinsulin processing by blocking V-ATPase function and inhibiting acidification.

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Insulin is secreted from pancreatic beta cells after the precursor proinsulin is processed by prohormone converting enzymes (PC) 1/3 and PC2 within secretory granules (SG). As diabetes progresses, proinsulin processing is impaired and thus, insulin biosynthesis is impaired in pancreatic beta cells. As a result, blood proinsulin levels increase. However, the exact mechanism by which proinsulin processing is impaired is unknown. Therefore, this study aimed to elucidate the effects of high glucose and high saturated fatty acid conditions observed in diabetic conditions on proinsulin processing. Electron microscopic analysis revealed that mouse islets treated with high glucose and high palmitic acid (HGPal) have an increased percentage of immature SGs that exhibit proinsulin accumulation. When the luminal acidity of SGs was assessed using a pH indicator in a pancreatic beta cell line, an increase in pH was observed upon HGPal stimulation. The pH of SGs is dependent on the function of V-ATPase, which acts as an important proton pump. The analysis of the assembly of the major domains V1 and V0 by fractionation assay and proximity ligation assay showed that HGPal stimulation decreased the formation of V1 and V0 aggregates. Furthermore, immunoblotting data showed that HGPal stimulation reduced PC1/3 and PC2 maturation in mouse islets and inhibited proinsulin processing. Furthermore, in diet-induced obese diabetic mice, ntraperitoneal glucose injection enhanced proinsulin secretion and impaired proinsulin processing in isolated islets was suggested. In summary, glucolipotoxicity alters the luminal acidity of secretory granules and inhibits proinsulin processing.

WPBS-03-2

Targeting PGC-1α by miRNA-374 simultaneously improve β-cell dysfunction and suppress hepatic glucose overproduction.

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Peroxisome proliferator-activated receptor gamma coactivator-1 (PGC-1α) plays a pivotal role in glucotoxicity-induced β-cell dysfunction and excessive hepatic glucose synthesis in diabetes. The impact of inhibition of high PGC-1α expression in the liver and pancreas in improving diabetes using a single miRNA has yet to be reported. In this study, we investigated miRNAs that can regulate PGC-1α and identified particles for efficient transport of miRNAs in vivo.

To search for appropriate target miRNAs, we analyzed miRNA expression patterns in primary rat islets and hepatocytes three days following exposure to glucotoxicity and identified that miRNA-374 as an optimal candidate. miR-374 significantly suppressed PGC-1α and hepatic glucose overproduction, and thereby improved glucotoxicity-induced β-cell dysfunction. Specific binding of miR-374 to the 3'-untranslated region (3'-UTR) of PGC-1α was confirmed. Targeted delivery of miR-374 was achieved using coated cationic lipoparticles (CCLs) containing miR-374 within the core and with a neutral coating, decorated with Ex-4 to target beta-cells. Optical imaging revealed that miR-374 was efficiently delivered to pancreatic β-cells. Notably, Ex-4-CCL-miR-374 reversed the pancreatic islet dysfunction induced by glucotoxicity and restored normal insulin secretory function of the pancreatic islets. Mechanistically, treatment with Ex-4-CCL-miR-374 improved hepatic insulin resistance by regulating glucose via activation of IRS2/PI3K/AKT signaling pathways, resulting in inhibition of hepatic gluconeogenesis. Ex-4-CCL-miR-374 represents a novel therapeutic target that can be used to reverse pancreatic dysfunction and improve hepatic insulin resistance in T2DM.

WPBS-03-3
Role of Nrf2 in glucose-stimulated insulin secretion from pancreatic β-cells

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In type 2 diabetes, glucose-stimulated insulin secretion (GSIS) from pancreatic β-cells is impaired. The disease is caused by oxidative stress due to excessive production of reactive oxygen species (ROS) associated with glucotoxicity and lipotoxicity; however, the detailed mechanism has not been clear. Nuclear factor erythroid 2p45-related factor 2 (Nrf2), a transcription factor that regulates genes related to the antioxidants, dissociates from regulatory factors such as Kelch-like ECH-associated protein 1 (Keap1) upon oxidative stress and then translocates into the nucleus. In the present study, we investigated the involvement of Nrf2 in the lipotoxic effect on GSIS.

Palmitate (0.5 mM) exposure for 48 hours decreased GSIS and increased intracellular ROS levels in INS-1 cells, a rat pancreatic β-cell line. Palmitate exposure decreased Nrf2 mRNA levels for 6~48 hours and Keap1 mRNA levels for 12 hours. The decrease in GSIS by palmitate exposure was completely restored by ROS scavengers (ascorbic acid + α-tocopherol). Knockdown of Nrf2 by siRNA in INS-1 cells decreased GSIS and increased intracellular ROS levels. Knockdown of Keap1 siRNA increased GSIS. The decrease in GSIS by Nrf2 deficiency was partially restored by ROS scavengers. Intracellular ATP levels were not changed by Nrf2 knockdown and were increased by Keap1 knockdown. Furthermore, Nrf2 knockdown tended to decrease NADPH levels under high glucose stimulation. These results indicate that decreased GSIS under lipotoxicity is attributed to increased ROS and suggest that Nrf2 regulates GSIS by mechanisms other than regulating antioxidant activity.

WPBS-03-4
Histone methylase MLL attenuates insulin secretion by reducing glucose sensitivity in mouse pancreas.

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MLL protein has been shown to have histone H3 lysine 4-methylation (H3K4-HMT) activity. In addition, the function of MLL protein as a histone methylase has been reported in the gene region involved in metabolism regions. Here, we analyzed the involvement of MLL in glucose metabolism in the pancreas using MLL knockout mice. Since the homozygotes of MLL knockout mice are embryonic lethal, we analyzed them using Heterozygous mice. MLL heterozygous mice showed significantly weight loss compared to the wild type mice. MLL heterozygous mice showed no difference in food intake compared to wild type mice. MLL heterozygous mice showed impaired glucose tolerance in IPGTT. However, ITT showed no insulin resistance and decreased insulin secretion during glucose loading. In GSIS tests, Islets isolated from heterozygous mice pancreas have been observed to decrease insulin secretion in the response to glucose stimulation. In comprehensive gene analysis using Microarray analysis of mRNA extracted from mice islet, the gene expression changes related insulin secretion have been revealed in MLL heterozygous mice. Histological search showed no decrease in β-cell number, and immunohistological search showed no difference in insulin, glucagon, and TUNEL staining. And also, MLL knockdown was performed in a cultured cell line. The result of insulin secretion was same as mice. Both MLL knockout mice and MLL knockdown cell line, the expression levels of GLUT1 and GLUT2 were decreased. In conclusion, MLL attenuates insulin secretion by reducing glucose sensitivity in mouse pancreas.

WPBS-03-5
Effect of thyroid hormone signaling on the differentiation from human iPS cells into pancreatic β cells.

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[Objective] Thyroid hormone transporter MCT8-mediated transmembrane transport, iodothyronine deiodinases-mediated intracellular deiodination, and thyroid hormone receptor (TR)-mediated gene transcription constitute the basis for cellular thyroid hormone signaling. Type 3 iodothyronine deiodinase (D3) converts 3,5,3'-triiodothyronine (T3) to 3,3'-diiodothyronine (T2) and decreases the intracellular T3 levels. D3 is expressed in human and mouse pancreatic β cells. Mice with targeted disruption of D3 gene were found to be impaired β cell function and subsequently insulin secretion and glucose homeostasis. These results suggest that it is necessary to keep the intracellular T3 level low at specific stage(s) for normal pancreatic β cell differentiation.The purpose of the current study was to clarify the effect of thyroid hormone signaling on the differentiation from human induced pluripotent stem cells (hiPSCs) into pancreatic β cells.

[Methods] To generate pancreatic β cells (C-peptide+/Nkx6.1+) from hiPSCs, stepwise directed differentiation was used. The proportion of key transcription factors were analyzed at each stages by flow cytometry. Real time PCR was used to analyze the mRNA levels of D3, TR α and β, and MCT8.

[Results] D3 mRNA levels were significantly increased, and TR β and MCT8 mRNA levels were significantly decreased, respectively, compared with those of undifferentiated cells at 4days after differentiation (definitive endodermal stage).

[Conclusions] Increased D3 expression and decreased TRβ and MCT8 expression may decrease the intracellular T3 signaling at 4 days after differentiation. These results suggest that decrease of intracellular T3 signaling at definitive endodermal stage may be necessary for appropriate differentiation from hiPSCs to pancreatic β cells.

WPBS-03-6
Accelerating the Differentiation of Neonatal Porcine Pancreatic Cell Clusters into β Cells in Alginate-Microcapsule

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Neonatal porcine pancreatic cell clusters (NPCCs) have been proposed as an alternative source of β cells for islet transplantation because of their low cost and growth potential after transplantation. However, the delayed glucose lowering effect due to the immaturity of NPCCs and immunologic rejection remain as a barrier to NPCC's clinical application. Here, we demonstrate immune-tolerant NPCCs with accelerated differentiation by microencapsulation and in vitro chemical treatment. NPCCs isolated from 3-day-old piglets were cultured in F-10 media and then microencapsulated with alginate on day 5. Differentiation of NPCCs was facilitated by media supplemented with activin receptor-like kinase 5 inhibitor II, triiodothyronine and exendin-4 for 2 weeks. Marginal number of microencapsulated NPCCs to cure diabetes with and without differentiation were transplanted into immune competent diabetic mice and observed for 8 weeks. The proportion of insulin-positive cells and insulin mRNA levels of NPCCs were significantly increased in the differentiated group compared with the undifferentiated group in vitro. Blood glucose levels decreased eventually after transplantation of microencapsulated NPCCs in diabetic mice and normalized after 7 weeks in the differentiated group. In addition, the differentiated group showed nearly normal glucose tolerance at 8 weeks after transplantation. In contrast, neither blood glucose levels nor glucose tolerance were improved in the undifferentiated group. Retrieved graft in the differentiated group showed greater insulin response to high glucose compared with the undifferentiated group. In vitro differentiation of microencapsulated immature NPCCs increased the proportion of insulin-positive cells and improved transplant efficacy in diabetic mice without

immune rejection.

WPBS-03-7

Exendin-based positron emission tomography for noninvasive evaluation of pancreatic β cell mass: from bench to bedside

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Objective: Pancreatic β cell mass (BCM) has central importance in the pathophysiology of diabetes mellitus; clinical BCM evaluation remains challenging due to lack of practical and noninvasive methods. We have synthesized a novel exendin-based PEGylated probe labeled with fluorine-18, [^{18}F]FB(ePEG12)12-exendin-4 (^{18}F-Ex4) for positron emission tomography (PET) imaging. Following our preclinical biodistribution study, we investigated the clinical utility of ^{18}F-Ex4 through quantitative BCM assessments using ^{18}F-Ex4 PET/ CT in healthy subjects and a patient with type 1 diabetes mellitus (T1DM) who had received simultaneous kidney–pancreas transplantation (SPK).

Methods: In our preclinical biodistribution study, pancreatic uptake values in male ddY mice were analyzed after administration of ^{18}F-Ex4 (0.74 MBq/ mouse). We conducted a first-in-human phase 1 study of ^{18}F-Ex4 PET/CT, in which six healthy male subjects (22.0±0.3 years) were enrolled. Subsequently, a 46-year-old male patient with T1DM who underwent ^{18}F-Ex4 PET/CT following SPK.

Results: In the preclinical study, ^{18}F-Ex4 showed good accumulation in the pancreas. In the phase 1 study, 60.3±6.5 MBq of ^{18}F-Ex4 was administered; ^{18}F-Ex4 PET/CT allowed successful visualization of the pancreas and demonstrated reasonably high standardized uptake value (SUV)means (3.71±0.38 at 60 min, 3.19±0.44 at 120 min). No serious adverse events were observed. In the patient with T1DM, ^{18}F-Ex4 PET/CT revealed simultaneous and distinct accumulation in both the donor and native pancreas (2.96 and 1.97 at 60 min, respectively; 3.08 and 2.25 at 120 min, respectively).

Conclusion: ^{18}F-Ex4 is promising for clinical PET imaging that enables noninvasive quantitative BCM assessment.

WPBS-03-8

Deconvolution of Sirtuin 3 deficiency islet function origin heterogeneity with single cell analysis

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Objective:Our team has showed that loss of Sirtuin 3 (Sirt3) in pancreatic β cells enhances β cell de-differentiation and dysfunction under metabolic stress, and further impairs insulin secretion. However, gene expressions, functional alterations, and the interaction between islet cells induced by Sirt3 deletion in β cells are under-explored. In the present study, we aim to investigate the compartmental and transcriptional alterations induced by Sirt3 deficient ß-cell under metabolism stress.

Methods: β cell-specific Sirt3 knockout (Sirt3f/f;Cre/+) mice were subjected to high fat diet feeding to induce metabolic stress. The bulk RNA sequencing (RNA-seq) and single RNA sequencing (scRNA-seq) of the abovementioned mice islets were used to analyse the differential gene expression and unravel the intra-islet cluster profile and gene ontology transcript origin.

Results: Differential expression in bulk RNA-seq revealed a series of gene (DEGs) sets that were up- or down-regulated with Sirt3 deficient status. Some of the gene sets associated had been reported with endocrine and autocrine functions namely Tph1, Tph2, Enpp2, located mainly within ß cell clusters and were enriched in Sirt3 knockout mice (Sirt3f/f;Cre/+) . In addition, sc-RNAseq showed 10 cell clusters which were identified within the islets including endocrine, exocrine, and immune cells. Upregulated DEGs from RNA-seq Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis were applied to scRNA-seq and revealed the intra-islet paracrine meditation resulting from Sirt3 deficiency.

Conclusion: Our study shows that Sirt3 in ß cells plays a key role in maintaining intra-islet homeostasis

WPBS-03-9

The cell-cell interaction between islet endothelial cells and islet stellate cells

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Objective: The islet vasculature, comprised primarily of islet endothelial cells, is a key contributor to the maintenance of normal beta cell function. However, the cell-cell interaction between endothelial cells and other cells within islet, especially non-endocrine cell types, remains poorly understood. We aimed to examine whether islet endothelial cells (IECs) can communicate with islet stellate cells (ISCs) and to determine its contribution to the development of type 2 diabetes.

Methods: Immortalized islet endothelial cells were treated with conditioned medium of activated or quiescent ISCs or co-cultured with ISCs. Cell viability, proliferation and migration capacity were determined. Protein level of activation markers in ISCs treated with conditioned medium from IECs were examined by immunofluorescent staining and western blot. Islet capillary abundance and ISCs activation level were also determined in pancreases from diabetic db/db mice using confocal microscopy.

Results: Conditioned medium derived from activated ISCs could enhance cell viability, proliferation rate and cell migration of immortalized islet endothelial cells, which is ameliorated for quiescent ISCs. Also, the proportion of Ki67 positive endothelial cell (proliferating cell) increased when co-cultured with ISCs. In turn, the expression of activation markers of ISCs decreased when treated with endothelial cell-derived conditioned medium or in a co-culture system. Islets from db/db mice exhibited increased expression of markers of ISCs activation along with decreased capillary density compared with non-diabetic mice.

Conclusion: Islet endothelial cells could interplay with islet stellate cells, and it may prove a promising target for the development of new therapies or prevention strategies for diabetes.

WPBS-04-1

The effects of exercise and detraining on each white adipose tissue in young OLETF rats

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Objective

Since childhood obesity leads to adulthood obesity and obesity-related health problems, it is necessary to prevent or treat childhood obesity, such as by exercise. However, it is unclear the obesity-preventive effects of childhood exercise in adulthood after detraining. This study aimed to investigate the effects of childhood exercise and following detraining on obesity in adulthood, focusing on adipose tissue localization.

Methods

Four-week-old male Otsuka Long-Evans Tokushima Fatty (OLETF) rats as obesity model animals were randomly divided into a sedentary (Sed) group and an exercise (Ex) group; the rats in the Ex group exercised from 4- to 12-week-old and detrained from 12- to 20-week-old. The subcutaneous, epididymal, retroperitoneal, and mesenteric white adipose tissues (scWAT, eWAT, rWAT, mWAT) were collected at 12- and 20-week-old. The wet weight and adipocyte diameter were measured.

Results
At 12-week-old, tissue wet weight and adipocyte diameter were significantly lower in the Ex group than in the Sed group for each types of WAT. At 20-week-old, there was no difference in adipocyte diameter for each types of WAT between the Sed and Ex groups. However, tissue wet weight of scWAT, eWAT, and rWAT was still significantly lower in the Ex group than in the Sed group.

Conclusions
Childhood exercise could prevent fat accumulation in the whole body. Lipids were accumulated due to adipocyte hypertrophy during the detraining period. But adipocyte hyperplasia in scWAT, eWAT, and rWAT may have been prevented by childhood exercise. Fat accumulation may differ depending on the localization of adipose tissue.

WPBS-04-2
Imeglimin affects mitochondrial function and DNA content in 3T3-L1 adipocytes

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Imeglimin, a novel oral anti-diabetes drug, is known to affect mitochondrial function in pancreatic beta cells and hepatocytes, but its effects on adipocytes are not clear. In this study, we investigated the effects of imeglimin on adipocyte mitochondria. We examined the effects of imeglimin on adipocytes using differentiated 3T3-L1 adipocytes as an adipocyte model. The results showed that imeglimin inhibited Complex I activity and increased AMP. In addition, western blot analysis revealed that imeglimin promoted the phosphorylation of AMP-kinase. On the other hand, imeglimin increased the expression of PGC-1alpha and TFAM genes as well as mitochondrial DNA. This increase in mitochondrial DNA induced by imeglimin was inhibited by compound C, an inhibitor of AMP-kinase. These results indicate that imeglimin affects mitochondrial function and DNA content in adipocytes.

WPBS-04-4
CLSTN3 gene variant and CLSTN3B associates with obesity risk and contributes to dysfunction in white adipose tissue

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Objective: White adipose tissue (WAT) is a major metabolic regulator. Calsyntenin 3 (CLSTN3) is a transmembrane protein that promotes synapse development in brain. Calsyntenin 3B (CLSTN3B) is an adipocyte-selective product of the CLSTN3 locus. As the role of *CLSTN3* and *CLSTN3B* in WAT is unknown yet, we aim to assess their expression pattern in human adipose tissue and investigate the regulatory impact on WAT function.
Methods: The phenotypic effect of *CLSTN3* gene variant in humans was analyzed by genetic association study and expression quantitative trait loci analysis. Adeno-associated virus-mediated human *CLSTN3* overexpression in mouse inguinal WAT was conducted to assess energy and lipid metabolism. What's more, we continued to detect the expression of *CLSTN3B* in abdominal subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) from 210 individual and analyze the correlation with metabolic parameters.
Results: We found that *CLSTN3* was routinely expressed in human SAT and *CLSTN3* gene variant rs7296261 was associated with human obesity risk. Local *CLSTN3* overexpression in mouse iWAT exacerbated diet-induced adipose dysfunction and metabolic deficiency including impaired lipolysis. Mechanistically, CLSTN3 could interact with amyloid precursor protein (APP) and increase APP accumulation in mitochondria. Moreover, we found that *CLSTN3B* was also expressed in human WAT and differed greatly between individuals. *CLSTN3B* expression was negatively correlated with BMI and a variety of metabolic parameters.
Conclusion: Our study provides the evidence for a novel role of *CLSTN3* and *CLSTN3B* in modulating WAT function, thereby targeting *CLSTN3* and *CLSTN3B* may be a potential approach for the treatment of obesity.

WPBS-04-6
The protective effect of stevioside on TNF-α-induced insulin resistance in 3T3-L1 adipocytes: a metabolomics approach

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Objective: Stevioside (SVS), the main constituent of *Stevia rebaudiana* Bertoni, has several therapeutic effects for metabolic syndrome, including reducing blood glucose levels and improving insulin sensitivity. The aim of this study was to unravel the protective effect of SVS in a cell culture model of insulin resistance using metabolomics.
Methods: 3T3-L1 adipocyte cells were stimulated with 1.0 ng/mL TNF-α for insulin resistance and treated with SVS. The cell lysate was harvested and analysed by liquid chromatography-mass spectrometry-quadrapole time-of-flight analysis (LC/MS-QTOF). Principal component analysis (PCA) was used to identify statistically distinct metabolites for SVS in TNF-α induced insulin resistance 3T3-L1 adipocytes, and metabolomics pathway analysis (MetPA) was used to analyse and visualise the metabolic pathways involved.
Results: A total of 24 metabolites were identified as potential biomarkers for SVS treatment in TNF-α induced insulin resistance 3T3-L1 adipocytes. The major metabolic pathways altered by SVS were glycine, serine, and threonine metabolism, arginine and proline metabolism, phenylalanine, tyrosine, and tryptophan metabolism, alanine, aspartate, and glutamate metabolism, glycerophospholipid metabolism, arachidonic acid metabolism, linoleic acid metabolism, pentose and glucuronate interconversions metabolism, retinol metabolism, and thiamine metabolism.
Conclusion: The regulation of SVS on metabolic biomarkers in insulin resistance may increase antioxidant defence, reduce pro-inflammatory cytokines, upregulate the pentose phosphate pathway and glycolysis, and increase membrane fluidity, implying that SVS has a protective effect in insulin resistance.

WPBS-05-1
Revisit Sialic Acid and Diabetes Mellitus: A Computational Study

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Objective: Sialic acids are a family of monosaccharides with highly diverse structures. While recent studies focused on the potential predictive value of serum sialic acids (total, bound and free forms) as biomarkers for indications of type 2 diabetes mellitus and its microvascular complications, previous in vitro studies demonstrated that addition of sialic acids to insulin-resistant cells led to increased insulin action. The present study aimed to evaluate the anti-diabetic potential of sialic acids using a computational approach.

Methods: The two-dimensional structures and SMILES notation of N-Acetyl-Neuraminic acid (Neu5Ac), N-Glycolyl-Neuraminic acid (Neu5Gc) and Keto-Deoxy-Nonulonic acid (KGN) were obtained from the PubChem database. Structure-based inverse dockings of Neu5Ac, Neu5Gc and KGN were performed through high-performance computing server via the DIA-DB system. The oral bioavailability, as well as absorption, distribution, excretion, and toxicity (ADMET) properties of the molecules were computed using the SwissADME web tool. Molecular interaction analysis was subsequently determined via BIOVIA Discovery Studio.

Results: Inverse virtual screening revealed that the three selected sialic acids molecules could potentially bind to corticosteroid 11-beta-dehydrogenase isozyme 1 (HSD11B1) and peroxisome proliferator-activated receptor gamma (PPARG), with the lowest binding energy score ranging from -6.6 to -7.3 Kcal/Mol. The sialic acids included in present analysis were presented with

favourable ADMET properties by passing the Lipinski rule of five and Veber rules, which indicate potential use as orally active compounds.

Conclusion: The present findings suggest multi-targeted actions of sialic acids in diabetes mellitus which are worth further exploration on deciphering its interaction underpinning insulin resistance and glucose metabolism.

WPBS-05-2

Sleep recovery following sleep fragmentation induces glycometabolism, gut microbiome and adipose transcriptome changes

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Objective

Chronic sleep fragmentation (SF) is prevalent in contemporary human society and has detrimental effects on many biological systems. Whether sleep recovery (SR) can reverse the adverse effects caused by SF remains largely unknown. Therefore, in this study, we aim to explore the influence of SR following chronic SF on glucose metabolism, gut microbiota, and transcriptome of inguinal white adipose tissue (iWAT).

Methods

Mice were exposed to SF for 8 weeks, then allowed to recover sleep for 2 weeks. Glucose tolerance was measured by intraperitoneal glucose tolerance tests, gut microbiota was evaluated by 16s rDNA amplicon sequencing, and transcriptome alterations of iWAT were assessed by RNA-sequencing.

Results

SR following chronic SF still resulted in significant glucose intolerance, subtle gut microbiota changes, and transcriptome alterations of iWAT. The transcriptional responses of iWAT were mainly involved in cardiac muscle contraction, hypertrophic cardiomyopathy, and pathways of dilated cardiomyopathy. We identified three hub genes of iWAT, namely non-SMC condensin I complex subunit G (Ncapg); centromere protein E (Cenpe) and TTK protein kinase (Ttk). Moreover, the relative abundance of the differential microbiome was associated with glucose parameters and the hub genes of iWAT.

Conclusion

Short SR can still not reverse the detrimental effects caused by chronic SF. And the alterations in gut microbiota might be a critical factor in deciphering the enduring adverse influence of SF, which provides some novel evidence and targets for combating SF.

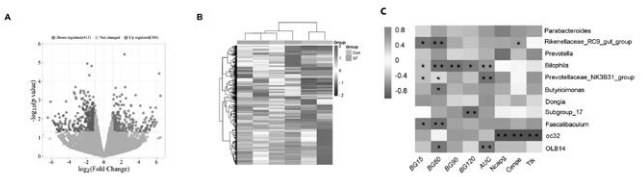

Fig.1. **A** Volcano plot illustrating differentially expressed genes (DEGs) between SF and control mice. Genes with $|\log_2(\text{foldchange})| \geq 1$, $p < 0.05$ highlighted in red for significantly upregulated (306 genes) and blue for significantly downregulated (413 genes) after sleep recovery following SF. Genes not significantly differentially expressed are in grey. **B** The heatmap showing the most DEGs filtered by $|\log_2(\text{foldchange})| \geq 1$, $p < 0.05$ in each group. SF, sleep fragmentation for 8 weeks, then sleep recovery for 2 weeks; Con, control. **C** Heatmaps of Spearman correlation analysis of altered gut microbes with glucose parameters and hub genes. Crosses show the correlation coefficients (r). * $p < 0.05$, ** $p < 0.01$. BG15, blood glucose level at 15 min of ipGTT; BG60, blood glucose level at 60 min of ipGTT; BG90, blood glucose level at 90 min of ipGTT; BG120, blood glucose level at 120 min of ipGTT; AUC, area under the curve of ipGTT; Ncapg, non-SMC condensin I complex subunit G; Cenpe, centromere protein E; Ttk, TTK protein kinase.

WPBS-05-3

Morphological analysis and drug effects on retina in salt-loaded type 2 diabetes model mice

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Objective:

One of the microvascular complications of diabetes is retinopathy, which is induced and exacerbated by risk factors such as salt intake and/or high fat diet. In this study, we morphologically investigated the effects of salt and high fat/sucrose (Quick fat: QF) diet on the retina of KK-Ay mice, a model of type 2 diabetes, and the effects of fenofibrate and dapagliflozin. We also investigated the effects of these drugs on another diabetes model, db/db mice.

Methods:

After male C57BL/6 mice and KK-Ay mice were loaded with 1% sodium chloride (NaCl) in drinking water and fed QF diet for 12 weeks, retinal thickness was measured at 250 μm from the optic nerve head. For drug treatment, KK-Ay mice or db/db mice loaded with NaCl and/or QF diet were fed fenofibrate (equivalent to 30 and 100mg/kg) or dapagliflozin (equivalent to 0.3 and 1mg/kg) in the diet for 12 weeks.

Results:

Retinal thinning was observed in KK-Ay mice compared to C57BL/6 mice. Salt loading caused retinal thinning in C57BL/6 mice, but not in KK-Ay mice. On the other hand, little effect of QF diet was observed in KK-Ay mice. No drug had a noticeable effect on retinal thickness in KK-Ay mice, but in db/db mice a low dose of dapagliflozin significantly increased retinal thickness.

Conclusion:

Insulin resistance and diabetes are strongly implicated in retinal thinning in KK-Ay mice, suggesting that high fat/high sucrose may also influence retinopathy. It is possible that insulin resistance is a factor in strain differences in efficacy.

WPBS-05-4

Components in coffee improve glucose metabolism by upregulating PGC-1α and FNDC5 in muscle

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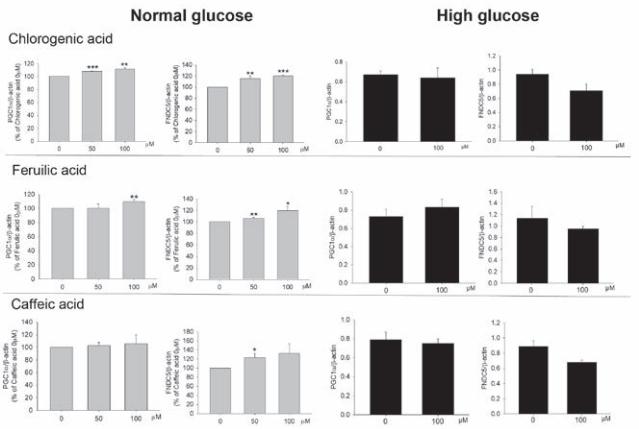
Objective: Several clinical investigations showed that coffee consumption could prevent the development of type 2 diabetes. PGC-1α and FNDC5 expression in muscle were associated with glucose metabolism and insulin sensitivity. We explored the PGC-1α and FNDC5 expression in myocytes after treating chlorogenic acid, ferulic acid, or caffeic acid.

Methods: Murine myoblasts (C2C12) were treated with different concentrations of chlorogenic acid, ferulic acid, or caffeic acid after well differentiation in normal (6mM) or high glucose (25mM) for 48-72 hours. PGC-1α and FNDC5 expression were measured by Western blot.

Results: After being treated with chlorogenic acid and ferulic acid, PGC-1α and FNDC5 expression in C2C12 cells increased significantly. In the caffeic acid group, FDNC5 expression increased mildly in muscle cells, but PGC-1α expression showed no significant difference after treatment. In high glucose group, PGC-1α and FNDC5 expression in muscle cells disclosed no significant difference between without and with the treatment of chlorogenic acid, ferulic

acid, or caffeic acid.
Conclusion: The anti-oxidative components of coffee with chlorogenic acid, ferulic acid, and caffeic acid upregulated the expressions of PGC-1α and FNDC5, which may improve glucose metabolism in muscle. However, the beneficial effects of chlorogenic acid, ferulic acid, and caffeic acid in muscle diminished in high glucose.



WPBS-05-5
Impacts of Glucose-Dependent Insulinotropic Polypeptide on Bone Remodeling

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OBJECTIVE:Glucose-dependent insulinotropic polypeptide (GIP) exhibits extrapancreatic effects through the receptor for GIP (GIPR). In this study, we investigated the impact of GIP on traction force-induced bone remodeling.
METHODS:Ni-Ti was attached between the maxillary bone and the maxillary left first molar (M1) of Mice lacking GIPR (GIPRKO) and wild type mice (WT), and mechanical load was applied by pulling the M1 in the mesial direction. Micro CT analyses and immunohistological evaluation were performed two weeks after the installation of the coil spring.
RESULTS: GIPRKO showed a significant increase in tooth movement distance and a significant decrease in residual alveolar bone mass. GIPRKO exhibited significantly decreased number of trabeculae and increased trabecular separation by orthodontic tooth movement compared with the corresponding changes in the WT. Histological analyses revealed a decreased number of steady-state osteoblasts in the GIPRKO. The orthodontic tooth movement induced bone remodeling, which was demonstrated by an increase in osteoblasts and osteoclasts around the forced tooth in the WT. The GIPRKO exhibited no increase in the number of osteoblasts; however, the number of osteoclasts on the coil-loaded side was significantly increased in the GIPRKO compared to that in the WT.
Conclusion:These results demonstrate the impacts of GIP on the dynamics of bone remodeling. We revealed that GIP exhibits the formation of osteoblasts and the suppression of osteoclasts in force-induced bone remodeling.

WPBS-05-6
Lysine-specific demethylase LSD1 acts as an 'epigenetic barrier' against environmental stresses in skeletal muscle

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[Objective]
Skeletal muscle exhibits remarkable plasticity in response to environmental cues, with stress-dependent effects on the fast-twitch and slow-twitch fibers. However, the underlying mechanisms which regulate stress-induced gene expression that causes fiber type-specific responses in the muscle have not been well understood. To elucidate the mechanisms, we focused on lysine-specific demethylase-1 (LSD1), an epigenetic factor which is reported to regulate the alternation of the metabolism in response to environmental stresses in various cells.
[Methods]
To investigate the role of LSD1 in muscle plasticity in vivo during postnatal life, we generated tamoxifen-inducible-, skeletal muscle-specific LSD1-knockout (LSD1-mKO) mice. We treated LSD1-mKO mice with dexamethasone (dex) as environmental stress which induces fast fiber-specific muscle atrophy. We also subjected the mice to voluntary wheel running (VWR), an exercise that induces the hypertrophy of slow-fiber dominant muscles.
[Results and Conclusion]
Using LSD1-mKO mice and in vitro approaches, we found that LSD1 loss exacerbated dex-induced atrophy in the fast fiber-dominant muscles, with reduced nuclear retention of Foxk1, an anti-autophagic transcription factor. LSD1 and Foxk1 formed a complex and regulated the expression of atrophy and myofiber-related genes. Furthermore, LSD1 depletion enhanced endurance capacity and hypertrophy of slow fiber-dominant muscles after VWR, through increased expression of ERRγ, a transcription factor that promotes oxidative metabolism genes. Thus, LSD1 serves as an 'epigenetic barrier' that optimizes fiber type-specific responses and muscle mass under environmental stresses. We also confirmed that LSD1 expression in skeletal muscles was decreased with aging, indicating that LSD1 modulators provide emerging therapeutic and preventive strategies against sarcopenia.

WPBS-05-7
Role of brain selenoprotein P in mental disorders associated with type 2 diabetes

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OBJECTIVE. Type 2 diabetes is associated with mental health problems, particularly anxiety disorders (Smith et al., J Psychosom Res 2013). A diabetes-associated hepatokine selenoprotein P (SeP, encoded by *Selenop* in mice, Cell Metab 2010) is also produced by astrocytes in the central nervous system (CNS) and delivered to neurons via the ApoEr2 receptor (Burk et al., FASEB J 2014). The present study investigated the role of SeP in altered behaviors associated with type 2 diabetes.

METHODS. C57BL/6 male mice and genetically matched neuron-specific *Selenop* knockout (KO) were fed a standard chow followed by 2 months of high-fat high-sucrose (HFHS) diet and underwent anxiety-like behavior testing in an elevated plus maze (EPM) test before and after the diet. We measured SeP mRNA expression by RT-qPCR, protein contents by ELISA method, and peripheral insulin resistance by glucose tolerance test.

RESULTS. HFHS diet reduced the time mice spent in the open arms of the EPM, representing more anxiety-like behavior compared to standard chow-fed controls. *Selenop* KO mice spend more time in the open arms than WT mice on either standard chow or HFHS diet. There is no significant difference in weight, locomotor activity, and glucose tolerance between the genotypes.

CONCLUSION. *Selenop* deficiency in CNS does not affect weight or glucose

tolerance but attenuates anxiety-like behavior in mice.

WPBS-05-8
Effects of electrical microstimulation of peripheral sympathetic nerve on blood glucose control in rats

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Objective: We previously reported that electrical microstimulation (MS) of the peripheral sympathetic nerve elevated glucose uptake in rats. In the present study, we evaluated the effects of MS on blood glucose (BG) control.
Methods: At 11 weeks of age, sympathetic nerve activity in rats were detected with a microelectrode in the unilateral sciatic nerve under anesthetic condition. The MS was conducted via the electrode for 60 min with monitoring of BG and lactate levels (MS group; n=5-7). At the end of MS, we measured mRNA expression in the soleus and extensor digitorum longus (EDL) and liver, and hepatic glycogen content, and compared them with non-stimulated, control rats (n=6).
Results: The MS showed significant increase in lactate level (P<0.01) whereas little change was seen in BG. *Pgc-1α* expression in the bilateral soleus and EDL in the MS group tended to be higher than those in the control group while *Glut4* expression in the bilateral EDL was significantly lower (P<0.05). Although *G6Pase* expression in the liver was significantly higher (P<0.01) in the MS group than in the control group, the liver glycogen content in the MS group was higher (P<0.05).
Discussion: Since PGC-1α regulates glucose uptake via GLUT4, the MS might elevate glucose uptake in the soleus but not in EDL. The little change in BG may be attributed to balance between glucose uptake and hepatic glucose production by *G6Pase*. Moreover, the MS might enhance glycogen synthesis derived in part from lactate.

WPCS-01-1
Relationship of PLR and NLR with mild cognitive impairment in patients with type 2 diabetes

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Objective: Two major indices relevant to systemic inflammation—platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR)—have been shown to be correlated with diabetes and its complications. This study evaluated the association between PLR, NLR, and mild cognitive impairment (MCI) among diabetic patients.
Methods: A total of 404 T2DM patients were enrolled in this study. The clinical characteristics and neuropsychological functions of T2DM were collected and divided into two groups (nMCI, n=243; MCI, n=164) according to the Montreal Cognitive Assessment (MoCA) scores. Through correlation analysis and univariate and multivariate regression, we further explored the association between PLR, NLR, and MCI. Furthermore, we investigated the effect of PLR and NLR on risk reclassification of MCI.
Results: The PLR and NLR levels were significantly higher among MCI patients than among nMCI patients. After fully adjusting for co-founders, NLR, as a continuous variate, remained an independent risk factor for MCI. Although PLR was not independently associated with MCI as a continuous variable, the upper 50th percentiles of PLR contributed to a 1.278-fold risk to the presence of MCI in the fully adjusted MCI model. Although a combination of PLR and NLR also failed to improve the clinical diagnostic efficacy, the addition of age, education, and glycated hemoglobin A1c (HbA1c) resulted in a model with increased diagnostic performance.
Conclusion: Our results showed that increased PLR and NLR levels were associated with MCI in T2DM, which may help to identify high-risk patients in a timely manner and provide clues for further prevention of cognitive dysfunction in T2DM patients.

WPCS-01-3
Associations of Lower Time in Range with Cognitive Dysfunction and Hippocampal Damage in Adults with Type 2 Diabetes

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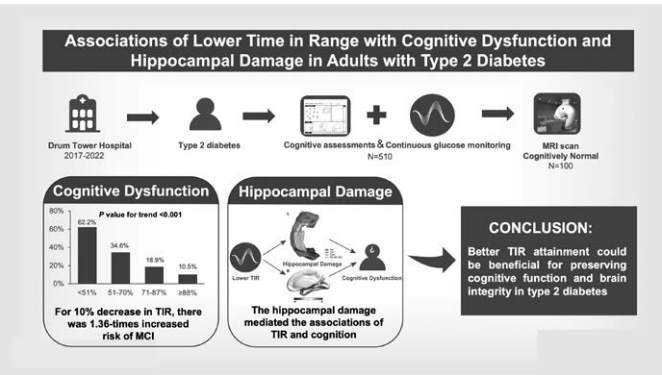
Objective
This study aimed to investigate the cross-sectional associations between time in range (TIR) and cognitive dysfunction, and the underlying hippocampal manifestations in patients with type 2 diabetes.
Methods
A total of 510 participants with type 2 diabetes who completed continuous glucose monitoring and comprehensive cognitive evaluations were enrolled. Among them, 100 patients with normal cognition underwent 3.0T magnetic resonance imaging to assess brain structural and functional changes.
Results
The prevalence of mild cognitive impairment (MCI) was significantly associated with lower TIR quartiles (*P* for trend <0.001). The multivariable-adjusted odds ratios (ORs) of MCI associated with TIR quartiles (Q1: ≥88% [reference group], Q2: 71-87%, Q3: 51-70%, Q4: <51%) were 1.00, 1.60 (95% CI: 0.66-3.83), 3.02 (95% CI: 1.14-8.04), and 7.67 (95% CI: 2.56-23.02) respectively (*P* for trend <0.001). Furthermore, the multivariable-adjusted OR for every 10% decrease in TIR was 1.36 (95% CI 1.20-1.52) for MCI. Decreased TIR was associated with cognitive decline in immediate memory, language, attention, delayed memory and processing speed. Importantly, cognitively normal patients with lower TIR showed reduced volume of left hippocampal subregions and decreased activation of right parahippocampal gyrus, and these hippocampal alterations mediated the association between lower TIR and cognitive dysfunction
Conclusion
Lower TIR is associated with the elevated prevalence of cognitive impairment in individuals with type 2 diabetes, and such association is mediated by hippocampal damage in type 2 diabetes. These findings underscore the clinical relevance of better TIR attainment could be beneficial for preserving cognitive function and brain integrity in type 2 diabetes.



WPCS-01-4
Association between brain imaging biomarkers and glycemic control indices in patients with type 2 diabetes mellitus

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Aims: Although there is substantial epidemiologic evidence linking type 2

diabetes mellitus (T2DM) to an increased risk of dementia, it is unclear whether T2DM is causally related to specific brain imaging changes. The aim of this study was to investigate the association between CGM-derived glycemic control indices and brain imaging biomarkers assessed by magnetic resonance imaging.
Methods: This cross-sectional study included 150 patients with T2DM. In this study, the degree of medial temporal lobe atrophy assessed by voxel-based morphometry and severity of deep and subcortical white matter hyperintensity (DSWMH) and periventricular hyperintensity (PVH) and were evaluated as brain imaging biomarkers. A retrospective CGM was worn to each participant for 14 days, and glycemic control indices were calculated.
Results: The results of this study showed that CGM-derived time in range (TIR) and glycemia risk index (GRI) were associated with severity of cerebral white matter lesions. Independent of the presence of hypertension, binomial logistic regression analysis revealed a significant association between TIR and severity of DSWMH [OR 0.973 (95% CI: 0.955-0.992), P = 0.006]. Logistic regression analysis showed that there was also a significant association between severity of PVH [OR 0.967 (95% CI: 0.945-0.989), P = 0.004] and TIR, but no association between medial temporal lobe atrophy and TIR [OR 0.991 (95% CI: 0.967-1.017), P = 0.501].
Conclusions: According to the findings of this study, CGM-derived TIR was associated with severity of cerebral white matter lesions independent of presence of hypertension.

WPCS-01-5
RAGE in circulating immune cells is essential for neuroinflammation and cognitive decline due to metabolic endotoxemia

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Objective: Metabolic endotoxemia has been proposed as a key mediator of metabolic syndrome (MetS) in relation to dietary factors, with translocation of lipopolysaccharide (LPS) into the bloodstream from a leaky gut, which are increasingly becoming recognized as risk factors for MetS-related comorbidities. However, it is not known whether metabolic endotoxemia induces MetS-related brain inflammation and cognitive decline.
Methods and Results: In this study, metabolic endotoxemia induced by low-dose LPS-infusion for four weeks in C57BL/6J mice induced MetS features, which were associated with cognitive decline and brain inflammation characterized by microgliosis, monocyte infiltration and endothelial inflammation, without significant changes in circulating cytokines. These changes as well as cognitive impairment were rescued in receptor for advanced glycation end products (RAGE)-knockout mice or chimeric mice lacking RAGE in bone marrow cells generated by bone marrow transplantation. Glucose transporter-1 (Glut-1) expression by monocytes, a critical mediator for inflammatory response, was induced by LPS-infusion in wild-type but not RAGE-knockout mice. These changes induced by LPS-infusion in the wild-type mice were ameliorated by an adenoviral increase in circulating endogenous secretory RAGE (esRAGE). Meanwhile, chimeric RAGE-knockout mice possessing RAGE in myeloid cells were resistant to cognitive decline and brain inflammation.
Conclusions: These findings indicate that RAGE in inflammatory cells is necessary but not by itself sufficient to mediate stimuli of chronic endotoxemia that cause brain inflammation and cognitive decline, potentially by orchestrating monocyte activation via regulation of Glut-1 expression. Additionally, esRAGE-mediated inflammatory regulation is a potential therapeutic option for cognitive dysfunction in metabolic endotoxemia.

WPCS-01-6
Gamma-glutamyl transferase and risk of dementia

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Objective : This study was designed to evaluate the association between gamma-glutamyl transferase (GGT) and incidence of dementia.
Methods : We used the Korean National Health Insurance Service (HNIS) datasets of Claims and Health Check-ups. The incidence of dementia was analyzed using KaplanMeier estimates, and the log-rank test was used to compare differences among groups. Hazard ratio (HR) and 95% confidence interval (CI) values were analyzed using the Cox proportional-hazards analysis with multivariable-adjustment. Statistical Analysis Systems software (version 9.3, SAS Institute, Cary, NC, USA) was used.
Results : Among a study population, 9.7% of subjects had diabetes. The higher the cumulative numbers of the highest GGT quartile, the higher the more percentage of subjects with diabetes. The cumulative numbers of the highest GGT quartile showed positive association with the incidence of dementia. Subject without diabetes showed more prominent association between the cumulative numbers of the highest GGT and incidence of vascular dementia.
Conclusion : This retrospective longitudinal study showed that GGT had positive correlation with dementia incidence.

WPCS-01-7
Association of use of anti-depressants and diabetes complications in type 2 diabetes – a territory-wide cohort study

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Objective
Mental illness is a major cause of hospitalisation in young people with type 2 diabetes in Hong Kong. We investigated the association between depression and diabetes complications.

Methods
We conducted a retrospective analysis of people with type 2 diabetes who participated in the Hong Kong Hospital Authority Risk Assessment and Management Programme in 2000-2019. People with comorbid depression were identified by the use of antidepressant at the time of first assessment. Using Cox regression, we estimated the hazard ratio (HR) of depression with major clinical outcomes adjusted for age, sex, diabetes duration, assessment year, smoking, alcohol use, HbA1c, blood pressure, lipid, kidney function, history of complications and medications at baseline.

Results
The analysis included 19,045(3.5%) people with type 2 diabetes and comorbid depression (mean age 60.9(SD:12) years, median diabetes duration 2 (IQR:0,6) years, 6,591(34.6%) men) and 524,136 people with type 2 diabetes alone (mean age 61.9(11.8) years, median diabetes duration 2(0,7) years, 269,698(51.5%) men). People with comorbid depression had a higher risk of severe hypoglycaemia (adjusted HR (aHR) =1.49 (95%CI:1.37-1.63), p-value<0.001), stroke (aHR=1.33 (1.20-1.48), p-value<0.001), heart failure (aHR=1.16 (1.03-1.31), p-value=0.018) and all-cause mortality (aHR=1.28 (1.21-1.36), p-value<0.001) but not end-stage kidney disease or cancer, versus people without depression. Stronger association was found in younger patients for severe hypoglycaemia (interaction p-value<0.001) and all-cause mortality (interaction p-value<0.001).

Conclusion
Comorbid depression is linked to higher risks of some complications in type 2

diabetes. The risk association of depression with severe hypoglycaemia and all-cause mortality is greater in younger population.

WPCS-01-8
Sensorineural Hearing Loss in Type 2 Diabetes Mellitus: an Overlooked Diabetes Complication

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Objective: Type 2 diabetes and sensorineural hearing loss both are common health problems manifested with ageing. However, hearing loss is commonly overlooked among other diabetes complication. A preliminary case control study was conducted, aim to evaluate the hearing function in type 2 diabetes who do not complain of hearing problem.
Methods:
Type 2 diabetes patient who attend outpatient diabetes center clinic at Prof. IGNG Ngoerah Hospital were enrolled in this study, and hearing function were tested by performing true audiometry and tympanometry. Patient with hearing loss were grouped as case and patient without hearing loss were grouped as control. Body mass index (BMI), systolic and diastolic blood pressure, blood sugar, HbA1c, and lipid profile were tested and compared between two group.
Results:
Mild hearing loss detected in 15 subjects, all of them were mild sensorineural hearing loss, none was conductive hearing loss. Subject with sensorineural hearing loss, were dominantly (66.7%) male, while in control group 40% were male. Subject with sensorineural hearing loss were older than subject without hearing loss (mean age 53.8±5.25 vs 48.46±8.57 years old, p=0.049). Other parameters including BMI, blood pressure, blood glucose level, HbA1c and lipid profile were not significantly different among two group.
Conclusions:
In this study, among type 2 diabetes patient, sensorineural hearing loss were mostly without any particular hearing complaint and symptoms and found by hearing function testing true audiometry and tympanometry. Whether hearing loss is associated with diabetes independent of glycemic control remains to be determined.

WPCS-01-9
Association between glucose tolerance and liver-related events and cardiovascular events in chronic hepatitis C

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Aim: Hepatitis C complicated with diabetes mellitus (DM) has been considered a risk factor for not only progression of fibrosis but also development of hepatocellular carcinoma and cardiovascular diseases. However, many previous studies may not have made an appropriate diagnosis of glucose intolerance. We aimed to examine the risk of abnormal glucose intolerance in developing liver-related and cardiovascular diseases in hepatitis C patients accurately diagnosed with impaired glucose tolerance.
Methods: This longitudinal retrospective study included 368 patients with chronic hepatitis C admitted to Ehime University Hospital for anti-hepatitis C therapy between September 1991 and January 2015. Patients were classified into normal glucose tolerance (NGT), prediabetes, and diabetes mellitus (DM) groups using a 75-g oral glucose tolerance test.
Results: Univariate analysis revealed that the DM group had a significantly higher incident rate of liver-related and cardiovascular events than the NGT group. Multivariate analysis adjusted for age, sex, body mass index, platelet, alanine transaminase levels, history of interferon and direct-acting antiviral therapies, sustained virological response, hypertension, and dyslipidemia revealed a significant association between the DM group and incidence of liver-related and cardiovascular events. In contrast, no significant association was observed between the prediabetes group and incidence of liver-related and cardiovascular events.
Conclusions: Patients with hepatitis C complicated by DM demonstrated a higher incidence of liver-related and cardiovascular diseases compared with those with hepatitis C complicated by prediabetes. Appropriate follow-up for patients with hepatitis C is required based on glucose tolerance status.

WPCS-02-1
Effects of pemafibrate on left ventricular diastolic function in patients with type 2 diabetes mellitus: A pilot study

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Aims/Introduction Diabetic cardiomyopathy (DCM) is characterized primarily by early diastolic dysfunction. Multiple DCM mechanisms involve changes in energy substrate utilization. Recent studies indicate that PPARα plays an important role in the pathogenesis of lipotoxic cardiomyopathy. Pemafibrate is known to be a selective PPARα modulator (SPPARMα). We thus investigated the effects of pemafibrate on cardiac diastolic function in patients with type 2 diabetes.
Materials and Methods Seventeen patients with type 2 diabetes (T2D) and hypertriglyceridemia were screened and treated with pemafibrate at a dose of 0.2 mg/day for 8-16 weeks. Fourteen patients were eligible for analysis. Echocardiography was used for assessment of diastolic function. Early diastolic filling velocity (E), late atrial filling velocity (A) and the E/A ratio were included in this study. Peak early diastolic annular velocities (e') were also assessed using color tissue doppler images. The primary endpoints were changes in the ratio of E to A (E/A), e', and the ratio of E to e' (E/e') from baseline.
Results Pemafibrate significantly increased average e' (7.24 ± 0.58 vs 7.94 ± 0.67, p = 0.019) and a significant reduction in E/e' (9.01 ± 0.94 vs 8.20 ± 0.91, p = 0.041). The increase in e' was significantly related to increases in fasting blood glucose (r = 0.607, p = 0.021) and non-esterified fatty acid (r = 0.592, p = 0.026).
Conclusion Pemafibrate improved diastolic function in patients with T2D and hypertriglyceridemia, suggesting that PPARα activation by pemafibrate prevents the development of DCM at an early stage.

WPCS-02-3
Dulaglutide prevents perilipin 2-induced myocardial steatosis and atrial fibrillation in mice

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Introduction:
Diabetes and obesity are the risk factors for atrial fibrillation (AF). Diabetes and obesity are also associated with myocardial steatosis, which leads to intracellular lipotoxicity. We previously reported that cardiac-specific overexpression of perilipin 2 (PLIN2) induced myocardial steatosis and AF in mice. Glucagon-like peptide-1 receptor agonist (GLP-1 RA) has been shown to have beneficial effects on cardiovascular disease and mortality, although the effect on AF has not been clarified. Thus we investigated the effect of a GLP-1 RA dulaglutide on AF and myocardial steatosis in the PLIN2-transgenic mice (PLIN2-Tg).

Methods:
Dulaglutide (0.5 mg/kg) or saline was administered every 4 days for 8 weeks to wild-type mice (WT) and PLIN2-Tg aged 12 to 15 months. Blood glucose, triacylglycerol (TAG), and atrial TAG content, surface electrocardiograms were measured after 8 weeks of treatment. AF was induced by transesophageal electric burst pacing, and the frequency of AF induction and its mean duration time were measured.
Results:
There was no difference in blood glucose or TAG levels between the groups. In the saline group, atrial TAG content was 3-fold greater in PLIN2-Tg compared to WT. However, the TAG content was 60% lower in PLIN2-Tg treated with dulaglutide compared to those treated with saline. PLIN2-Tg showed 3-fold greater frequency and duration of AF compared to WT, whereas dulaglutide treatment significantly diminished those parameters in PLIN2-Tg.
Conclusions:
Dulaglutide ameliorates atrial steatosis and prevents AF. Dulaglutide might be a potent drug for the treatment of AF in patients with myocardial steatosis.

WPCS-02-4
Insulinopenic diabetes accelerates steatohepatitis in mice: liver pathology and single-cell RNA seq signatures

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Background and Aims
Nonalcoholic fatty liver disease (NAFLD) is a growing health hazard that causes liver cirrhosis and hepatocellular carcinoma. We previously found that reduction in HbA1c and insulin treatment independently contribute to the alleviation of liver fibrosis during histological course of human NAFLD. The present study investigated the effect of insulinopenic diabetes on steatohepatitis and established a novel mouse model of diabetic steatohepatitis.
Methods
The 7-week-old C57BL/6J male mice were fed a 60% high-fat diet (HFD). Liver inflammation and fibrosis were induced by injecting carbon tetrachloride (CCl4) once in 3 days for 8 weeks. Insulinopenic diabetes was induced by injecting a low dose (50 mg/kg/d) streptozotocin (STZ) injection for 7 days.
Results
The HFD+CCl4+STZ group showed more advanced liver steatosis, hepatocyte ballooning, fibrosis, and regenerative nodules than other groups compared with the HFD+CCl4 group. Single-cell RNA-seq analyses for non-parenchymal cells showed unique macrophage fractions were increased or decreased in the HFD+CCl4+STZ group. Liver sinusoidal endothelial cells (LSECs) at both central and portal, natural killer (NK) cells, and B cells were globally reduced in the HFD+CCl4+STZ group.
Conclusion
We have established the novel diabetic steatohepatitis model by combining HFD, CCl4, and STZ. The STZ-mediated insulinopenic diabetes enhanced the HFD+CCl4-induced steatosis, hepatocyte ballooning, fibrosis, regenerative nodule formation, and macrophage M1/M2 ratios. Diabetes damages LSECs and exerts significant signatures in specific immune cell clusters. Investigating the target pathways linking hyperglycemia, LSECs, and immune cells may help understand molecular mechanisms underlying how diabetes accelerates NASH.

WPCS-02-5
Associations of thigh subcutaneous fat with incidence and remission of non-alcoholic fatty liver disease

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Objective: No prospective studies have examined the association between thigh subcutaneous fat distribution and non-alcoholic fatty liver disease (NAFLD). We investigated the associations of thigh subcutaneous fat distribution with incidence and remission of NAFLD based on a community-based prospective cohort.
Methods: We followed 1787 subjects who underwent abdominal ultrasonography, abdominal and femoral magnetic resonance imaging scans, and anthropometric assessments. Associations of thigh subcutaneous fat area (TSFA)/abdominal fat area (AFA) ratio and thigh circumference (ThC)/waist circumference (WC) ratio with incidence and remission of NAFLD were estimated using the modified Poisson regression model.
Results: Over a mean 3.6-year follow-up, 239 incident cases of NAFLD and 207 regressed cases of NAFLD were identified. Increasing TSFA/AFA ratio was associated with a lower risk of incident NAFLD and a higher likelihood of remission of NAFLD (risk ratio [RR] per standard deviation [SD]: 0.69, 95% confidence interval [CI] 0.59–0.81; 1.20, 95% CI 1.07–1.34, respectively). Each one SD increase in ThC/WC ratio was associated with a 16% lower risk of incident NAFLD (RR 0.84, 95% CI 0.76–0.94) and a 22% higher likelihood of remission of NAFLD (RR 1.22, 95% CI 1.11–1.34). Additionally, the effects of TSFA/AFA ratio on incidence and remission of NAFLD were mediated through adiponectin (14.9% and 26.6%), homeostasis model assessment of insulin resistance (9.5% and 23.9%), and triglyceride (7.5% and 19.1%).
Conclusion: A favorable fat distribution, characterized by a relatively greater ratio of thigh subcutaneous fat to abdominal fat, had a protective role against NAFLD.

WPCS-02-6
The association between thyroid hormones and non-alcoholic fatty liver disease in patients with type 2 diabetes

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Objective
Non-alcoholic fatty liver disease (NAFLD) comprises of a wide spectrum of liver pathologies. Thyroid dysfunction is associated with NAFLD, because free thyroxine (FT4) and triiodothyronine (T3) directly regulate hepatic lipid metabolism. This study aimed to investigate the relationship between each thyroid hormones and NAFLD in patients with type 2 diabetes (T2DM).

Methods
This cross-sectional study enrolled a total of 3,117 patients with T2DM, after excluding excessive alcohol drinking and presence of hepatitis B/C virus. Overt hypo-or hyperthyroidism, and atypical patterns such as non-thyroidal illness were also excluded. Liver ultrasonography was used to define the presence of NAFLD. The indices for liver steatosis/fibrosis were calculated as well.

Results
Serum T3 level (119.8 ± 19.4 vs. 114.7 ± 19.0 ng/dL, P<0.001) was significantly higher and TSH level (2.5 ± 2.1 vs. 2.7 ± 2.3 uIU/ml, P=0.019) was significantly lower in NAFLD group than in non-NAFLD group, while serum FT4 level did not differ. Increase in T3 level (per 10 ng/dL) was significantly and independently associated with the presence of NAFLD (OR=1.12, 95% CI=1.05–1.19, P<0.001) in a multivariate model. TSH level was inversely associated with the presence of NAFLD (OR=0.93, 95% CI=0.89-0.97, P=0.002). However, FT4 level did not correlate with NAFLD. Only T3 level was significantly associated with the severity of NAFLD and the indices for hepatic steatosis/fibrosis.

Conclusions

Higher serum T3 level even within normal to subclinical range was significantly associated with the presence of NAFLD, more severe NAFLD, and the degree of hepatic steatosis/fibrosis in patients with T2DM.

WPCS-02-7

Greater severity of steatosis is associated with a higher risk of incident diabetes

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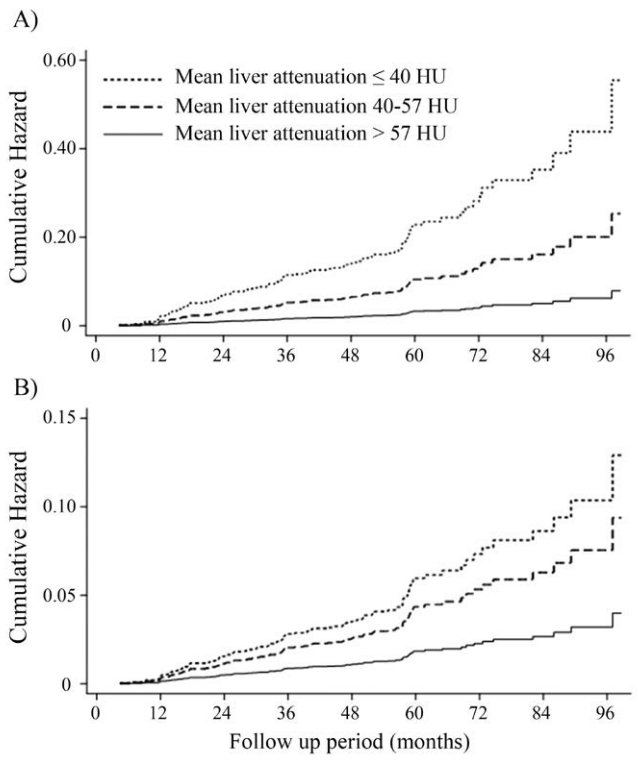
Objective: The aim of our study was to evaluate the association between hepatic steatosis and incident diabetes and determine if there are differences in these associations based on the degree of hepatic steatosis.

Methods: We analyzed data from 1,798 subjects who underwent a comprehensive health check-up and abdominal CT scan between 2010 and 2013. All subjects were categorized into three groups based on the baseline liver attenuation value on non-contrast CT images: without hepatic steatosis (>57HU), mild hepatic steatosis (41-57 HU), and moderate to severe hepatic (≤40HU). The risk of incident diabetes was assessed in each group.

Results: Of the participants, 43.0% had mild hepatic steatosis and 5.8% had moderate to severe hepatic steatosis. During a median follow-up of 5 years, 5.8% of study subjects progressed to diabetes. The incidence of diabetes was 17.3% in the moderate to severe hepatic steatosis group and 9.0% in the mild steatosis group, while only 2.9% of subjects without hepatic steatosis developed diabetes. In a multivariate adjustment model, subjects in the moderate to severe steatosis group had a hazed ratio (HR) of 3.24 (95% CI 1.64 to 6.42) for the development of diabetes and those in the mild steatosis group had a HR of 2.33 (95% CI 1.42 to 3.80), compared with subjects without hepatic steatosis.

Conclusions: The degree of hepatic steatosis was associated with a higher risk of incident diabetes. Our findings suggest that degree of steatosis could be an important factor in evaluating the risk of diabetes in patients with hepatic steatosis.



WPCS-02-8

Determination of serum ferritin levels in Mongolian men and women and its relationship with serum lipids and glucose

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Objective: To determine serum ferritin levels in Mongolian adults and compare serum ferritin with serum lipid and glucose levels by gender

Methods

The cross-sectional study involved 900 people (610 men and 290 women) from the Health preventive center, Erdenet Medical Hospital among the workers of Erdenet Mining Corporation in 2022. We analyzed serum levels T-Chol, TG, HDL, LDL, GLU and evaluated them in relation to ferritin levels.The clinical characteristics of the groups were compared using Independent Samples test.

Results

Serum ferritin levels were different between males (419.75±297.77) and females (169.71±175.49) (P<0.001). When comparing the analysis of men and women, serum ferritin, triglyceride , total cholesterol , LDL, glucose were higher, and HDL was lower in men (<0.05).

Conclusion: In males, TG and glucose were higher in the group with increased ferritin while HDl was low. On the other hand, women in the normal ferritin group had lower total cholesterol, LDL, and Tg than those in the elevated ferritin group.

№	Units	Men (n=610)			Women (n=290)		
		Ferritin high (n=235)	Ferritin normal (n=375)	P value	Ferritin high (n=82)	Ferritin normal (n=208)	P value
1.	Age (year)	46.69±10.38	44.15±11.38	<0.006*	54.96±8.38	47.07±10.96	<0.001**
2.	T-Chol (mmol/L)	5.18+0.93	5.03+0.97	<0.078	5.38+1.05	4.78+0.87	<0.001**
3.	TG (mmol/L)	1.71+1.53	1.30+0.88	<0.001**	1.26+0.76	0.95+0.44	<0.001**
4.	HDL (mmol/L)	1.27+0.28	1.33+0.26	<0.015*	1.51+0.30	1.53+0.26	<0.659
5.	LDL (mmol/L)	3.13+0.88	3.10+0.85	<0.710	3.28+2.82	2.82+0.74	<0.001**
6.	GLU (mmol/L)	6.10+2.01	5.64+1.27	<0.002*	6.17+3.04	5.31+0.94	<0.015*

WPCS-02-9

Prevalence of MAFLD and alcohol-related liver disease in young male Japanese adults

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Objective: Metabolic dysfunction-associated fatty liver disease (MAFLD) is an increasing cause of chronic liver disease in Japan. Concerning the increase of diabetes mellitus/impaired glucose tolerance in young adults, MAFLD may be escalating in the same generation. However, the prevalence in young adults has not yet been demonstrated. We, therefore, assessed the incidence of MAFLD and alcohol-related liver disease (ALD) in young male Japanese adults, and the role of health checkups in disease screening.

Methods: We recruited 313 male graduate students (mean age; 23 years) at an annual health checkup in April 2022. MAFLD was diagnosed on the basis of health checkup data and hepatic steatosis identified by ultrasonography. ALD was diagnosed with an alcohol consumption of > 30 g/day. To identify the value of health checkup items, logistic regression and receiver-operating characteristic curve analyses were used.

Results: MAFLD and ALD were observed in 11% and 1%, respectively. Serum alanine aminotransferase (ALT) levels were useful in identifying MAFLD with an optimal cutoff value of 26 IU/L (area under the curve [AUC], 0.86; sensitivity, 0.82; specificity, 0.77). The AUDIT was also helpful in identifying

ALD with an optimal cutoff value of 12 points (AUC, 0.97; sensitivity, 1.00; specificity, 0.96).
Conclusion: Our study revealed a prevalence of more than 10% of MAFLD in young male Japanese adults. Additionally, it was found that health checkups, including the measurement of ALT and AUDIT, were important for the screening MAFLD and ALD in younger people.

WPCS-03-1
Association between serum dehydroepiandrosterone sulfate levels and annual eGFR changes in people with type 2 diabetes

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[Background and Purpose]
Dehydroepiandrosterone sulfate (DHEAS) is thought to be associated with life span. Although renal dysfunction has often been found in people with diabetes, the clinical significance of DHEAS in renal prognosis remains unclear. Therefore, we aimed to determine whether DHEAS is associated with renal function in subjects with type 2 diabetes (T2D).
[Subjects and Methods]
To clarify the relationship between baseline serum DHEAS levels and longitudinal eGFR changes in people with T2D, we retrospectively evaluated 233 subjects (133 males and 100 females; mean age of 67.8±10.8 years) in whom 12-month longitudinal eGFR values were recorded after baseline serum DHEAS measurement at Anan Medical Center between April 2020 and March 2021. Associations of serum levels of DHEAS with values of the eGFR slope were statistically analyzed.
[Results]
The mean baseline HbA1c in the subjects was 7.1 ± 1.5% and the mean baseline eGFR was 72.8 ± 20.1 ml/min/1.73 m^2. Forty-four subjects (18.9%) were being treated with insulin. Multivariate regression analysis with confounding factors for determinants of eGFR slope showed that baseline HbA1c (p=0.020) and DHEAS (p=0.007) were independently and inversely associated with eGFR slope. Moreover, those associations remained significant even after adjustment of medications used.
[Conclusion]
In the present study, we found an inverse relationship between serum DHEAS levels and eGFR slope in people with T2D. The results suggest that early intervention for glycemia and hypertension is essential for renal protection in people with T2D who have high serum DHEAS levels.

WPCS-03-2
Singlecell transcriptomics reveals the cellular and molecular mechanisms of losartan in the treatment of in DKD mice.

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Angiotensin receptor blockers (ARBs) have been used for patients with DKD. However, the cellular and molecular mechanisms of ARBare incompletely understood. The changes of renal cells and differentially expressed genes before and after losartan (LST) of DKD were analyzed by single nuclear transcriptome sequencing (snRNA seq) technology. It was found that LST increased the number of proximal renal tubular cells (PT) and type A podocytes (POD-A). GO enrichment analysis showed that POD-A. Further, GSVA analysis revealed that ARB affected oxidative stress, apoptosis, membrane potential, ATP synthesis, mitochondrial dynamics and mitochondrial autophagy of PT, thus improving mitochondrial homeostasis. Pseudotime analysis provides the characteristic expression genes during the transformation from type B to type A podocytes after LST treatment.PT subgroup cells regulating oxidative stress and apoptosis transformed into regulating mitochondrial autophagy and antiinflammatory phenotype. Therefore, we speculate that the cells represent three phenotypes in the renal tubular cell phenotype spectrum, and thismay undergo the transformation of cell phenotype, which will have an effect on losartan treatment.The therapeutic mechanism of LST on PT cells is mainly reflected in inhibiting apoptosis and oxidative stress, promoting mitochondrial autophagy, and the therapeutic mechanism on POD cells is mainly reflected in maintaining the integrity of cytoskeleton.

WPCS-03-3
2-Deoxy-D-Ribose Induces Ferroptosis Through Inhibition of Cystine Transport in Renal Tubular Epithelial Cells

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Ferroptosis of renal tubular epithelial cells (RTECs) is involved in the development of diabetic nephropathy and acute kidney injury. The aim of this study was to verify whether 2-Deoxy-D-ribose (dRib) can induce ferroptosis in RTECs.
Intracellular cystine uptake, GSH content, and cell viability were measured in NRK-52E and rat primary RTECs. Lipid peroxidation was evaluated by C11-BODIPY staining and intracellular malondialdehyde and 4-hydroxynonenal levels. The xCT gene was overexpressed using a lentivirus.
The mRNA expression of Nrf2, ATF4, SLC7A11, ACSL4, CHAC1, and PTGS2 and the protein expression of Nrf2 and CHAC1 in NRK-52E cells were increased in response to the varying concentrations of dRib. dRib stimulation reduced cystine uptake and induced GSH depletion, lipid peroxidation, and cytotoxicity. 2-Mercaptoethanol restored dRib-induced cystine uptake reduction, GSH depletion, lipid peroxidation, and cytotoxicity. Deferoxamine, ferrostatin-1, and liproxstatin-1 restored the levels of dRib-induced lipid peroxidation and cytotoxicity, whereas the effect of deferoxamine was offset by the addition of FeSO4. These results were repeatedly observed in primary RTECs. The dRib-induced cystine uptake reduction, GSH depletion, lipid peroxidation, and cytotoxicity were almost completely restored by the xCT gene overexpression.
These findings suggest that dRib induces ferroptosis by inhibiting the intracellular cystine transport via the system χc- in RTECs. Therefore, it is thought that diabetic nephropathy and acute kidney injury could be prevented through regulation of the system χc-.

WPCS-03-4
A risk-prediction model for diabetic kidney disease based on machine-learning methods

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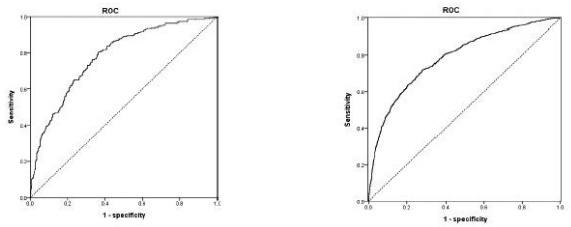
Objective: Even with controlled multiple risks, the number of chronic kidney disease (CKD) in patients with type 2 diabetes (T2DM) is still increasing. We aimed to find the residual risk factors of T2DM-related CKD and establish a risk-prediction model using machine learning.
Methods: In this retrospective observational study, subjects were enrolled in two independent T2DM cohorts: the derivation group (n=7,363, male 62.2%) and the validation group (n=4,490, male 61.9%). The CKD-predicting model in T2DM patients has established endeavors to use machine-learning methods, including Neural Network/XGBoost/Random-Forest, and traditional logistic regression analysis.
Results: Following machine learning training, the Random-Forest method with the best area under the receiver operating characteristic curve (AUC) was selected. Based on the feature importance and summary of SHAP (SHapley Additive exPlanations) values, serum uric acid, age, and low hemoglobulin were selected as the top 3 factors by the Random Forest method. The CKD-predicting model was constructed using clinical risk factors consisting of old age, systolic blood pressure, HbA1C, hyperuricemia, triglycerides, and anemia.

The AUC of the CKD predicting model among the derivation cohort and validation cohort was 0.779 and 0.784, respectively. (Fig 1).

Conclusion: In addition to traditional metabolic abnormalities, hyperuricemia, and anemia were identified as residual risk factors of CKD in T2DM patients. By machine learning, a CKD prediction model for T2DM patients selected six modifiable factors and with good accuracy.



A B

Figure 1. Area under the receiver operating characteristic curve for prediction of CKD in T2DM patients.

A. The derivation cohort

AUC	(95% CI)	*p-value*	Sensitivity	Specificity	Accuracy
0.779	(0.749-0.807)	<0.001	75.07%	67.83%	70.91%

B. The validation cohort

AUC	(95% CI)	*p-value*	Sensitivity	Specificity	Accuracy
0.784	(0.771-0.796)	<0.001	71.73%	71.62%	71.65%

AUC: area under the receiver operating characteristic curve; CI: confidence interval

WPCS-03-5
Influence of high-protein diet on diabetic nephropathy in SDT fatty rats

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[Objective] Protein-intake is limited in patients of DKD. Urea and creatinine are produced in proteolysis, these processing has burden to kidneys. Therefore, high-protein diet (HP) is known to contribute to the exacerbation of DKD. This examination investigated the effect of HP feeding on diabetic model rats and also confirmed the usefulness of the model animal.

[Methods] Male and female five-week-old SDT fatty rats were fed basal diet or HP *ad libitum* for 17 weeks. At necropsy, blood and kidneys were sampled for blood biochemistry test, gene expression analysis and histopathological analysis.

[Results] BUN was significantly increased in HP groups. Creatinine tended to increase in female HP group. As a results of histopathological analysis and gene expression, inflammation and fibrosis were increased in HP groups. Especially, fibsosis was observed on tubulointerstitium. Furthermore, more calcification was observed in HP group than standard diet group.

[Conclusion] These results suggested that HP may cause calcification, induce to interstitial nephritis. The factor of calcification was considered phosphorus contained in protein. The phosphorus was bound and deposited with calcium, as a result, HP induced calcification. Therefore, HP is one of the risk factors for DKD, and SDT fatty rat is useful as a animal model to test the effect of nutritional components on DKD.

WPCS-03-6
p-Cresol suppresses gluconeogenesis in cultured hepatocytes

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<Objective>

Diabetic patients with decreased renal function are prone to hypoglycemia, although the underlying mechanisms remain unclear. In this study, we aimed to investigate the effects of p-cresol, a representative uremic retention solute, as well as p-cresyl sulfate and indoxyl sulfate, on hepatic gluconeogenesis.

<Methods>

Rat hepatoma cells (Fao cells) were cultured in RPMI 1640 medium containing 10% fetal bovine serum until they reached confluence. After overnight serum starvation, the cells were exposed to a gluconeogenic medium consisting of glucose-free DMEM medium containing 3 mM sodium pyruvate and 30 mM sodium lactate. Simultaneously, p-cresol (25, 50, or 100 μg/mL), p-cresyl sulfate (100 μg/mL), or indoxyl sulfate (213 μg/mL) was added to the medium. After 6 hours, glucose concentration in the medium was measured and the cells were collected for examination of mRNA expression levels of phosphoenolpyruvate carboxykinase (PEPCK) and glucose 6 phosphatase (G6Pase), which are rate-limiting enzymes in gluconeogenesis.

<Results>

Glucose release into the medium decreased in a concentration-dependent manner in the p-cresol group compared to the control group, whereas no changes were observed in the p-cresyl sulfate or indoxyl sulfate groups. PEPCK mRNA expression did not change in the p-cresol group, but G6Pase mRNA expression decreased. We then investigated the mechanism of p-cresol's inhibitory effect on gluconeogenesis and found that p-cresol promoted phosphorylation of Erk1/2. Treatment with 20 μM U0126, an Erk1/2 inhibitor, partially restored the decrease in G6Pase mRNA expression induced by p-cresol.

<Conclusion>

p-Cresol suppresses gluconeogenesis in Fao cells by decreasing G6Pase mRNA expression.

WPCS-03-7
Metabolomics signature for the prediction of diabetic nephropathy in Chinese patients with type 2 diabetes

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Objective:

Diabetic nephropathy (DN) is the leading cause of end-stage kidney disease (ESKD). The current study aimed to identify circulating metabolites that are associated with incident DN by metabolomics profiling analysis in Chinese patients with type 2 diabetes (T2D).

Methods:

A nested case-control metabolomics profiling study, using the Q600 Metabolite Array kit, was conducted in patients with T2D recruited from the Hong Kong West Diabetes Registry (HKWDR). Serum samples of 40 individuals who had developed DN and 40 age, sex and T2D duration-matched individuals who remained free from DN throughout the follow-up period were investigated. Potential predictive metabolites were selected by the Boruta analysis. The associations between the identified metabolites and incident DN were examined and their predictive ability were assessed.

Results:

Over 500 metabolites were successfully detected in the metabolomics analysis.

Boruta analysis selected 10 metabolites as potential predictors of incident DN. Multiple conditional logistic regression analyses showed that L-Threonine, malonylcarnitine, L-Lactic acid, malic acid, together with two metabolites not previously reported, PC aa C30:3 and sulfolithocholylglycine, were independently and significantly associated with incident DN after adjustment for the clinical risk factors (all p-value<0.05 and q-value<0.1). Inclusion of five metabolites to the clinical risk model significantly increased the area under the receiver operating characteristics curve (AUROC) from 0.75 to 0.87 (DeLong p-value=0.023).

Conclusion:
Metabolites showing novel associations with incident DN were identified. The addition of five metabolites significantly improved the prediction of DN beyond the clinical risk model. Further validation in independent cohorts with larger sample size are warranted.

WPCS-03-8
An artificial intelligence based prediction model for diabetic kidney disease progression: DrAnswer 2.0

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Objective: Since the progression of diabetic kidney disease (DKD) is highly variable, it is crucial to identify patients at risk for DKD progression. We aimed to establish and validate a prediction model for DKD progression within 5-years based on artificial intelligence (AI) algorithms.
Methods: In patients with type 2 diabetes, we defined the progression of DKD as a development of eGFR <30 mL/min/1.73m^2 or an end stage renal disease. A prediction model for DKD progression was built using random forest model. The model was trained and tested on a database of three hospital electronic health record (n=20,938), and externally validated on a single hospital medical records (n=4,636). Data augmentation that combines three time points among the patient's multiple visit points and the concept of GFR slopes (short-term and long-term changes, respectively) were used to improve the model accuracy.
Results: Within 5 years, 2,131 patients (8.3%) showed DKD progression. Age, gender, age at diagnosis, fasting glucose, BUN, eGFR, medical comorbidities and medical history were included in our models. The prediction model showed excellent performance with mean accuracy 0.89, sensitivity 0.86, specificity 0.90, and AUC 0.88, respectively. The model was validated with mean accuracy greater than 0.92 in an external dataset (sensitivity 0.95, specificity 0.91, and AUC 0.93, respectively).
Conclusion: AI algorithms can accurately predict DKD progression over time in patients with T2DM. We expect that estimating individual risk for DKD progression could be a cornerstone of personalized approach to optimize outcomes for patients with DKD.

WPCS-04-1
Usefulness of Dietary Support for Patients with Borderline-Diabetes Mellitus Utilizing AGEs Value (first report)

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INTRODUCTION
People with borderline-diabetes have little access to hospitals and little opportunity to receive education about diet. We focus on AGEs as a biomarker of lifestyle because we believe that non-invasive measures of life can motivate the implementation of a healthy diet.
OBJECTIVES
This study was to analyze the relationship between diet, self-efficacy, and AGEs in borderline-diabetic patients and to obtain implications for the usefulness of AGEs in dietary support.
Methods
Participants were borderline-diabetic patients who were attending the clinic or working at University A and had undergone a staff health examination. Questionnaires were administered and health data were analyzed using descriptive statistics.
RESULTS
There were 7 participants. AGEs values ranged from 0.42 to 0.71 (mean 0.55). Self-efficacy scores ranged from 32 to 72 out of 90 (mean 55.4). When participants' AGEs values were compared to the SD of AGEs for healthy individuals in each age group, four participants had AGEs values higher than the SD.
Discussion
Borderline-diabetes is an important process in which improvement in lifestyle habits can prevent the transition to type 2 diabetes. It is a well-known fact that weight and BMI values are associated with type 2 diabetes, but there are people with standard body size in the borderline stage, and many are unaware of their risk. Since low self-efficacy tends to worsen AGEs values in this study, AGEs values, which can be measured easily and with little burden, may provide an opportunity to review lifestyle habits and help prevent the transition to diabetes.

WPCS-04-2
Eating order and blood glucose level - A case study

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Backround
The International research studies have suggested eating vegetables and protein before carbohydrates in order to control insulin and blood sugar levels.
Objective
The aim of study is to compare a mixed and an ordered meal effect on blood glucose level.
Methods
In our case study participated 2 nurses with and without diabetes who are working in a diabetes clinic. During lunch time they ate an ordered meal for 5 days and mixed meal for 5 days. The ordered meal was as follows: Vegetables first, protein and fats second, starches and sugars last. We are measured fasting and postprandial glucose levels.
Result
Fasting and postprandial blood glucose level range was 5.2-6.5 and 5.0-5.7 mmol/l for healthy nurse, but 6.1-11.1 and 6.1-12.3 mmol/l for nurse with diabetes, during the mixed meal. Fasting and postprandial blood glucose level range was 5.1-5.5 and 5.4-6.4 mmol/l for healthy nurse, 4.3-11.2 and 4-12.3 mmol/l for nurse with diabetes, during the ordered meal. Mean postprandial blood glucose level of mixed and ordered meals of healthy nurse's was 5.44±0.29 and 5.66±0.42 mmol/l (p=0.462), but response of nurse with diabetes was 9.48±2.98 and 6.78±3.20 mmol/l (p=0.343).
Conclusion
A mean postprandial blood glucose level was lowered by 2.7 mmol/l in diabetic patients after an ordered meals. We should continue a large sample study in future.

WPCS-04-3
Vitamin D and Type 2 diabetes mellitus

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OBJECTIVE
International studies of the relationship between diabetes and vitamin D have shown that vitamin D affects glucose control by stimulating insulin secretion. Among Mongolians vitamin D deficiency is common. The aim of this study was to evaluate plasma vitamin D levels in diabetic patients.

METHODS
Clinic based cross-sectional study was included a hundred (64 men and 36 women) diabetic patients. Physical examination and laboratory tests were determined. Fasting glucose, HbA1C, Insulin, C-peptide, lipid profiles and vitamin D were measured.

RESULTS:
Diabetic patients' mean age was 54.2±10.9 years old, Body weight 79.74±15.7kg; BMI 28.65±5.0 kg/m^2 ; BF 35.38±9.9%; BM 26.46; VF 10.4±5.55%; Fasting blood glucose 11.96±5.3 mmol/l; HbA1C 9.1±2.8%. Mean plasma vitamin D level of diabetic patients was 17.7±10.28 Among diabetic patients very severe, severe, suboptimal, optimal level and upper normal level of Vitamin D was 6%, 21%, 36%, 27%, 9% and 1%.

CONCLUSION:
Among diabetic patients Vitamin D deficiency is common.

WPCS-04-4
Managing risk of sarcopenia in elderly diabetic patients.

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Objective: Sarcopenia and its complications are seen most frequently in elderly diabetic patients; nutritional intervention is thought to be important for both prevention and management of the condition. We investigated the relationship between body composition, physical measurements, and clinical data as well as food intake by survey in elderly diabetic patients visiting our hospital.
Methods: The subjects were diabetic patients aged 65 years or older who visited our hospital from April 2020 to January 2021. Patients on maintenance dialysis, those with severe cognitive impairment or physical inability due to long-term bed rest or having active malignant tumors or inflammatory disease were excluded. Sarcopenia was diagnosed using the AWGS2019 sarcopenia diagnostic criteria. We quantified the relationship between the presence or absence of sarcopenia and age, anthropometric measurements, HbA1c, eGFR, and FFQ results.
Results: The study included 6 males and 52 females, of whom 21 males and 15 females showed evidence of sarcopenia, which was increased with age but remained rare in subjects with BMI ≥25 and <30. The prevalence of sarcopenia tended to be higher with use of SGLT2 inhibitors, low energy and protein intake, and low physical activity, although the differences were not significant.
Conclusion: The results of this study suggest that optimization of BMI and total energy and protein intake along with adequate exercise, is important for the prevention and control of sarcopenia in elderly diabetic patients. In addition, caution should be exercised in the use of SGLT2 inhibitors in susceptible individuals.

WPCS-04-5
Validation of improved 24-hour dietary recall using a portable camera among the Japanese population

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Objective
The collection of weighed food records (WFR) is a gold standard for dietary assessment. We propose using the 24-h recall method combined with a portable camera and a food atlas (24hR-camera method). Our study examined the validity of the 24hRcamera method against WFR by comparing the results.

Methods
Study subjects were 30 Japanese males, aged 31–58 years. For validation, we compared the estimated food intake (24hR-camera method) and weighed food intake (WFR method). The 24hR-camera method uses digital photographs of all food consumed during a day, taken by the subjects, and a 24-h recall questionnaire conducted by a registered dietitian, who estimates food intake by comparing the participant's photographs with food atlas photographs. Food intake was calculated for each food group and nutrient using the 24hR-camera vs. weighed methods.

Results
Correlation coefficients between the estimated vs. weighed food intake were 0.7 or higher in most food groups but were low in food groups, such as oils, fats, condiments, and spices. For other food groups, the percentages of the mean difference between estimated vs. weighed food intake were -22.1% to 5.5%, with no significant differences between the methods. The correlation coefficients between the two methods were 0.774 for energy, and 0.855, 0.769, and 0.763 for the macronutrients, proteins, lipids, and carbohydrates, respectively, demonstrating high correlation coefficients: greater than 0.75.

Conclusion
The 24hR-camera method satisfactorily estimated the intake of energy and macronutrients (except salt equivalents and potassium) in Japanese males and was confirmed as a useful method for dietary assessment.

WPCS-04-6
Dietary FODMAP intake and metabolic parameters in Chinese individuals with impaired glucose tolerance

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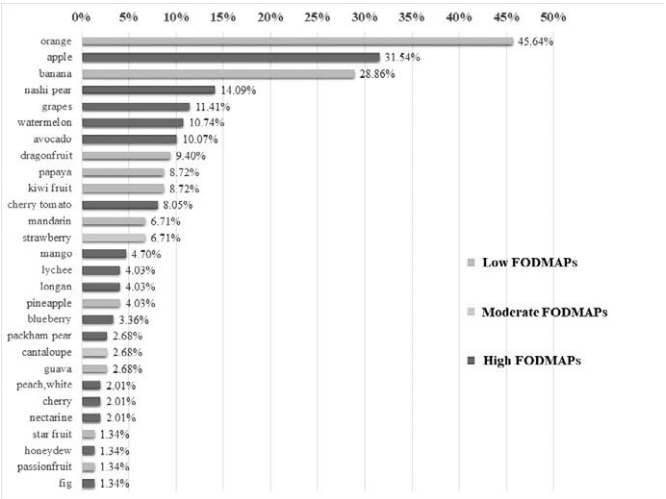
Objective: Dietary FODMAPs (Fermentable, Oligo-, Di-, Mono-saccharides And Polyols) affect metabolic-related microbiota in patients with irritable bowel syndrome. The relationships between FODMAP content of habitual diets and metabolic parameters, in people with prediabetes or diabetes are unknown.
Methods: In a cross-sectional study, we evaluated the association of habitual FODMAP intake with metabolic parameters in 149 Hong Kong Chinese with impaired glucose tolerance (IGT) who underwent 75g oral glucose tolerance test with C-peptide, body composition by bioelectrical impedance and completed food records over 3 days.
Results: The median (interquartile range) age was 59 (53-62) years with 60% women. Thedaily FODMAP intake was 6.9 g/d (4.6-10.3), derived predominantly from foods high in fructans [1.8(1.4-2.5) g/d) and lactose [1.7 (0.27-4.4) g/d]. Obese subjects had the lowest daily FODMAP intake compared with their non-obese and non-overweight counterparts [5.7(3.9-7.9) vs 7.1(5.0-11.3) vs 9.9(4.1-22.4) g/day, p=0.024] despite having similar total daily energy intake. The total content of FODMAPs was negatively correlated with body fat. After adjustment for age and gender, total FODMAPs were negatively associated with body mass index (BMI) and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). This remained significant after adjustment for macronutrients (p=0.032) and physical activity (p=0.036). Amongst the high FODMAP foods, apples were consumed most frequently followed by shiitake mushroom.
Conclusion: Hong Kong Chinese with IGT had low FODMAP intake especially amongst the obese subjects with lower FODMAP intake being independently associated with higher BMI and insulin resistance. These data provide the basis for designing dietary interventions for prevention of diabetes.



WPCS-04-7

Emotional Eating as a Pitfall of Poor Glycemic Control in Type 1 Diabetic Adolescent: A Case Report

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Objective:
Emotional eating is a condition defined as overeating in response to negative affect without particular mood or emotions. This condition becomes one of the causes of poor glycemic control in type 1 diabetic adolescent in which stress and confusion are experienced more than depressed mood.

Methods:
To describe a case of poor glycemic control of 18-year-old type 1 diabetic adolescence patient with emotional eating based on DEPS-R questionnaires.

Results:
An 18-years-old male patient was diagnosed with type 1 diabetes with initial a1c level was 9%. Initially, patient had insulin with dose titration to 3x20 unit of aspart insulin with correctional dose 1 unit for each 25 mg/dl increase of blood glucose and 1x30 unit of glargine insulin subcutaneously. The a1c level were between 7.7% and 8.9% with consistent used of insulin. The major problem of uncontrolled blood glucose was food restriction. Self-monitoring blood glucose was done 6 to 7 times a day with recurrent episodes of hypoglycemia. Patient's mood seemed to be depressed and his body weight was increased 10 pounds for the last two years. His DEPS-R score was 20 which concludes that the patient is an emotional eater.

Conclusion:
Emotional eating is a common problem in type 1 diabetic adolescent. Changes in neurotransmitters such as dopamine and hormones may be contributed in emotional disturbances which lead to increase appetitive drive and affect imbalance in adolescent. Early recognition and treatments may help achieve stable glycemic control in order to reduce complications and morbidities in type 1 diabetes.

WPCS-04-8

A Multicenter, Randomized Trial Comparing Low-carbohydrate Diet to Canagliflozin for Diabetes Treatment

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Aims/Introduction: In most previous studies, low-carbohydrate diets (LCDs) were compared with low-fat or low-calorie diets in terms of glycemic control. In this study, we used canagliflozin, a sodium-glucose co-transporter-2 (SGLT2) inhibitor, as the positive control drug and aimed to demonstrate that LCD is non-inferior to canagliflozin in blood glucose control.

Methods: We conducted a 3-month, multicenter, randomized trial involving patients with type 2 diabetes. Participants were randomly assigned in a 1:1 ratio to receive canagliflozin (100 mg/day) or LCD (carbohydrate intake < 20% of the total energy intake). The change in HbA1c level and the pharmacoeconomic effects of both interventions were evaluated.

Results: In total, 120 participants were enrolled; 60 were administered canagliflozin and 60 were administered LCD. After the 3-month intervention, the mean change in HbA1c levels was -1.73% with canagliflozin and -2.27% with LCD (estimated difference, -0.54%; 95% confidence interval [CI], -0.95 - -0.13; P = 0.011). After adding canagliflozin, 5 of 37 patients who had been using antidiabetic drugs (13.5%) discontinued one oral antidiabetic drug or reduced their insulin doses, whereas in the LCD group, 10 of 36 patients who had been using antidiabetic drugs (27.8%) discontinued one oral antidiabetic drug or reduced their insulin doses.

Conclusions: Our study showed that LCD was non-inferior to canagliflozin in glycemic control. Patients in the LCD group showed greater decline of HbA1c levels than those in the canagliflozin group. LCD reduced the cost of antidiabetic drugs.

WPCS-04-9

Does Intermittent Fasting Reverse The Clinical Progression of Type 2 Diabetes Mellitus ? : A Meta-Analysis

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Objectives
Intermittent Fasting (IF) is an emerging dietary behaviour defined as alternating periods of abstinence from caloric intake followed by normal diet in non fasting periods. This review aims to analyses the role of IF in glycemic control, Type 2 Diabetes Mellitus (T2DM) management, and diabetes remission based on current relevant clinical trials.

Methods
We performed a comprehensive literature screening through several electronic database such as Pubmed, Google Scholar, and The Cochrane Library. We collected randomized controlled trials that were published between March 2013 to March 2023. We pooled and analyzed the data based on the standardized mean differences (SMD) with 95% confidence interval (CI). Data heterogeneity was analysed using I^2 statistical approach, followed by calculating the average difference with random-effect or fixed-effect meta analysis models.

Result
Twelve trials (n=865 participants) met the inclusion criteria and underwent risk-of-bias assessment. After intervention, Glycated hemoglobin A1c (HbA1c) reduced by 1.05 (95% CIs: -1.51 ; -0.59) and HOMA IR decreased by 0.28 (95%CIs : -0.38 ; -0.17) in experimental group compared to control. Insulin plasma levels was reduced although non significantly. Secondary outcome

analyses showed significant BMI reduction and improvement of several metabolism indicators such as Triglyceride Glucose Index (TyG). In pre-diabetes population, IF showed promising result to achieve glycemic control.

Conclusion

Our findings suggested that IF serves as a potential non-pharmacological therapy for T2DM patients. However, long-term studies with wider participants are needed to further explore the sustainability of the practice and possible adverse events.

WPCS-05-1

THE CORRELATION BETWEEN INSULIN RESISTANCE AND SOLUBLE THROMBOMODULIN AS A COAGULATION FACTOR IN T2DM

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Objective: The aim of the study is to find out the correlation between insulin resistance and soluble thrombomodulin as a coagulation factor in type 2 diabetes mellitus patients.

Methods: This is a cross sectional study. The sample is selected by consecutive sampling at the metabolic endocrine outpatient clinic in Dr. M. Djamil General Hospital.

Results: On 30 patients, 66.7% were women and 33.3% were men. The mean levels of this study variables are mean soluble thrombomodulin level 4,059.13 (1114.14) pg/ml and HOMA-IR 5.09 (7.05). There is significant positive correlation between soluble thrombomodulin and HOMA-IR (p=0.003, r=0.519), but not significant between soluble thrombomodulin and fibrinogen (p=0.23, r=0.225).

Conclusion: There is correlation between insulin resistance and soluble thrombomodulin as a coagulation factor in type 2 diabetes mellitus patients.

Keywords: diabetes mellitus, insulin resistance, soluble thrombomodulin, coagulation

WPCS-05-2

Personalized Exercise Prescription in Type 2 Diabetes Patients in the Context of Integrative Medicine

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Abstract

Objective: This study aimed to investigate the application and effects of personalized exercise prescription in type 2 diabetes patients in the context of integrative medicine.

Methods: 120 type 2 diabetes patients admitted to our hospital from March 2022 to September 2022, were randomly divided into a control group and an observation group, with 60 patients in each group. All patients received routine examination and treatment upon admission, with the control group receiving routine nursing education and the observation group receiving personalized exercise prescription guidance on the basis of routine nursing education. The levels of glycemic and lipid metabolism indicators (fasting blood glucose [FBG], 2-hour postprandial blood glucose [2hPG], glycosylated hemoglobin [HbA1c], and body fat percentage) were compared between the two groups before and 3 months after intervention.

Results: 60 patients in each group completed the 3-month intervention and follow-up. Before intervention, there was no significant difference in glycemic control and body fat percentage between the two groups (P>0.05). After 3 months of intervention, the levels of FBG, 2hPG, HbA1c, and body fat percentage in both groups decreased compared to before intervention (P<0.05), with the observation group showing greater improvement than the control group, and the difference was statistically significant (P<0.05).

Conclusion: Personalized exercise prescription guidance for type 2 diabetes patients can effectively reduce body fat percentage and improve glycemic control, with better results than routine nursing education alone.

WPCS-05-4

Risk factors and clinical profile of early-onset type 2 diabetes in urban Indonesians

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Objective: To investigate the prevalence, risk factors, characteristics and complications of early-onset type 2 diabetes among urban Indonesians.

Methods: This cross-sectional study included type 2 diabetes patients at a private specialized diabetes clinic. Patients diagnosed before the age of 40 years were classified as early-onset and those diagnosed at the age of ≥40 years were classified as late-onset. Data were extracted from hospital electronic medical record.

Results: As many as 24.4% (139/569) of our study patients had early-onset type 2 diabetes. Risk factors associated with early-onset, instead of late-onset, were male [adjusted OR, 2.18 (95% CI, 1.41-3.37)], obesity [1.71 (1.11-2.65)], and diabetes family history [1.73 (1.12-2.70)]. Early-onset patients were younger (median, 37 vs 56 years, p <0.001) and more likely to use insulin [31.7% vs 13.3%, OR 3.03 (1.93-4.77)], had higher body mass index (27.8 kg/m^2 vs 25.9 kg/m^2, p <0.001), HbA1C (9.5% vs 8.3%, p <0.001), triglyceride (179 mg/dL vs 153 mg/dL, p=0.050), and lower HDL levels (39 mg/dL vs 44 mg/dL, p=0.002), compared to those of late-onset patients. In those with diabetes duration <5 years, early-onset had lower risks of macroangiopathy [OR, 0.26 (95% CI, 0.10-0.67)], diastolic dysfunction [0.07 (0.01-0.52)], nephropathy [0.32 (0.15-0.66)], and neuropathy [0.07 (0.01-0.50)]; those with diabetes duration ≥5 years, early-onset had lower macroangiopathy [0.19 (0.06-0.57)] but higher retinopathy [4.93 (1.22-19.98)] risks compared to the corresponding late-onset.

Conclusion: Despite worse metabolic control, chronic complications were less common in early-onset type 2 diabetes which might be due to the younger age compared to late-onset.

WPCS-05-5

Cysteine post-translational modifications targeted by selenoprotein P-mediated reductive stress in type 2 diabetes

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The diabetes-associated with the hepatokine selenoprotein P (SeP, encoded by *Selenop* in mice) causes pathology of type 2 diabetes (T2D), such as insulin resistance, exercise resistance, and impaired thermogenesis (Cell Metab 2010, Nat Med 2017, Cell Rep 2022). The present study focuses on comprehensive identification of the cysteine post-translational modifications (C-PTMs) impacted by the SeP-mediated reductive stress.

We used the liver of male *Selenop*-KO and wild type (WT) mice fed with high-fat and high-sucrose diet for 4 months, performed a differential alkylation-based redox labeling, followed by a trypsin digestion, and analyzed by triplicate the labeled peptides using a LC-MS. The resulting number of C-PTMs were analyzed by bioinformatic tools to organize, filter, align, and classify the data. Moreover, we estimated the differential altered proteins in the liver of male *Selenop*-KO and WT mice (fold change of ≥ ±1.2 and p.Adj.value ≥ 0.05) and assessed their relationship with biological processes using gene ontology enrichment analyses.

We identified the number of C-PTMs in oxidized and reduced state, only 0.8% of the total C-PTMs were identified as potential targets of the SeP-KO mediated reductive stress and of these C-PTMs 33.3% were in mitochondria. We obtained more oxidized proteins in the liver of *Selenop*-KO mice (39.8%) compared to that of WT mice (27.8%). Also, we found some biological processes significantly altered in *Selenop*-KO mice related to mitochondrial function.

These results suggest that SeP-mediated reductive stress modifies mitochondrial function via modifying C-PTMs of target proteins, which might be potential therapeutic targets against T2D.

WPCS-05-6
Dietary habits among newly diagnosed patients with type 2 DM; A cross sectional study in Sabaragamuwa, Sri Lanka

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Objective: To study dietary habits of newly diagnosed patients with type 2 diabetes mellitus (T2DM) who attended the diabetes Clinic, Kegalle Teaching Hospital, Sabaragamuwa Province, Sri Lanka.

Methods: A cross-sectional study was conducted to collect data on dietary habits in 172 patients with newly diagnosed T2DM Individuals with known hyperlipidemia, hypertension, renal, liver, cardiac, respiratory, thyroid, psychiatric, and any other chronic or acute diseases, and pregnant women were excluded. A pre-tested, newly developed, interviewer administered questionnaire was utilized in the data collection. Body mass and height were measured. The descriptive statistics were analyzed using SPSS software 25.0 version.

Results: Of all study subjects, 66 % were overweight or obese (mean BMI; 26.97±3.13 kg/m^2). Mean age of the participants were 49±7 years of all patients, 37.97 % consumed rice and curry for breakfast, lunch, and dinner. Only 15% depended on food made from wheat flour for the breakfast. Of the newly diagnosed T2DM patients, 13% had skipped breakfast. A total number of 74 patients (47%) had intake at least one fruit per day. The majority of the entire study group (61%) depended on full cream milk for the morning tea. It was shown that 17.08% of the patients had green leaves. Only 13% of patients practiced the recommended consumption of five servings of fruits and vegetables per day.

Conclusion: Most newly diagnosed patients with T2DM were overweight or obese. The
present study revealed the first sound research evidence on dietary habits of newly diagnosed T2DM patients.

WPCS-05-7
Hip fracture and the risk of incident diabetes: a retrospective cohort study in the Real-world Hip Fracture Cohort.

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Objective: Robust evidence shows that incident fractures and changes in bone metabolism are a consequence of Type 2 Diabetes Mellitus (T2DM), however, no studies have examined the relationship of indicators of bone health on the risk of developing T2DM. Here, we aimed to evaluate the risk of incident T2DM in hip fracture patients.

Methods: This is a retrospective cohort study conducted in the Hong Kong population. Patients aged ≥ 65 who were admitted to the hospital with a diagnosis of accidental fall from 1 Jan, 2008 to 31 Dec, 2015 were included in the study. Patients with hip fracture on admission were PS matched to controls (1:1) and followed from the date of discharge till first diagnosis of T2DM, death or study end (Dec 31, 2020). With death being the competing event, we used competing risk regression to evaluate the risk of incident T2DM in patients with hip fracture.

Results: 46,328 participants were followed-up for 236,595.6 person-years. The incidence rates for T2DM were 11.947 and 14.505 per 1000 person-years in the hip fracture and control groups respectively. After accounting for competing risk of death, hip fracture patients had a significantly lower risk of developing T2DM (HR=0.771, 95% CI 0.719-0.827, p<0.001).

Conclusion: For the first time, we show that hip fracture, an indicator of bone health, is associated with a reduced risk of developing T2DM. These results provide further insight into the cross-talk between bone health and T2DM, warranting further research into the relationship between bone and glucose metabolism.

WPCS-05-8
Comparison of beta-cell function between Chinese with young-onset and late-onset type 2 diabetes in Hong Kong

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Objective

We compared the trajectory in beta-cell function in Chinese with type 2 diabetes (T2D) diagnosed at age <40 years (young-onset diabetes, YOD) and ≥40 years (late-onset diabetes, LOD).

Methods

In two cohorts of people with T2D recruited in 1996-2012 (n=4543) and 2020-2021 (n=799), we used multivariable linear regression models to compare fasting C-peptide and Homeostasis Model Assessment (HOMA2-%B) across diabetes duration at enrolment between YOD and LOD.

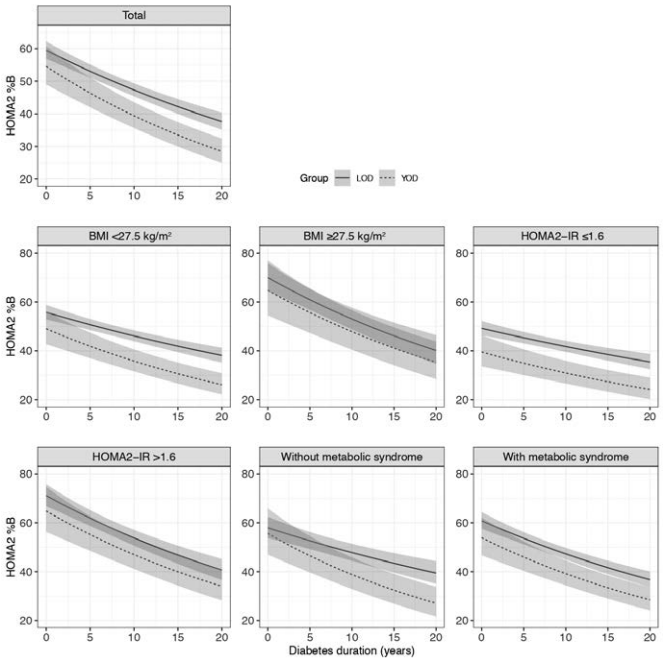
Results

The YOD group (n=1894, mean [SD] age: 40.0 [7.6] years, median [IQR] diabetes duration: 6 [2-12] years) was more likely to have obesity (41.9% vs. 26.7%), dyslipidaemia (61.9% vs. 55.3%) and worse glycemic control (mean HbA1c 7.7% vs. 7.4%) than those with LOD (n=3448; age: 61.2 [10.7] years, diabetes duration: 5 [1-10] years). The YOD group had lower fasting C-peptide (log-transformed, β = -0.21, p <0.001) and HOMA2-%B (log-transformed, β= -0.10, p <0.001) adjusted for year at enrollment, diabetes duration, sex, weight, glycemic and lipid indices. Fasting C-peptide and HOMA2-%B decreased with increasing diabetes duration in both groups. The slopes of decline were greater in YOD than LOD (fasting C-peptide, β for interaction = -0.01, p =0.03; HOMA2-%B, β for interaction = -0.01, p =0.04). In subgroup analysis, the slope difference was restricted to people with BMI <27.5 kg/m^2 and those without metabolic syndrome.

Conclusion

Chinese with YOD had worse beta-cell function and trajectory than those with LOD.

Figure. Comparison of HOMA2 %B in people with YOD and LOD, adjusted for calendar year and sex



WPCS-05-9

Alanine transaminase and aspartate transaminase ratio is associated with dysglycaemia

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Background and aims: Alanine transaminase and aspartate transaminase ratio (ALT/AST) , a marker of severity and prognosis of hepatic diseases. Recent studies showed that ALT/AST is also closely related to insulin resistance, metabolic syndrome and diabetes. However, the relationship between ALT/AST with dysglycaemia in general Chinese population is still limited. Therefore, this study aimed to address this gap.

Methods: A total of 5,001 subjects aged≥18 years were included in the baseline survey. Among them, 1,803 participants with normoglycaemia completed a 3-years follow-up. Diagnosis of prediabetes and diabetes were according to the WHO 1999 criteria. Multiple logistic regression analyses were used to assess the relationship between ALT/AST and dysglycaemia.

Results: In cross-sectional analyses, the odds of prediabetes and diabetes were increased by 28% and 51% for every 1-standard deviation increment of ALT/AST after multivariable-adjustment. In longitudinal analyses, 334 participants developed prediabetes and 66 participants developed diabetes during a 3-year follow-up period, baseline ALT/AST was positively associated with the risk of prediabetes and diabetes (P for trend < 0.05). And also found that baseline ALT/AST correlated positively with fasting plasma glucose, 2h plasma glucose after OGTT, insulin resistance (assessed by triglyceride-glucose index) and negatively correlated with insulin sensitivity (assessed by single-point insulin sensitivity estimator) at follow-up.

Conclusions: ALT/AST was significantly associated with prediabetes and diabetes in general Chinese population.

WPCS-06-1

The Promotion and Application of Standardized Injection of Insulin in clinical in China

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Background: Our research team selected 77 hospitals and 1666 nurses nationwide to investigate the status quo of insulin injection behavior of clinical nurses in China, and result showed that nearly 40% of nurses have non-standard operation during insulin injection. There is no standard of insulin injection in China. Objectives: Formulate a national standardized insulin injection operation specification and promote it in clinical nationwide in China. Material and methods: We adopt the expert meeting method to set standards, and from April 3, 2021 to December 27, 2022, we used online video display and offline salon for training and promotion in hospital nationwide. Then, a self-made questionnaire was used to investigate the status quo of nurses' clinical operation of insulin after training. Results: A total of 46817 nurses participated in the training, and 10260 nurses participated in the survey. Half of the nurses (50.73%) believed that the main difficulty in implementing this standard was the low number of offline training and lack of systematicness. Half of the nurses (43.04%) put forward other suggestions, such as making the operation process into a picture manual, making a sleeve book for everyone, making a official account and QR code training website, etc. Conclusion: The standardized injection of insulin is very needed in China, but there are difficulties in clinical application at present. It is necessary to build and develop offline promotion programs and operation tools according to the feedback of nurses, form a suitable paradigm.

WPCS-06-2

Usefulness of insulin injection technique using a covered needle for needle phobia

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[Objective] To investigate the usefulness of insulin self-injection using a hidden needle for needle phobia.

[Results] Our case was a 39-year-old woman. She was diagnosed with gestational diabetes at 15 weeks of gestation and started self-monitoring of blood glucose (SMBG). She could perform SMBG by herself because the needle was hidden. At 17 weeks of gestation, insulin therapy became essential, but insulin self-injection was refused because the needle was visible. When using the AutoShield Duo™ pen needle without needle exposure, self-injection could be performed from the day of its introduction. A database search found another case in which a person with needle phobia was introduced to insulin self-injections with the AutoShield Duo™ pen needle and could subsequently self-inject with a regular needle. Furthermore, it was reported that continuous subcutaneous insulin infusion (CSII) could also be introduced to needle phobia due to similar reasons.

[Discussion] Insulin self-injection is associated with anguish in needle phobia. The AutoShield Duo™ pen needle features double-ended automatic cover to prevent needlestick injury and reduces needle exposure. Based on our experience and previous reports, people could self-inject insulin from the day of its introduction by using a device with a structure in which the needle was hidden.

[Conclusion] A covered needle (e.g., AutoShield Duo™ pen needle and CSII) is useful for insulin self-injection in needle phobia and may reduce psychological distress.

WPCS-06-3

Comparison of laser and traditional lancing device for capillary sampling in diabetic patients with high bleeding risks

Min Jeong Park[1], Soo Yeon Jang[1], Ahreum Jang[1], Eyun Song[1], Kyung Mook Choi[1], Sei Hyun Baik[1], Da Young Kim[2], Ji A Seo[2], Ji Hee Yoo[2], Inha Jung[2], Nan Hee Kim[2], Hye Jin Yoo[1], Joo Won Kim[3], Hwan-Jin Hwang[3], Suk Hwan Yun[3]

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Objective: Patients with diabetes(DM) taking anti-platelet agents or with thrombocytopenia have high bleeding risks. Despite self-monitoring capillary blood glucose(SMBG) is important for DM management, patients with bleeding tendency reluctant to do SMBG in fear of bleeding. Recently, laser lancing devices (LMT-1000) that can collect capillary blood was developed. We compared bleeding time(BT) of capillary sampling with LMT-1000 and traditional lancet in DM patients with high bleeding risks.

Methods: DM patients with thrombocytopenia (50,000≤ platelet <120,000/uL) or on dual-antiplatelet agent(DAPT) were recruited. We performed capillary sampling with LMT-1000 in one hand, and with lancet in the other hand. BT was measured by Duke method absorbing blood with filter-paper in every 15seconds until hemostasis. We checked glucose, HbA1c using each device and surveyed the pain, satisfaction score using numeric rating scale(NRS) and visual analog scale(VAS).

Results: Among 102patients, 82subjects(80.4%) used DAPT and 21patients(20.6%) have thrombocytopenia. Strong positive correlation was seen (r=0.962, P<0.001) between glucose levels measured by LMT-1000(197.7±81.5mg/dL) and lancet(199.3±85.1mg/dL). Capillary blood HbA1c sampled by two devices exhibited high correlation (r = 0.963, P <0.001, LMT-1000: 7.507±1.5, lancet: 7.506±1.5). LMT-1000 reduced puncture pain by 50.0% (NRS 1 vs 2, *p*=0.003) and increased satisfaction by 23.1% (VAS 8 vs 6.5, p <0.001) compared to lancet. BT of capillary sampling using LMT-1000 was shorter than lancet (60 vs 85 seconds, *p*=0.024) especially in patients with thrombocytopenia

Conclusion: Capillary blood sampling using LMT-1000 is favorable for DM patients with high bleeding tendency, since LMT-1000 reduces BT and puncture pain while providing reliable glucose, HbA1c value.

WPCS-06-4

Relationship between time in range and corneal nerve fiber loss in asymptomatic patients with type 2 diabetes

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Objective: Corneal confocal microscopy (CCM) is a noninvasive technique to detect early nerve damage of diabetic sensorimotor polyneuropathy (DSPN). Time in range (TIR) is an emerging metric of glycemic control which was reported to be associated with diabetic complications. We sought to explore the relationship between TIR and corneal nerve parameters in asymptomatic patients with type 2 diabetes (T2DM).

Methods: In this cross-sectional study, 206 asymptomatic inpatients with T2DM were recruited. After 7 days of continuous glucose monitoring, the TIR was calculated as the percentage of time in the glucose range of 3.9 to 10.0 mmol/L. CCM was performed to determine corneal nerve fiber density, corneal nerve branch density, and corneal nerve fiber length (CNFL). Abnormal CNFL was defined as≤15.30 mm/mm^2 .

Results: Abnormal CNFL was found in 30.6% of asymptomatic subjects. Linear regression analyses revealed that TIR was positively correlated with CCM parameters both in the crude and adjusted models (all P < 0.05). Each 10% increase in TIR was associated with a 28.2% (95% CI: 0.595–0.866, P = 0.001) decreased risk of abnormal CNFL after adjusting for covariates. With the increase of TIR quartiles, corneal nerve fiber parameters increased significantly (all P for trend <0.01). The receiver operating characteristic curve indicated that the optimal cutoff point of TIR was 77.5% for predicting abnormal CNFL in asymptomatic patients.

Conclusion: There is a significant independent correlation between TIR and corneal nerve fiber loss in asymptomatic T2DM patients. TIR may be a useful surrogate marker for early diagnosis of DSPN.

WPCS-06-5

A research study on the discomfort and coping methods experienced during the use of CGM in diabetic patients

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ObjectAlthough the use of CGMs in diabetic patients is rapidly increasing, side effects such as skin side effects, discomfort at the attachment site, and bleeding have not been investigated.

MethodsFrom January to December 2021, 1010 patients receiving treatment at four general hospitals in Korea were surveyed using an online questionnaire targeting patients who had experience using CGM.**Rsults**There were 207 patients who experienced falling off during use, and it appeared in the order of falling off when putting on and taking off clothes, showering, sweating, and exercising. Discomfort experienced when using CGM was surveyed by 588 people, followed by discomfort during activity, skin problem, pain, bleeding, inflammation, and numbness in the limbs. There were 47 inquiries to the customer center, 45 consultations by medical experts, and 19 consultations. Regarding future use of CGM, 827 people wanted to continue using it and 183 people would not use it.**Conclusion**Sufficient education should be provided during diabetes education to minimize the occurrence of discomfort in using the CGM and to use the equipment well.

WPCS-06-6

Real usage of continuous glucose monitoring in pediatric patient with Type 1 and Type 2 diabetes in single center

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Objective: We investigate usage status and effectiveness of continuous glucose monitoring (CGM) among pediatric patients with diabetes mellitus. Method: We have selected 30 pediatric patients with diabetic mellitus who have been treated in Jeonbuk national university children's hospital and used CGM over at least one years. History, laboratory data and AGP report of CGM has been reviewed retrospectively. Result: 30 pediatric patients composed of 18 male and 12 female patients. All of male patients were diagnosed of type 1 diabetes mellitus (T1DM) and 15(83%) of male patient have used sixth generation (G6) Dexcom CGM. 10(83%) female patients were diagnosed of T1DM. 9(75%) of female patient have used G6 Dexcom CGM. All of pediatric patient under the age of 10yr have used G6 Dexcom CGM at the diagnosis while 4 (57%) of male and 5 (83%) of female patient at 10-15yrs group have used CGM at the diagnosis. Hemoglobin A1C (HbA1c) for all patient during use of CGM has been observed to significantly decrease (p =0.004 for male, p=0.008 for female). Analysis of AGP report have shown time in range (TIR) value have decreased gradually as time has passed. And CGM activation also have been observed to decrease among older age group.

Conclusion: Real time and continuous scanned CGM was more preferred by pediatric patient under 10 years old. Although Usage of CGM have been helpful to pediatric patient with diabetes mellitus, patient education and medical staff effort are required to keep TIR and CGM activation time being high.

WPCS-06-7

Internet-based glucose monitoring system improves glycaemia in people with insulin-treated type 2 diabetes

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Department of Endocrinology, Singapore General Hospital

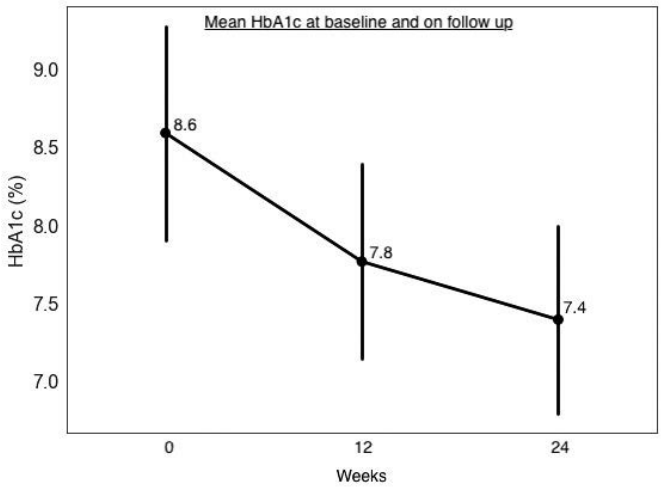
Self-monitoring of blood glucose (SMBG) using online platforms has shown promise in improving glycaemia among people with type 2 diabetes (T2D), though its effectiveness in a heterogenous Asian population such as in Singapore remains unclear.

T2D subjects treated with premixed insulin and HbA1c of 7.5%-10% were enrolled into an internet-based glucose monitoring system (ALRT Diabetes Solution) entailing SMBG twice daily and weekly direct glucometer uploads. The system then offered insulin dose suggestions and alerts to the primary physician. HbA1c and fasting plasma glucose (FPG) were measured at baseline and at week 12 and 24.

25 subjects were recruited (44.0% female, 58.9 ± 7.0 years, 52.0% Chinese). All subjects experienced reduction in HbA1c, with mean HbA1c falling 1.2%; from 8.6 ± 0.7% to 7.4 ± 0.6% at 24 weeks ($p < 0.01$). Mean FPG decreased 1.6 mmol/L; from 8.7 ± 2.0 mmol/L to 7.1 ± 1.4 mmol/L at 24 weeks ($p<0.01$). Adherence to prescribed SMBG frequency was 100% in 56.0% (14/25) of subjects.

Hypoglycaemia (BG <4.0 mmol/L) was reported in 48.0% (12/25) of patients during the study, comparable to the self-reported baseline of 44.9% (11/25). These were more frequent at weeks 13-24 (72 episodes) than weeks 1-12 (24 episodes), and predominantly (85/96 episodes) confined to level 1 (BG 3.0 - 3.9 mmol/L). There were no severe episodes of hypoglycaemia.

An internet-based glucose monitoring system with automated insulin dose suggestions led to significant reductions in HbA1c and FPG in our cohort. Mild hypoglycaemic episodes were more frequent with tighter glycaemic control.



WPCS-06-8

Blood Glucose Monitoring Device is associated with Glycemic Outcomes and Patients' Perspective in Chinese T1D Patients

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Department of Endocrinology, the First Affiliated Hospital with Nanjing Medical University

Background: Continuous glucose monitoring (CGM) is transforming the present situation of blood glucose monitoring (BGM), we aimed to investigate the situation in Chinese patients with type 1 diabetes (T1D), and evaluate the effects of self-monitoring of blood glucose (SMBG) and CGM on metabolic control and the patients' subjective feedbacks.

Methods: Online surveys presented 24-item questionnaire. Statistical analyses evaluated the choice of the BGM methods and their association with glycemic outcomes.

Results:197 participants returned the questionnaire. The median (IQR) age was 29.0(6.2-8.2) years and the disease duration was 4.5(1.5-11.0) years. 57.4% of participants were female. The CGM percent use was 61.4%. HbA1c (P=0.002), sex (P=0.011), educational background (P=0.011), current treatment (P=0.003), residential area (P=0.008) and glycemic monitoring expense(P<0.001) were significantly different between the SMBG and CGM group. 90.9% of the CGM group considered their blood glucose as "greatly improved" or "improved". The financial burden was the most disadvantaged part of CGM. Furthermore, sex (OR=2.33, P<0.01), age (OR=0.98, P<0.05) and residential area (OR=0.55, P<0.01)were associated with a higher percentage of CGM usage.

Conclusion: The use of CGM for diabetes management is increasing tremendously in the real-world setting in China and is associated with glycemic outcomes. However, the financial burden was still a problem that could not be ignored.

WPCS-06-9

Association of adherence to continuous glucose monitoring with glycemic control in adults with type 1 diabetes

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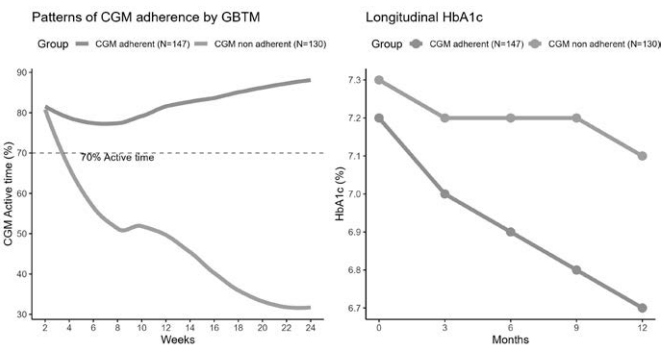
Objective: Many diabetes guidelines recommend that the percentage of active time for continuous glucose monitoring (CGM) needs to be at least 70% of the data for at least 14 days. We aimed to identify how patterns of CGM adherence over a 6 month-period measured at 2-week intervals affected long-term glycemic control in adults with type 1 diabetes.

Methods: We included adults with type 1 diabetes who were new CGM users (N=277). Percentage of active time of CGM was collected at 2-week intervals from baseline to 6 months through cloud-based data repository. HbA1c was measured at baseline and at three, six, nine, and 12 months. Group-based trajectory modeling (GBTM) was performed to classify groups of patients with similar trajectories using the percentage of active time in the CGM measured every 2 weeks for 6 months. We used linear mixed models to identify quantitative changes in repeated measures of HbA1c.

Results: Participants were classified by GBTM into a CGM adherent (N=147) and a non-adherent group (N=130). Subjects between CGM adherent and non-adherent group did not differ in baseline characteristics. There was a significant difference from 6 months and it became greater to -0.4% (P value=0.007) at 12 months. The increase in HbA1c every 3 months in CGM non-adherent group was 0.08% (95% CI: 0.03 to 0.13) compared with CGM adherent group.

Conclusion: There was a significant association between the pattern of CGM adherence over six months and longitudinal HbA1c, and an intervention strategy for CGM non-adherent group is needed.



WPCS-07-1
Association of Central Obesity and BMI with Cardiovascular Disease Risk Factors

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Objective: We aimed to investigate the clinical utility of the combined approach using body mass index (BMI) and waist circumference (WC) for assessing subsequent cardiovascular disease (CVD) risk factors.

Methods: We studied health checkup data from 14,170,134 adults aged 20 or older between 2009 and 2015. Participants had no history of type 2 diabetes, hypertension, or dyslipidemia at baseline. BMI was categorized into 5 subgroups, and WC cut-off points for central obesity were 90cm in men and 85cm in women. We divided participants into 10 subgroups based on central obesity and BMI ranges and analyzed the incidence risk of CVD risk factors (at least one from type 2 diabetes, hypertension or dyslipidemia) using a multivariable Cox's proportional hazard model.

Results: During the 5.3-year follow-up period, 1,857,307 participants developed CVD risk factors. Hazard ratio (HR) for CVD risk factors increased by 8.2% for every 1kg/m^2 increase in BMI. Participants with central obesity had significantly increased multivariable-adjusted HRs for CVD risk factors across all BMI categories, as compared to the reference group (BMI 18.5 to 23 kg/m^2 without central obesity): 1.00 to 1.27 for BMI 18.5 to 23.0 kg/m^2, 1.45 to 1.64 for BMI 23.0 to 25.0 kg/m^2, 1.83 to 2.10 for BMI 25.0 to 30.0 kg/m^2, and 2.56 to 3.08 for BMI over 30.0 kg/m^2.

Conclusions: Our study found that evaluating central obesity, in addition to BMI, has clinical utility in predicting CVD risk factors in Korean populations, even among individuals with a normal body weight.

WPCS-07-2
A matched cohort study evaluating effectiveness of pragmatic preventive program to delay long-term progression to T2DM.

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Objective: To evaluate the effectiveness of a hospital based Pragmatic Diabetes Preventive Program (PDPP) integrating cognitive behavioral therapy compared with the standard care in participants with prediabetes.

Methods: We performed a matched cohort study of patients 18-90 years with prediabetes, receiving a PDPP between 2013-2015 and matched 1:1 to those receiving a usual care. The one-year diabetes preventive program is composed of a 5-main session and of online group gamification in-between, in which, each session consisting of prediabetes self-management education, hand on self-practice workshop, psychosocial intervention and online group activities. The primary outcome was 60-month incidences of T2DM estimated using Kaplan–Meier analysis and Cox regression models.

Results: 190 of 192 participants and 190 of 10,260 were enrolled into intervention group and usual care group. The baseline characteristics of the participants were almost similar in both groups. After 60 months, the incidence rate (per 1000 person-year) of diabetes was 17.0 (95%CI 8.1,26.0) in the intervention group, and 35.02 (22.7,47.4) in the control group. Compared with usual care, the multivariable-adjusted HRs for incident diabetes in intervention group was 0.46 (0.21,0.98).

Conclusion: PDPP can halve the long-term incidence rate of diabetes in people with prediabetes. Therefore, health professionals should encourage individuals with prediabetes to attend the program to delay progression to diabetes.

WPCS-07-3
Low dose of diazoxide attenuates visceral fat obesity via correcting hyperinsulinemia in non-diabetic obese subjects.

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[1]Diabetes and Lifestyle-Related Disease Center, Tomishiro Central Hospital; [2]University of the Ryukyus; [3]Fukushima Medical University

Objective: Diazoxide, a mitochondrial KATP channel opener, is used as an inhibitor of insulin secretion in patients with adult insulinoma or infants with persistent hyperinsulinemic hypoglycemia. Reportedly, diazoxide has an anti-obese effect in hyperinsulinemic obese subjects (JCEM 1998;83:1911). We studied effects of low dose diazoxide on visceral fat obesity and daily glucose profiles in non-diabetic obese subjects (jRCT registration s071200028). Study design: Five subjects (2 men and 3 women: 43 years old) with visceral fat area >100 cm^2 were treated with diazoxide at 25, 50 and 75mg per day and were evaluated by 75g oral glucose tolerance test (OGTT) and flash glucose monitoring (FGM). Waist circumference, subcutaneous fat area and visceral fat area were determined by abdominal computed tomography (CT). Results: 75mg of diazoxide revealed a phased decrease of body weight (-0.6kg; p=0.016), waist circumference (-1.6cm; p=0.010) and visceral fat area (-18.2cm^2; p=0.021) and decreased area under the curve of plasma insulin (InsulinAUC) (-8225ngxmin/ml; p=0.013) without causing hyperglycemia (GlucoseAUC) (-1047mgxmin/dl; p=0.092). Conclusions: Low dose of diazoxide attenuates visceral fat area via correcting hyperinsulinemia in non-diabetic obese subjects, suggesting that diazoxide could be beneficial in hyperinsulinemic obese subjects.

WPCS-07-4
Metabolic Rewiring in Diabetes: Reprogramming GLUT4 Expression via Amino Acid Starvation

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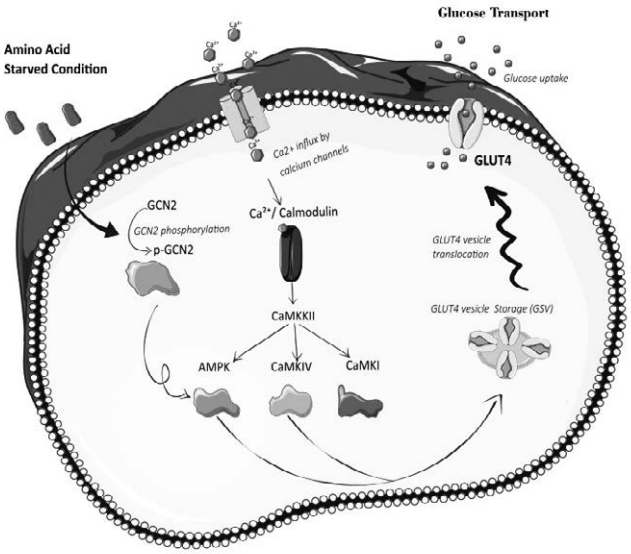
Objective Growing evidence suggest that dietary/caloric restrictions without malnutrition helps to alleviate inflammatory symptoms and protect the host against cellular damages. General control non- derepressible 2 kinase (GCN2), a nutrient sensor, is an eIF2 kinase that plays a central role in sensing and programming cellular metabolism as an adaptation to the conditions of amino acid restriction (AAR). While hyperglycaemia cripples the majority of Type 1 and Type 2 Diabetes patients, this study aims to closely observe upregulated Glucose uptake resulting from GCN2 activation and its cross talk with the AAR signalling pathway elements besides calcium influx and insulin dependency.

Methods Primary glucose transporters 1, 2, 3 and 4 were screened and GLUT4 was observed to display correlation to GCN2 upon activation. Flow Cytometry based experiments analysing GLUT4, glucose uptake and the signalling pathway elements is performed in GCN2 WT and KO MEFs and C2C12 cells *in vitro*. Finally, AAR induction is carried out *in vivo* in the STZ induced Type 1 and Type 2 Diabetes murine model.

Results A novel therapeutic approach to diabetes was observed wherein, glucose dysregulation is corrected via upregulation of GLUT4 in an insulin independent signalling pathway. Maintenance of pancreatic integrity is also observed besides upregulated insulin production in *in vitro* and *in vivo* murine models.

Conclusion In conclusion, this study proposes to layout the possible manner of unfolding of the AAR signalling pathway that could majorly affect metabolic regulation of inflammation and immunity involved during the pathogenesis of Diabetes and thereby promise a novel therapeutic.



WPCS-07-6

Association Between Trajectory of Metabolic Syndrome and Knee Pain Over 11 Years in Middle-Aged Adults

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[1]Menzies Institute for Medical Research, University of Tasmania; [2]Clinical Research Centre, Zhujiang Hospital, Southern Medical University, China; [3]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

Objective: Metabolic syndrome (MetS) is characterised by the clustering of central obesity with metabolic abnormalities. We aimed to describe the association of MetS and trajectories of MetS over 10-13 years with knee symptoms in general population-based middle-aged adults.

Methods: Fasting blood biochemistry, waist circumference and blood pressure measures were collected during Childhood Determinants of Adult Health (CDAH)-1 study (year:2004-6;n=2447; mean age:31.48±2.60) and at 10-13 years at CDAH-3 (year:2014-2019;n=1549; mean age:44±2.90). Participants were defined as having MetS as per International Diabetes Federation (IDF) definition. Knee symptoms were assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale at CDAH-3 (mid-adulthood).

Results: The prevalence of MetS increased from 8% in young adulthood (female:52.06%) to 13% in mid-adulthood (female:53.78%) over 10-13 years. Presence of MetS at mid-adulthood was associated with knee symptoms at mid-adulthood [ratio of means (RoM): 1.33; 95%CI:1.27,1.39]. Four MetS trajectories were identified—'No MetS' (85.01%), 'Improved MetS' (2.14%), 'Incident MetS' (8.81%), and 'Persistent MetS, (4.04%). Compared to 'No MetS', 'Persistent MetS' [RoM:1.15; 95%CI:1.06,1.25], 'Incident MetS' [RoM:1.56; 95%CI:1.48,1.65], and 'Improved MetS' [RoM:1.22; 95%CI:1.05,1.41] was associated with higher knee symptoms. Notably, 'Incident MetS' was strongly associated with knee symptoms [RoM: 1.56; 95%CI:1.48,1.65] and pain [RoM:1.52; 95%CI:1.37,1.70] at mid-adulthood.

Conclusion: In this sample of middle-aged adults, there was a positive association between MetS and knee symptoms. Relative to those without MetS at either life stage, the elevation in mean knee pain scores was more pronounced for those who developed MetS after young adulthood than those who had MetS in young adulthood.

Table 1: Characteristics of the participants at CDAH-1 and CDAH-3 follow-ups

Variable	CDAH-1		CDAH-3	
	N	Mean±SD	N	Mean±SD
Participants, N	2447	2447	1549	1549
Age, years	2322	31.48±2.60	1549	44.00±2.90
Female, n (%)	2447	1274 (52.06)	1549	833 (53.78)
BMI, kg/m^2	2444	25.53±4.71	1540	27.11±5.28
WOMAC total¶	2447	NR	1324	9.99±20.90
WOMAC pain	2447	NR	1325	2.59±5.19
WOMAC pain prevalence,%	2447	NR	1325	571 (43.09)
WOMAC stiffness	2447	NR	1333	1.45±2.65
WOMAC disfunction	2447	NR	1330	5.93±14.16
MetS measures,[ł] n (%)	2447	196 (8.01)	1549	205 (13.23)
High waist circumference,[a] n (%)	2278	664 (29.15)	1539	724 (47.04)
Hyperglycaemia,[b] n (%)	2372	241 (10.16)	1518	94 (6.19)
Hypertriglyceridemia,[c] n (%)	2373	343 (14.45)	1518	262 (17.26)
Low HDL-C,[d] n (%)	2373	423 (17.83)	1546	257 (16.62)
Hypertension,[e] n (%)	2321	490 (21.11)	1545	424 (27.44)

Values are expressed as mean±SD unless otherwise indicated.
BMI: body mass index, CDAH: Childhood Determinants of Adult Health, COMP: cartilage oligomeric matrix protein, HDL-C, high-density lipoprotein cholesterol, n: number of patients at the respective time point, MetS, metabolic syndrome. NR: not recorded, SD: standard deviation, WOMAC: Western Ontario MacMaster osteoarthritis score.
¶WOMAC total denotes overall knee symptoms
[ł] MetS based on IDF definition,
According to the new IDF definition, for a person to be defined as having the metabolic syndrome, they must have: Central obesity (defined as waist circumference* with ethnicity-specific values) plus any two of the following four factors ([b-e])
[a]Defined as waist circumference ≥94 cm in males or ≥80 cm in females.
[b]Defined as fasting glucose ≥5.6 mmol/L. Or previously diagnosed type 2 diabetes
[c]Defined as serum triglycerides ≥1.7 mmol/L. Or specific treatment for this lipid abnormality
[d]Defined as HDL-C <1.03 mmol/L in males or <1.3 mmol/L in females. or specific treatment for this lipid abnormality
[e] Defined as blood pressure ≥130/85mm Hg. Or treatment of previously diagnosed hypertension

WPCS-07-7

Histological changes in adipose tissues of KHK global knockout mice with metabolic syndrome models

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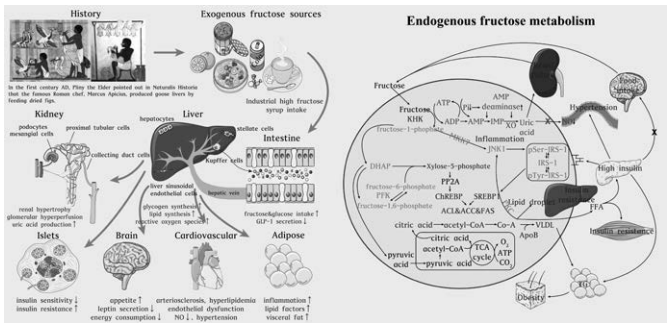
Objective: Modern industrial development of fructose is widely used to make food; its excessive intake can cause metabolic syndrome harm is seriously underestimated. Our team has been innovative in proposing a new concept of both fasting serum fructose and fructose kinase, KHK, as endogenous fructose markers and discovered its relationship with metabolic syndrome. The aim of this study was to explore the histological staining changes of adipose tissues in the models of metabolic syndrome for KHK global knockout mice.

Methods: Genetic engineering was used to construct the KHK global knockout mice and their control wild-type mice. After successful identification by sequencing and PCR and establishment of diabetes and obesity models with a high-fat diet and streptozotocin injection, six types of adipose tissues were collected with Hematoxylin-Eosin staining for observation.

Results: Based on successful genotype construction via sequencing and PCR identification, the model of metabolic syndrome was successfully established by testing serum physical indicators. Staining observations showed that adipose tissues of various parts in KHK global knockout mice changed to different degrees.

Conclusion: Under the metabolic syndrome model, adipose tissues in KHK global knockout mice were altered, indicating that KHK may be closely related to the fat distribution in metabolic syndrome. The study is conducive to the pathophysiological mechanism of metabolic syndrome and the development of targeted drugs.



WPCS-07-8

Prediabetes Phenotype Influences the Effect of Lifestyle Interventions on Diabetes Incidence: A Meta-Analysis

Thirunavukkarasu Sathish[1,2], Kamlesh Khunti[3], K.M. Venkat Narayan[2,4], Viswanathan Mohan[5], Melanie J Davies[3,6], Thomas Yates[3], Brian Oldenburg[7,8], Kavumpurathu R Thankappan[9], Robyn J Tapp[1], Ram Bajpai[11], Ranjit M Anjana[5], Mary B Weber[2,4], Mohammed K Ali[1,2,4], Jonathan E Shaw[7]

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Objective

To examine whether the effect of lifestyle interventions on diabetes incidence differs by prediabetes phenotype.

Methods

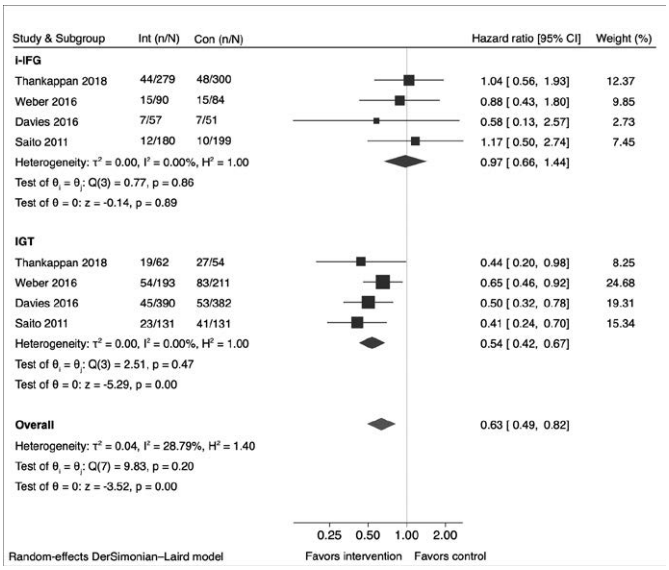
We searched MEDLINE, Embase, Scopus, and ClinicalTrials.gov from inception to March 01, 2023. Randomized controlled trials that recruited adults (age ≥18 years) with impaired glucose tolerance (IGT: fasting plasma glucose [FPG] <126 mg/dl and 2-hr plasma glucose [2-hr PG] 140-199 mg/dl) and isolated impaired fasting glucose (i-IFG: FPG 100-125 mg/dl and 2-hr PG <140 mg/dl), which evaluated the effect of lifestyle interventions on diabetes incidence were eligible. The primary outcome was incident diabetes (FPG ≥126 mg/dl or 2-hr PG ≥200 mg/dl or taking antidiabetic medications). Individual participant data were pooled from trials and analyzed through two-stage random-effects models using the within-trial interactions approach.

Results

Four trials with 2,794 participants (mean age 51.6 years, 60.6% men) were included; 1,240 (44.4%) had i-IFG, and 1,554 (55.6%) had IGT at baseline. Over 2.7 years of median follow-up, compared with the control arms, diabetes incidence was significantly lower in the intervention arms in IGT (Hazard ratio [HR] 0.54, 95% CI 0.42-0.67) but not in i-IFG (HR 0.97, 95% CI 0.66-1.44), with an interaction HR of 0.63 (95% CI 0.43-0.92, P=0.01). All four studies were at low risk of bias, and the certainty of the evidence was moderate.

Conclusion

Lifestyle interventions, as implemented in studies to date, effectively reduce diabetes incidence in people with IGT but not in those with i-IFG. Therefore, different interventions are likely required for individuals with IGT and i-IFG to prevent progression to diabetes.



WPCS-07-9

BMI Category-specific Waist Circumference Thresholds for Predicting the Risk of Type 2 Diabetes

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Objective: This study aimed to determine ethnicity-specific and body mass index (BMI) category-specific waist circumference (WC) thresholds and their clinical utility in assessing the risk of obesity-related diseases through a longitudinal study.

Methods: A prospective assessment was conducted on a population-based cohort of 5,852,702 subjects using data from the Korea National Health Insurance System. BMI was classified into six subgroups (<18.5, 18.5–22.9, 23.0–24.9, 25.0–29.9, 30.0–34.9, and ≥35.0 kg/m^2), and time-dependent receiver operating characteristic curve analysis was used to determine BMI category-specific WC thresholds for predicting the development of type 2 diabetes and at least one other cardiometabolic risk factor (hypertension and/or dyslipidemia). The hazard ratios (HRs) and 95% CIs for outcomes were obtained by using Cox proportional hazard models.

Results: During an average follow-up of 8.2 years, 130,106 subjects were diagnosed with the main outcomes. Optimal BMI category-specific WC thresholds were identified for men and women, ranging from 73 to 104 cm for men and 66 to 100 cm for women across different BMI categories. These thresholds showed a better balance between sensitivity and specificity than the recommended single WC thresholds, particularly for normal-weight and overweight individuals. The HRs for developing type 2 diabetes and comorbidities increased significantly with increasing WC thresholds for a given BMI category (P <.001, respectively).

Conclusion: This study determined optimal BMI category-specific WC thresholds, which can help identify individuals at high risk of developing type 2 diabetes and comorbidities.

WPCS-08-1

Effects on blood glucose metabolism of Pasireotide-LAR treatment in patients with acromegaly

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Purpose: To observe the efficacy and effects on blood glucose metabolism of pasireotide-LAR, a kind of long-acting release somatostatin receptor ligands

(SRLs) , monotherapy in patients with acromegaly.
Method: In this monocentric prospective study within a tertiary university hospital in Chengdu, 21 consecutive acromegalic adults (9 male and 12 female, average age 37. 48 ±8.10 years) were enrolled. Of these, 19 had undergone transsphenoidal surgery (TSS) and 15 had received radiation therapy (Gamma Knife). Patients received pasireotide-LAR injection once every 28 days (16 with 40 mg/month; 5 with 60 mg/month). Growth hormone (GH) and insulin-like growth factor (IGF-1) concentration were determined and glucolipid metabolism were evaluated from baseline to week 12 and 24.
Results:
The level of IGF1 was significantly decreased after the treatment (41.79 ±26.09μg/L vs. 79.86±29.41μg/L, t=5.362, P=0.000). 1/21 patients stopped Pasireotide-LAR due to intolerance.20/21 patients completed the study with Pasireotide-LAR for a median of 24 weeks with IGF-1 levels≤1.3 ULN. and 13 patients (65%)achieved complete biochemical control (remission). HbA1c and fasting plasma glucose were elevated during the treatment of pasireotide-LAR (HbA1c 5.62 ±0.42% vs. 6.26 ±0.61%,P = 0.00;FBG.38 ±0.69 mmol/L vs. 6.36 ±0.85 mmol/L, P = 0.000, respectively). 8/20 patients had hyperglycemia-related AEs and required initiation of oral antidiabetic treatment.
Conclusion: Pasireotide-LAR could effectively control the secretion of GH and IGF-1, suggesting a potency therapeutic alternative in acromegalic patients. Meanwhile, it also has a risk of raising plasma glucose and HbA1c in patients with acromegaly.

WPCS-08-2
Clinical usefulness of targeted next-generation sequencing panel testing for the diagnosis of monogenic diabetes

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[1]Department of Neurology, Hematology, Metabolism, Endocrinology and Diabetology, Yamagata University Faculty of Medicine; [2]Genomic Information Analysis Unit, Department of Genomic Cohort Research, Yamagata University Faculty of Medicine

Objective: We aimed to verify the usefulness of targeted next-generation sequencing (NGS) technology for clinical sequencing studies in a single center.
Methods: We designed an amplicon-based NGS panel targeting 34 genes associated with known monogenic diabetes and performed resequencing in 56 patients with autoantibody-negative diabetes mellitus diagnosed at <50 years who had not been highly obese. By bioinformatic analysis, we filtered significant variants based on allele frequency (<0.005 in East Asians) and functional prediction. We estimated the pathogenicity of each variant upon considering the patient's clinical features and family history.
Results: Overall, 16 candidate causative variants were identified in 16 patients. Among them, two previously known heterozygous nonsynonymous single-nucleotide variants (SNVs) associated with monogenic diabetes were confirmed as causative variants: one each in the *GCK* and *WFS1* genes. The former was found in two independent diabetes-affected families. Two novel putatively deleterious heterozygous variants were also assumed to be causative from the family history: one frameshift and one nonsynonymous SNV in the *HNF4A* gene. The other twelve variants were supposed to have the possibility of affecting gene function, but there was no supporting evidence of an association with the development of diabetes mellitus.
Conclusion: Targeted NGS panel testing was useful to diagnose various forms of monogenic diabetes in combination with familial analysis, but additional ingenuity would be needed for practice.

WPCS-08-3
A male presentation of autoimmune mediated diabetes as part of polyglandular autoimmune syndrome type 3

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Objective
Autoimmune polyglandular syndrome type 3 is an autoimmune condition that affects the body's endocrine glands, and typically affect woman during their middle age life.

Methods
Case report

Results
A 30 years old man came with symptoms of tachycardia and losing weight. Patient was diagnosed with Grave's disease with free T4 level > 7,7ng/dL, TSHs at < 0,003 mIU/mL and TRAb 4.11 IU/L. Thyroid US shows diffuse goiter with hypervascularization. Four months later having white discoloration of skin and spread through out the body. Vitiligo was diagnosed and treated with desoksimetasone 0,25% cream, pimecrolimus 1% cream, sunblock with SPF30 and phototherapy with narrow band UVB. Three months later, patient came to ER with general weakness and blood sugar at level 537 mg/dL. Laboratories result shows HbA1c at 14,6%, blood glucose at 537 mg/dL, negative ketone, normal pH, bicarbonate at 24,3, plasma osmolarity 359 mOsm/kg, anion gap 10,7, ANA test negative. Patient was diagnosed with Hyperosmolar Hyperglycemic State. Full evaluation performed and found C-peptide level was at 0,1 ng/mL. There is no similar history found in patient's family.

Conclusion
Important pathogenesis in polyglandular failure was cellular autoimmunity. Many family and population studies showed that PAS type 3 related to strong genetic background. PAS type 3 associated with HLA class II genes, but can also multigenetic involvement. Like IMD which related to several loci in non-HLA genomic regions, autoimmune thyroiditis also polygenic. With advanced of genome identification methods, there are possibilities for candidate gene approach therapies for this patient in future.

WPCS-08-4
Nilotinib Induced Diabetes

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[1]Department of Internal Medicine, University of Indonesia; [2]Metabolic and Endocrine Division,Department of Internal Medicine, University of Indonesia

Introduction
Discovery of Tyrosine kinase inhibitor dramatically changed prognosis of chronic myeloid leukaemia patients. Nilotinib is a 2nd generation TKI that has been used for first line or second line treatment of CML that already well-known for its glucometabolic effect compare to imatinib. It's hypothesized to increase insulin resistance and lower insulin secretion causing impaired glucose tolerance, diabetes mellitus until metabolic syndrome.
Case
Female 48 years old, without history of diabetes in the family. She already received imatinib for 7 years until resistance and changed to 2x400mg nilotinib. After a year of using nilotinib, she was found to have diabetes and dyslipidaemia during routine check-up without any symptom. Based on the Naranjo algorithm, this reaction is classified as possible ADR. She is now under insulin and oral therapy, with last A1C is 9.4%. She is still in nilotinib until now, and the result for her CML is remarkable.
Discussion
Nilotinib is found to reduced adiponectin and causing insulin resistance, furthermore it also increased body weight that increased risk of diabetes. Therefore, routine metabolic screening should be done for patient receiving nilotinib. Especially looking at CML patients' demography. There should be further study to elaborate underlying mechanisms behind nilotinib glucometabolic effect to help control metabolic panel in these patients.

WPCS-08-5
Functional analysis, inheritance and pathogenesis of first Glu59Gln mutation in NeuroD1 gene in a Chinese MODY family

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Objective: To investigate whether *NEUROD1* is responsible for Chinese MODY, we screened its mutation in MODY pedigrees and explored the potential pathogenesis.

Methods: PCR-sequencing was performed to screen *NEUROD1* mutations in 32 Chinese MODY probands who were negative for MODY2, MODY3 and MODY5 genes. The functional significances of newly identified mutations were analyzed by studies on clinical phenotypes, pathophysiology and three-dimensional (3D) structure.

Results: 1) Glu59Gln (E59Q, c.175 G>C), a heterozygous mutation in *NEUROD1* gene, was identified in a MODY family. 2) Glu59 residue in NeuroD1 is highly conserved across mammalian species. 3) Four diabetic patients (proband, her son, brother and sister) carrying the mutation were thinner with BMI of 21.0 (20.3-21.2). In comparison with unaffected relatives (n = 6), E59Q carriers showed obviously decreased insulin secretion at fasting and postprandial status (all $p<0.05$). The proband's father with E59Q mutation was normal glucose tolerance, suggesting non-penetrants. 4) The E59Q mutation was not detected in other probands or in the 201 non-diabetic control subjects. 5) The negatively charged Glu59 forms hydrogen bonds and strong salt bridges with the surrounding positively charged Arg54 and Lys88, while the salt bridges of Gln59 side chain was disrupted, a new hydrogen bonds was formed between Gln59 and Arg54.

Conclusion: NEUROD1-E59Q mutation clearly affected the interaction between E59 and its surrounding amino acids and thus changed the molecular conformation of NeuroD1, which may decrease the E59Q mutant binding to the insulin promoter and activity of insulin transcription, therefore causing MODY6 subtype with defected insulin secretion.

WPCS-08-6
Copy number variations in Maturity-Onset Diabetes of the Young: Copy number analysis in *HNF1B* by computational tool

Sandra T.F. Tsoi[1], Cadmon Lim[1,2], Ronald C.W. Ma[1,2,3], Eric S.H. Lau[1], Baoqi Fan[1], Elaine Chow[1,2,3], Alice P.S. Kong[1,2,3], Juliana C.N. Chan[1,2,3], Andrea O.Y. Luk[1,2,3]

[1]Department of Medicine & Therapeutics, The Chinese University of Hong Kong; [2]Hong Kong Institute of Diabetes and Obesity, The Chinese University of Hong Kong; [3]Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong

Objective:

Copy number variations (CNV) account for 50% of *HNF1B*-MODY. Next-generation sequencing (NGS), widely used in genetic variant screening, is insufficient in identifying CNV which requires additional tests such as multiplex ligation-dependent probe amplification (MLPA). We employed a computational tool to detect CNV in *HNF1B* from NGS data in patients with young-onset diabetes to report the prevalence of *HNF1B*-MODY and assess the usability of the tool.

Methods:

Targeted sequencing of monogenic diabetes genes was conducted for 1,021 Chinese with non-type 1 diabetes diagnosed aged ≤40 years in the Hong Kong Diabetes Register. Copy numbers of *HNF1B* region were analyzed from the sequencing reads using an open-source CNV detection algorithm CNVPanelizer. CNV were then validated by MLPA when screened positive.

Results:

From the sequencing data of 1,021 patients, no pathogenic variants were identified in *HNF1B*. Using CNV detection algorithm, 3 (0.3%) patients were newly detected for heterozygous *HNF1B* whole-gene deletion and 1 (0.1%) patient for whole-gene duplication, confirmed on MLPA. Two out of 3 patients with deleted *HNF1B* gene copy exhibited *HNF1B*-MODY-associated clinical features, including single kidney, renal cysts and chronic kidney disease without retinopathy. Notably, the patient with extra *HNF1B* gene dosage also had renal cysts and persistent albuminuria.

Conclusion:

Using bioinformatic methods, we identified 4 (0.4%) cases of *HNF1B* CNV in this young Chinese diabetes cohort not otherwise detected on standard analysis of NGS data. Computational methods are useful to screen for CNV at no additional cost and time.

WPCS-08-7
Targeted gene panel provides advantages over whole-exome sequencing for diagnosing obesity and diabetes mellitus

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A small fraction of patients diagnosed with obesity or diabetes mellitus has an underlying monogenic cause. Here, we constructed a targeted gene panel consisting of 83 genes reported to be causative for monogenic obesity or diabetes. We performed this panel in 481 patients to detect causative variants and compared these results with whole-exome sequencing (WES) data available for 146 of these patients. The coverage of targeted gene panel sequencing was significantly higher than that of WES. The diagnostic yield in patients sequenced by the panel was 32.9% with subsequent WES leading to an additional three diagnoses with two novel genes. In total, 178 variants in 83 genes were detected in 146 patients by targeted sequencing. Three of the 178 variants were missed by WES although the WES-only approach had a similar diagnostic yield. For the 335 samples only receiving targeted sequencing, the diagnostic yield was 32.2%. In conclusion, taking into account the lower costs, shorter turnaround time, and higher quality of data, targeted sequencing is a more effective screening method for monogenic obesity and diabetes compared to WES. Therefore, this approach could be routinely established and used as a first-tier test in clinical practice for specific patients.

WPCS-08-8
Utility of SGLT-2 Inhibitors in a Case of Type A Insulin Resistance Syndrome with a Novel Gene Mutation

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Type A insulin resistance syndrome is caused by abnormalities of genes related to insulin receptor and signal transduction. Conventionally, insulin-sensitizing agents such as metformin and thiazolidinedione have been used for patients with mild phenotype, and large doses of insulin and recombinant human IGF-1 have been used for patients with severe phenotype. However, maintaining good glycemic control for these patients is challenging and refinement of therapeutic strategy is warranted. Recently, several reports have suggested the utility of sodium-glucose cotransporter 2 (SGLT-2) inhibitors. In this article, we report a case of type A insulin resistance syndrome with novel heterozygous mutation in tyrosine kinase domain (Asp1110His) of INSR, for whom we administered SGLT-2 inhibitors and achieved good glycemic control while alleviating hyperinsulinemia. We further discuss the importance of early diagnosis and the utility of SGLT-2 inhibitors in treatment of type A insulin resistance syndrome.

WPCS-08-9
New Mechanism in small intestine for Oxyhyperglycemia by Excess Thyroid Hormone

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Objective: Oxyhyperglycemia is a special type of impaired glucose tolerance. It shows characteristic and transient glucose spike after an oral intake of glucose. Excess thyroid hormone causes oxyhyperglycemia. The mechanism still remains to be elucidated. We focus on SGLT1 (sodium-glucose transporter) which plays an important role of nutrient absorption in small intestine. This

study hypothesized that thyroid hormone regulates SGLT1 gene expression.
Methods: The rats were injected by T4 and fasting treatment for overnight. We divided small intestine into three parts, termed A, B and C from stomach side. The mice were rendered hyperthyroid by injected by T4 for 14 days. We measured glucose levels by OGTT (Oral glucose tolerance test) or IPGTT (intraperitoneal glucose tolerance test) in mice. We measured serum free T4 levels and analyzed the expression of the SGLT1 mRNA levels in small intestine by QPCR in both rats and mice.
Results: T4 treatment increased serum free T4 levels compare to sham in both rat and mice. T4 treatment increased mRNA levels of SGLT1 in small intestine B and C in rats, and similar changes were observed mice. Glucose levels were increased at 60 mins in OGTT with T4 treatment compared to sham. However, there were same glucose levels in IPGTT with or without T4 treatment in mice.
Conclusion: Thyroid hormone up-regulates the mRNA levels of SGLT1 in small intestine. Our data suggests that excess thyroid hormone caused oxyhyperglycemia via up-regulated the SGLT1 mRNA in small intestine.

WPCS-09-1
Sodium–glucose cotransporter 2 inhibitor combined with medical nutrition therapy for hyperglycemia in acute stroke

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Background: Effective and safe glucose-lowering treatment is needed in patients with hyperglycemia in an acute stroke phase. We investigated the effectiveness and safety of lowering blood glucose (BG) levels as medical nutrition treatments involving total energy restriction (TER) combined with a high (60%) carbohydrate (carb) or moderate (40%)-carb restriction diet with or without sodium-glucose cotransporter 2 inhibitors (SGLT2i).**Methods:** We included patients with acute stroke admitted between 2011 and 2019 who 1) had glycated hemoglobin A1c level ≥6.5%, BG level ≥11.1 mmol/L, and an estimated glomerular filtration rate ≥60 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$ at admission; and 2) underwent a fasting BG (FBG) test on day 7. The 40%-carb-TER diet (C40) group was divided into the C40 with SGLT2i [C40_SGLT2(+)] and without SGLT2i [C40_SGLT2(-)] subgroups. We defined FBG <7 mmol/L by day 7 as the target FBG and neither sulfonylurea (SU) use nor insulin analog use as the safety endpoint. **Results:** Eighty-four patients were eligible: 26 and 58 in the C60 and C40 groups, respectively [36 patients in the C40_SGLT2(+) and 22 in C40_SGLT2(-) subgroups]. SGLT2i use was an independent factor for the efficacy endpoint, and both SGLT2i and a 40%-carb-TER diet were associated with no SU use. **Conclusions:** A 40%-carb-TER diet combined with SGLT2i may achieve the day 7 target FBG level without SU use in patients with hyperglycemia at the acute stroke stage.

WPCS-09-2
Association of insomnia and coexisting habitual snoring with risk of cerebrovascular events in type 2 diabetes

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Background and aims:
Obstructive sleep apnoea(OSA) and insomnia are common sleep disorders in type 2 diabetes(T2D) and potentially increase risk of cerebrovascular events(CVE). Nonetheless, the effects of insomnia and comorbid OSA on CVE outcomes are underexplored. We hypothesized insomnia increases CVE risk both independently and in combination with habitual snoring(HS), a proxy of OSA, in T2D.

Methods:
Clinical information was collected from T2D enrolled in Hong Kong Diabetes Register(July 2010-June 2015). Shift workers and history of CVE at baseline were excluded. Eligible participants were categorized into 4 groups: non-HS-non-Insomnia (control), HS-alone, Insomnia-alone and HS+Insomnia; and prospectively followed up for incident CVE till 31 December 2019. Sleep habits were assessed by validated sleep questionnaires with HS defined as a frequency≥3/week and insomnia defined as Insomnia Severity Index>14.

Results:
A total of 2774 patients [mean(standard deviation) age = 54.3(8.5) years; duration of diabetes = 8.2(7.1) years; HbA1c = 7.5(1.5) %; 58.3% men; 59.4% control, 31.9% HS-alone, 4.7% Insomnia-alone, 4.0% HS+Insomnia] were included. After a median (inter-quartile range) follow-up of 7.8 (1.6) years, 2.1% developed CVE. Analysis of the entire cohort showed no significantly increased hazards of incident CVE for all three groups (HS-alone, Insomnia-alone or HS+Insomnia groups) compared to control. Sensitivity analysis revealed significant risk association of Insomnia-alone [HR 4.025 (1.003-16.153), $p = 0.050$] and HS+Insomnia [5.165 (1.022-26.101), $p = 0.047$] with incident CVE in women, which were absent in men.

Conclusion:
Insomnia increased risk of CVE in women with T2D with further risk escalation when comorbid with habitual snoring.

WPCS-09-3
Increased fibroblast growth factor 23 levels are associated with vascular smooth muscle dysfunction in type 2 diabetes

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Aim: Fibroblast growth factor 23 (FGF23) is a key regulator of phosphate metabolism. Recently, increased FGF23 levels were shown to be associated with the risk of cardiovascular disease in the general population. In this study, we investigated the association between serum FGF23 levels and vascular function in patients with type 2 diabetes.
Methods: This study included 283 Japanese patients with type 2 diabetes. Flow-mediated dilatation (FMD) and nitroglycerin-mediated dilatation (NMD) of the brachial artery were measured by ultrasonography to evaluate vascular endothelial function and smooth muscle function, respectively. Serum intact FGF23 levels were determined by a sandwich enzyme-linked immunosorbent assay.
Results: The median values of FMD, NMD, and serum FGF23 were 6.0%, 14.0%, and 27.3 pg/mL, respectively. Serum FGF23 levels were inversely associated with NMD, but not with FMD, and the association was independent of atherosclerotic risk factors, estimated glomerular filtration rate (eGFR), and serum phosphate levels. Furthermore, the relationship between serum FGF23 levels and NMD was modified by kidney function and was more pronounced in subjects with normal kidney function (eGFR ≥ 60 $mL/min/1.73m^2$).
Conclusions: This study demonstrated that an increased serum FGF23 levels was an independent determinant of impaired NMD in patients with type 2 diabetes, especially in those with normal kidney function. This study suggests that an increased serum FGF23 levels is a novel biomarker for vascular smooth muscle dysfunction in patients with type 2 diabetes.

WPCS-09-4
ASSESMENT OF CARDIOVASCULAR RISKIN PATIENTS WITH DIABETES MELLITUS

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BACKROUND: In Mongolia, the number of cardiovascular diseases and related causes of death is expected to steadily increase due to the increasing prevalence of non-communicable diseases such as obesity and diabetes among

the population.
OBJECTIVES: 1. Assessment of the risk of cardiovascular diseases in patients with diabetes mellitus. 2. Study of the relationship between glycemic control and the risk of cardiovascular diseases
METHODS: The study included 120 patients with diabetes mellitus who are under the supervision of an endocrinologist at the second state central hospital. Cardiovascular risk was assessed using a CARDIOCAL calculator recommended by the World Health Organization and Pan American Health Organization. This calculator inclides age, smoke, systolic blood pressure (mm. Hg), total cholesterol (mg/dl). Cardiovascular risk assessment with this calculator is classified as follows: Low <10%, moderate (10-20%), high (20-30%), very high (>30%).
RESULTS: The median age of patients 60.34±4.5, and 55% (n=66) were male. Duration of diabetes: 5-10 years 20,8% (n=25), 11-15 years 34,2% (n=41), 16-20 years 27,5% (n=33), 21-25 years 17,5% (n=21). Assessment of cardiovascular risk: low-32,5 % (n=39), moderate-35,8% (n=43), high-27,5% (n=33), very high-4,2% (n=5). The average of HbA1C-9,1% and the risk of cardiovascular diseases varied depending on the level of glycemic control. According to the glycemic index: 25,2% (n=29) good control, 74,7% (n=86) bad control. The difference between glycemic control and cardiovascular disease risk was statistically significant (P<0,01).
CONCLUSION: Diabetic patients have a high risk of cardiovascular diseases, and one of the contributing factors is glycemic control.

WPCS-09-5
Overexpression of MnSOD suppresses progression of atherosclerosis in apolipoprotein B-deficient mice

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Background: Manganese superoxide dismutase (MnSOD), which scavenges mitochondrial reactive oxygen species (mtROS), improves hyperglycemia-induced dysfunction of endothelial cells. However, effectiveness of MnSOD for diabetic macrovascular complication is unclear. Therefore, we investigated the effect of overproduction of MnSOD in endothelial cells (ECs) on atherosclerotic lesion formation in apolipoprotein-E deficient (ApoE-KO) mice.
Methods: ApoE-KO mice with vascular endothelium-specific overexpression of MnSOD (eTg-MnSOD/ApoE-KO) (12 weeks of age) were fed with normal chow (NC) or high fat diet (HFD) for 8 weeks. Atherosclerotic lesion formation (ALF) of whole aorta and aortic sinus were evaluated by Oil red O staining. Expression of ICAM-1, MCP-1 and IL-6 mRNA in human aortic endothelial cells (HAECs) were evaluated by real-time RT-PCR. mtROS generation in HAECs was evaluated by mitotrucker-Red.
Results: There was no difference on ALF between NC-fed ApoE-KO and eTg-MnSOD/ApoE-KO mice. However, ALF in HFD-fed eTg-MnSOD/ApoE-KO mice was significantly smaller than that in HFD-fed ApoE-KO mice, without affecting glucose and lipid metabolism. Moreover, ROS generation in ALF of HFD-fed eTg-MnSOD/ApoE-KO mice was reduced. LPS significantly induced mtROS generation, which was suppressed by overexpression of MnSOD in HAECs. Moreover, LPS-induced ICAM-1, MCP-1 and IL-6 mRNA expression were suppressed by overexpression of MnSOD.
Conclusion: Overexpression of MnSOD suppressed LPS-induced expression of adhesion molecules and inflammatory cytokines in vascular ECs, and ALF in HFD-fed ApoE-KO mice. Considering the report that HFD-fed mice show increased blood LPS levels, LPS-induced overproduction of mtROS in vascular endothelium may be one of the important factors in HFD-induced progression of atherosclerosis.

WPCS-09-6
DPP4 deficiency induces M2 macrophage polarization, and suppresses progression of atherosclerosis in apoE-KO mice

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Background: Dipeptidyl peptidase-4 (DPP4) inhibitors suppressed progression of atherosclerosis in atherosclerotic mouse models. However, the role of DPP4 on the progression of atherosclerosis is not clear. We investigated the effect of DPP4 deficiency on the progression of atherosclerosis in DPP4 and apolipoprotein-E double knockout (DPP4/ApoE-DKO) mice.
Methods: ApoE-KO mice and DPP4/ApoE-DKO mice were fed with normal chow until 20 weeks of age. Whole aorta and aortic sinus were stained with Oil red O. Expression of iNOS, MCP-1, TNF-α and IL-1β mRNA (M1 markers), and arginase-1, Mgl2 and Ym1 mRNA (M2 markers) in bone marrow-derived macrophages (mφ) were evaluated by real-time RT-PCR, and mφ polarization was evaluated by flowcytometry.
Results: The blood glucose levels upon glucose tolerance test were significantly decreased in DPP4/ApoE-DKO mice. The size of atherosclerotic lesions was significantly smaller in DPP4/ApoE-DKO mice. There was no difference between wild-type mφ and DPP4-KO mφ in LPS+IFNγ-induced the mRNA expression of M1 markers, but the mRNA expression of M2 markers were significantly increased in DPP4-KO mφ. The number of iNOS (M1 marker)-positive cells were increased by LPS+IFNγ, which was comparable between wildtype mφ and DPP4-KO mφ. On the other hand, the number of CD206 (M2 marker)-positive cells was higher in DPP4-KO mφ than that in wildtype mφ.
Conclusion: This study suggests that DPP4 deficiency suppresses the progression of atherosclerosis in apoE-KO mice. Moreover, DPP4 deficiency increases the polarization of M2 mφ. These findings may indicate the involvement of DPP4, at least in part, in the development of diabetic macrovascular complications.

WPCS-09-7
Syndecan-1, a Marker of Endothelial Glycocalyx Degradation, is Associated with Arterial Stiffness in Type 2 Diabetes

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The endothelial glycocalyx (EG) covers the luminal surface of vascular endothelium that mediates or protects the endothelium from various stress associated with vascular injury. Circulating syndecan (SDC)-1 that is extracellular domain of transmembrane heparan sulfate proteoglycan shed by inflammatory mediators is considered as a marker of EG degradation associated with vascular damage. Although diabetes is known as one of the causes of EG degradation, no study has thus far investigated the relationship between EG degradation and atherosclerosis in type 2 diabetes. This study aimed to investigate the association between EG degradation assessed by serum SDC-1 levels and arterial stiffness in patients with type 2 diabetes.
This study enrolled 276 Japanese patients with type 2 diabetes and assessed arterial stiffness by pulse wave velocity (PWV). Patients with severe kidney dysfunction whose estimate glomerular filtration rate (eGFR) was less than 30 mL/min/1.73m^2 or those with history of cardiovascular diseases were excluded. Median values of serum SDC-1 level and PWV were 26.4 ng/mL and 1042 cm/sec, respectively. In univariate analyses, serum SDC-1 levels were not correlated with PWV ($p = 0.222$). In multivariate analysis, serum SDC-1 levels were independently associated with PWV ($b = 0.100$, $p = 0.031$) after adjustment for known other risk factors including age, body mass index, HbA1c, LDL-cholesterol, and eGFR.
In conclusion, serum SDC-1 level is an independent determinant of PWV in patients with type 2 diabetes. This study suggests a potential role of the EG degradation in arterial stiffness in type 2 diabetes.

WPCS-10-1

Hypoglycemia in hospitalized older patients with diabetes--An 0bservational study

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Objective: To evaluate the incidence and predisposing risk factors of hypoglycemic episodes in elderly hospitalized diabetic patients, and discusses the prevention and treatment measures of hypoglycemia in elderly subjects with type 2 diabetes mellitus.

Methods: In this mono-center observational study, we retrospectively analyze the time distribution and frequency of hypoglycemic episodes in elderly diabetic patients(age>65 years) hospitalized in West China Hospital of Sichuan University from January 1, 2022 to March 31, 2022.We defined hypoglycemia as a recorded self-monitored blood glucose (SMBG) results< or =3.9mmol/L. We also reported all predisposing factors for each hypoglycemic episode. Recorded and analyzed the temporal and spatial characteristics of hypoglycemia.

Results: There were a cohort of 475 elderly diabetic patients who were diagnosed with diabetes, with a history of diabetes of 12.2 years. The blood glucose management system detected a total of 894 hypoglycemic episodes, the time distribution of hypoglycemia was 333 times (37.2%) during the day, 561 (62.8%) hypoglycemic episodes occurred at night, most were symptomatic, and 199 cases (42.9%) of recurrent hypoglycemia (≥ 2 times) within one week. Statistical analysis showed that the incidence of hypoglycemia was higher in non-surgical departments than in operating departments. The first predisposing risk factors were attributed to missing a meal (nearly 60%)followed by inappropriate exercise, and medication increase.

Conclusion: The time distribution of hypoglycemia is mostly nighttime, and the course of disease and the recent fluctuation range of blood glucose are closely related to the occurrence of hypoglycemia.

Period of monitoring	Occurrence of blood glucose	First phase of hypoglycemia	Second phase of hypoglycemia
0:00-2:00	42	27	15
2:00-4:00	37	27	10
4:00-6:00	30	26	4
6:00-8:00	304	275	29
8:00-10:00	55	47	8
10:00-12:00	57	44	13
12:00-14:00	38	33	5
14:00-16:00	91	76	15
16:00-18:00	37	30	7
18:00-20:00	55	45	10
20:00-22:00	110	88	22
22:00-24:00	38	25	13

Table 1: The time and extent distribution of hypoglycemia.

WPCS-10-2

Diabetes Mellitus in the Elderly Adults in Korea: the Korean National Health and Nutrition Examination Survey 2019-2020

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Background: We evaluated the prevalence and management of diabetes mellitus in elderly Korean patients with DM based on nationally representative data from the Korean National Health and Nutrition Examination Survey (KNHANES).

Methods: A total of 3,371 adults aged 65 years and older (21.8% of total population) were analyzed using KNHANES from 2019 to 2020. Prevalence, awareness, treatment, and control rates, and comorbidities were analyzed. Lifestyle behaviors and energy intake were also measured by a self-administered questionnaire.

Results: In this elderly population, the prevalence of DM and prediabetes based on the KNHANES criteria was 29.6% and 50.5%, respectively. The awareness, treatment and control rates were 76.4%, 73.3%, and 28.3%, respectively. The control rate was 77.0% if A1C <7.5% criteria was used. The mean A1C value of individuals with known DM was 7.1%, and 14.5% of this population had A1C ≥8.0%. Abdominal obesity, hypertension, and hypercholesterolemia were combined with DM in 63.9%, 71.7%, and 70.7% of this population, respectively, and the rate of integrated management was 34.9% (A1C <7.5%). A total of 40.1% of those with DM walked regularly. The percentage of energy intake from carbohydrates was higher in those with DM than in those without DM, while that of fat was lower in those with DM than in those without DM, especially in women.

Conclusion: In 2019-2020, three of ten elderly adults in Korea had DM, and approximately 70% of them had comorbidities. A strategy for more individualized comprehensive care for the elderly with DM is urgently needed.

WPCS-10-3

Factors Associated with Treatment Burden in Patients of Elderly Diabetes Patients with Multi-comorbidities

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Patients with chronic multiple comorbidities have a high burden of treatment, which will affect the quality of life and treatment compliance, thereby increasing the hospitalization rate and mortality. This study is to explore the factors that affect the treatment burden of elderly patients with type 2 diabetes mellitus (T2DM) accompanied with multi-comorbidities. A cross-sectional study was conducted to facilitate sampling and collection of T2DM patients over 60 years old with chronic comorbidities. From November 2021 to October 2022, a total of 206 cases who were managed in a diabetic specific hospital were studied. Basic data, diabetes-related emotional distress, social support, and chronic disease treatment burden were analyzed with questionnaires (Short-Form Chinese-Version PAID Scale, Diabetes Social Support Scale, Chinese Multimorbidity Treatment Burden Questionnaire). 53.4% were women, mean age was 71.2 ± 6.4 years, the mean DM duration was 15.1 ± 7.9 years, 77.2% were married, 88.3% were financially independent, and 61.7% with poly-pharmacy. Treatment burden was observed in 193 subjects (93.7%), the mean HbA1C, education level, type of medical insurance, source of income, number of chronic diseases, poly-pharmacy, diabetes-related emotional distress, and social support status were significantly associated with degrees of treatment burden. By a multiple regression analysis, education level, type of medical insurance, number of chronic diseases, diabetes-related emotional distress, and social support were significantly related factors to the burden of chronic treatment R2=53.2%, p<0.001. Our study revealed that treatment burden is commonly presented in elderly T2DM patients with multi-comorbidity, and there are multiple domains associated with treatment burden.

WPCS-10-4

Risk of cause-specific mortality across glucose spectrum in elderly people: a nationwide population-based cohort study

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Background: Diabetes mellitus (DM) is associated with premature mortality. We aimed to investigate the risk of cause-specific mortality according to glucose tolerance status in elderly Koreans.

Methods: A total of 1,292,264 subjects with age ≥65 who received health examination in 2009 were identified from the National Health Information Database. Subjects were classified as normal glucose tolerance (NGT),

impaired fasting glucose (IFG), newly-diagnosed DM, early DM (oral hypoglycemic agents, OHA ≤2), or advanced DM (OHA ≥3 or insulin). The risk of organ-specific and disease-specific death was estimated by multivariate Cox proportional hazard analysis.

Results: During a median follow-up of 8.41 years, 257,356 death events were recorded. DM was associated with higher risk of all-cause mortality (HR 1.58, 95% CI 1.57-1.60), death due to circulatory (HR 1.49, 95% CI 1.46-1.52), respiratory (HR 1.51, 95% CI 1.47-1.55), genitourinary systems (HR 2.22, 95% CI 2.10-2.35), and neoplasm (HR 1.30, 95% CI 1.28-1.32). DM was related to higher risk of death due to ischemic heart disease (HR 1.70, 95% CI 1.63-1.76), cerebrovascular disease (HR 1.46, 95% CI 1.41-1.50), pneumonia (HR 1.69, 95% CI 1.63-1.76), and kidney diseases (HR 2.23, 95% CI 2.09-2.38). The risk of mortality step-wisely increased according to the glucose spectrum (P for trend <0.0001 for every cause). Presence of stroke, heart failure, or chronic kidney disease accentuated the risk of all-cause mortality in every stage of glucose intolerance.

Conclusion: A linear association between the risk of mortality from various causes and severity of glucose tolerance status was noted in elderly population.

WPCS-10-5

The impact of pay-for-performance program on glycemic overtreatment in old patients with type 2 diabetes in Taiwan

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Background and Aims: In 2001, the Bureau of Nation Health Insurance (NHI), Taiwan implanted a pay-for-performance (P4P) program for diabetes to promote better glycemic control. In 2006, the NHI launched the "Personal Annual Incentive by Performance" which includes the proportion of enrollees with HbA1c <7% as one of the four performance indicators. We aimed to evaluate the impact of annual Incentive on glycemic overtreatment in old patients with type 2 diabetes mellitus (T2DM).

Materials and Methods: Data of patients with T2DM in 2006, 2011, and 2016 were collected from 2 tertiary referral medical centers. The inclusion criteria were age ≥65 years old, using insulin, sulfonylureas, or glinides. The definition of glycemic overtreatment were healthy patients with HbA1c <6.5%, intermediate health with HbA1c <7.0%, and poor health with HbA1c <7.5%. The Student's t test and the chi-square test were used to compare continuous and categorical variables, respectively.

Results: A total of 30,195 patients were included, of whom 8,671 (28.7%) patients was overtreated with an increasing rate overtime (27.0% in 2006, 28.2% in 2011, and 30.2% in 2016). The overtreated trend was similar in both P4P participants and non-P4P participants. P4P participants had lower overtreated rate than non-P4P participants. The older the age and the lower the estimated glomerular rate had the higher overtreated rate. Nephrologist had the highest overtreated rate (38.1%); similar rate between endocrinologist and family physician, 24% vs 23.8%.

Conclusions: The glycemic overtreatment is increasing overtime. P4P program lowered overtreatment rate. Subspecialty education of individualized treatment goal is needed.

WPCS-10-6

Serum Osmolality Predicts Diabetes Onset with Kidney Function Decline in Non-diabetes: A 4-Year Longitudinal Study

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OBJECTIVE

To assess the prognostic value of serum osmolality on long-term kidney-related outcomes and incidence of diabetes in patients without diabetes.

METHODS

From January 2016 to December 2019, a serial check-up annually of the general population was conducted in a rural area in middle Taiwan, and data were collected on patient demographics, biochemical indexes tests, and anthropometric parameters. Their serum osmolality was calculated and fasting blood glucose of more than 126 mg/dl was to be identified as diabetes onset. For assessing long-term kidney-related outcomes, based on the age- and sex-specific distribution, we analyzed the changes in estimated glomerular filtration rate (eGFR), proteinuria, and the onset of diabetes.

RESULTS

We retrospectively analyzed 4-year longitudinal data from 24071 participants and identified 1543 patients without diabetes. The baseline prevalence rates for impaired fasting glucose (IFG) and euglycemia were 38.7% (597/1543) and 61.3% (946/1542), respectively. A total of 101 participants faced the onset of diabetes during the study period. There was a progressively significant increase in new-onset diabetes associated with estimated serum osmolality (x2 for trend, $p < 0.001$). Using the area under a receiver operating (ROC) curve, the Youden index analysis presented 301 mosmol/kg to be the optimal cutoff value of serum osmolality.

CONCLUSION

Higher serum osmolality closely correlates with the combined risk of diabetes onset and worsening kidney function in participants without diabetes. These findings encourage the aggressive screening of these people to optimize the risk stratification of diseases.

WPCS-10-7

Effect of aging on glucose metabolism in Japanese healthy subjects (The Koshi Study)

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Background: Aging is one of the risk factors for diabetes, however the reason for that is controversial whether it is due to impaired insulin secretion or increased insulin resistance. In natural history for type 2 diabetes, insulin resistance is revealed prior to impaired insulin secretion in each individual, but the effect of aging is still not clear.

Method: To investigate the effect of aging on glucose tolerance, we performed 75-gram oral glucose tolerance test for 160 healthy Japanese whom are dispersed in four groups (young-aged: 20-40 years old n=30, middle-aged group: 41-59 years old n=44, senior-aged group: 60-74 years old n=58, elderly-group: over 75 years old, n=28).

Result: Among 160 subjects, 16 out of 160 was revealed diabetes, 31 out of 160 was revealed IGT. There was correlation between age and HbA1c ($r=0.44$, $p<0.001$), but there was no correlation between BMI and age. Although there was no significant change in HOMA-IR and Matsuda-DeFronzo Index between four groups, insulinogenic index (1.14 ±0.94, 0.75±0.61, 0.59±0.46,

0.58±0.68)and HOMA-b (88.2±65.5, 62.9±29.6, 54.2±34.3, 58.9±37.9) was significantly decreased with aging when compared with young- aged group ($p<0.05$).
Conclusion: Aging induces impaired insulin secretion in Japanese healthy subjects, which may be the reason why aging is the risk for diabetes in Japanese.

WPCS-10-8
Level of Serum Pentosidine and esRAGEs in Women with Type 2 Diabetes Mellitus as a Predictor of Bone Quality

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Objective: To determine the level of serum pentosidine, serum esRAGE, ratio of serum esRAGE/pentosidine in T2DM and non T2DM patients, with correlation of serum esRAGE/pentosidine ratio to serum P1NP. All factors were believed as surrogate markers for bone quality assessment.
Methods: A cross-sectional study was conducted to 38 premenopausal women, who experienced T2DM for more than 5 years, compared to 36 non-T2DM women within similar age range at several hospitals in Jakarta, Indonesia. Simple random sampling was done. Serum pentosidine and serum esRAGE level were evaluated by ELISA method and serum P1NP level was evaluated by ECLIA method.
Results: T2DM patients had higher serum pentosidine level (p=0.028), lower serum esRAGE level (p=0.248), lower esRAGE/pentosidine ratio (p=0.001) than non-T2DM patients. Serum pentosidine level were 5406 ± 1911 pmol/ml and 3145 ± 1892 pmol/ml with median ratio of serum esRAGE/pentosidine were 0.03 pg/pmol and 0.06 pg/pmol, between T2DM patients and non-T2DM patients, consecutively. There was no correlation between serum esRAGE/pentosidine ratio and serum P1NP in T2DM patients.
Conclusion: Hyperglycemia in T2DM patients lead to high serum pentosidine levels without elevated serum esRAGE levels. As addition, there was a decrease level of serum esRAGE/pentosidine ratio in T2DM patients with no correlation between level of serum esRAGE/pentosidine ratio and level of P1NP as a marker for bone formation in T2DM patients.

WPCS-10-9
Correlation between Calcium serum with T Score Spine among Patients with Diabetes

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Objective: Diabetes is the most common in all over the wolrld especially in developing countries. Diabetes is also a chronic inflammation process, and also related to decrease of calcium serum and T score femur. Until now, the association between calcium and with T-Score level is still not clear. This study aims to investigate correlation between calcium serum and T Score spine among diabetes patients.
Method: This study is an analytical study with a cross-sectional design conducted in I Goesti Ngoerah Gde Ngoerah Teaching Hospital from September to October 2022. The data was taken using the consecutive sampling method; 42 samples were collected— the analysis using univariate and bivariate analysis. The correlation between calcium serum and T Score spine was analysed using the Pearson correlation.
Results: The mean age in this study was 53.35 ±10.18 ; Calcium level 9.02 ± 0.504 mg/dL. Pearson correlation analysis showed that calcium serum has significant statically with T score spine among diabetes (r= 0,402, p=0.008 < 0.05).
Conclusion: Calcium serum is positively correlated with T score spine among diabetes population
Keyword: diabetes, calcium, T Score Spine, moderate correlation

WPCS-11-1
Whole-exome sequencing identifies rare mutations of *CALCR*, *GIPR*, *GPR151* and *GPR75* in individuals with severe obesity

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A recent study identified four brain-expressed G protein–coupled receptors (CALCR, GIPR, GPR151, and GPR75) for which the burden of rare nonsynonymous variants was associated with BMI. To detect rare variants for these genes in Chinese obese cohort, we collected 120 obese patients who underwent laparoscopic sleeve gastrectomy from January 2011 to July 2019. Whole exome sequencing was carried out to detect the rare mutations for the four genes, and the pathogenic variants were screened by multiple bioinformatics methods. Seven rare variants were identified in nine patients (9/120) for the four genes, and two of the variants were novel in East Asian population. This study screened rare mutations of four G protein–coupled receptors genes in Chinese obese cohort, providing new clues to the pathogenesis of obesity.

WPCS-11-2
Newly diagnosed diabetes characteristics: preliminary results from Mongolian Diabetes Registration Study (MONDIA)

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Objective
To study anthropometric and laboratory characteristics of newly diagnosed patients with type 2 diabetes in Mongolia
Methods
Since January 2023, we have started national diabetes registry program (MONDIA diabetes registration) in Mongolia. Data collection included demographic, anthropometric (body mass index, BMI, waist circumference) and laboratory findings (glycated hemoglobin, lipid profiles) from patients records. As planned to collect the data, we trained doctors from 30 units in Mongolian rural and urban areas. In this preliminary analysis, we included data from 3 units with all necessary data collected during January and February in 2023.
Results
A total of 1015 patients with diabetes was registered in the MONDIA Diabetes Registry. Among those, 91 patients were newly diagnosed patients (8.7%). The mean age was 53.2 ± 11.6 and 49.5% (n=45) were males. Mean BMI was 28.3 ± 5.3 kg/m^2 and 82.4% (n=75) were obese and overweight. Prevalence of metabolic syndrome was 41.8% among newly diagnosed patients. Among them 87% of all patients were hypertensive. Dyslipidemia was 50% and the main type of dyslipidemia was increased triglyceride. Newly diagnosed patients were classified as diagnoses: on a health check-up (33.1%) and because of presenting symptoms of hyperglycemia (25.3%), because of acute and chronic diabetic complications (9.8%) and because of other diseases (31.9%).
Conclusion
The prevalence of newly diagnosed patients was higher amongst registered diabetic patients in Mongolian diabetes registry. The most common features of newly diagnosed patients were obesity and metabolic abnormalities.

Keywords
obesity, metabolic syndrome, hypertension

WPCS-11-3
Remote preconditioning increases glucose utilization via hepatic glucose transporter-4 and improves hepatosteatosis

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Objective: Considering that hindlimb ischemia–reperfusion (IR) or remote

preconditioning decreases blood sugar levels by suppressing hepatic gluconeogenesis and enhances glucose uptake via the parasympathetic nervous system, this study aimed to analyze the effects of IR on factors associated with liver energy metabolism.

Methods: Male C57BL/6J mice subjected to streptozotocin (STZ)-induced diabetes (DM) were studied, followed by IR.

Results: Hepatic mRNA expression levels of glucose transporter type 4 (GLUT4) were remarkably upregulated by IR, whereas GLUT1, GLUT2, GLUT5, GLUT8, and GLUT9 were unaffected. In each hepatic lobule zone (zone 1, periportal area; zone 2, intermediate area; and zone 3, central area), IR increased the GLUT4 protein expression. The PAS-positive glycogen levels were significantly higher in all zones, specifically zone 1, in IR-treated livers than in the control liver. Compatibly, in primary hepatocytes, acetylcholine distinctively upregulated the GLUT4 expression, specifically on the cytoplasmic membrane. Alternatively, IR significantly suppressed serum ketone body levels in mice with STZ-induced DM. The pyruvate dehydrogenase activity, which converts pyruvate into acetyl-CoA linking glycolysis with the tricarboxylic acid (TCA) cycle, was also significantly upregulated by IR. The activity of aconitase and concentration of fumarate, key components in the TCA cycle, were non-significantly increased in IR-treated DM mice

Conclusion: Increased glucose uptake via GLUT4 overexpression may induce glycogen storage in IR-treated livers. Moreover, the average-size of fat droplets within the IR-treated liver of db/db mice as type II DM model was significantly smaller (p=0.0250). These results suggested that IR may improve nonalcoholic fatty liver disease associated with DM.

WPCS-11-4

The interaction of insulin resistance and diabetic genetic risk score on development of diabetes in Asian population

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Background Insulin resistance (IR) and genetic background of diabetes were related to diabetes development. However, the interaction of IR and diabetic genetic background remained unclear.

Methods A predictive algorithm of IR derived from US National Health and Nutrition Examination Survey (NHANES) and Taiwan MAJOR database to the non-diabetic participants was applied to non- diabetic participants in Taiwan biobank. Five clusters of T2D genetic risk score were also calculated for each participant. The primary endpoint is new development of diabetes during follow up study. Interaction of IR and individual genetic clusters was tested.

Results

Overall, 7365 participants were enrolled in this study and 360 patients (4.9%) developed diabetes in the follow up period. After multivariable adjustment, the predicted insulin resistance by algorithm significantly increase risk of new diabetes (Odds Ratio(OR)=7.248, p<0.001). In addition, the OR of new- onset diabetes for each standard deviation of genetic risk scores was 1.247 (p<0.001),1.186(p=0.003), 1.114(p=0.04), 1.163(p=0.007) and 1.091(p=0,11) for genetic clusters of reduced beta cell function, low pro-insulin levels, obesity mediated, lipodystrophy-like fat distribution, and disrupted liver lipid metabolism, respectively.

The interaction between predictive insulin resistance and genetic risk scores only reached statistically significant in reduced beta cell function (p for interaction=0.006). Genetic risk of reduced beta cell significantly increased risk of future diabetes in people without insulin resistance (OR=1.369,p<0.001), but not significant in people with insulin resistance at baseline (OR=0.973,p=0.801).

Conclusion

IR and diabetic genetic risk scores were related to diabetes development, particularly score of reduced beta cell function in people without IR.

WPCS-11-5

Cumulative exposure to metabolic syndrome is associated with type 2 diabetes risk in young adults

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Background: Metabolic syndrome is associated with type 2 diabetes and its prevalence is increasing worldwide in young adults. We aimed to determine whether cumulative exposure to metabolic syndrome is associated with type 2 diabetes risk in young adults.

Methods: Data of 1,376,540 participants aged 20–39 years without a history of type 2 diabetes and who underwent four annual health check-ups were collected. In this large-scale prospective cohort study, we evaluated the incidence rates and hazard ratios (HRs) of diabetes according to cumulative frequencies of metabolic syndrome over 4 years of consecutive annual health check-ups (burden score 0–4). Subgroup analyses were performed by sex and age.

Results: During 5.18 years of follow-up, 18,155 young adults developed type 2 diabetes. The incidence of type 2 diabetes increased with burden score (P < 0.0001). The multivariable-adjusted HRs for type 2 diabetes were 4.757, 10.511, 18.288, and 31.749 in participants with a burden score of 1 to 4, respectively, compared to those with 0. In subgroup analyses, the risk of incident diabetes was greater in women than men and in the 20–29 years age group than the 30–39 years age group. The HRs were 47.473 in women and 27.852 in men with four burden scores.

Conclusions: The risk of type 2 diabetes significantly increased with an increase in the cumulative burden of metabolic syndrome in young adults. Additionally, the association between cumulative burden and diabetes risk was stronger in women and the 20s age group.

WPCS-11-6

The Characteristics of Prediabetes Patients associated with Insulin Resistance in Padang, Indonesia

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Objective: The study aims to determine the characteristics of prediabetic patients associated with insulin resistance in a high carbohydrate consumption city, Padang (West Sumatera Province, Indonesia).

Methods: This research is a cross-sectional study where the sample is selected by consecutive sampling in 2021-2022. We screened the family of diabetes patients in the outpatient clinic in M. Djamil General Hospital Padang, Indonesia. Prediabetes was defined according to the American Diabetes Association (ADA) criteria.

Results: People living in Padang have a high risk of high carbohydrate consumption. That eating habits are risk factors for prediabetes and diabetes mellitus. Of 80 prediabetic patients, 58 (72.5%) were men, and 22 (27.5%) were women. The characteristics are age 32.71 (5.09) years old, waist circumference (WC) 112.18 (13.95) cm, body mass index (BMI) 31.09 (5.67) kg/m^2, systolic blood pressure 125.25 (10.55) mmHg, diastolic blood pressure 80.5 (6.17) mmHg, fasting plasma glucose (FPG) 94.89 (9.72) mg/dl, postprandial plasma glucose (PPG) 113.14 (18.14) mg/dl, HbA1c 5.91 (0.21) %, HOMA-IR 3.82 (1.81). We found a correlation between HOMA-IR with BMI, WC, and HbA1c but not with FPG dan PPG.

Conclusion: The characteristics of prediabetic patients in Padang are obesity with normal blood pressure, FPG, and PPG. We found that insulin resistance has arisen in these patients correlated with BMI, WC, and HbA1c.

WPCS-11-7

Association between triglyceride to high-density lipoprotein ratio and waist circumference in Mongolian adults

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Objectives: To investigate the triglyceride and high-density lipoprotein ratio as an insulin resistance marker in Mongolian adults in relation to waist circumstances.

Materials and Methods: This cross-sectional study included 365 individuals. Data on anthropometric measurements (weight, height, waist circumference, BMI, and blood pressure) and blood draws for fasting blood glucose, insulin, and lipid profiles (total cholesterol, TG, HDL, and LDL) were collected. Triglyceride/HDL ratio (TG/HDL) was calculated by dividing triglycerides by HDL level. HOMA-IR was calculated according to the formula: fasting insulin (microU/L) x fasting glucose (nmol/L)/22.5. The association between TG/HDL and HOMA-IR was studied in groups of waist circumference as dividing into 25th, 50th, and 75th percentiles using Spearman's correlation analysis.

Results: The subjects comprised 135 males (37%), with a mean age of 46.79±8.79 years. Mean fasting insulin was 10.04±6.56, 12.22±6.82, 16.35±12.07 in groups of 25th, 50th and, 75th percentiles of waist circumference respectively. The correlation coefficients of HOMA-IR with TG/HDL increased depending on waist circumference (r=0.241, r=0.337, and r=0.469 in waist circumference tertiles). TG/HDL-C cut-off was 1.2 (AUC=0.77, p<0.001, Sensitivity=56%, Specificity=90%) in men and 0.69 (AUC=0.649, p<0.001, Sensitivity=46%, Specificity=80%) in women in a group of 25th percentiles respectively.

Conclusion: TG/HDL was significantly associated with waist circumference. This suggests that the TG/HDL ratio could be used to indicate insulin resistance among Mongolians.

Keywords: Insulin resistance, lipid profiles, waist circumstance, HOMA-IR

WPCS-11-8

Central obesity and glucose intolerance among Mongolian military personnels

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Objective: To study the prevalence of central obesity and glucose intolerance among Mongolian military personnels. **Methods:** This study was conducted in Ulaanbaatar, Mongolia between June and August 2022, including officers and leaders aged 30-55 working in military units. Body measurements included body weight, height, BMI, waist circumference, blood pressure, and hand grip strength. Impaired glucose metabolism was identified using 2 hour oral glucose tolerance test (between 7.8 and 11.0 mmol/l and above 11.1 mmol/l as defined as prediabetes and diabetes separately). Central obesity was defined is IDF criteria for Asians (>90 cm in men and >80 cm in women). A statistically significant probability was considered when the P value was at <0.05. **Results:** A total of 141 people participated in the study, and the mean age was 37.6±5.5. The 70.9% (n=100) of the respondents were male and 76.6% (n=108) had a bachelor's degree or higher. According to BMI, overweight and obesity were 56% (n=79) and 19.1% (n=27) respectively. The prevelance of central obesity regarding to waist circumference was 63.1% (n=89). Regard to OGTT, glucose intolerance was 13.5% including 5.0% of diabetes mellitus. Pearson's correlation analysis, waist circumference was positively correlated with fasting glucose (r=0.219) and age (r=0.223). These associations were statisctically signifcant. **Conclusions:** The prevalence of central obesity among military personnel was 63.1% and glucose intolerance was 13.5%.

Keywords: armed forces, BMI, central obesity, OGTT

WPCS-11-9

Validation and reliability of the Mongolian version of the Dietary Variety Score and Cumulative Lifestyle Index

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Objective: This study aimed to reliable and validate a Mongolian version of the Dietary Variety Score (DVS) and Cumulative Lifestyle Index (CLI).

Methods: DVS and CLI questionnaires were translated into Mongolian and back-translation. After language validation, the questionnaires were administered twice (test n=37 and retest n=244) to healthcare workforces in First Central Hospital of Mongolia. Internal consistency (by Cronbach's alpha) and test-retest reliability were evaluated.

Results: Translation and back translation revealed no major difficulties. DVS and CLI questionnaire's cross-correlation between the subscale for the test-retest studies reliability ranged from r=0.13-0.50 and r=0.13-0.30, respectively (p<0.001). The test-retest studies showed that the total alpha coefficient of the DVS and CLI questionnaires was higher than α> 0.70 (α> 0.93 and α> 1.01), which provided excellent internal consistency and reliability (Table 1).

Conclusion: The Mongolian version of DVS and CLI had reliability and validity, and it is a useful instrument for measuring the eating and lifestyle habits in healthcare workforces.

Table 1. DVS and CLI reliability and validity

DVS and CLI	Coefficient Cronbach's α			
	Number of items	The sum of the item variance	Variance of total score	Overall Cronbach's α
Test (n=37)				
DVS	10	5.84	34.18	**0.92**
CLI	6	1.20	7.88	**1.01**
Total	16	7.05	56	**0.93**
Retest (n=244)				
DVS	10	6.41	231.36	**1.08**
CLI	6	5	52.08	**1.08**
Total	16	11.31	231.36	**1.01**
Item deleted	0	-	-	-

Data are presented Cronbach's alpha coefficient, A significance level of α> 0.70

WPCS-12-1

Effect of SGLT2 Inhibitor on Plasma Carnitine levels in patients with Type 2 Diabetes

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Objective: Carnitine is essential for fatty acid transport into the mitochondoria and it is thought to be an index of beta-oxidation. SGLT2 inhibitors inhibit glucose reuptake in the kidney, and it promote the catabolic processes of metabolism accompanied by increased ketone levels. Little is known the changes in plasma carnitine levels after administration of SGLT2 inhibitors. The aim of our study was to understand the metabolic changes by assessing the serum carnitine and ketone body levels after the administration of SGLT2 inhibitors in type 2 diabetic patients. Methods: The subjects were 15 patients with type 2 diabetes (age: 43.7±9.8 years). The plasma ketone body, free carnitine, and acylcarnitine concentrations were measured 2, 4, and 8 weeks after the administration of ipragliflozin (50 mg). Results: Ipragliflozin resulted in a significant HbA1c reduction, and body weight reduction after 8 weeks. The 3-hydroxybutyrate levels significantly increased after 2 weeks. The plasma acylcarnitine levels were significantly increased after 4 and 8 weeks. Eight weeks after the administration of ipragliflozin, an acute reduction in eGFR was -0.34±10.4ml/min/1.73m^2. The increase in acylcarnitine levels showed significant negative correlation with the decrease in HbA1c level and the decrease in eGFR. Conclusion: These results suggest that the SGLT2 inhibitor increased fatty acid catabolism in the early stages after administration of SGLT2 inhibitor. The changes in plasma acylcarnitine levels may be one of

the marker of the fuel metabolism and the acute eGFR change after administration of SGLT2 inhibitor.

WPCS-12-2

Renoprotective effects of SGLT2 Inhibitors in type 2 diabetes patients, in routine clinical practice

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Aims/Introduction:
Sodium glucose cotransporter 2 inhibitors (SGLT2is) have been shown to have renoprotective effects
in several randomized controlled trials. However, there are not enough reports on the effects of SGLT2is in clinical practice.
Therefore, we retrospectively examined the effects of SGLT2is on renal function in patients with type 2 diabetes, using estimated glomerular filtration rate(eGFR) slope, an index of annual change in eGFR, as well as the effects on each parameter measured simultaneously in routine clinical practice.
Materials and Methods:
We evaluated the annual eGFR slope in 101 type 2 diabetes mellitus patients, treated with SGLT2is ≥1 years. The calculation of the annual change in eGFR for each patient was obtained by acquired eGFR data before and after at least 1 years of the initial SGLT2is administration, followed by analysis of the changes in the mean eGFR slope.
Results:
The mean age , BMI, HbA1c and eGFR at SGLT2is administration were 58.3 years, 28.2 kg/m^2, 7.9% and 87.1 mL/min/1.73 m^2, respectively.
The mean annual eGFR slope after SGLT2is administration (- 0.6 ± 0.65 (± SE) mL/min/1.73 m^2/year) was significantly slower than before SGLT2is administration (- 2.8 ± 0.65 (± SE) mL/min/1.73 m^2/year;P =0.017).
Additionally, the slowing in eGFR slope was more pronounced in the group with eGFR<60 mL/min/1.73 m^2 at the start of SGLT2is , compared with eGFR≧60 mL/min/1.73 m^2 group.
Conclusions:
The administration of SGLT2is agents significantly slowed the decline in eGFR and
suggesting that it may be more effective in patients with eGFR< 60 mL/min/1.73 m^2.

WPCS-12-3

Glucose lowering pharmacological treatment options of diabetic patients

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Objective
The aims of this study were to evaluate glucose lowering pharmacological treatment options of diabetic patients.
Methods
We used web based diabetes registration data from 2016-2021, provided by 26 medical centers of Mongolia. Glucose lowering pharmacological treatment options evaluated by registered glucose-lowering agents in Mongolia such as Biguanides, DPP-4 inhibitors, Thiazolidinediones, GLP-1 receptor agonist, Sulfonylureas, and Insulins.
Results
Web based diabetes registration data was included total 12384 (6283 male, 6101 female) diabetic patients' information. Among registered diabetic patients T1DM, T2DM, GDM and Other type of DM was 2.3%(286), 95.2%(11794), 0.5%(63) and 0.5%(66), respectively. Among registered diabetic patient with Biguanides, DPP4 inhibitors, Thiazolidinediones and Sulfonylureas were 58%(7181), 23.3%(2890), 0.7%(91) and 28.3%(3504), respectively. But, among total diabetic patients on rapid, short-acting, long-acting, ultralong-acting, premixed insulin and on insulin pump were 1.0%(125), 6.1%(754), 9.3%(1152), 8.3%(1023), 11.0%(1364) and 0.5%(67), respectively.
Conclusions
During the 2016-2021 most of prescribed glucose lowering pharmacological treatment options for diabetic patients in Mongolia was Biguanides, Sulfonylureas and DPP4 inhibitors. Among insulin treatment premixed and long-acting insulin are dominant.

WPCS-12-4

Efficacy of SGLT2 inhibitors in elderly type 2 diabetes with and without renal dysfunction

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Background: The efficacy of SGLT2 inhibitors (SGLT2i) in diabetes individuals with and without renal dysfunction is being established. Presently, it is recommended to use the drug with caution in the elderly. We compare glycemic control by SGLTis in elderly diabetes people with and without renal dysfunction.
Methods: Elderly type 2 diabetes individuals (>=65 years) who started SGLT2i between May 2015 and October 2020 were included in the study. Pre- and post-treatment (one year) data (e.g., HbA1c) were compared. Patients aged >=75 years and those with renal dysfunction (eGFR <60 and <45) were examined separately.
Results: Of the 213 individuals included in the study. Of the 194 individuals remaining on the drug, 70 were aged >=75 years, 77 had eGFR <60 and 26 had eGFR <45. The median HbA1c [25th percentile, 75th percentile] was 7.30% [6.70, 8.13] before treatment, which improved to 6.80% [6.20, 7.50] after treatment (p<0.001). Individuals aged >=75 years (HbA1c 7.00% [6.48-8.03] showed improvement of HbA1c to 6.70% [6.18-7.43], p<0.001); those with renal dysfunction (eGFR <60: 7.20% [6.60-8.10]) improved to 6.80% [6.30-7.50], p<0.001 and those having eGFR <45: 7.60% [6.80-8.20] to 7.22% [6.70-7.73], p=0.012) also showed improvement. However, the degree of improvement in HbA1c tended to be less in individuals with more severely impaired renal function (p for trend = 0.078).
Conclusions: SGLT2i exerts a consistent beneficial hypoglycemic effect in elderly people including those aged >=75 years. While similar effects are seen in people with renal dysfunction, the benefit of the drug tends to be somewhat less.

WPCS-12-5

Benefits of SGLT2 inhibitors for hyperglycemia due to high-dose corticosteroid therapy in patients with type 2 diabetes

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Objective: High-dose corticosteroid administration is a mainstay of treatment for several diseases; in patients with diabetes, the resultant blood-glucose rise usually requires additional medication such as insulin. We evaluate the benefits of SGLT2 inhibitors (SGLT2i) for hyperglycemia resulting from high-dose intravenous corticosteroid pulse in patients with type 2 diabetes.
Methods: We collected inpatient data of patients with type 2 diabetes hospitalized for treatment of facial palsy or idiopathic hearing loss from April 2014 to March 2022. These patients were treated with intravenous corticosteroid therapy at 200mg of prednisolone sodium succinate daily for three days followed by 100mg daily for three days and 50mg for another three days. Patients were excluded if they were discharged before the ninth hospital day or if preprandial blood glucose was not measured three times a day in the hospital. Medications, anthropometric data, HbA1c, and preprandial blood glucose were retrospectively extracted from medical records by the medical

information unit. The effects of SGLT2i on the mean preprandial blood glucose during the 7-day hospital stay were analyzed by multiple regression.

Results: Thirty-nine patients were included. HbA1c and age at the time of admission were selected as confounders. SGLT2i use was a significant variable in the multiple regression analysis for lowering mean preprandial blood glucose.

Conclusion: SGLT2i use may be effective by itself for lowering glucose due to high-dose corticosteroid therapy for facial palsy or idiopathic hearing loss in patients with type 2 diabetes.

WPCS-12-6

Long-term risk of hyponatremia in patients with diabetes mellitus receiving SGLT2-inhibitors

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Background

There're case reports of hyponatremia events in people receiving sodium-glucose cotransporter-2 inhibitors (SGLT2i).

There' no study yet to evaluate the risk of hyponatremia among people receiving SGLT2i in the long time. Thus, we use our nationwide database to check the risk of hyponatremia under combination of SGLT2i in diabetes patients.

Method

We enrolled 11,399 diabetic patients treated with SGLT2is and 11,399 diabetic patients treated without SGLT2is from the Longitudinal Generation Tracking Database (LGTD) in the study after propensity score matching (PSM). Adjusted hazard ratios (aHR) and the corresponding 95% CI were estimated by multivariate Cox proportional hazards models with covariates of sex, age, diuretics, and comorbidities.

Result

The diabetic patients treated with SGLT2is were at significantly lower risk of hyposmolality and hyponatremia in those aged more than or equal to 60 years (aHR = 0.45, 95% CI = [0.23, 0.88]) and those with hypertension (aHR = 0.47, 95% CI = [0.27, 0.82]) and hyperlipidemia (aHR = 0.53, 95% CI = [0.30, 0.94]) when compared to diabetic patients treated with diuretics only. The risk of hyposmolality and hyponatremia decreased along with the increase of days of supply of SGLT2is (141-330 days: aHR = 0.47, 95% CI = [0.27, 0.82]; 331+ days: aHR = 0.13, 95% CI = [0.04, 0.41]).

Conclusion

SGLT2i are associated with lower risk of hyponatremia compared with diuretics among people with diabetes mellitus.

WPCS-12-7

Effects of DPP-IV inhibitor Gemigliptin on stress induced accelerated senescence

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Obejective: Senescent cells have important roles in inflammation and atherosclerosis. DPP (dipeptidyl peptidase)-IV inhibitors increase approximately 70 proteins along with active GLP-1 which are degraded by ubiquitous DPP-IV. We tested the anti-aging effects of DPP-IV inhibitor Gemigliptin through its pleiotropic biological actions beyond glucose control.

Method: We used HUVEC and streptozotocin injected type 1 diabetic C57BL6J mice. H_2O_2 was used for oxidative stress on HUVEC. High fat feeding to diabetic mice were performed (glucolipotoxicity). DPP-IV inhibitor Gemiglipin was used with various concentrations. Molecular markers of cell senescence, cell cycle analysis, and the signaling molecules involved in cell survival and apoptosis were studied.

Results: Gemigliptin exhibited significant protection on stress induced apoptosis and accelerated senescence in cultured HUVEC and the cells of high fat feeding type 1 diabetic mice aorta. The size and the number of atherosclerotic plaques in aorta were significantly reduced, and the aortic wall thickness was reduced by Gemigliptin. Expressions of senescence markers, i.e. p16, p21, p27, p53, and SA-β-Gal positivity were significantly reduced by Gemigliptin, while the markers of cell defense and survival (PGC-1α, eNOS, Sirt1) were increased. Cell cycle analysis on HUVEC revealed that the cells in subG1 phase were reduced and G0/G1 phase were increased by Gemigliptin.

Conclusion: Gemigliptin is effective for the protection of stress induced apoptosis and accelerated senescence of HUVEC and mouse aorta. Anti-senescence effect of Gemigliptin is not related with glucose lowering. Further studies are needed to clarify the clinical significance of these findings. (This work was supported by LG Chem)

WPCS-12-8

Relation between prolonged utilization of Dipeptidyl peptidase-4 inhibitors and the risk of pancreatic cancer

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Objective

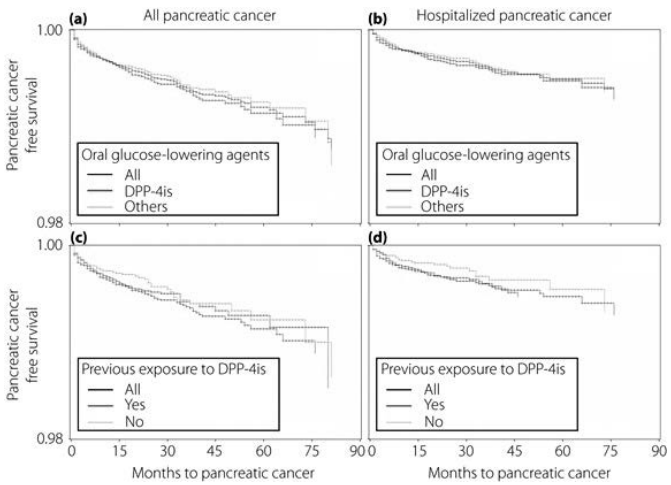
The primary objective of this study was to determine whether long-term use of dipeptidyl peptidase-4 inhibitors (DPP-4is) is associated with the risk of pancreatic cancer (PC) in individuals with diabetes in Japan.

Methods

We utilized the JMDC Claims Database, which contains medical information on individuals aged <75 years in Japanese employment-based health insurance programs. Pancreatic cancer was established through a claim for ICD-10 code C25. The study compared the risk of PC in patients prescribed DPP-4is versus other oral glucose-lowering agents (GLAs) using Kaplan-Meier (KM) curve analysis, log-rank tests, and Cox proportional hazard models.

Results and Conclusion

The study included 61,430 patients who were given DPP-4is and 83,304 patients who were given other oral GLAs. The median follow-up period was 17 months for DPP-4is and 14 months for other oral GLAs. According to the log-rank test, the distribution of all PCs and PCs requiring hospitalization was comparable between the two groups (all PCs: p=0.7140, PCs requiring hospitalization: p=0.3446). The KM curves for time to all PCs and PCs requiring hospitalization were also similar. The use of DPP-4is did not increase the adjusted risk of PC, as calculated using Cox proportional hazard models (all PCs: p=0.6518 HR(95%CI)=1.1 (0.8-1.3), PCs requiring hospitalization: p=0.6662, HR(95%CI)=1.1 (0.8-1.4)).The findings of this study, which utilized a database approach, did not provide evidence of a significant association between the use of DPP-4is over the long-term and an increased risk of PC among individuals with diabetes in Japan.



WPCS-12-9

The glycemic role of leptin and ghrelin after treatment of SGLT2 inhibitors in type 2 diabetes

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OBJECTIVE:
To compare the change of leptin and ghrelin with glycemic control in patients with type 2 diabetes who were treated with dapagliflozin.
RESEARCH DESIGN AND METHODS:
97 patients were enrolled and assigned to receive dapagliflozin 10mg daily. Serum leptin and ghrelin were check before and after 3 months treatment of dapagliflozin 10mg/day. All participants were divided to 2 groups by HbA1c of 7%, group in target (n=45) and group above target (n = 52). Additional analysis was done by the change of body weight, weight loss group (n = 60), weight gain group (n = 37). Changes of serum leptin and ghrelin were compared between two groups.
RESULTS:
The mean HbA1c was 6.7 ± 0.1 % in group in target, and 7.3 ± 0.2 % in group above target. Serum leptin and ghrelin changes were non significant differences. Serum leptin changes showed significant decrease from 7.54 ± 3.51 ng/ml to 6.60 ± 2.40 ng/ml ($P < 0.001$) in weight loss group and significant increase from 7.58 ± 2.61 ng/ml to 8.24 ± 3.09 ng/ml ($P < 0.001$). Serum ghrelin level was significant decrease from 873.6 ± 252.6 ng/ml to 798.4 ± 200.8 ng/ml (P= 0.029) in weight loss group, but no significant change of 791.8 ± 216.6 ng/ml to 818.8 ± 208.6 ng/ml ($P = 0.493$) in weight gain group.
CONCLUSIONS:
Serum leptin and ghrelin decrement are related to weight loss with treatment of dapagliflozin 10mg/day. Further investigations are required to overcome weight gain after treatment of SGLT2i.

WPCS-13-1

Fatty acid profile in patients with different titers of GADA in patients with latent autoimmune diabetes in adults

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Fatty acid profile in patients with different titers of GADA in patients with latent autoimmune diabetes in adults
Objective To study if the fatty acid profile were different in patients with different titers of GADA in patients with latent autoimmune diabetes in adults (LADA).
Methods: GADA≥176u/ml and FCP<200pmol/L was defined as H-t1dm, GADA ≥30 and <176 and FCP<200 as L-t1dm, GADA ≥176 and FCP≥200 as H-LADA, GADA ≥30 and < 176 as L-LADA, GADA<30 and FCP<200 as I-t1dm, GADA<30 AND FCP≥200 and <600 as NI-t2dm, and GADA<30 and FCP≥600 as HI-t2dm.
Results: Nonglycemic indices Heatmapping found H-LADA, L-LADA were grouped together with type 2 diabetes while I-t1dm, H-t1dm, L-t1dm were grouped together. The main decriming indices were waist, BMI, systolic blood pressure and anthrogenic index plasm. Using 23 fatty acids, H-t1dm, L-t1dm, I-t1dm, H-LADA, L-LADA were grouped in one group while the two type 2 diabetes subgroups grouped together. The main differentiating fatty acids were C20:0, C22:0, C24:0, C22:1 and C24:1, C20:5 and C22:5. They are significantly higher in any type 1 diabetes and LADA subyptes while no different were found among type 1 diabetes subtypes and LADA subtypes.
Conclusion Titers of GADA does not influence fatty acid profiles, but can differentiate autoimmune diabetes from type 2 diabetes.

WPCS-13-2

Clinical features of adults with type 1 diabetes mellitus

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Objective:
The purpose of our study is to study the clinical characteristics of adults with T1DM in Ulaanbaatar, Mongolia.
Methods:
A hospital-based study included 111(64 women, 47 men) from 206 adults with T1DM of 9 districts of Ulaanbaatar city. T1DM clinical characteristics data collected by questionnaire, physical examination and laboratory tests.
Results:
The mean age of adults with T1DM was 31.3±7.6(18-54) years old. The mean age at first diagnosis of diabetes was 21.2±8.9(3-51) years old and diabetes duration was 10.1±6.5(0-37) years. At the time of first diagnosis T1DM adults with clear clinical symptoms and signs and with diabetic ketoacidosis, was 32.4% and 26.1% respectively. T1DM adults with low, normal, high level of insulin was 21.7%, 76% and 2.1%, but low, normal and high level of c-peptide was 67.5%, 30% and 2.5%, respectively. Anti-GAD65 positive patients was 67.5%. By level of HbA1C patients with good, moderate and bad control was 5.96%, 4.47% and 89.6%. But patients with elevated cholesterol was 83%, triglycerides was 68.7% and LDL was 86.3%. T1DM adults any time of life with ketoacidotic coma was 48.6% and with hypoglycemic coma was 39.6%. A mild hypoglycemia 69.4% and nocturnal hypoglycemia was 36.9%. T1DM adults with any diabetic complications was 71.2%, with eye 52.2%(58), kidney 17.1%(19), nerve 32.4%(36), stroke 0.9%(1), heart attack 2.7%(3) respectively.
Conclusions:
T1DM incidence is 2.57 per 10.000 populations among adults in Ulaanbaatar, Mongolia. Among adults with T1DM patients with clear clinical symptoms, normal insulin levels, positive Anit-GAD65, dyslipidemia, poor control are dominant.

WPCS-13-3

Detectable proinsulin levels after the onset of fulminant type 1 diabetes: TIDE-J study

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(Objective) Persistent proinsulin secretion has been reported in long-standing type 1 diabetes with undetectable serum C-peptide. Fulminant type 1 diabetes (FT1D) is characterized by the rapid destruction of pancreatic β-cells, leading to almost complete insulin depletion early after the onset. In this study, we aimed to clarify proinsulin levels in Japanese patients with acute onset type 1 diabetes (A1TD) and FT1D.

(Methods) We measured serum proinsulin levels by radioimmunoassay in T1D patients [AT1D: n = 19; FT1D: n = 7] enrolled in the Japanese Type 1 Diabetes Database Study (TIDE-J) at onset, 1 year and 2 years later.

(Results)

The median proinsulin levels in AT1D at the onset, 1year and 2 years later were 5.6(3.1-24.6), 12.4(3.1-50.9), 9.4(3.1-43.7) pmol/L, respectively. The median proinsulin levels in FT1D at the onset, 1year and 2 years later were 3.1(3.1-5.8) ,3.1(3.1-16.7) ,3.9(3.1-36.1) pmol/L, respectively.

Proinsulin levels at the onset in FT1D patients were significantly lower than those in AT1D patients (Wilcoxon rank sum test, p=0.03). Among AT1D patients, 7 of 19 patients presented undetectable proinsulin level at the onset. Only 1 patient remained undetectable proinsulin level throughout 2 years. Among FT1D patients, 6 of 7 patients presented undetectable proinsulin level at the onset. Of these, only 3 patients remained undetectable proinsulin level throughout 2 years.

(Conclusion) In Japanese patients with fulminant type 1 diabetes, some recovered proinsulin secretion. This result suggests that immature pancreatic β-cells secreting proinsulin might have been regenerated even in FT1D patients several years after disease onset.

WPCS-13-4

Acute hepatitis-type liver injury with iron deposition in a male withnewly onset anti-GAD antibody-positive T1 diabetes

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BACKGROUND: Aminotransferase elevation is a frequent cause of consultation for hepatologist, in out/in-patient settings, but identifying the origin of these biochemical alterations may be challenging. Glycogenic hepatopathy is a cause of liver damage in poorly controlled type 1 and occasionally type 2 diabetes, but its occurrence is often overlooked 1)2)3).

CASE RECORD: A forty-year-old male admitted to a suburban diabetes department with chief complaints of thirsty and nocturia for a month. His FPG 7.2 mmol/l, FCPR 0.92 ng/ml, HbA1c 9.3 % in NGSP, and anti-GAD antibody titer 690 IU/ml made diagnosis as type 1 diabetes. Before insulin Aspart multiple daily injection was applied, transaminase was within normal on slight fatty liver. However, after herpes zoster infection on valacyclovir, his AST/ALT was worsen to 117/339 IU/L, in spite of insulin Lispro. Given elevated anti-mitochondrial M2 antibody titer in 11.2 units/L, autoimmune hepatitis, and several potential causes of damage 2) could be hypothesized, including celiac hepatitis, and fatty liver 3). Liver biopsy revealed no finding in liver cirrhosis, non-alcoholic steatohepatitis, nor primary biliary cirrhosis; Around hepatocyte centrilobular necrosis, Berlin-blue staining show diffuse, fine, and dense hemosiderin deposition along with histiocyte (Figure). These findings hypothesized precedent hemochromatosis. Insulin Lispro had not worsen transaminase.

DISCUSSIONS/CONCLUSIONS: Liver staining with periodic acid-Schiff with or without diastase should be performed because a marked accumulation of glycogen indicates the presence of a glycogenic hepatopathy associated with poorly controlled type 1 diabetes 1).

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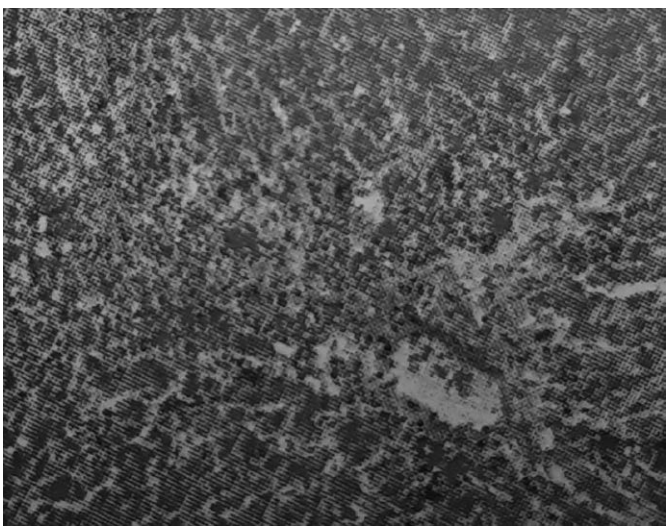

WPCS-13-5
Efficacy of immunotherapies on β-cell preservation in patients with T1D: a systematic review and meta-analysis

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Objective
We conducted this systematic review and meta-analysis to assess the effects of immunotherapies on blood glucose control and β-cell preservation in patients with type 1 diabetes (T1D).
Methods
We searched four databases from inception to July 2021. We included clinical trials of immunotherapy conducted in patients with T1D with reported changes from baseline in at least one of following outcomes: glycated hemoglobin (HbA1c) levels, daily insulin dosage, 2-h and 4-h mixed-meal-stimulated C-peptide area under the curve (AUC). The results were evaluated as the weighted mean differences (WMDs) and 95% confidence intervals (CIs).
Results
In total, 39 clinical trials were included. No significant differences were observed in changes of HbA1c (WMD, -0.03%, 95% CI, -0.16 to 0.10%, P=0.69) and changes of daily insulin dosage (WMD, -0.03 units/kg/day, 95% CI, -0.07 to 0.01units/kg/day, P=0.15) between immunotherapy and control group. Immunotherapy contributed to preservation of 4h C-peptide AUC (WMD, 0.07nmol/L, 95% CI, 0.03 to 0.11nmol/L, P=0.002), but showed no significant differences in changes of 2h C-peptide AUC when compared with the control group(WMD, 0.01 nmol/L, 95% CI, -0.01 to 0.04nmol/L, P=0.29).
Conclusion
In patients with T1D, immunotherapies were associated with a significantly elevated 4h C-peptide AUC when compared with the control group, while immunotherapies did not contribute to a substantial reduction in HbA1c level or daily insulin dosage.

WPCS-13-6
DIABETIC KETOACIDOSIS IN LATENT AUTOIMMUNE DIABETES IN ADULTS WITH GRAVES' DISEASE: A RARE CASE

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Objective: Latent autoimmune diabetes in adults (LADA) and Graves' disease are autoimmune disorders in endocrinology that are rarely found in single patients. Both autoimmune diseases can be found in autoimmune polyglandular syndrome (APS) type 3. Type 3 APS are also subdivided into 3A, 3B, 3C, and 3D. Infections such as urinary tract infections and pneumonia can trigger diabetic ketoacidosis (DKA) in these patients.
Methods: Case report
Results: A 23-year-old man presents with breathlessness since one day ago. The patient complains of intermittent fever followed by a cough. Physical examination results were compos mentis, heart rate 117 x/minute, temperature 37.40 C, breathing 28 x/minute. White blood cells were 32.230/mm3, random blood glucose 352 mg/dl, urine ketone +2, HbA1c 14,6%, HOMA IR 1.8, C-Peptide 0.3 ng/mL, TSH <0.05 uIU/mL, FT4 25 pmol/L, and TRAb 9.35 IU/L. From thyroid USG, we found toxic diffuse goiter. The patient was diagnosed with diabetic ketoacidosis, LADA, Graves' disease, and community-acquired pneumonia. The patient was treated with DKA and sepsis management. On the second day, the management of DKA was resolved, and continued with the administration of regular insulin. There is no specific therapy for managing LADA and these patients' co-incidence of Graves' disease.
Conclusion: Diabetic ketoacidosis (DKA) in this patient was successfully treated. The presence of LADA and Graves' disease in this patient suggests the possibility of APS type 3A, in which autoimmune thyroiditis with immune-mediated diabetes mellitus is found.
Keywords: diabetic ketoacidosis, latent autoimmune diabetes in adults, Graves' disease, autoimmune polyglandular syndrome (APS) type 3

WPCS-13-7
Thinking from a case of fulminant type 1 diabetes(FT1D)

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We met a patient of FT1D after virus infection last November. A 30-year-old female (BMI 20.2 kg/m^2) presented to our hospital due to nausea and vomit for two days. 4 days ago, the patient developed a fever over 38.0 °C with anorexia and muscle pain after drinking. She was diagnosed with diabetes and severe diabetic ketoacidosis (DKA). Laboratory findings showed a near normal HbA1c)(6.1%), positive GADA(109IU/ml) and low serum c-peptide(<0.02ng/ml), high serum insulin(77.7uU/ml), high cTnI (8.163ng/ml) and CKMB(34u/L) besides with hyperglycemia, ketosis, severe metabolic acidosis (aterial pH 6.85) at presentation. After treating with fluid resuscitation and intravenous insulin infusion, DKA was resolved promptly. She was in good health previously and not on any medication and without family history of diabetes. Five days latter cTnI and CKMB returned to normal range and 14 days latter serum insulin decrease to low quarter of normal range (6.8uU/ml) and GADA decreased to nearly normal range (44.2IU/ml). At presentation the frequency of PD-1+ CD4+ and PD-1+ CD8+ cells was high and cytomeglovirus IgG was positive in this patient. The patient was placed on CSII for glycemic control and wore CGMS for glucose monitoring after outside of hospital. The latest TIR is 72.8% with TAR 19.2 and TBR 5.3%. Cases with FT1DM due to immune-related factors virus infection have been reported. T-cell autoimmunity may be involved in FT1D. In our patient cytomeglovirus infection triggered the onset of autoimmune which led to rapidly destroy of islet cells completely.

WPCS-13-8
Is TyG-index an Indicator of DKA Severity in the Patients with Ketosis-prone Diabetes

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Objective
Previous studies have shown that the triglycerides and glucose index (TyG) could be a reliable predictor of insulin resistance, and higher HbA1c levels lead to recurrent diabetic ketoacidosis (DKA). However, there is no description of the association of higher TyG with the severity of DKA in patients with ketosis-prone diabetes(KPD).

Methods
Patients admitted to West China Hospital with DKA between January 1, 2020 and December 31, 2022 were analyzed. They were classified as type 1," "type 2," or "atypical" based on fasting C-peptide, autoimmune condition, and treatment history. Patients with KPD were divided as three subgroups based on the degree of severity of DKA (mild: pH 7.2–7.3; moderate: pH 7.1–7.2; severe: pH <7.1),TyG-index were calculated as the in [fasting triglycerides(TG) (mg/dL) ×FPG (mg/dL)/2]. Spearman correlation analyzed the data for 112 patients included in the study.

Results
Of 112 patients, 58(51.79%) who presented with DKA had type 1 diabetes, while 39(34.82%) had type 2 diabetes and 15 (13.39%) had been typed as "atypical diabetes". HbA1c for mild, moderate, and severe DKA groups were 11.51(±0.4)%, 11.56(±0.43)%, and 12.54(±0.52)%, respectively. The duration of diabetes mellitus did not affect the FBG level and TyG-index. Meanwhile, FBG level did not show a statistical correlation with blood pH levels. Blood pH and TyG returned a negative correlation (correlation coefficient, −0.57; p<0.001). Likewise, the HbA1c level correlated positively with the 3 groups of DKA (correlation coefficient, 0.62; p<0.05).

Conclusion
A higher TyG and HbA1c were associated with more severe DKA in patients with KPD.

WPCS-13-9

Characteristics of HLA class Ⅱ genes of patients with type 1 diabetes and those with autoimmune thyroid disease

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【Objective】Clinical features like the manner of onset (acute (AO)/ slowly-progressive (SP) /fulminant (FO)) as well as the presence of autoimmune thyroid disease (AITD) of patients with type 1 diabetes (T1DM) were examined regarding HLA haplotypes.【Methods】We genotyped the HLA class II (DR/DQ) gene of all 48 patients with T1DM (22 AO, 19 SP and 7 FO) who admitted and underwent HLA testing at Gunma University Hospital since 2016. The complication rate of AITD was 41.9%, of which 16.7% were Graves' disease (GD) and 39.5% were Hashimoto thyroiditis.【Results】As previously reported, DRB1*0901-DQB1*0303 (DR9) and DRB1*0405-DQB1*0401 (DR4) were frequent (43.8%) in our study. However, DRB1*0802-DQB1*0302 (DR8), which is reported to be frequent in childhood-onset was only 8.3%. AO and FO had similar haplotypes but SP was different: 32% of SP did not have those susceptible HLA. There was a high frequency of homozygous for both DR9 and DR4 in patients with T1DM and GD. Moreover, DR8 was not found in patients with AITD.【Conclusion】These data supported the previous report regarding HLA haplotypes of Asian patients with T1DM and may be useful for predicting future onset of AITD.

WPCS-14-1

Semaglutide for non-alcoholic fatty liver disease: a switch from other glucagon-like peptide-1 receptor agonists

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Objective

Non-alcoholic fatty liver disease (NAFLD) is an important liver comorbidity in individuals with type 2 diabetes (T2D). Although some glucagon-like peptide-1 receptor agonists (GLP-1RAs) have preferable effects on NAFLD, the efficacy of once-weekly semaglutide, especially after a switch from other GLP-1RAs, has not been clarified.

Methods

In this subanalysis of a multi-center, prospective, randomized, parallel-group comparison trial, individuals with T2D treated with liraglutide or dulaglutide were assigned to continue their GLP-1RAs (CTRL) or switch to semaglutide (SWITCH) for a further 24 weeks (SWITCH-SEMA1 trial). Participants were not habitual drinkers and were suspected to have NAFLD (fatty liver index (FLI) ≥ 30).

Results

In total, 62 of 100 participants met the criteria for this subanalysis. There were no statistical differences in baseline characteristics between the SWITCH (n = 33) and CTRL groups (n = 29). The FLI significantly improved in the SWITCH group (70.4 to 64.8) compared with the CTRL group (69.5 to 70.9) ($p < 0.01$). Improvement in the FLI in the SWITCH group was significantly correlated with lower body mass index ($p < 0.001$), higher age ($p = 0.014$), and a switch from dulaglutide ($p = 0.031$). Glycemic control, liver function, or kidney function did not affect the efficacy of semaglutide on the FLI.

Conclusion

A switch from conventional GLP-1RAs to once-weekly semaglutide might be a useful option for managing NAFLD in individuals with T2D.

WPCS-14-2

Personalized glucose-lowering effect of Chiglitazar in Type 2 Diabetes: a post-hoc analysis of clinical trials

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Chiglitazar (carfloglitazar) is a peroxisome proliferator-activated receptor (PPAR) pan-agonist presenting comparable glucose-lowering efficacy with sitagliptin in patients with type 2 diabetes. To identify the subgroup with higher benefit with chiglitazar, a post-hoc analysis using machine learning algorithm was applied in ChiglitAzar Monotherapy with Placebo (CAMP) and ChiglitAzar Monotherapy with Sitagliptin (CAMS) study. We constructed a phenomap based on 13 baseline variables of 1069 patients with diabetes assigned to chiglitazar (32 mg or 48 mg, N=822) and sitagliptin (N=247). Personalized HbA_{1c} decline at week 24 was estimated using least-squares regression weighted for phenotypic distances in each participant. High-benefit group (HBG) was defined as patients with higher predicted HbA_{1c} decline in chiglitazar than sitagliptin, and low-benefit group (LBG) was the opposite. 677 (63.3%) patients were allocated to HBG and 392 (36.7%) were allocated to LBG. Chiglitazar led to a greater HbA_{1c} decline than sitagliptin in the HBG (relative decline: 0.66%, 95%CI [0.50, 0.83]) and small decline in the LBG (-0.93% [-1.18, -0.68], $p_{interaction}<0.001$). There was no significant inter-group heterogeneity in changes in HOMA-IR, HDL, triglyceride, or body weight. Most participants receiving chiglitazar treatment (N=635, 77.3%) gained more glucose-lowering benefits from chiglitazar 48 mg than 32 mg. To facilitate efficient identification of HBG in clinic, we developed ML-PANPPAR, which showed robust performance (AUC=0.933 in the internal validating subset) to recognise HBG using 5 features (sex, BMI, $HbA_{1c,}$ HDL and fasting insulin). Our phenomapping-derived tool facilitates the identification of chiglitazar responders in clinic and provided precision allocation of this drug among diabetes patients.

WPCS-14-3

Clinical factors and glycemic control in Japanese patients with type 2 diabetes treated with 0.75 mg/ week Dulaglutide

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Objective: A post-hoc analysis of the AWARD study showed that the GLP-1 receptor agonist Dulaglutide given at a dose of 0.75 mg or 1.5 mg/week lowered HbA1c levels regardless of gender, BMI, or duration of diabetes. Because the approved dose of dulaglutide is only 0.75 mg in Japan, we aimed to clarify glycemic control-related factors in Japanese people with type 2 diabetes who were treated with dulaglutide.

Methods: We retrospectively studied 152 Japanese people with type 2 diabetes who received newly initiated treatment with 0.75 mg/week of dulaglutide for at least 6 months and had no history of GLP-1 agonist treatment. We statistically evaluated the correlations of clinical factors including physical measurements, biochemical data and DPP4 inhibitor use prior to dulaglutide treatment with reduction of HbA1c or achievement of HbA1c < 7.5% after the dulaglutide treatment.

Results: In multivariable analysis for determinants of HbA1c reduction after dulaglutide treatment, hypertension (p=0.016) and duration of diabetes (p=0.017) were inversely associated with HbA1c reduction. In contrast,

baseline HbA1c (p<0.001) was positively associated with HbA1c reduction. In logistic regression analysis for determinants of achievement of HbA1c < 7.5% after dulaglutide treatment, baseline HbA1c (p<0.001) and hypertension (p=0.020) were inhibitory factors for the achievement. A history of DPP4 inhibitor use prior to dulaglutide treatment had no influence on glycemic control.

Conclusions: In Japanese people with type 2 diabetes treated with 0.75 mg/week of dulaglutide, baseline HbA1c, duration of diabetes, and presence of hypertension should be taken into consideration for predicting the therapeutic effect.

WPCS-14-4

Exercise improves quality of life in adults with type 2 diabetes: a systematic review and meta-analysis

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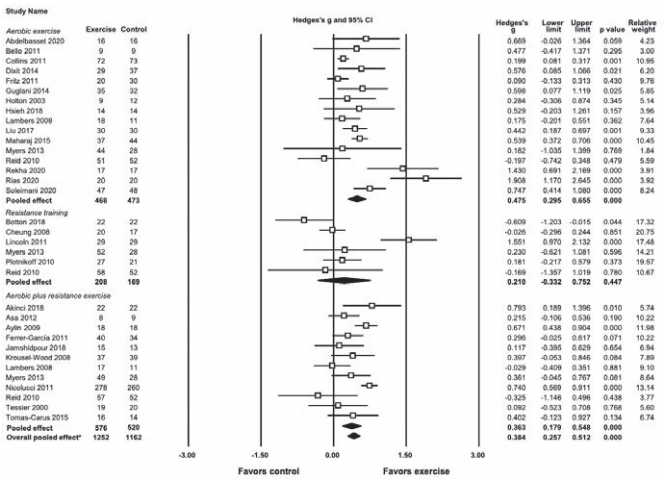
Aims: The primary aim of this study was to determine the effect of regular exercise on quality of life (QoL) in adults with T2D. A secondary aim was to determine the effect of different exercise modalities on QoL. The third aim was to determine whether improvements in QoL were associated with improvements in glycated hemoglobin (A1C).

Methods: Relevant databases were searched to May 2022. Eligible studies included randomized trials involving ≥2 weeks of aerobic and/or resistance exercise and assessed QoL using a purpose-specific tool. Mean differences and 95% confidence intervals (CIs) were calculated as standardized mean difference (SMD) or weighted mean difference. A regression analysis was undertaken to examine the interaction between change in QoL with change in A1C.

Results: Of the 12,642 studies retrieved, 29 were included involving 2,354 participants. Exercise improved QoL when compared with control (SMD=0.384, 95%CI:0.257,0.512, p<0.001). Aerobic exercise, alone (SMD=0.475, 95%CI:0.295,0.655, p<0.001) or in combination with resistance training (SMD=0.363, 95%CI:0.179,0.548,p< 0.001) improved QoL whereas resistance training alone did not. Exercise improved A1C (mean difference:-0.509%, 95%CI:-0.806,-0.212, p=0.001) and this change was associated with improvements in QoL (β=-0.305, p=0.030).

Conclusion: These results provide robust evidence that regular aerobic exercise alone or in combination with resistance training is effective for improving QoL in adults with T2D. Such improvements are associated with improved blood glucose control. Further studies should be undertaken to determine the relative importance of exercise duration, intensity, and frequency on patient-reported outcomes such as QoL.



WPCS-14-5

The impact of weight loss on metabolic control among type 2 diabetes patients: a retrospective real-world study

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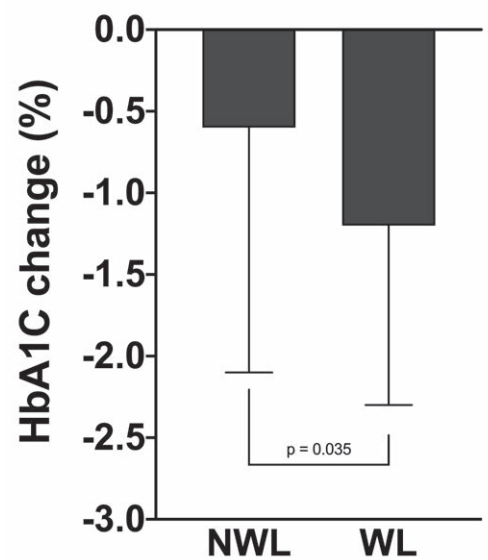
Objective: To investigate the impact of weight loss on metabolic control among type 2 diabetes patients in real-world practice.

Methods: This retrospective observational real-world study was conducted at an Indonesian private hospital diabetes center. Patients with type 2 diabetes whose at least baseline and one other body mass index (BMI), blood pressure (BP), and HbA1C data from electronic medical record within a year from their first visit were included. Patients with weight loss ≥ 5% from baseline (WL) was compared to those who did not lose weight ≥ 5% (NWL). Outcomes included change in HbA1c and low-density lipoprotein (LDL) levels, and glycemic (<7% or <8% in elderly), LDL (<70 mg/dL), and BP (<140/90 mmHg) targets achievement.

Results: A total of 513 and 112 patients were included as NWL and WL group, respectively. Patients in WL group had greater HbA1C reduction (median, -1.2% vs -0.6%, p=0.035) compared to those in NWL group. Those in WL group who were obese, but not those who were overweight or lean, were more likely to achieve glycemic target even after adjustment for age, sex, baseline BMI, and last-first visit interval (adjusted OR [aOR] 1.67 [95% CI 1.01-2.78]) compared to those in NWL group, especially those with poor baseline glycemic control (aOR 2.01 [95% CI 1.10-3.66]). No association was found between WL and LDL or BP control.

Conclusion: In line with recent guideline, weight management in clinical practice had significant impact on glycemic control for type 2 diabetes patients with obesity.



WPCS-14-6

Association of Insulin Antibody Subclasses with Glucose Control in Insulin-Treated Type 2 Diabetes Mellitus

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Objective To examine the distribution and effects of the subclass of insulin antibodies on glucose control and side events in patients with type 2 diabetes treated with premixed insulin analog. 17

Methods A total of 516 patients treated with premixed insulin analog were

sequentially enrolled from the First Affiliated Hospital of Nanjing Medical University from June 2016 to August 2020. Subclass-specific insulin antibodies (IAs) (IgG1-4, IgA, IgD, IgE, and IgM) were detected in IA-positive patients by electrochemiluminescence. We analyzed glucose control, serum insulin, and insulin-related events between IA-positive and IA-negative groups, as well as among patients with different IA subclasses. Results Overall, 98 of 516 subjects (19.0%) were positive for total IAs after premixed insulin analog therapy; of these participants, 92 had subclass IAs, and IgG-IA was the predominant subclass, followed by IgE-IA. IAs were associated with serum total insulin increase and local injection-site reactions but not glycemic control and hypoglycemia. In the subgroup analysis in patients with IA-positive, the IgE-IA and IA subclass numbers were more associated with increased serum total insulin levels. Additionally, IgE-IA might be correlated more strongly with local responses and weakly with hypoglycemia, while IgM-IA might be correlated more strongly with hypoglycemia. Conclusion We concluded that IAs or IA subclasses might be associated with unfavorable events in patients receiving premixed insulin analog therapy, which can be used as an adjunctive monitoring indicator in clinical insulin trials.

WPCS-14-7
Elucidation of Metabolic Regulatory Mechanisms in Liver by SGLT2 Inhibitors

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Objective

Sodium glucose co-transporter 2 (SGLT2) inhibitors are anti-diabetic drugs for type 2 diabetes that lower blood glucose and body weight. It is of special interest that SGLT2 inhibitors also improve liver metabolism and fatty liver. Liver is an important organ in regulation of energy metabolism, but the metabolic action of SGLT inhibitor in liver remains unclear.

Methods

We investigated the factors associated with the beneficial effects of dapagliflozin, a SGLT2 inhibitor, in the liver after confirming its glucose-lowering and weight loss effects using an obesity and diabetes mouse model. We also performed clinical study of patients with type 2 diabetes to explore candidate biomarkers that reflect the beneficial action of dapagliflozin in the liver.

Results

In animal study, dapagliflozin induced autophagy in the liver, and valine and leucine were increased in plasma as well as in liver. Thus, increased plasma valine and leucine levels are potential biomarkers for improved liver metabolism. Clinical study found that valine and leucine levels were markedly higher in patients treated with dapagliflozin than those not treated after one week intervention.

Conclusion

Dapagliflozin improves liver metabolism via hepatic autophagy, and plasma valine and leucine levels may reflect its metabolic effect.

WPCS-14-8
Investigation of the Insulin-secretory and anti-apoptotic effect of apigenin on the functionof INS-ID pancreatic β-cell

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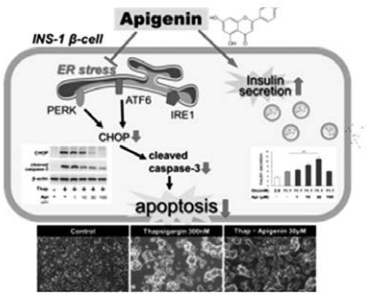
Endoplasmic reticulum (ER) stress has been identified as a key player role in the pathogenesis of diabetes mellitus, contributing to pancreatic β-cell dysfunction, β-cell apoptosis, decreased insulin secretory response, and cell death. The alleviation of ER stress and β-cell dysfunction would therefore provide viable therapeutic approach to prevent and/or treat type 2 diabetes mellitus. Naturally occurring polyphenols, known as flavonoids, has received considerable attention for the improvement of type 2 diabetes mellitus.

In the present study, we explored the anti-diabetic effect of apigenin, a trihydroxy flavone, on glucose-stimulated insulin secretion and apoptosis, and the mechanism underlying its anti-diabetic effects in INS-ID β-cell line. Our findings showed that apigenin concentration-dependently facilitated 11.1-mM glucose-induced insulin secretion, which peaked at 30 μM. The expression of ER stress signaling proteins, CHOP and cleaved caspase-3, which was elevated by thapsigargin in INS-1D cells, was concentration-dependently inhibited and silenced by apigenin treatment, with peak suppression at 30 μM. This was strongly correlated with the results of the flow cytometric analysis of annexin V/propidium iodide staining, DNA fragmentation analysis, and phase contrast microscopy. Moreover, these beneficial effects of apigenin were accompanied by a concomitant concentration-dependent suppression of thioredoxin-interacting protein (TXNIP) expression, which was initially elevated by thapsigargin.

Overall, these results suggest that apigenin is an attractive natural product with remarkable facilitation of glucose-stimulated insulin secretion and anti-apoptotic effects on β-cells, and that its anti-apoptotic effect may be mediated by reduced expression of CHOP, cleaved caspase-3, and TXNIP, thus promoting β-cells survival and function.



WPCS-14-9
Antidiabetic drugs selection and its influencing factors in patients with type 2 diabetes in the last five years

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Trend of antidiabetic drugs selection and its influencing factors in patients with type 2 diabetes in the last five years

Objective To investigate the trend in antidiabetic agents use or selection in our patients discharged during January 2017 to December 2021 and possible influencing factors over 5 years.

Method Retrive data of 3865 patients admitted during index years. Physical examination, biochemical indice and medication before and at discharge were recorded excluding type 1 and critical illness.

Results Use of Meformin (around 50%)and DPP-4i (9.9%-17.9%)remained constantly over the five years, acarbose, sulphonylurea decreased sharply while SGLT2i increased from 0.4% in 2019 to over 50% in 2021. Basal insulin and premix insulin remained stable over the five years while basal bolus intensive insulin decreased from 17.9% to 9.8%, GLP-1RAs increased from 3% to 24.7%. Coronary heart disease was the main influencing factor for choosing SGLT2i and BMI was the main influencing factor for chosing GLP-RAs.

Conclusion Medication for diabetes changed significantly in recent years, Selection of GLP-1RAs and SGLT2i did still not fully comforms corrent recommendations.

WPCS-15-1
Coexisting diabetes at cancer diagnosis is associated with type of cancer treatment

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Objective: Little is known about how coexisting diabetes affects the types of

cancer treatment of patients with cancer. In this study, we examined the association between coexisting diabetes and types of cancer treatment in patients with cancer.
Methods: We used cancer registries and administrative data of patients diagnosed with all cancer type from 2010 to 2015 at 36 hospitals in Osaka Prefecture, Japan. The diagnosis of diabetes was estimated by the presence or absence of diabetes medication and set as the target exposure. Multivariate logistic regression models were used to analyze types of cancer treatment and multivariate Cox regression models were used to analyze 3-year mortality.
Results: Of the 131,701 cancer patients analyzed, 6,135 (4.7%) had diabetes at the time of cancer diagnosis. The odds ratio for patients with coexisting diabetes of receiving tumor resection was 0.75 (95% CI, 0.70–0.72), the odds ratio of receiving chemotherapy was 0.67 (0.63–0.72), and the odds ratio of receiving radiotherapy was 0.78 (0.71–0.86), when compared to those without diabetes. The unadjusted 3-year survival rates were 61.4% (95%CI, 60.0–62.7) for the coexisting diabetes group and 77.3% (77.0–77.5) for the non-diabetes group. The hazard ratio for 3-year mortality for coexisting diabetes was 1.42 (1.36–1.48).
Conclusion: Patients with cancer and coexisting diabetes are less likely to receive tumor resection or chemotherapy. These differences may be associated with poorer prognosis in patients with comorbid diabetes.

WPCS-15-2
Glycemic Excursion, Side Effects and Self-Management in Diabetes Patients Undergoing Chemotherapy: A Literature Review

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Purpose: The purpose of this study was to identify the state of self-management in patients with diabetes who undergoing chemotherapy, by referring to fluctuations in glycemic excursion and adverse drug reaction.
Methods: Literature research was conducted in February 2023 using PubMed, CINAHL, and Ichushi-Web databases with “Cancer AND Diabetes AND Chemotherapy” as keywords. Based on our criteria, 31 articles were selected, and a review matrix sheet was created for the analysis of fluctuations in glycemic excursion and any adverse drug reaction to diabetes in patients undergoing chemotherapy.
Results: Substantial increases and unpredictable fluctuations in glycemic excursion were observed in these patients. In addition, an increase or change in the treatment dose was prevalent. Primarily, peripheral neuropathy and infection were reported as common adverse drug reactions. The risk of adverse drug reactions was especially high for patients with diabetes undergoing chemotherapy; furthermore, among this cohort, the detrimental effects were more likely to exacerbate into a severe condition that required special attention. Almost inevitably, the implementation rate of diabetes self-management programs decreased on the eighth week after the commencement of chemotherapy.
Conclusion: Considering the findings of large individual differences in fluctuation in this cohort, tailored assistance that is appropriate for each patient’s chemotherapy regimen or blood glucose level is of paramount importance. Support of patient self-management to achieve stable blood glucose levels and thus prevent adverse drug reaction was a key component in the successful completion of chemotherapy and improved patient outcomes for this group of special needs patients.

WPCS-15-3
Association of comorbid type 2 diabetes and cancer with risk of depression

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Objective: Type 2 diabetes (T2D) may increase risk of depression, resulting in huge challenges for clinical management of T2D. T2D is one of the common comorbidities in mid- to long-term cancer survivors who are also at high risk of depression. There is little epidemiologic evidence on risk of developing depression in individuals who had both T2D and cancer.
Methods: Using nationally representative data from the Korean Health Insurance Service database, 1,763,912 adults with T2D aged≥20 years without a history of depression were enrolled between 2015-2016 (mean follow-up of 3.6 years) after excluding those with any secondary or unclassified cancers. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated for risk of depression, after adjusting for sociodemographic, lifestyle, and metabolic risk factors.
Results: We identified 175,581 (10.0%) incident depression cases that occurred at least 1 year after enrollment. Having a comorbid cancer was associated with increased depression risk (HR 1.11, 95% CI 1.09-1.14) in individuals with T2D. By cancer type, those who had comorbid stomach (HR 1.24, 95% CI 1.18-1.30), pancreatic (HR 1.49, 95% CI 1.17-1.90), lung (HR 1.23, 95% CI 1.09-1.40), and prostate (HR 1.30, 95% CI 1.20-1.41) cancer, compared to those without the comorbid corresponding cancer. A comorbid gynecologic or breast cancer was not associated with increased depression risk.
Conclusion: The increased risk of depression in individuals with both T2D and cancer highlights the need to evaluate the risk of depression in healthcare settings. Further research is needed to explain differential associations by cancer type.

WPCS-15-4
Association of insulin resistance and Physical Activity With Survival Among Cancer Survivors

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Background
Insulin resistance (IR) and physical activity may influence survival after cancer.

Objective
To examine the independent and joint associations of insulin resistance and physical activity with mortality outcomes among cancer survivors.

Methods
A prospective non-diabetic cohort with age greater than 40 years (n = 27972) from UK biobank were linked to mortality data through November 12, 2021. Insulin resistance was accessed by a predictive algorithm. Physical activity was calculated by weekly metabolic equivalent of tasks (METs).

Results
Among 27972 non-diabetic cancer survivors (62.9% females), 6113 (27.2%)

patients were estimated as insulin resistance by predictive algorithm. During the follow-up period of up to 14 years, there were 4100 deaths (cancer, 2923; heart diseases, 404; other causes, 773). Multivariable models showed that being IR was associated with higher risks of all-cause (hazard ratio [HR], 1.143; 95% CI, 1.041-1.256) and cancer-specific (HR, 1.176; 95% CI, 1.052-1.314) mortality compared with non-IR. Compared with physical activity <10 (METs)/week exercise, the hazard ratio of cancer mortality were 0.799 (0.714-0.894), 0.68 (0.599-0.771), 0.68(0.581-0.768) and 0.681(0.618-0.751) for physical activity of 10-19, 20-29, 30-39, ≥40 (METs)/week exercise, respectively. In the joint analyses, compared with weekly physical activity <10 METs in non-IR patients, the corresponding risk of cancer mortality were 1.079 (0.892-1.305), 0.818 (0.66-1.014), 0.871(0.692-1.098),0.847(0.646-1.112) and 0.815(0.681-974) for IR with physical activity of <10,10-19, 20-29, 30-39, ≥40 (METs)/week exercise.

Conclusion

The beneficial effect of physical activity is greater in individuals without insulin resistance, particularly for physical activity greater than 20 (METs)/week exercise.

WPCS-15-5

The Development of Fulminant Type 1 Diabetes during Non-immune-checkpoint-inhibitor Chemotherapy for Breast Cancer

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It is well known that immune checkpoint inhibitors (ICI) cause various immune-related endocrinopathy including fulminant type 1 diabetes. However, there have been only few reports showing that non-ICI cancer chemotherapy induces fulminant type 1 diabetes. Here, we report a case of fulminant type 1 diabetes during non-ICI chemotherapy for breast cancer.

A 42-year-old woman with a history of breast cancer was receiving non-ICI chemotherapy with bevacizumab (anti–vascular endothelial growth factor antibody) and paclitaxel (tubulin inhibitor).She visited our hospital due to fever and general fatigue. Her laboratory data revealed the presence of urinary ketones, hyperglycemia (584mg/dl), metabolic acidosis with anion gap level of 18.5 mEq/L, and HbA1c level of 6.8% with serum C-peptide level of 0.1 ng/ml. In the glucagon stimulatory test, her serum C-peptide level was still 0.1 ng/ml after glucagon injection. Accordingly, we diagnosed fulminant type 1 diabetes although her anti-glutamic acid decarboxylase antibody was positive.

The development of fulminant type 1 diabetes during non-ICI chemotherapy for malignancy is a rare, but potentially fatal condition. More cases and further studies are needed to investigate the pathogenesis of the non-ICI-induced fulminant type 1 diabetes.

WPCS-16-1

Diabetes mellitus and Methicillin-resistant staphylococcus aureus (MRSA) infection

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Objective

The number of patients with methicillin-resistant staphylococcus aureus (MRSA) infection is high among people with diabetes mellitus. The aim of study was to evaluate MRSA infection among hospitalized diabetic patients.

Methods

Cross sectional study was included 201 (47 males, 53 females) diabetic patients, aged 22-79 and admitted to hospital. Body composition (body mass index, body fat, body muscle, body age and visceral fat), Blood glucose and HbA1C were measured. MRSA infection and antibiotics use data was collected from the hospital medical record.

Results

A total of 100 diabetic patients used antibiotic. Prevalence of methicillin-resistant staphylococcus aureus (MRSA) infection was 28%. Diabetic patients mean age 57.4±11.2 years old, body weight 77.2±15.8 kg, height 165.4±9.0 cm, BMI 27.9±5.2 kg/m², body fat (BF) 33.7±8.4%, muscle (BM) 44.5±10,2%, body age 67.8±14.9 years old, visceral fat (VF) 10.7±4.1%, metabolic rate 1316±263.7 kcal, waist circumference 99.2±13 cm, FBG 12.0±3.6 mmol/l, HbA1C 10.5±2.8%, Insulin 14.1±9.1 µIU/ml and C-peptide 2.7±1.5 ng/ml. MRSA positive and MRSA negative groups was no significantly different by HbA1C (10.1±1.9 vs 10.7±3.7; p=0.77) and Fasting glucose (11.1±3.7 vs 10.5±3.5; p=0.44) levels. Among hospitalized and MRSA infected diabetic patients foot ulcer and soft tissue infection was 64.3%(18) and 35.7%(10), respectively. All of MRSA positive patient was used Vancomycin.

Conclusion

1 of 2 hospitalized diabetic patients was infected and used antibiotics. Prevalence of methicillin-resistant staphylococcus aureus (MRSA) infection is 28%. Foot ulcer and Glycopeptides (Vancomycin) use are more frequent among hospitalized diabetic patients with MRSA.

WPCS-16-2

Antibiotics use of hospitalized diabetic patients

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Objective

Infection and antibiotics use are more common among diabetic patients. The aim of study was to evaluate antibiotics usage among the hospitalized diabetic patients.

Methods

Cross sectional study was included 201 (47 males 53 females) diabetic patients, aged 22-79 and admitted to hospital. Body composition (body mass index, body fat, body muscle, body age and visceral fat), Blood glucose and HbA1C were measured. Antibiotics use data was collected from the hospital medical record.

Results:

A total of 100 hospitalized diabetic patients out of 201 used antibiotics. Diabetic patients mean age was 57.4±11.2 years old, body weight 77.2±15.8 kg, height 165.4±9.0 cm, BMI 27.9±5.2 kg/m², body fat (BF) 33.7±8.4%, muscle (BM) 44.5±10,2%, body age 67,8±14,9 years old, visceral fat (VF) 10.7±4.1%, metabolic rate 1316±263.7 kcal, waist circumference 99.2±13, FBG 12.0±3.6 mmol/l, HbA1C 10.5±2.8%, Insulin 14.1±9.1 µIU/ml and C-peptide 2.7±1.5 ng/ml. Among hospitalized and antibiotics used diabetic patients urinary tract infection, soft tissue infection, foot ulcer and ketoacidosis was 50%, 28%, 18% and 4%, respectively. Cephalosporin and glycopeptides consumption was 73% and 27%, respectively.

Conclusions:

1 of 2 hospitalized diabetic patients was infected and used antibiotics. Urinary tract infections and cephalosporin use are more frequent among diabetic patients with infection.

WPCS-16-3

Serum chemokine CC-motif ligand 17 is a predictive marker of severe COVID-19 in patients with diabetes.

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Objective

In mild or moderate COVID-19 patients, chemokine CC-motif ligand 17 (CCL17) was reported to be a predictive marker for severe COVID-19; however, the validity of CCL17 among patients with diabetes is fully unknown. Objective of this study is to evaluate the predictive ability of CCL17 to predict severe COVID-19 in diabetic patients.

Methods

This retrospective observational study enrolled 176 diabetic patients with mild or moderate COVID-19 at hospitalisation (mean age 73 ± 14 years; 61.0%

male). Receiver operating characteristic and logistic regression analyses were used to examine the predictive validity of indices for severe COVID-19. To evaluate improvement in risk prediction with the addition of CCL17, we calculated net reclassification improvement (NRI) and the integrated discrimination improvement (IDI).

Results

During hospitalization, 41 patients developed severe COVID-19. Serum CCL17 collected at admission exhibited a higher area under the curve value (0.744) compared with that of other indicators including ferritin and C-reactive protein for the prediction of severe COVID-19. The optimal cut-off value for CCL17 was 140.0 pg/ml. A multi-variate logistic analysis revealed that CCL17 was negatively associated with severe COVID-19 (Odds ratio, 0.997; P = 0.047) even after adjustment for covariates. The addition of the CCL17 to a model consisting of vaccination, albumin, C-reacting protein and N/L ratio significantly improved classification performance for severe COVID-19 using the NRI (0.50, P = 0.004) and IDI (0.05, P < 0.001).

Conclusion

CCL17 levels in patients with diabetes infected with mild or moderate COVID-19 predict risk of developing severe COVID-19.

WPCS-16-4
THYROID HORMONE CHANGES DURING AND AFTER COVID-19 INFECTION

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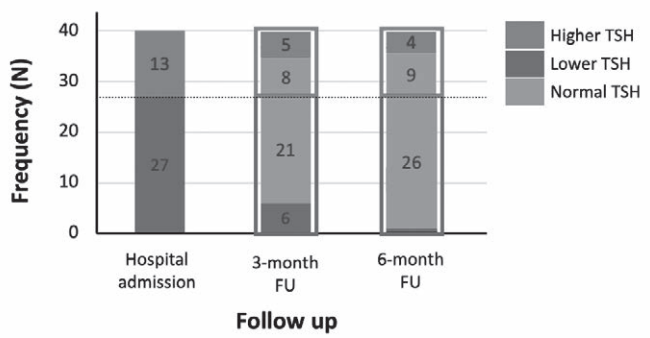
Objective: to detect and follow-up of non-thyroid illness hormone changes among COVID-19 patients

Materials and methods: This study was conducted among patients who treated in the First State Central Hospital and the National Center for Infectious Diseases. Participants with thyroid hormone changes were followed-up after 3 and 6 months. A total of 116 people were enrolled and according to the exclusion criteria, (anti-TPO, anti-TG and TSHR-ab positive and other criteria), 26 people were excluded and a total of 90 people were analyzed.

Result: The mean age was 56.8 ± 15.9 and 20.0% (n=18) were male. In terms of severity of COVID-19, 7.8% was severe. Among total patients, 46.6% had thyroid hormone changes. Of those changes (46.6%, n=41), 31.1% (n=28) and 14.4% (n=13) had decreased and increased TSH separately. Changes in TSH hormone (37.9% decreased, 13.8% increased) were observed in 51.7% (n=15) of people with mild COVID-19 infection while 100% (n=7) showed changes in TSH hormone in severe cases. Among them 83.3% in severe COVID-19 infection had decreased TSH hormone, while 16.7% had an increased TSH (p=0.017). When the changes in the thyroid hormone test were repeated after 3 and 6 months, 72.5% (n=29) of those who had TSH changes in the repeated test after 3 months, and 87.5% (n=35) after the 6- month test returned to normal ranges.

Conclusion: Thyroid function abnormality was 46.6% of COVID-19 patients, commonly occurred with the changes in TSH. At 6-month follow-up, 87.5% of all patients' TSH levels recovered to normal ranges without any treatment.



WPCS-16-5
Association of serum glycemic variability and severity of COVID-19 in Patients type 2 diabetes in Korea

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Background/Aims: Not only just simple value of blood sugar, serum glycemic variability also affects the control of diabetic complications and infections. This study is about the association between severity of COVID-19 and variety of blood glucose in Korea.

Methods: We conducted the study retrospectively with data from a cohort of 211 confirmed COVID-19 cases enrolled between July 2020 to July 2021 at Meoung-ji hospital in Korea. The severity of COVID-19 was divided into three subtypes: severe, critical, death.

Severe subtype was defined if a patient need O2 supply with nasal prong or facial mask. Critically severe patients are defined if other advanced treatment is needed such as non-invasive ventilation or high flow O2 or invasive ventilation or other multi-organ failure/ECMO/CRRT. About mean value of glucose and the glycemic variability, the standard deviation(SD) and coefficient of variation(CV) of these values were calculated and matched with each patient's severity.

Result: Clinic characteristics were collected from a total of 147 patients out of 211 confirmed cases of COVID-19. The excluded 64 patients were excluded due to lack of data. Patients were classified into three groups depending on their severity. Mean glucose value of patients were 160.42, 170.16, 201.81(SD 56.27, 157.92, 185.48) in severe, critical, death subtypes, and a ratio of CV in the three subtypes were 4.28, 2.04, 2.72 respectively.

Conclusions: This study found that those who have greater glycemic variability, tend to show high severity of COVID

WPCS-16-6
Ischemic stroke in patients with diabetes during COVID-19 pandemic in South Korea

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Objective: COVID-19 results in sub-optimal care for diseases requiring prompt management, such as ischemic stroke. Patients with diabetes mellitus (DM) were compromised with routine diabetic care during pandemic, despite COVID-19 patients with DM have higher risk of stroke. We examined stroke management and healthcare-associated behavior change during pandemic in DM patients.

Methods: 11,734 patients diagnosed of acute ischemic stroke and underwent intravenous thrombolysis (IVT) or endovascular thrombectomy (EVT) during January 2019 to December 2020 were recruited using data of National Emergency Department Information System. Rates of intensive care unit (ICU) admission were compared between pandemic and reference period and risk stratification according to age and DM status was performed. Treatment modality, time delay of visitation to emergency department (ED) were analyzed.

Results: Incidence of stroke available for procedures increased during outbreak(6,081 vs 5,653). Increase of stroke incidence was noted during post first outbreak period (109 vs 118,p=0.04). The rate of IVT increased (total:1450 vs 1737, p<0.01, DM:226 vs 272,p=0.20), while that of patients applied mechanical ventilation decreased (total:767 vs 739, p<0.02, DM:161 vs 121,p<0.01). ICU admission rate increased especially in DM patients aged more than seventies (316 vs 419,p<0.01). There was time delay of symptom to ED(1.50 vs 1.55,p<0.01), but hospital stay and in-hospital mortality were preserved in pandemic.

Conclusion: During the COVID-19 pandemic, the incidence of ischemic stroke requiring urgent procedure increased, and older patients with DM showed a higher ICU admission rate. It emphasizes the significance of consistent care for chronic metabolic diseases for non-COVID-19 related diseases prevention.

WPCS-16-7
Is there anything changed about diabetic ketoacidosis cases over the past 3 years?

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Background and aims: The etiology of diabetic ketoacidosis (DKA) was mainly type 1 diabetes mellitus(T1DM) and less frequent uncontrolled type 2 diabetes mellitus (T2DM). The purpose of the present study was to assess the prevalence of DKA among patients with T1DM and T2DM during the COVID-19 pandemic.

Patients and methods: A retrospective study included a cohort of 420 patients, who were hospitalized in the Department of Endocrinology and Metabolism, West China Hospital due to episodes of DKA or diabetes ketosis during January 1, 2020 to December 31, 2022. Clinical profiles and hospital mortality were analyzed.

Results: Among the 420 patients, 174 had DKA. Of them,80 (46.0%) had mild DKA, 78 (44.83%) had moderate DKA, whereas 16 patients (9.17%) had severe DKA. 122 patients (70.11%) developed DKA as the first manifestation of T1DM, 52 patients (29.89%) developed DKA in type 2 diabetes (T2DM), It was mainly caused by infections and medical noncompliance. Five patients died in the hospital due to severe infection and DKA (1.19% of all episodes),which is higher than the previous studies before 2019.

Conclusions: The prevalence of DKA admissions increased during the COVID-19 pandemic. severe infection and DKA increased mortality.

WPCS-16-8
A prospective one-year follow-up of glycaemic status of COVID-19 survivors with dysglycaemia in acute COVID-19

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Objective: We evaluated changes in glycaemic status, over one year, of COVID-19 survivors with dysglycaemia at baseline.

Methods: COVID-19 survivors who had dysglycaemia(defined by HbA1c 5.7–6.4% or random glucose≥10.0 mmol/L)in acute COVID-19 were recruited from a major COVID-19 treatment centre from September–October 2020. Non-COVID controls matched for age, sex, BMI and HbA1c were recruited from community. 75-gram oral glucose tolerance test(OGTT)were performed at baseline (six weeks after discharge from hospitalization for acute COVID-19) and one year after acute COVID-19, with HbA1c, insulin and C-peptide measurements. Progression in glycaemic status was defined by progression from (i)normoglycaemia to prediabetes/diabetes, or (ii)prediabetes to diabetes.

Results: 52 COVID-19 survivors were recruited(age:61.2±8.8years; 50%men). Compared with non-COVID controls, they had higher C-peptide($p<0.001$) and trend towards higher HOMA-IR($p=0.065$). At one year, 43 COVID-19 survivors attended reassessment. HbA1c increased from 5.5±0.3% to 5.7±0.2%($p<0.001$), with increases in glucose on OGTT at fasting($p=0.089$), 30-minute($p=0.126$), 1-hour($p=0.014$) and 2-hour($p=0.165$). At baseline, 19 subjects had normoglycaemia, 23 had prediabetes, and 1 had diabetes. Over one year, 10 subjects(23.8%; of the 42 non-diabetes subjects at baseline)had progression in glycaemic status, without significant change in C-peptide levels(0.67pmol/L to 0.67,$p=0.835$) and HOMA-IR. There was a trend of increase in BMI from 24.4±2.7kg/m^2 to 25.6±5.2($p=0.083$). Subjects with progression in glycaemic status had more severe COVID-19 illness than non-progressors($p=0.030$).

Conclusion: Subjects who had dysglycaemia in acute COVID-19 were characterised by insulin resistance. Over one year, ~25% had progression in glycaemic status, especially those with more severe COVID-19 illness. Importantly, there was no significant deterioration in insulin secretory capacity.

WPCS-16-9
Association of HOMA-IR (HI) with severity and worsening of confirmed COVID-19 patients

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Objectives:To determine the proportion and characteristics of COVID19 patients whom the Insulin resistance (IR) occur,as well as to analyze the relationship between HI and clinical outcomes of COVID19 patients. **Methods**:The subject was confirmed COVID-19 patients at RSCM-Jakarta in December 2020-March 2021.Worsening of the disease is defined as the degree of disease becomes ≥1 degree worse than at the time of admission and/or occurred death.Determination of the IR is carried out based on HI value ≥3.70 which is based on references.The design is a cross-sectional study for the relationship between HI and COVID-19 severity,and a retrospective cohort study for the relationship between HI and worsening degrees of disease. Multivariate analysis was carried out to analyze the association.**Results**:Total of 288 subjects were included.The characteristics in IR group were quite the same such as in the total group.HI showed an increase in values with increasing degree of disease,and the difference was significant.In the multivariate analysis,HI was associated with severity of COVID-19 ,but after adjustment with confounding variables the association was statistically insignificant.HI value was associated with the worsening of the disease (RR:1.994;95%CI:1.325-3.002;p=0.001),but after adjustment,the association was not statistically significant.**Conclusion**:The similar characteristics between IR and non-IR group gave rise to the thought that the IR is an acute one caused by COVID-19 .There is no proven association between HI and the severity of COVID-19 at admission,nor in the association between HI with the worsening of COVID-19.It is assumed that in the relationship between SARS-CoV-2 infection and inflammation,IR plays the role but is not the sole factor.

WPCS-17-1
Nocturnal hypertension and left ventricular diastolic dysfunction in diabetic patients with pre-heart failure phase

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Background: Diabetes is an important risk factor of heart failure (HF) and is associated with left ventricular (LV) diastolic dysfunction. However, integrated importance of diabetes and its comorbid conditions, such as altered nocturnal blood pressure (BP) variation, as predictors of diastolic dysfunction is not known in pre-HF period. The present study was conducted as longitudinal examination of the predictive value of nocturnal hypertension profiles on progression of LV diastolic dysfunction in propensity score-matched diabetic and non-diabetic patients without heart diseases.

Methods and Results: Pre-heart failure 422 subjects (154 diabetes, 268 non-diabetes) were followed for a mean 36.8 ± 18.2 months. The relationships among the patterns of nocturnal hypertension (extreme-dippers, dippers, non-dippers and riser) and the outcome of LV diastolic dysfunction, defined as increase in E/e' >14, were investigated in the patients with and without diabetes. After propensity score matching, there were 143 in each group. Kaplan-Meier analysis results revealed that diabetic patients with non-dipper ($p=0.034$ vs. dipper) and riser ($p=0.028$ vs. dipper) had a significantly greater risk for a diastolic dysfunction event. Furthermore, multivariable Cox proportional hazards analysis revealed that non-dipper (HR: 2.76; 95% CI: 1.00–7.58, $p = 0.049$) and riser (HR: 3.00; 95% CI: 1.01–8.85, $p = 0.046$) patterns were significantly associated with elevated risk of outcome

independent of classical risk factors. In contrast, no similar significant associations were found in non-diabetic patients.

Conclusions: During pre-HF periods, nocturnal hypertension is an important predictor for progression of LV diastolic dysfunction in diabetic patients.

WPCS-17-2

NT-proBNP as an Early Cardiovascular Risk Biomarker in Chinese Patients with Type 2 Diabetes: A Cross-sectional Study

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Objective

N-terminal pro-brain natriuretic peptide (NT-proBNP) is a cardiac biomarker that is strongly associated with heart failure diagnosis and predicting cardiovascular (CV) risk. Patients with Type 2 Diabetes (T2DM) are encouraged to receive regular diabetes mellitus complication assessment (DMCA) which is useful for predicting microvascular complications but rather insufficient for early CV risk detection. This study aimed to evaluate the feasibility of incorporating NT-proBNP in the regular DMCA for early assessment of CV risk in Chinese T2DM patients.

Methods

This study recruited 240 Chinese T2DM patients from a community health awareness program in Hong Kong. All participants underwent measurement of NT-proBNP (Roche Diagnostics) in addition to the regular DMCA. High CV risk was defined as NT-proBNP level >125 pg/ml.

Results

The participants had a mean age of 62.0±0.6 years, diabetes duration of 11.3±8.5 years, and NT-proBNP level of 69.0±156.2 pg/ml. When comparing to the low CV risk group, the high CV risk group (n=25,10.4%) was significantly older, with a longer diabetes duration, lower BMI, more conventional CV risk factors, and CKD history (all $p<0.05$). Both the number of conventional CV risk factors and albuminuria were significant predictors for elevated NT-proBNP. Compared with patients without albuminuria, the risks of elevated NT-proBNP for those with microalbuminuria and macroalbuminuria were 5.5-fold and 10.9-fold, respectively (both $p<0.001$).

Conclusion

Elevated NT-proBNP had shown prognostic value. This simple blood test may be included in the regular DMCA for early identification of Chinese T2DM patients with high CV risk, which can facilitate further investigations and timely treatments.

WPCS-17-3

The Relationship between Body Shape and Cardiovascular Disease in People with Metabolically Healthy Obesity

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Many studies reported inconsistent results about the development of cardiovascular disease (CVD) in individuals with metabolically healthy obesity (MHO). This study aimed to evaluate the effect of body shape on CVD outcomes in individuals with MHO. We analyzed the data of 8,416 participants from the Korean Genome and Epidemiology Study. To evaluate the participants' body shape, we calculated the Z-score of log-transformed A Body Shape Index (LBSIZ) and divided the participants into the following groups: metabolically healthy normal weight (MHNW), MHO, metabolically unhealthy normal weight (MUNW), and metabolically unhealthy obesity (MUO). Then, each group was classified into four subgroups based on the LBSIZ quartile. A multivariate logistic regression analysis was performed to evaluate the effect of LBSIZ for CVD events according to obesity phenotypes. 696 CVD events occurred in the participants. In the multivariate Cox regression model, MHO individuals did not have an increased risk of CVD compared with MHNW individuals. However, the further analysis with LBSIZ showed that the MHO participants with 3rd and 4th LBSIZ quartiles had a significantly higher hazards ratio for CVD events, whereas those with 1st and 2nd LBSIZ quartiles did not have an elevated risk of CVD compared to the MHNW participants with 1st quartile. In the restricted cubic spline regression, LBISZ showed a linear relationship with CVD events regardless of obesity phenotypes. The MHO individuals with a high quartile of LBSIZ have a significant increased risk for CVD events.

WPCS-17-4

Correlation between Insulin Resistance with Severity of Coronary Artery Stenosis in non-Diabetes Subject

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Objective : To determine the correlation between IR with severity of coronary artery stenosis in non-diabetes subject.

Method: Observational research with cross sectional approach at Wahidin Sudirohusodo Hospital Makassar from July 2020 until April 2021. Subject is Acute Coronary Syndrome (ACS) patients which meet inclusion criteria. Insulin resistance assessed using Admission Insulin Resistance Index (AIRI). Severity of coronary artery stenosis assessed using clinical classification of ACS, Syntax score, and number of coronary artery lesion. Statistical analysis using Kruskall-Wallis, Spearman's rho, and Chi Square test. Statistical results are considered significant if p value < 0.05.

Result : Research conducted on 22 subjects which consists of 20 men and 2 women, mean age of 57.8±15.5 years, diagnosis of STEMI 10 patients, NSTEMI 8 patients, and UAP 4 patients, mean of AIRI 13.69±9.56, and median number of stenosis lesion 3.50. Study analysis did not find significant difference of AIRI value between UAP, NSTEMI, and STEMI (p>0.05). No significant correlation between value of AIRI and Syntax score (p>0.05). No significant relationship between value of AIRI and number of coronary artery stenosis lesion (p>0.05).

Conclusion : No significant correlation between insulin resistance with severity of coronary artery stenosis in non-diabetic subject.

WPCS-17-5

The association and joint effect of A-FABP and obesity phenotype with cardiovascular events

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Objective: To explore the association between serum adipocyte fatty acid-binding protein (A-FABP) levels and obesity phenotype, and their joint impact on incident cardiovascular events.

Methods: The prospective study included 1345 residents (579 men and 766 women) without baseline cardiovascular diseases in 2013–2014. In 2021–2022, cardiovascular events were recorded by telephone and medical records. Fat percentage (fat%) and visceral fat area (VFA) were measured by bioelectrical impedance analyzer and magnetic resonance imaging, respectively. Fat% ≥ 25% in men or fat% ≥ 35% in women was defined as high fat%. VFA ≥ 80 cm^2 was defined as high VFA. Obesity phenotype was classified into four categories: (1) low fat%–low VFA; (2) low fat%–high VFA; (3) high fat%–low VFA; (4) high fat%–high VFA.

Results: During a mean 7.6-year follow-up, per 1-unit increase in $\log_e$-transformed A-FABP levels conferred a 1.87-fold (95% CI 1.33–2.63) risk of cardiovascular events. The highest tertiles of fat% and VFA levels were related to higher risks of cardiovascular events, respectively (fat%: HR 2.38, 95%CI 1.49–3.81; VFA: HR 1.79, 95%CI 1.09–2.93). Stratified analyses showed that the association between A-FABP levels and cardiovascular events was more predominant in those with low fat%–low VFA and low fat%–high VFA. The joint effect of high A-FABP and obesity resulted in a greater risk of cardiovascular events.

Conclusion: Serum A-FABP levels were significantly associated with the risk of cardiovascular events, and the association pattern was more predominant among population with low fat%, regardless of VFA levels.

WPCS-17-6

Neck circumference predicts the occurrence of future cardiovascular events in a 7.6-year prospective cohort

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Objective: To investigate whether neck circumference (NC) could be used as a predictor for future cardiovascular events in a community-based Chinese cohort.

Methods: We enrolled 1435 participants aged 50–80 years (626 men and 809 women) from communities in 2013-2014. From 2021-2022, cardiovascular events were collected by phone calls and medical records. Cardiovascular events were a composite of first instance of ischemic heart diseases and cerebrovascular events. High NC was defined as NC ≥ 38.5 cm in men and NC ≥ 34.5 cm in women.

Results: Throughout the 7.6-year follow-up, 148 cardiovascular events (10.31%) occurred. For every 1-SD increase in NC, multivariable-adjusted hazard ratio (HR) of cardiovascular events was 1.45 (95% confidence interval [CI], 1.15–1.83) in the whole population. The dose-response association was significant in men (HR 1.37, 95% CI, 1.10–1.71), but not in women (HR 1.19, 95%CI 0.94-1.52). Similarly, compared with participants with low baseline NC, those with high baseline NC conferred a significantly higher risk of cardiovascular events in total population (HR 1.59, 95%CI 1.14–2.22). Stratified analyses showed that the association was significant in men (HR 1.90, 95% CI, 1.21–2.98), but not in women (HR 1.25, 95% CI 0.75–2.07). Besides, the predictive ability of NC for cardiovascular events was comparable to that of body mass index or waist circumference.

Conclusion: NC was significantly associated with the risk of future cardiovascular events in middle-aged and elderly population in China, and was a better predictor in men.

WPCS-17-7

Visceral Fat is a Significant Determinant of Diastolic Dysfunction Parameters in Type 2 Diabetes Mellitus Patients

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Background. Diastolic dysfunction failed to be diagnosed in 33% type 2 diabetes mellitus patients, thus controlling risk factors is crucial. Visceral fat is significantly correlated with increased insulin resistance, epicardial fat deposition, and lipotoxicity. However, correlation between visceral fat and diastolic dysfunction parameters in type 2 diabetes mellitus population has not been investigated

Objective. We aimed to determine correlations between visceral fat and diastolic dysfunction parameters including E/E', lateral E', septal E', tricuspid regurgitation velocity (TRV), and left atrial volume index (LAVI) in type 2 diabetes mellitus population.

Methods. We performed cross-sectional study on type 2 diabetes mellitus patients admitted to ten primary health care in Jakarta between November 2020-2021. Visceral fat was measured by bioimpendance analysis (BIA). Diastolic dysfunction parameters were assessed by echocardiography. Other clinical and laboratory data were also recorded.

Results. A total of 56 type 2 DM patients with normal ejection fraction, mean age 49.3 (8.7) years were analyzed. We found significant correlations between visceral fat and E/E' (r = 0.304; p= 0.023), septal E' (r= -0.363; p=0.006) and lateral E' (r= -0.271; p= 0.043). Multivariate analysis demonstrated that visceral fat is the most significant determinant for increased E/E' ratio (B= 0.303; p <0.018) and decreased lateral E' (B= -0.367; p <0.003) and septal E' (B= -0.311; p <0.043). There was no correlation between visceral fat and TRV or LAVI.

Conclusion. There were significant correlations between visceral fat and E/E', lateral E', and septal E' in type 2 diabetes mellitus population.

WPCS-17-8

CO-OCCURRING DIABETES AND HYPERTENSION MORE THAN A YEAR INCREASING THE RISK OF HEART FAILURE: BOGOR DIABETES STUDY

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Introduction. *High blood sugar levels in type 2 diabetes can cause serious health complications such as heart failure because it can cause damage to the blood vessels and cardiac nerves. Additionally, people with type 2 diabetes who have high blood pressure also have a higher risk of developing heart failure. In this study, we examined diabetes patient with hypertension who began experiencing symptoms of heart failure.*

Methods*. Cross sectional design was conducted among adult patients diagnosed with type 2 diabetes and hypertension in Bogor city, Indonesia from January 2018-March 2018. The patient was examined for heart failure symptoms and analyzed by chi-square and spearman test to determine the correlation.*

Results*. From 153 subjects, there is significant correlation between hypertension in diabetes patient and heart failures ymptoms (p=0.043; OR (CI 95%) 2.06 (1.027 – 4.131)); p (r) = 0.043 (0.166). Positive correlation showed that diabetic patients co-occurring with hypertension more than a year may have heart failure symptoms.*

Conclusion*. Co-occurring diabetes and hypertension more than a year may have developing heart failure.*

Keywords. *Diabetes, hypertension, heart failure.*

	Heart Failure Symptoms		Total	OR (CI 95%)	*p	**r	**p
Hypertension	Yes	No					
Yes	47 (30.7%)	51 (33.3%)	98 (64.1%)	2.060 (1.027 – 4.131)	0.043	0.166	0.040
No	17 (11.1%)	38 (24.8%)	55 (35.9%)	Ref			
Total	64 (41.8%)	89 (58.2%)	153 (100.0%)				

*Corelative analysis were analysed using Chi Square with significance value of p<0.05.
**Corelative analysis and Strength of Corelation were analysed using Spearman test with significance value of p<0.05.

WPCS-17-9

The Difference of Echocardiography Findings of Type 2 Diabetes Mellitus with Hypertension Patients in Bogor, Indonesia

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Objective: Cardiovascular complications and nephropathies are the most common complications in T2DM patients especially with hypertension, as it is in Indonesia. Bogor Diabetes Study already revealed that in T2DM patient with hypertension and proteinuria tend to have higher event of heart failure signs and symptoms compared to those who doesn't. This study aimed to describe the echocardiography findings in T2DM diabetes patients with hypertension.

Method: A total of 153 T2DM patients in Bogor with and without hypertension

were enrolled in this cross-sectional study, consecutively. We compared the diastolic systolic dysfunction findings by echocardiography between groups with E/A pattern and ejection fraction score to evaluate their heart function in a real-world setting.

Results: There was significant difference in echocardiography findings between groups (p=0.017). Diabetic patients with hypertension have higher risk in diastolic dysfunction (p=0,015) and higher risks of developing heart failure symptoms (p=0.043).

Conclusions: T2DM patients with hypertension have higher risk of cardiovascular symptoms and risks compared to without hypertension.

WPCS-17-10

Age-Related Diabetes Impact on All-Cause Mortality after Acute Myocardial Infarction

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OBJECTIVE

Little is known about the association of diabetes mellitus with post-acute myocardial infarction (AMI) clinical outcomes in younger adults. We sought to test the hypothesis that diabetes impact on outcomes may vary according to patients' age.

RESEARCH DESIGN AND METHODS

A total of 12,600 AMI patients from the Korea Acute Myocardial Infarction Registry-National Institute of Health (KAMIR-NIH) between November 2011 and December 2015, was classified into young (n=3,590 [28.5%]) and elderly (n=9,010 [71.5%]) patients. For the study, those under 55 years of age were considered young. We performed comparisons of baseline characteristics, in-hospital treatments, and outcomes between diabetes and non-diabetes after stratification according to age group.

RESULTS

The prevalence of diabetes mellitus was 26.5% in the young AMI group. In the multiple adjusted model of the entire cohort, diabetes was strongly associated with 3-year all-cause mortality (12.6% vs. 6.8%; adjusted hazard ratio [HR], 1.318; 95% confidence interval [CI], 1.138-1.526). When the entire cohort was subdivided into two age groups, young with diabetes showed a 107.0 % higher mortality rate than non-diabetes (adjusted HR, 2.070; 95% CI, 1.150-3.724). Meanwhile, elderly diabetic patients had a 25.3 % higher risk of mortality compared with non-diabetic patients (adjusted HR, 1.253; 95% CI, 1.076-1.459). The interaction of diabetes with age was significant (adjusted *P* for interaction =0.008).

CONCLUSIONS

Diabetes is not uncommon in young AMI patients, and the risk of long-term mortality is rather significantly higher in young patients. More aggressive treatments to prevent future cardiovascular events in younger patients after AMI are needed.

WPCS-18-1

Association between continuous glucose monitoring-derived metrics and albuminuria in type 2 diabetes

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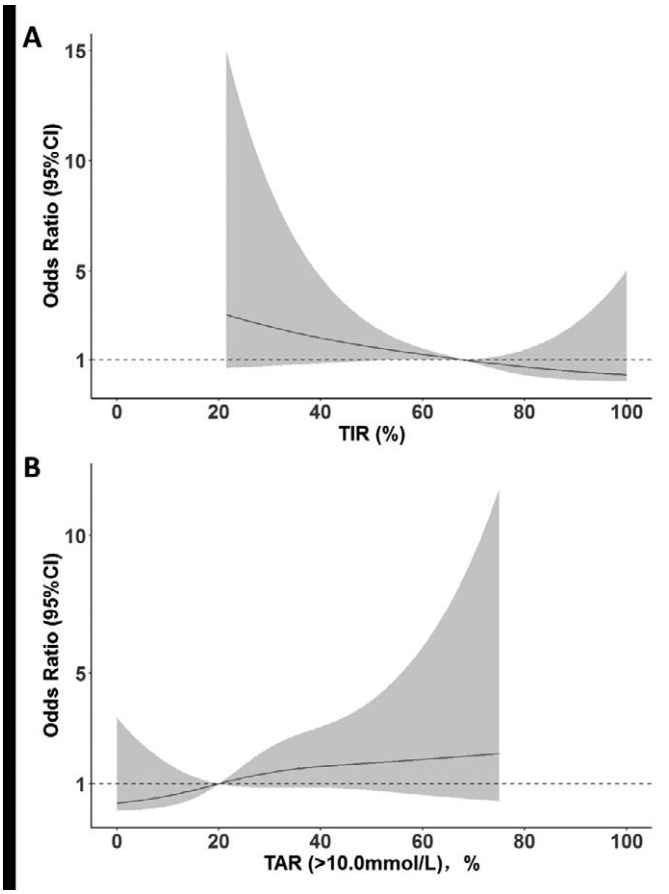
Objective The study intended to investigate the relationship between continuous glucose monitoring (CGM)-derived metrics, including time in target glucose range (TIR), time above target glucose range (TAR), and time blow target glucose range (TBR) and albuminuria in type 2 diabetes mellitus (T2DM) patients.

Methods A total of 135 inpatients with T2DM and received CGM between December 2017 and March 2021 were included in the study. The cohorts were divided into 3 groups based on tertiles of TIR, and subsequently analyzed the prevalence of albuminuria. The logistic regression model and restricted cubic spline were used to investigate the association TIR, TAR, and TBR and albuminuria after adjusted the confounders, including demographic characteristics, complications, medical treatment, and laboratory data.

Results The prevalence of albuminuria had a significant decrease with higher TIR tertiles (13.95% vs. 4.35% vs. 2.17%, P for trend=0.03). After adjusted the covariates, higher TIR was associated with a higher prevalence of albuminuria (odds ratio [OR]:0.94, 95% confidence interval [CI], 0.90-0.99). Meanwhile, higher TAR (>10.0 mmol/L) was associated with a higher prevalence of albuminuria.

Conclusion These results demonstrate that CGM-derived metrics, TIR and TAR, were associated with albuminuria in in T2DM patients. More attention to TAR in glycemic control with TIR might be beneficial in these patients.



WPCS-18-2

Urinary post-translation modified Fetuin-A: an early marker for progressive eGFR decline in subjects of Type 2 Diabetes

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Objective

There is an urgent need for additional biomarker(s) to predict renal function decline in patients with type 2 diabetes in early stage of kidney disease.

Methods

Subjects of type 2 diabetes without overt proteinuria in the cohort for a study of Validation of Early Diagnostics Biomarkers for Diabetic Nephropathy were included to assess the predictive role of post-translationally modified Fetuin-A in urine (uPTM-FetA). An eGFR decline ≥30% from baseline ere used as a kidney endpoint.

Results

In total, 258 patients with T2D (age 61.2 ± 9.9 years, 57% male, BMI 24.7±3.6

kg/m², with a diabetes duration of 11 [IQR: 7-16] years) were recruited, with a median uPTM-FetA/urinary creatinine (Cr) ratio of 10.32 [IQR: 6.39-21.30 ng/mg]. In survival analyses, we categorized the subjects according to the tertiles of UACR for those without microalbuminuria, and the group with microalbuminuria. We demonstrated a remarkable significant difference in 4 groups reaching the kidney endpoint during the follow up of 5 years by UACR category (p=0.014). Stratifying subjects with UACR and uPTM-FetA/uCr resulted in remarkable difference in survival curves (p=0.00013). A uPTM-FetA/uCr higher than the cut-off at 6.37 ng/mg was associated a HR of 6.32 (95% CI: 1.52 to 26.3) when adjusted for clinical variables including UACR and eGFR.

Conclusion

uPTM-FetA, a novel and independent of routine UACR and eGFR, was associated with renal function decline in patients with T2D without overt proteinuria. It was associated with renal function progression even in patients with T2D without microalbuminuria.

WPCS-18-3

Urinary cholesteryl as a predictor for the progression of renal dysfunction in early stage of diabetic kidney disease

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The prognosis of diabetic kidney disease (DKD) is currently assessed using urinary albumin or protein levels and the eGFR. However, previous studies have reported that eGFR decline is observed in certain DKD patients without albuminuria. Albumin-bound fatty acids (FAs) are reabsorbed in tubular cells, but excessive lipid accumulation induce lipotoxic tubular damage and detachment of cholesterol-accumulated tubular cells (RTEC) in the urine. Therefore, urinary lipids could provide valuable clinical information on DKD. Thus, we conducted a prospective study of the usefulness of urinary cholesterol (UCHO) as a predictor of the development of DKD in 220 outpatients with diabetes for a median of 60 months. UCHO was measured using a sensitive cholesterol assay system after treatment of the urine with cholesterol esterase.

UCHO increased along with DKD severity based on the KDIGO categories. Multivariate regression analysis showed that baseline UCHO was associated with the baseline eGFR, UACR, NGAL, L-FABP, RTEC and decline of eGFR per year even after adjusting for age, sex, BMI, blood pressure, HbA1c, use of RAS inhibitor, and SGLT2 inhibitor. Furthermore, UCHO was associated with NGAL, and RTEC even in A1 category. The development of end-stage kidney disease or the initiation of renal replacement therapy was increased in patients with the highest quartile of UCHO group (hazard ratio, 2.7; 95% CI, 1.1 to 6.7; p<0.05)

UCHO may be valuable for the assessment of tubular damage and prediction of the progression of renal dysfunction in early stage of DKD.

WPCS-18-4

Abelmoschus manihot compared with losatan for the treatment of stage 3 diabetic nephropathy: a non-inferior trial

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Objective: Huangkui capsule, an extract from the flowers of *Abelmoschus Manihot*, has been proved effective in improving chronic kidney disease. This study aimed to evaluate the efficacy and safety of Huangkui capsule in patients with diabetes and microalbuminuria.

Methods: This multicenter, randomized, open-label, parallel-controlled trial was conducted in six hospitals. The inclusion criteria were 30 mg/g ≤ albumin creatinine ratio (ACR) <300 mg/g, eGFR ≥ 60 mL/min/1.73 m^2, and type 2 diabetes with glycosylated hemoglobin ≤ 9%. We enrolled 239 patients who were randomly assigned to be treated with Huangkui capsule 2.15 g three times a day, or losartan potassium tablets 100 mg/day for 24 weeks. The primary outcome was the change in ACR from baseline and the secondary outcome was the change in eGFR.

Results: The ACR in the losartan group was 119.47±78.16 mg/g at baseline and 90.51±136.12 mg/g after 24 weeks of treatment, with a decrease of 30.46±134.16 mg/g (*P*=0.049). In the Huangkui group, the ACR decreased from 121.98±84.31 mg/g to 88.13±76.66 mg/g, with a drop of 31.94±91.66 mg/g (*P*=0.002). The change in eGFR was -3.58±10.35 mL/min/1.73 m^2 and -3.82±13.05 mL/min/1.73 m^2 in the losatan and Huangkui groups, respectively. In subgroup analysis of patients with baseline ACR ≥ 100 mg/g, losatan and Huangkui lowered ACR by 56.83 mg/g (*P*=0.044) and 78.72 mg/g (*P*<0.001), respectively. There were no significant differences between the two groups (*P*>0.05).

Conclusion: Huangkui capsule was non-inferior to canagliflozin in reduction of microalbuminuria and is a promising medicine for diabetic nephropathy.

WPCS-18-5

Finerenone Renal Efficacy and Safety in Diabetic Kidney Disease, a Meta Analysis, and Meta-regression

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Objective: *This study aims to determine the efficacy and safety of finerenone in patients with diabetic kidney disease (DKD).*

Methods: *Four selected databases including Pubmed, Cochrane Library, Scopus, and ClinicalTrials.Gov were searched using specific keywords up to February 2023. The effect size were estimated with risk ratio (RR) for dichotomous outcomes, and mean difference (MD) for continuous outcomes with 95% confidence interval (CI).*

Results: *A total of 4 randomized control trial (RCTs) including 13.929 patients were identified. Our pooled analysis showed that finerenone was associated with sustained estimated glomerular filtration rate (eGFR) reduction >40% (RR: 0.85 95% CI [0.78, 0.92], p=0.0002), and associated with higher* urine albumin to creatinine ratio *(UACR) reduction from baseline (MD: −0.30; 95% CI [−0.33, −0.27], I^2 = 0% , p<0.00001) when compared to placebo. Further regression analysis showed that this reduction was not significantly influenced by sex (p=0.101), age (p=0.3761), and HBA1c (p=0.2182). No significant difference was observed in the incidence of any adverse events between finerenone and placebo groups (RR: 1.00; 95% CI [0.98, 1.01], I^2 = 0%, p=0.65). However hyperkalemia was notably higher in finerenone compared to placebo (RR: 2.03; 95% CI [1.83, 2.26], I^2 = 0%, p<0.05).*

Conclusion: *Finerenone may ameliorate the kidney function in DKD, but with higher risk of hyperkalemia.*

Further well-designed RCTs are still required to confirm the results of our study.

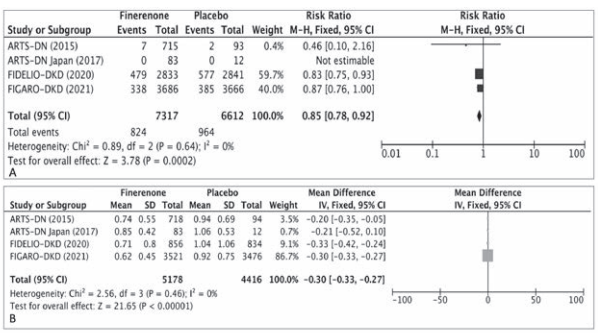

Figure.1 The efficacy of finerenone and placebo according to A. Sustained decrease eGFR >40%, B. UACR mean difference compare to baseline.

WPCS-18-6

Anthropometry measurements in hemodialysis patients: dialysis vintage stratified comparison

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Objective

This study compared the anthropometric measures of end-stage renal disease (ESRD) patients on maintenance hemodialysis (MHD) based on dialysis vintage (DV).

Methods

This cross-sectional study was done on ESRD patients (n=102) three times a week MHD at the hemodialysis center of the First State Central Hospital of Mongolia in 2023. Patients were divided into 2 subgroups d

Results

Out of 102 patients recruited in our study, 65.1% (n=65) were male. The mean age was 51.2 ± 14.8 years while the mean duration of HD was 4.6 ± 4.1 years. Dialysis vintage 2–4 years: when compared to early

Of the 102 patients[1] recruited, 65.1% (n=65) were male, and the mean age and duration of HD treatment were 51.2 ± 14.8 years and 4.2 ± 3.8 years, respectively. Patients in the late HD group (2-4 years of dialysis vintage) had significantly lower MAC (30±4.3 vs. 30.21 ± 3.84; OR=3.11; 95% CI 3.06-3.78; p< 0.05) and HGS (27.9 ± 3.12 vs. 22.4 ± 2.36; p< 0.046 in men and 18.6 ± 1.42 vs. 17.3 ± 5.6; p < 0.032 in women) compa

Conclusion

Anthropometry measurements of ESRD patients on MHD depend on the dialysis vintage, suggesting that the longer dialysis vintage might be related to the risk of sarcopenia. Therefore, management to prevent muscle weakness may be necessary in such patients.

Keywords

Hemodialysis, body composition, nutritional state, sarcopenia

Эндээс эхлээд засаад биччихлээ. Яахаар байна багшаа хараад хэлээд өгөөрэй

WPCS-18-7

Blood pressure and end-stage renal disease in older diabetes patients: a nationwide population-based study

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Background: There is insufficient evidence to determine a precise blood pressure target in older adults with diabetes mellitus. In this study, we evaluated the potential relationship between blood pressure levels and end-stage renal disease (ESRD) in older diabetes patients without ESRD using a nationwide longitudinal population dataset from the National Health Information Database (NHID).

Methods: We performed a retrospective, observational, cohort study including 267,156 older (≥ 65 years old) patients with diabetes and without ESRD from 2009 to 2018 based on the NHID. We divided the participants into eight groups based on their systolic blood pressure (SBP) and diastolic blood pressure (DBP). The primary composite outcome was ESRD.

Results: During a median follow-up of 7.26 years, the incidence rate of ESRD was 2.03 per 1,000 person-years. In multivariable Cox proportional hazard modeling, the risk of the primary outcome was the lowest in groups with an SBP of 100–119 mmHg and DBP of < 80 mmHg. In subgroup analysis according to the use of hypertension medication, there was a significant difference in DBP (p for interaction = 0.026) but no difference in SBP (p for interaction = 0.247). The risk of ESRD was the lowest in patients with an SBP of 110–129 mmHg taking hypertension medication and the highest in the group with an SBP of ≥ 160 mmHg.

Conclusion: Maintaining blood pressure at less than 120/80 mmHg might prevent progression to ESRD in older diabetes patients without cardiovascular disease

WPCS-18-8

Transcriptome meta-analysis of diabetic kidney disease and hub genes discovery

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Objective: To identify crucial genes correlated with diabetic kidney disease (DKD) and advance the understanding of pathogenesis of DKD by integrating transcriptome datasets.

Methods: Two meta-analysis methods, continuous variable summary meta-analysis and surrogate variable analysis (SVA) combat method, were conducted to integrate seven kidney gene expression profiles from human DKD expression datasets. Differentially expressed genes (DEGs) were identified by limma algorithm. Two machine learning methods, lasso regression and random forest analysis, were used to seek out hub DKD targets, and the CIBERSORT method was applied to explore the relation between hub genes and immune cells.

Results: 324 DKD glomerulus DEGs and 231 tubules DEGs were identified, which were enriched in immune infiltration functions and pathways. After the selections from two machine learning algorithms, CD44, CEBPD, CD53, and FN1 were identified as hub gene targets for DKD. Correlation analysis revealed that CD44 had negative correlations with naïve B cell and resting NK cells, while CEBPD showed positive correlations with activated NK cells; CD53 positively linked to M2 macrophages, but exhibited negative correlations with regulatory T cells and M0 macrophages; FN1 had negative correlations with regulatory T cells and M0 macrophages.

Conclusion: The study provides a comprehensive meta-analysis of DKD transcriptome based on currently available human kidney glomeruli/tubules gene expression datasets to identify 4 DKD-related hub gene targets and their correlations with detailed immune cells. A web-portal and new analytical tools have also been built to facilitate investigators to access the meta-analysis results for validation from cell culture and animal experiments.

WPCS-18-9

Effect of sacubitril/valsartan on both glycemic control and microalbuminuria in diabetic patients with hypertension

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Background: Diabetes is an independent risk factor for renal failure progression. Sacubitril/valsartan(sac/val), a combination angiotensin receptor-neprilysin inhibitor, reduces morbidity and mortality in patients with heart failure with reduced ejection fraction (HFrEF), compared with the angiotensin-converting enzyme inhibitor enalapril, and improves peripheral insulin sensitivity in obese hypertensive patients. However, little is known regarding the underlying mechanisms of sac/val effect on diabetic kidney disease in humans. We aimed to investigate the effect of sac/val, in comparison with valsartan, on HbA_{1c} and urinary microalbuminuria in patients with diabetes and hypertension.

Methods: We included fourteen diabetic patients with hypertension who were treated with valsartan. Their mean age was 66 yr. and diabetic history was 20 years. After switching from valsartan to sac/val for their treatment, we assessed changes in HbA_{1c}, urinary microalbumin, daily salt intake, eGFR and BMI in a mixed effect. Daily salt intake was evaluated by calculating the sodium and creatinine levels in urine samples. Treatment of glycemic control in these patients with oral drugs and insulin were not changed during this study.

Results: During the three months of follow-up, HbA_{1c} concentrations decreased by 0.46% (SD 0.85). Urinary albumin concentrations decreased by 10%($p<0.003$). Mean blood pressure also decreased 20 mmHg. No changes were observed in BMI, eGFR and daily salt intake.

Conclusion: Patients with diabetes and hypertension who received sacubitril/valsartan had a reduction both in HbA_{1c} and urinary microalbumin after switching from valsartan. These data suggest that sacubitril/valsartan might enhance glycemic control and prevent diabetic nephropathy in patients with diabetes and hypertension.

WPCS-18-10

Switching to pemafibrate improves renal function in diabetic kidney disease: a sub-analysis of the PARM-T2D study

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Objective

Fibrates can cause renal dysfunction, limiting their use by patients with diabetic kidney disease (DKD). However, pemafibrate is metabolized by the liver and has less toxicity on renal function. In the present analysis, we evaluated the outcome of pemafibrate on renal function in patients with or without DKD in a real-world clinical setting.

Methods

We performed a sub-analysis of data collected during a multi-center, prospective, observational study comparing the effects of pemafibrate on lipid metabolism in patients with type 2 diabetes complicated by hypertriglyceridemia (the PARM-T2D study). The participants were allocated to take add-on pemafibrate (ADD-ON), switch from current fibrate to pemafibrate (SWITCH), or continue conventional therapy (CTRL). The changes in eGFR over 52 weeks were compared between the groups and according to DKD status.

Results

Data for 520 participants (ADD-ON (n=166), SWITCH (n=96), and CTRL (n=258)) were analyzed, and 56.7% of them had DKD. The eGFR improved only in the SWITCH group, which was also true for the DKD subgroup (p<0.001), but this effect was abrogated in patients with severe renal dysfunction (G3b and G4) and/or macroalbuminuria. Multivariate analysis showed that older age, a switch from fenofibrate, and the absence of macroalbuminuria were associated with improvements in eGFR (all p<0.05).

Conclusion

Switching to pemafibrate may be associated with an improvement in renal function, but with lower extent in patients with poor renal function.

WPCS-19-1

Association between serum Tsukushi and liver fibrosis in type 2 diabetes

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Objective: Tsukushi (TSK), a small secreted protein of the leucine-rich proteoglycan family, is a newly identified hepatokine. We aimed to investigate whether circulating levels of TSK were related to metabolic-associated fatty liver disease (MAFLD) in individuals with type 2 diabetes.

Methods: 393 subjects with type 2 diabetes were recruited from the diabetes clinic. Vibration-controlled transient elastography was performed to determine the degree of hepatic steatosis and fibrosis, as reflected by controlled attenuation parameter (CAP) and liver stiffness (LS), respectively. MAFLD was defined as CAP ≥ 248 dB/m. Serum TSK was measured by ELISA.

Results: MAFLD was present in 276 subjects. There were no significant differences in age and duration of diabetes between subjects with or without MAFLD, but those with MAFLD were more obese (p<0.01) and had higher HbA1c (p<0.01). Serum TSK level was increased in subjects with MAFLD compared to those without [91.0 ng/ml (61.7 – 133.8) versus 82.5 ng/ml (60.9 – 118.5), respectively, p<0.05]. On univariate analysis, serum TSK level was significantly associated with the severity of steatosis and fibrosis, and correlated with CAP, LS, and liver transaminases. Serum TSK was also associated with BMI, serum triglyceride levels and inversely with HDL and eGFR levels. There was no correlation with HbA1c or fasting glucose. Linear regression analysis showed that LS and eGFR levels were significant independent determinants of serum TSK levels.

Conclusion: Serum TSK was increased in people with type 2 diabetes and co-existing MAFLD, and was associated with the severity of liver fibrosis.

WPCS-19-2

Improvement of insulin sensitivity and inhibition of hepatic gluconeogenesis by components in bitter melon fruits

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We previously reported that bitter melon extract has hypoglycemic effects and enhances insulin secretion from pancreatic β-cells; however, the effects on insulin sensitivity and gluconeogenesis remain unclear. To clarify the blood glucose regulatory mechanism of bitter melon fruit, we investigated the acute effects of bitter melon extract on insulin sensitivity and gluconeogenesis and the underlying mechanisms.

The green fruit of bitter melon was freeze-dried and extracted with methanol. The bitter melon fruit extracts were fractionated by hydrophobicity into an ethyl acetate-soluble fraction (A, hydrophobic), an *n*-butanol-soluble fraction (B, amphipathic) and a water-soluble fraction (C, hydrophilic). Single administration of fraction A or B to normal mice reduced blood glucose levels during the insulin tolerance test. Fraction A treatment activated the phosphorylation of Akt in the liver and white adipose tissue. In the liver, fraction A activated the phosphorylation of glycogen synthase kinase-3β and increased glycogen content. Fraction B treatment activated the phosphorylation of Akt in the skeletal muscle and white adipose tissue. On the other hand, single administration of fraction C reduced blood glucose levels during the pyruvate tolerance test and suppressed the expression of glucose 6-phosphatase and phosphoenolpyruvate carboxykinase, the gluconeogenesis rate-limiting enzymes in hepatocytes.

This study demonstrated improvement of insulin sensitivity in insulin-acting tissues by fraction A and B, activation of glycogen synthesis in the liver by fraction A, and suppression of gluconeogenesis in the liver by fraction C. Thus, bitter melon can acutely regulate blood glucose homeostasis via multiple actions.

WPCS-19-3

Endothelial cell-specific CNP overexpression does not improve insulin resistance in HFFCD-induced NASH model mice

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Objective: Previous reports have shown that mice with endothelial-cell-specific overexpression of CNP (E-CNP Tg mice) were protected against hepatic fibrosis and inflammation induced by high fat diet (HFD) feeding with improved insulin sensitivity and attenuated weight gain. Given that recently developed high-fat, high-fructose, high-cholesterol diet (HFFCD) is considered to be superior model in regard to the resemblance to human non-alcoholic steatohepatitis (NASH), in this study, we attempted to reveal whether these previous findings with E-CNP Tg mice on HFD can be observed in this newly developed NASH model.

Methods: E-CNP Tg mice were fed with HFFCD for 8 months, and glucose tolerance, insulin sensitivity, and the degree of liver inflammation and fibrosis were assessed.

Results and Conclusion: After 8 months feeding of HFFCD, the liver of E-CNP Tg mice and controls showed progressive fibrosis, which resembled the feature of human NASH. No significant differences, however, were observed in the degree of fibrosis between E-CNP Tg mice and controls, although there was a tendency of improvement in E-CNP Tg mice. Insulin resistances were developed by HFFCD with no differences between the genotypes. The expression levels of GC-B mRNA, a receptor for CNP, in the liver were suppressed by HFFCD diets, which were rather elevated by HFD. There is a possibility that the reduced levels of GCB may have weakened the action of CNP in the current model. Further studies will be needed to evaluate the therapeutic potential of CNP in NASH.

WPCS-19-4
Lobeglitazone inhibits LPS-induced NLRP3 inflammasome and inflammation in the liver

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Objective: : Nonalcoholic fatty liver disease (NAFLD), ranging from steatosis to cirrhosis, is a liver manifestation of metabolic syndrome. Diabetes is a major risk factor for the disease progression of NAFLD. Inflammation is a important mechanism of NAFLD and is related to disease progression to fibrosis. Kupffer cells (KC) is a macropahges in the liver and are involved in liver inflammation. Alterations in the functional activity of KCs are associated with liver diseases, including NAFLD. Lobeglitazone acts as a peroxisome proliferator-activated receptor gamma ligand, a type of thiazolidinedione, and is known to have anti-inflammatory effects. Still, there is no clear evidence of direct anti-inflammatory effects in the liver.

Methods : To study the liver inflammation effect of lobeglitazone, we used a mouse (C57BL/6) primary KCs, hepatocyte and hepatic stellate cells (HSCs). Cytokines were measured by real time RT-PCR analysis and ELISA. The expression levels of NLRP3 inflammasome markers were evaluated by western blot analysis.

Results : In this study, lobeglitazone reduces LPS-induced NLPR3 inflammasome activation and inflammatory cytokines in primary KC and hepatocyte. Cytokines secreted from activated KC increased hepatocyte inflammation and HSC activation, and lobeglitazone inhibited these responses. In addition, lobeglitazone suppressed liver fibrosis by inhibiting LPS-induced TGF-β secretion and TGF-β-induced CTGF expression.

Conclusion: The inhibitory effect of lobeglitazone on inflammasome activation was associated with inhibiting liver fibrosis. These results suggest that lobeglitazone may be a beneficial treatment option for inflammation and fibrosis in the liver.

WPCS-19-5
Insulin sensitivity affects hepatic ChREBP activity.

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(Objective) Glucose and insulin regulate lipogenic genes via Chrebp and Srebp1c, respectively. In contrast, gene regulation of other metabolic pathways appears to be different. In this study, we aimed to elucidate the regulation of hepatic metabolic gene expression by glucose and insulin.

(Methods) Ten-week-old male wild-type (WT) and Chrebp$^{-/-}$ mice were persistently treated with the insulin receptor antagonist S961 (240 nmol/kg BW/day) for four days. Real-time PCR and RNA sequencing (RNA-Seq) were used to assess comprehensive gene expression levels.

(Results) Blood glucose, insulin, and 3-OHBA levels increased after S961 treatment, consistent with decreased Akt phosphorylation. Chrebp deletion more potently decreased liver triglyceride contents than the S961 treatment. S961 treatment reduced Chrebp expression to approximately 40% of wild-type, and Chrebp deletion did not alter Srebp1 expression; S961 treatment and Chrebp deletion reduced Pklr, Fasn, Elovl6, and Scd1 expression. S961 treatment and Chrebp deletion also increased and decreased G6pc and Fbp1 expression, respectively. Finally, RNAseq results showed that S961 and Chrebp deletion decreased 140 of 2320 genes (6%), and S961 increase and Chrebp deletion decreased 19 of 2320 genes (0.82%).

(Conclusion) Chrebp and its known target genes were also reduced by S961, suggesting that the effect of S961 on gene expression is partially due to reduced Chrebp activity. Thus, insulin sensitivity may affect hepatic ChREBP activity.

WPCS-19-6
Amphiregulin promotes iNOS and COX-2 expression in hepatic inflammation via NF-κB and MAPK signaling pathways

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Objective: Inflammation is a major cause of hepatic tissue damage and accelerates the progression of nonalcoholic fatty liver disease (NAFLD). Amphiregulin (AREG), an epidermal growth factor receptor (EGFR) ligand, is associated with human liver cirrhosis and hepatocellular carcinoma. We aimed to evaluate the effects of AREG on hepatic inflammation during NAFLD progression, *in vivo* and *in vitro*.

Methods: AREG gene expression was measured in the liver of mice fed a methionine choline-deficient (MCD) diet for 2 weeks. We evaluated inflammatory mediators and signaling pathways in HepG2 cells after stimulation with AREG. Nitric oxide (NO), prostaglandin E2 (PGE2), inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 (COX-2) were analyzed using an enzyme-linked immunosorbent assay (ELISA) and western blotting. Nuclear transcription factor kappa-B (NF-κB) and mitogen-activated protein kinases (MAPKs), including extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), and p38-MAPK, were analyzed using western blotting.

Results: Pro-inflammatory cytokines (tumor necrosis factor-α [TNF-α], interleukin [IL]-6, IL-1β, and IL-8) and immune cell recruitment (as indicated by L3T4, F4/80, and ly6G mRNA expression) increased, and expression of AREG increased in mice fed the MCD diet. AREG significantly increased expression of IL-6 and IL-1β and production of NO, PGE2, and IL-8 in HepG2 cells. It also activated the protein expression of iNOS and COX-2. AREG activated NF-κB and MAPKs signaling, and together with NF-κB and MAPKs inhibitors, AREG significantly reduced the protein expression of iNOS and COX-2.

Conclusion: AREG plays a role in hepatic inflammation by increasing iNOS and COX-2 expression via NF-κB and MAPKs signaling.

WPCS-19-7
Increased O-GlcNAcylation in hepatocytes via sodium-glucose cotransporter 2 drives non-alcoholic steatohepatitis

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AIMS: Steatosis reducing effects of sodium-glucose cotransporter 2 (SGLT2) inhibitors in non-alcoholic steatohepatitis (NASH) has been consistently reported in humans but their mechanism remains uncertain. In this study, we examined the expression of SGLT2 in human livers and investigated the crosstalk between SGLT2 inhibition and hepatic glucose uptake, intracellular O-GlcNAcylation, and autophagic regulation in NASH.

METHODS: Human liver samples obtained from individuals with/without NASH were analyzed. For in vitro studies, human normal hepatocytes and hepatoma cells were treated with SGLT2 inhibitor under high-glucose and high-lipid conditions. NASH in vivo was induced by a high-fat, -fructose, and -cholesterol Amylin liver NASH (AMLN) diet for 10 weeks followed by an additional 10 weeks with/without SGLT2 inhibitor (empagliflozin 10 mg/kg/day).

RESULTS: Liver samples from individuals with NASH were associated with increased SGLT2 and O-GlcNAcylation expression compared with controls. Under NASH (in vitro condition with high glucose and lipid) intracellular O-GlcNAcylation and inflammatory markers were increased in hepatocytes and SGLT2 expression was upregulated; SGLT2 inhibitor treatment blocked these changes by directly reducing hepatocellular glucose uptake. In addition, decreased intracellular O-GlcNAcylation by SGLT2 inhibitor promoted autophagic flux through AMPK-TFEB activation. In the AMLN diet-induced NASH mice model, SGLT2 inhibitor alleviated lipid accumulation, inflammation, and fibrosis through autophagy activation related to decreased

SGLT2 expression and O-GlcNAcylation in the liver.
CONCLUSIONS: This study firstly demonstrates increased SGLT2 expression in NASH and secondly reveals the novel effect of SGLT2 inhibition on NASH by activating autophagy mediated by inhibition of hepatocellular glucose uptake and consequently decreasing intracellular O-GlcNAcylation.

WPCS-19-8
The prevalence and the predictive factors of NAFLD diagnosed by Transient Elastography in Thai people with prediabetes.

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Objective: To investigate the prevalence and to develop a simple clinical predictive score for detecting NAFLD in Thai people with prediabetes
Methods: A cross-sectional analysis was conducted from a baseline cohort of people with prediabetes. NAFLD was diagnosed by a transient elastography with a controlled attenuation parameter >275dB/m and/or a liver stiffness measurement ≥7.0kPa and without secondary causes of hepatic steatosis.
Results: Of 400, 375 participants (Female 68%, age 62.1±9.9 years, BMI 26.3±4.6 kg/m2, FPG 96.5±10.3 mg/dL, HbA1c 5.8±0.3%) without secondary causes were recruited. The prevalence of NAFLD in our study was 35.7%. In multivariate logistic regression analysis, the most practical model comprised FBS≥110 mg/dL and HbA1C≥6.0%, sex-specifics cut-offs HDL, ALT≥30, and BMI of <23, 23-<25 and ≥25 kg/m2 can provide a good predictive performance with an area under the receiver operating characteristic curve of 0.715 (95%CI 0.692,0.738). Sensitivity and specificity were 70.86% and 72.14% with PPV and NPV were 58.6% and 81.65% respectively, at the cut-off value of 4.5. The likelihood ratio of testing positive for NAFLD was 2.54.
Conclusion: This practical score, which has a good predictive performance, must be beneficial for clinicians in emphasizing necessities for the investigations among participants with prediabetes, particularly in resource-limited settings. Early detection and management of NAFLD could ameliorate the future burden of liver complications.

WPCS-19-9
Inhibition of GPR120 signaling in intestine ameliorates insulin resistance and fatty liver under high-fat diet feeding.

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Objective: G-protein-coupled receptor (GPR) 120 is expressed in enteroendocrine cells secreting glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic polypeptide/gastric inhibitory polypeptide (GIP), and cholecystokinin (CCK). Although GPR120 signaling in adipose tissue and macrophages ameliorate obesity and insulin resistance on high long-chain triglyceride (LCT) diet, intestine-specific roles of GPR120 are unclear.
Methods: We generated intestine-specific GPR120-knockout ($GPR120^{int-/-}$) mice to measure intestinal hormones after single administration of LCT. Following 15 weeks of high-LCT diet, we evaluated insulin sensitivity, weight of liver and white adipose tissue (WAT), Akt phosphorylation, and gene expression of inflammatory cytokines and lipogenic molecules.
Results: $GPR120^{int-/-}$ mice exhibited reduced GIP secretion and CCK action without change of insulin, GLP-1, or peptide YY (PYY) after single administration of LCT. Under a high-LCT diet, $GPR120^{int-/-}$ mice showed amelioration of insulin resistance and fatty liver. Moreover, liver and WAT of $GPR120^{int-/-}$ mice exhibited increased Akt phosphorylation and reduced gene expression of suppressor of cytokine signaling (SOCS) 3, which inhibits insulin signaling. Gene expression of inflammatory cytokines in WAT and lipogenic molecules in liver were reduced in $GPR120^{int-/-}$ mice.
Conclusion: Inhibition of GPR120 signaling in intestine ameliorates insulin resistance and fatty liver under high-LCT diet feeding.

WPCS-20-1
Diabetes Incidence and Risk Factors in a Japanese Cohort

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【Background】Diabetes has been reported to be associated with cardiovascular diseases and diseases that reduce quality of life, such as sarcopenia. Although it is well known that the prevalence of diabetes has increased in Japan with changes in lifestyle and social environment after World War II, few reports have examined the long-term incidence of diabetes in the Japanese population.
【Purpose】To examine the long-term trends in the diabetes incidence and the factors related to the diabetes incidence
【Methods】In a cohort of A-bomb survivors and their controls in Hiroshima and Nagasaki followed for 60 years since 1958, we examined 9,131 subjects who participated in the health examination study at least twice from 1969 to 2015.
【Results】During the follow-up period, 1,417 subjects newly developed diabetes. The incidence of diabetes increased throughout the follow-up period and was higher in men than in women.
Diabetes incidence was also higher in the younger birth cohort. Family history of diabetes and current smoking were risk factors for the diabetes incidence
As for the effects of radiation exposure, an association was suggested between higher doses of radiation exposure and incidence of diabetes among those exposed at a younger age in Hiroshima.
【Conclusions】The diabetes incidence increased throughout the follow-up period and was higher in men and in the younger birth cohort. Family history of diabetes and current smoking were associated with diabetes incidence. An association with radiation exposure was suggested in some dose ranges.

WPCS-20-2
Association between proinsulin level and hepatic steatosis in individuals with type 2 diabetes

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Objective: Increased proinsulin secretion is an indicator of pancreatic beta-cell exhaustion. Our previous research demonstrated that proinsulin (PI) levels positively associated with the degree of hepatic steatosis in a population-based study. This current study investigates whether a similar association is also observed in individuals with type 2 diabetes.

Methods: Data from our prospective, cross-sectional observational study in individuals with type 2 diabetes were analyzed. Individuals with a history of alcohol consumption or those with missing data were excluded. The degree of hepatic steatosis was evaluated using a fatty liver index (FLI). A total of 191 individuals were divided into three groups: low FLI group (FLI <30), moderate FLI group (30 ≤FLI <60), and high FLI group (FLI ≥ 60). Fasting serum PI levels were compared among the three groups.

Results: In the crude analysis, logarithm-tranformed PI in the high FLI group was significantly higher than in the moderate and low groups. A significant difference was also observed between the moderate FLI group and the low FLI group. Similar results were observed when adjusted for age and sex ($p<0.01$).

Conclusion: Our data showed that PI levels increase proportionally with hepatic steatosis progression in this cohort. This elevation of proinsulin further supports the existence of a direct relationship between hepatic steatosis and beta-cell exhaustion in individuals with type 2 diabetes.

WPCS-20-3

Diabetes under peritoneal dialysis improved less in mortality age than those without diabetes on peritoneal dialysis.

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DM is the most common underlying cause of ESKD. Those with ESKD must undergo hemodialysis, peritoneal dialysis or kidney transplant. This study analyzed whether diabetes patients' prognoses have recently improved after receiving PD. From 2006 to 2018, we examined their age of death and the cause of mortality.

The National Statistics Information Service provided mortality information, and the Korean NHIS provided data from their National National Health Insurance database. The NSIS death records from 2006 to 2018 were combined with the NHIS claims data. We included only those who underwent PD.

11,174 deaths in all were recorded (4,818 individuals with DM and 6,356 individuals without DM). Among people with and without DM, the age at death increased by 0.11 and 0.44 years/year, respectively. Males with DM experienced the lowest changes in mortality age (0.10 years/year), while female without DM experienced the largest changes (0.47 years/year). For those with DM getting PD, DM itself, cardio-cerebrovascular illnesses, and cancer were the main reasons of mortality.

In conclusion, this study showed that people with DM getting PD had a slight rise in death age during a 12-year period, but the shift was considerably less pronounced than in people without DM. The prognosis of the DM patient who underwent PD should be improved in light of these findings. It would also be crucial to determine the particular cause of mortality as well as the best management approach in this population.

WPCS-20-4

Serum Glucagon-like peptide 1 effected to the pathophysiological role of type 2 diabetic patients

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Glucagon-like peptide 1 (GLP-1), regulates glucose metabolism by inducing beta cell mass, insulin secretion and suppressing glucagon secretion. GLP-1 is a potent anti-hyperglycemic hormone, inducing the beta cell of the pancreas to release the hormone insulin response to rising glucose, while suppressing glucagon secretion. GLP-1 has a half-life of less than 2 minutes, due to rapid degradation by the enzyme dipeptidyl peptidase-4 (DPP-4). However, plasma GLP-1 level correlated to blood glucose and insulin and to prove that low GLP-1 levels was a risk factor Mongolian population with type 2 diabetes mellitus (T2DM). Methods:Plasma insulin, active and total GLP-1 concentration in type 2 diabetic subjects measured by ELISA. In glucose tolerance test (GTT), 75g glucose was orally injected into type 2 diabetic subjects followed by blood sampling from the vein for glucose and insulin measurements.Serum total and active GLP-1, insulin and blood glucose level were measured on fasting and postprandial state at 15, 30, 60 and 120 minutes in 14 newly diagnosed T2DM and 28 subjects with normal glucose tolerance, were enrolled in the study as the control group. Results:Both fasting and postprandial total GLP-1 levels were significantly lower in subjects with T2DM than control subjects. In postprandial state, blood glucose level was potently higher and serum total GLP-1, insulin levels were significantly lower in T2DM. Conclusion:The lower level of postprandial active GLP-1 potently correlated to impairment at glucose-induced insulin release and hyperglycemia in T2DM. This result indicate that impairment at postprandial GLP-1 secretion may have pathophysiological role to develop T2DM.

WPCS-20-5

Association of bone mineral density with the risk of incident type 2 diabetes in Hong Kong: A prospective cohort study

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Objective: There is emerging evidence that bone and energy metabolisms are interrelated. Several cross-sectional studies have been conducted examining the relationship between bone turnover markers and glycaemic traits, but the findings were inconsistent. In particular, the temporal relationship of bone mineral density (BMD) with incident type 2 diabetes mellitus (T2DM) remains unknown. The aim of the present study is to examine the association of BMD with the risk of T2DM using a prospective cohort in Hong Kong.

Methods: 7,160 eligible participants from the Hong Kong Osteoporosis Study (HKOS) were included. Baseline examination was conducted from 1995 to 2010. Participants were followed for a median of 16.8 years until 2020. BMD was measured at the hip, femoral neck, and lumbar spine. T2DM incidents were assessed using electronic health records. Cox proportional hazard regression was used to estimate the hazard ratio (HR) of T2DM, with adjustment for potential confounders, including BMI.

Results: BMD of total hip and femoral neck (per 0.1g/cm2 increase) was significantly associated with an increased risk of T2DM (HR: 1.143, 95% CI: 1.077 - 1.214, $p<0.001$; and HR: 1.103, 95% CI: 1.034-1.178, $p=0.003$, respectively). Patients with osteoporosis were associated with a reduced risk of T2DM when compared to participants with normal BMD (HR: 0.703, 95% CI: 0.552-0.897, $p=0.004$).

Conclusion: The present prospective study provided novel evidence that higher BMD is associated with a higher risk of T2DM. Future study evaluating the potential of BMD being a clinical target for diabetes management is warranted.

WPCS-20-6

Epidemiology, clinical features, diagnosis, treatment, and prognosis of calciphylaxis: A review from 1519 patients

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Importance: Calciphylaxis is a rare, devastating, but underrecognized disease. Currently, there is no systematic information regarding its diagnosis and management.

Objective: We aimed to perform a systematic review of calciphylaxis to identify its clinical features, diagnosis, treatment, and prognosis.

Evidence Review: We systematically searched 7 databases from inception to December 2022.

Findings: A total of 1519 patients were included. Calciphylaxis was more frequent in females than males (5:2). The mean age at onset was 56.35±15.77 years. Most patients had end-stage renal disease (75.12%), and diabetes (28.24%). Calciphylaxis is a systemic disease, with the skin being the most frequently affected organ (1351 cases, 88.94%). Skin lesions typically develop bilaterally (75.8%). The typical skin manifestation was painful necrotizing ulcers covered with black eschar, however, other patients with calciphylaxis develop milder lesions such as erythema, livedo and plaques. No specific laboratory markers were identified. Although calcium and phosphate products were assumed to beassociated with calcium deposits, the majority of calciphylaxis patients had normal serum calcium levels (62.58%). However, the serum phosphate levels were elevated in 65.94% of patients. Currently, there is no widely accepted standard for diagnosing calciphylaxis. Thus, many patients are initially misdiagnosed. The most common misdiagnoses were vasculitis.

Conclusions and Relevance: A diagnostic criterion was proposed after reviewing current literature, with biopsy and radiological imaging being the most useful tools. Multidisciplinary management which includes pain management, local wound care, infection prevention and control, restoration of calcium and phosphate metabolism, and reversion of vascular calcification, is usually preferred in patients with calciphylaxis.

WPCS-20-7

The Impact of Parity on the Risk of Type 2 Diabetes: A prospective cohort study of UK Biobank Participants

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Objective

The aim of our study was to investigate the association between parity and the risk of type 2 diabetes using a large, well-established prospective UK Biobank cohort.

Methods:

Definition of incident type 2 diabetes was based on self-report in an in-person interview at enrollment or on diagnostic and procedure codes in electronic health records. Parity was defined as the number of live births (0, 1, 2, 3, 4, or ≥5). Parity and the risk of diabetes were estimated by Cox proportional hazard regression models, adjusting for demographic, clinical, and lifestyle factors.

Results:

A total of 242,159 women with full data available (mean age 56.8 years and BMI 26.8 kg/m2) were included in the analysis. During the median follow-up of 8.9 years, 4,045 (1.7%) women developed type 2 diabetes. Parity was significantly associated with the risk of type 2 diabetes even after adjusting for potential risk factors. Among the subgroup with ideal lifestyle habits, parity was not associated with the risk of type 2 diabetes. In contrast, among the subgroup with poor lifestyle habits, the risk of type 2 diabetes substantially increased as parity increased.

Conclusion:

In this study, we found an association between multiparity and the risk of type 2 diabetes. However, multiparous women with a healthy lifestyle did not show an increased future risk of type 2 diabetes. Therefore, this study suggests that lifestyle interventions may help prevent type 2 diabetes among women with high parity.

WPCS-20-8

Postprandial CPR index is valuable in assessing beta-cell function in Japanese patients with type 2 diabetes

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Onset of type 2 diabetes(T2D) is based on the insulin secretion(loss of b-cell function) and resistance. Residual b-cell function is a key factor in achieving optimal glycemic control in T2D patients. Glucagon stimulates insulin, therefore glucagon stimulation test(GST) is a reliable marker for b-cell function. Fasting C-peptide(CPR) to glucose ratio(CPR[ng/ml] / glucose[mg/dl] x100; F-CPR-index) is used as a marker of insulin secretion. We evaluated the efficacy of postprandial CPR to glucose ratio(P-CPR-index) for evaluating b-cell function in T2D.

500 of Japanese T2D patients with inadequate glycemic control(HbA1c>7.0) were eligible in the study. HbA1c, fasting CPR and glucose, postprandial(120 min after breakfast) CPR and glucose were measured, and F-CPR-index and P-CPR-index were calculated. GST was performed as follows: 1mg of glucagon was injected intravenously, CPR was determined before and 6 min after injection, GSTDCPR(CPR[6 min] – CPR[0 min]) was calculated. Factors correlated with GSTDCPR were analyzed using simple and multiple stepwise regression analysis. P value<0.05 was defined as statistically different.

F-CPR-index, P-CPR-index and GSTDCPR were 1.60±0.95, 2.67±1.92 and 1.93±1.21, respectively. Simple regression analysis showed that GSTDCPR was significantly correlated with age, height, body weight(BW), BMI, waist circumference, duration of diabetes, retinopathy, insulin therapy, urinary CPR, F-CPR-index and P-CPR-index. Multiple stepwise regression analysis revealed that independent factors contributing to GSTDCPR were BW(b=0.336), duration of diabetes(b= -0.107), presence of retinopathy(b= -0.121), use of DPP-4i(b= -0.099), metformin(b= -0.109), SGLT2i(b= -0.108, p=0.002) and P-CPR-index(b=0.432).

Our date demonstrated that P-CPR-index was valuable and simple method in assessing residual beta-cell function in daily clinical practice.

WPCS-20-9

Risk of diabetes complication among different type 2 diabetes subtypes in Korean - A cluster analysis

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Background: Little is known about the subtypes of type 2 diabetes (T2D) and their association with clinical outcomes in Asians.

Methods: We performed data-driven cluster analysis in patients with newly diagnosed drug-naive T2D (n = 756) from the Korean Genome and Epidemiology Study. Clusters were based on five variables (age at diagnosis, BMI, HbA1c, and HOMA2 β-cell function, and insulin resistance).

Results: We identified four clusters of patients with T2D according to k-means clustering: cluster 1 (22.4 %, severe insulin-resistant diabetes [SIRD]), cluster 2 (32.7 %, mild age-related diabetes [MARD]), cluster 3 (32.7 %, mild obesity-related diabetes [MOD]), and cluster 4 (12.3 %, severe insulin-deficient diabetes [SIDD]). During 14 years of follow-up, individuals in the SIDD cluster had the highest risk of initiation of glucose-lowering therapy compared to individuals in the other three clusters. Individuals in the MARD and SIDD clusters showed the highest risk of chronic kidney disease and cardiovascular disease, and individuals in the MOD clusters showed the lowest risk after adjusting for other risk factors ($P < 0.05$).

Conclusions: Patients with T2D can be categorized into four subgroups with different glycemic deterioration and risks of diabetes complications. Individualized management might be helpful for better clinical outcomes in Asian patients with different T2D subgroups.

WPCS-21-1

SCREENING TEST FOR T2DM: OGTT OR HYPERINSULINEMIA

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Objective: Detection of hyperinsulinemia during the screening of T2DM.

Method: Hospital based cross-sectional study was included 354 (94 male, 260 female) participants. Screening of T2DM was included diabetes risk score questionnaire, physical examination and laboratory tests. FBG, OGTT, HbA1C, serum insulin, c-peptide were measured and we calculated HOMA-IR, HOMA-B, HOMA-S indices.

Results: The mean age of the participants was 42.4±13.7 years old. Mean body weight 80.4±14.9 kg, BMI 30.1±4.8 kg/m2BF, 39.4±8.6%, VF 9.8±3.4% and FBG 5.9±0.8 mmol/l, OGTT 2 hours blood glucose 8.9±2.6mmol/l, HbA1C 5.8±1.2%; Insulin 24.6±16.7 mkU/ml, C-peptide 3.6±2.5mkU/ml, HOMA-IR 2.9±1.5, HOMA-B 142.7±70.5%, HOMA-S 46.9±31.8%.

Results of OGTT: There were 18.4% (65) normal, 81.6% (289) abnormal (prediabates 66.4% (235), diabetes 15.3% (54)). Among the prediabetes were IFG alone (60), IGT alone (47) and IFG +IGT (128).

Insulin resistance were respectively diagnosed 33.8%(22) in normal group, 70%(42)in IFG group, 76.5%(36) in IGT group, 69.5%(89) in IFG+IGT group, 96.1%(49) in DM newly diagnosed group.

Conclusion:

1 in 3 people was diagnosed as insulin resistance in normal OGTT. The onset of hyperinsulinemia maybe an early sign in T2DM.

WPCS-21-2
Serum Soluble CD81 in subjects with type 2 diabetes mellitus

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Objective

CD81 are cell surface proteins involved in cell development, activation, growth and motility. Recent studies suggest that CD81 marks dedifferentiated β-cells under metabolic stress, such as the progression of diabetes. However, the clinical significance of changes in serum soluble CD81 (sCD81) in diabetic subjects remains unknown. We measured serum sCD81 during a 75g oral glucose tolerance test (OGTT) in diabetic patients and subjects with normal glucose tolerance.

Methods

101 subjects who had an OGTT were recruited. The test results were divided into diabetes (DM) and normal glucose tolerance (NGT) groups. Results with prediabetes were excluded. During the OGTT, sCD81 levels were measured at 0 and 120 minutes and changes in sCD81 were compared between groups.

Results

In all subjects, serum sCD81 were reduced from 0.65 ± 0.66ng/mL at baseline to 0.57 ± 0.52ng/mL at 120 minutes OGTT (*P = 0.014*). In DM group, serum sCD81 were significantly higher than normal group at baseline and 120 min OGTT (*P=0,006* and *.030*, respectively). The serum sCD81 of the NGT group remained unchanged, while the DM group showed a significant decrease during the OGTT. (from 0.44 ± 0.50 ng/mL to 0.42 ± 0.40 ng/mL, *P = 0.635* in the NGT group; from 0.76 ± 0.72 ng/mL to 0.64 ± 0.56 ng/mL, *P = 0.011* in the DM group).

Conclusion

Serum sCD81 levels were elevated in type 2 diabetics, with changes in sCD81 during OGTT only in DM group. Serum sCD81 may have potential as a new diagnostic marker for type 2 diabetes.

WPCS-21-3
MATSUDA AND ORAL DISPOSITION INDICES FOR TYPE 2 DIABETES MELLITUS

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OBJECTIVE

The aim of study determination of insulin sensitivity and glucose tolerance by Matsuda and Oral disposition indices (oDI) in type 2 diabetes mellitus (T2DM) patients.

MATERIALS AND METHODS

Case control study included 30 T2DM patients and 30 Healthy subjects (HS). Physical examination and laboratory tests were determined. Plasma glucose, insulin were measured at 0, 30, 60, and 120 min of the oral glucose tolerance test (OGTT). Matsuda and oDI indexes were calculated for glucose and insulin levels at the 0 and 30 minutes of the OGTT.

RESULTS

The mean age of the participants was 46.7±9.96 years old. Comparing mean results of the physical characteristics of the T2DM and HS: weight 87.9±11.3 and 66.3±14.5kg (p=0.001), BMI 31.6 and 24.8kg/m^2 (p=0.0016), body fat 35.2 and 31.8% (p=0.0002), visceral fat 12.0 and 7.8% (p=0.02), muscle 28.2 and 24.5% (p=0.0002). According to the laboratory parameters of the case and control groups, fasting glucose (p<0.001), HbA1C (p=0.001), insulin (p=0.002), HOMA-S (p<0.001) was statistically different, HOMA-IR (p=0.053) and HOMA-B (p=0.055) were not different. Matsuda index or insulin sensitivity was low for case group (2.31±1.23 vs 4.99±2.89; p=0.001) and oDI or beta cell function was high for case group (4.27±2.70 vs 0.5±0.63; p=0.0001), respectively.

CONCLUSION

Insulin sensitivity reduced and betta cell function is increased in newly diagnosed T2DM patients.

WPCS-21-4
Approach to Diagnosis and Management Latent Autoimmune Diabetes in Adults : A Case Report

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Introduction.

Latent Autoimmune Diabetes in Adults (LADA) is used to describe a form of autoimmune diabetes that has a later onset and a slower progression toward an absolute insulin requirement. The presence of pancreatic auto antibodies especially to Glutamic acid decarboxylase (GAD65) is the best single marker required to diagnose LADA.

Case Illustration.

A 35-year old male came to emergency room with shortness of breath since two days before admission.There was a weight loss of 10 kg in the last 1 month.Blood sugar level was 422 mg/dL, blood ketone was 5.6 mmol/L, and the blood gas analysis showed metabolic acidosis. Cpeptide level was 0.35 ng/mL (1.1 - 4.4 ng/mL). Patients was positive for glutamic acid decarboxylase autoantibodies. Patients was diagnose with LADA and treated with basal insulin 1x36 unit and prandial insulin 3x20 unit.

Discussion.

Cpeptide is mostly undetectable in classical T1DM and normal or high in patients with newly diagnosed T2DM, whereas individuals with LADA tend to have low but still detectable C-peptide values at the time of diagnosis. Thus, islet autoantibodies screening, especially GADA, should be required as a second step for patients with adult-onset diabetes showing low serum C-peptide. To date, evidence shows that patients with LADA should be treated with insulin at an earlier stage.

Conclusion.

Routine GADA screening should be considered. However, since testing for islet-cell autoantibodies may not always be indicated because of high costs, C-peptide measurement may be a useful tool to rule out diagnosis of LADA in case of low clinical suspicion.

WPCS-21-5
35 YEAR OLD WOMANWITH INSULINOMA, HASHIMOTO THYROIDITIS, AND UTERINE MYOMA

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Dr. Kariadi Hospital

Introduction

Insulinoma is a rare neuroendocrine tumor (NET). Hashimoto thyroiditis (HT) is an autoimmune thyroid disease causing hypothyroidism. Both insulinoma and HT are predominantly in women. Uterine myoma is the most common solid pelvic tumor. Concomitant diseases of insulinoma, HT, and uterine myoma is extremely rare.

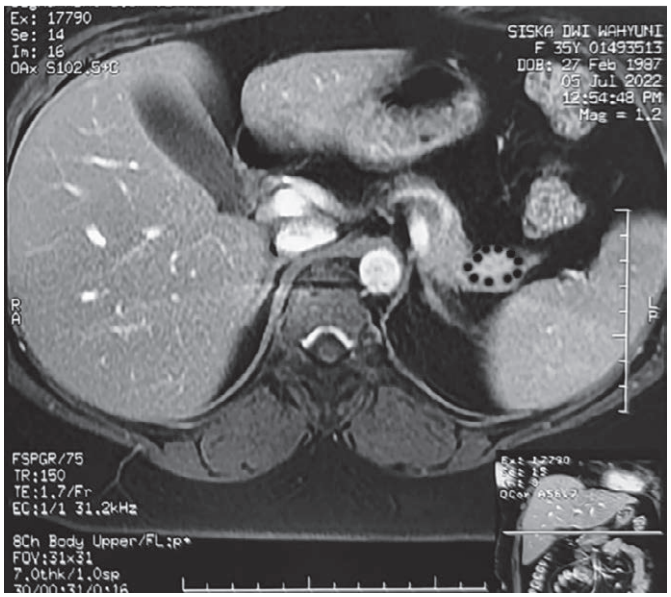
Case Presentation

History taking: 35 year old woman was referred by a neurologist to endocrinologist due to recurrent hypoglycemia. She formerly complained of recurrent epileptic episode followed by transient decreased consciousness. Regular treatment with anti-epileptic agent showed no benefit. She also had an extreme weight gain and irregular period. **Physical examination**: obese class II (BMI 33,6 kg/m^2). Vital sign normal. **Laboratory findings**: FG 49 mg/dL, 2h ppg 100 mg/dL, HbA1c 4,1%. Fasting insulin 17 IU/mL (upper normal). TSHs 5,15 uIU/mL (N: 0,51-4,94), freeT4 13,92 (N: 10,6-19,4). Anti-TPO level 42,25 IU/mL (N: <5,61). **Radiology finding**: abdominal CT: mass on the pancreatic tail and uterine. **Management**: Thyroid hormone supplementation, pancreatic tail mass resection, and myomectomy. **Histopathology finding**: consistent with insulinoma and uterine myoma. **Result**: excellent well being after surgery.

Discussion

Diagnosis of insulinoma based on recurrent hypoglycemia, high fasting insulin level, pancreatic tail mass, and hystopatology. HT based on the subclinical hypothyroidism and high anti-TPO level. Uterine myoma based on uterine

mass and hystopathology. Hyper-insulin and hypothyroidism both can trigger extreme weight gain. High circulating insulin might stimulate cell proliferation and tumor progression. Despite those facts, correlation among pancreatic NET, thyroid autoimmunity, and pelvic solid tumor remains unclear.



WPCS-21-6

Monogenic diabetes caused by KCNJ11 gene abnormality without abnormal glucose metabolism in the neonatal period.

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KCNJ11 gene encodes the KIR6.2 subunit of the KATP channel in pancreatic beta cells and has been widely reported as a causative gene of neonatal diabetes, and some have also been reported to develop diabetes in adolescence. In addition, some of these genes have been reported to cause diabetes in adolescence and are known as Maturity-onset diabetes of the young (MODY)13 genes. We report a case with diabetes caused by KCNJ11 gene abnormality, which was diagnosed before puberty without any apparent abnormalities in glucose metabolism in the neonatal period.

A 7-year-old boy. He was diagnosed as diabetic with fasting blood glucose of 133 mg/dl and HbA1c of 8.2%, and was referred to our hospital. His family history showed that his paternal grandfather had diabetes mellitus. At the time of examination, his fasting blood glucose was 154 mg/dl, HbA1c was 8.2%, islet autoantibodies were all negative, and a glucagon tolerance test showed C-peptide 0.79 ng/ml at fasting and a peak value of 1.78 ng/ml at 6 minutes post-load, indicating decreased insulin secretion. Genetic tests for glucose metabolism abnormalities were performed, and c.685G>A was found in KCNJ11 gene. Diabetes due to KCNJ11 gene abnormalities can cause diabetes before puberty and should be considered as a diagnostic differential in cases of diabetes due to atypical low insulin secretion.

WPCS-21-7

Clinic characteristics and heterogeneity in children and adolescents with ketosis-prone diabetes mellitus

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Background Ketosis-prone diabetes mellitus(KPDM) is a subtype metabolic disorder of type 2 diabetes mellitus that presents in obese children and adolescents. Limited studies are conducted in China.

Objective To assess clinical characteristics and heterogeneity of diabetic ketoacidosis(DKA) in KDPM, and their relative difference among children with newly diagnosed T1DM.

Methods This is a retrospective study of 32 newly diagnosed diabetes children and adolescents (≥14 yrs, KPDM,n=21 and T1DM, n=11) admitted for DKA in West China Hospital, a tertiary teaching hospital in Chengdu. The fasting plasma glucose(FBG), HbA1c, C-peptide, free fat acids (FFA) and β-hydroxybutyrate concentrations were measured. Data was analyzed using SPSS 20.0.

Results Of the total, 21 were KPDM patients. Polydipsia and polyuria (each 90.47%) were the predominant symptoms onset. Family history of diabetes and unknown precipitants the first episode of ketoacidosis were significantly different among the KDPM patients. Mean (±SD) body mass index of patients in the KPDM group was 29.0(±3.6)kg/m^2, and the waist circumference was 92.2(±9.7)cm, which was significantly higher than that in the T1DM group (P<0.001).FBG at admission was 23.3(±8.5)mmol/L and HbA1c was 11.5(±3.0)%, respectively, which elevated same as that in the T1DM group [12.7(±1.8)% , P >0.05]. FFA and β-hydroxybutyrate levels were markedly elevated in KPDM (1267.6±440.8 mmol/L v.s.1098.9±281.7 mmol/L, p>0.05, 1.59±1.05 mmol/L v.s. 1.44±0.20 mmol/L, p>0.05,respectively).No mortality was documented.

Conclusion Insulin resistance(IR) coexist in KPDM patients.Those had severe hyperglycemia, hypertriglyceridmia and high plasma FFA concentrations on admission, suggesting that glycolipid toxicity could result in serious IR, β-cell dysfunction and DKA in patients with KPDM.

WPCS-21-8

Changes of incretin effects and glucagon levels in different type of hyperglycemia

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We identified changes of Glucagon-like-peptide 1 (GLP-1) and glucagon levels in new diagnosed type 1 diabetes (T1D) (n=11) and T2D (n8) of adolescent, impairing glucose tolerance(IGT) of male(n=15) and female(n=15) , and gestational diabetes mellitus (GDM)(n=15). All patients undertook oral glucose tolerance test in a week of diagnosis except T1D with DKA. Analysis data included age, gender, body weight, BMI, PG, insulin, c peptide, GLP-1, glucagon, AUC_X, early ingulinogenic index (IGI,△I30 / △G30) and Matsuda index, which were tested and calculated. Results showed that incretin effects were impaired in both T1D, IGT, T2D and GDM, while fast GLP-1 levels and AUC_{GLP-1} in children were higher than those of adults, and fast GLP-1 levels and AUC_{GLP-1} of women in pregnant were also higher than in non-pregnant ones. At the same time , $AUC_{Glucagon}$ increased obviously during early stage of both T2D and T1D. The data suggested that impairment of incretin effects were through the process of diabetes independent with type differentiation. And hyperglucagonemia seemed not associated with disease history both in T2D and T1D.

WPCS-21-9

Monocyte CD300e expression analysis in Patients with Type 1 Diabetes and control subjects

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Type 1 diabetes (T1D) is characterized by immune-related pancreatic β-cell destruction. The CD300e antibody level increases during the acute phase of fulminant T1D (FT1D). Here, we investigated the contribution of CD300e to T1D development.

Monocytes were obtained from 20 patients with FT1D, 25 with acute onset T1D (AT1D), 14 with type 2 diabetes (T2D), and 17 healthy controls (HCs). Additionally, peripheral blood mononuclear cells (PBMCs) were obtained from 8 patients with FT1D, 12 with AT1D, 11 with T2D, and 9 HCs. Using flow cytometry, we analyzed CD300e expression in monocytes and myeloid dendritic cells in PBMCs. Tumor necrosis factor (TNF)-α was measured after the stimulation of monocytes with 3.3 ng/μL sphingomyelin (SM), a CD300e

ligand.
The percentage of CD300e-positive cells in the monocytes of patients with AT1D was higher than that in those of HCs (p = 0.006). The percentage of CD300e-positive cells was higher in female participants than in male participants, and was negatively correlated with the estimated glomerular filtration rate and age (sex p = 0.023, eGFR p = 0.028, age p = 0.023). There was no difference in SM-stimulated TNF-α production by monocytes among diabetic subtypes and gender. We showed differences in CD300e expression in human monocytes with diabetes type, sex, age, and renal function.
These results provide information on the physiological features of CD300e and insights into the role of CD300e in AT1D pathogenesis.

WPCS-21-10
Tramadol Induced Hypoglycemia in Type-2 Diabetes Mellitus Patient: A Case Report

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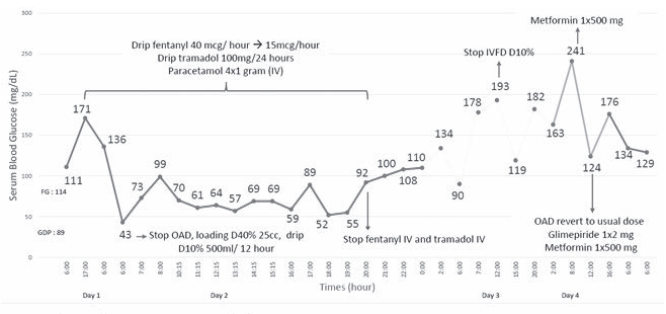
Introduction: Tramadol is opioid analgesics for alleviating moderate to severe pain. Hypoglycemia is an uncommon adverse effect of tramadol. We present an unique case of hypoglycemia as a variation of the tramadol's adverse effect in a patient with type 2 diabetes mellitus.
Case Illustration: A 84-year-old woman with type-2 diabetes mellitus routinely consumed 2 mg glimepiride and 500 mg metformin per day. She never had hypoglycemia episode before. She underwent a left total knee replacement because of severe osteoarthritis.
Three days after surgery and oral intake was adequate, she received 100mg/24 hours of tramadol, of which she then developed hypoglycemia with a blood glucose level was 43 mg/dL. Anti-diabetic agents were stopped, sugary drinks and intravenous glucose were given, but but her blood sugar levels remained low. Her blood glucose gradually returned to normal levels after we discontinued tramadol.
Discussion : The cause of hypoglycemia should be determined as soon as possible. In this case, tramadol is a potential cause of the hypoglycemia episode. The episodes of hypoglycemia aligned perfectly with the anticipated pharmacodynamic and pharmacokinetic of tramadol. The temporality of events after tramadol use in this patient fulfilled causality criteria. Tramadol-induced hypoglycemia may be severe in some cases.**Conclusion** : While tramadol-associated hypoglycemia is rare and the underlying mechanisms are poorly understood, we need to consider it in a case of hypoglycemia which match the temporality of tramadol use.
Keywords: hypoglycemia, tramadol, type-2 diabetes mellitus



WPCS-22-1
Risk of developing type 2 diabetes, hypertension and dyslipidemia in women with GDM: a nationwide cohort study in Taiwan

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Objective: An increasing trend in the prevalence of gestational diabetes mellitus (GDM) is reported in Taiwan. GDM has been linked to various adverse outcomes on mothers' health. However, evidence from nationwide cohort studies is limited. Furthermore, the results of GDM effect on developing type 2 diabetes mellitus (T2DM), hypertension (HTN) and hyperlipidemia (HL) are inconsistent.
Methods: This is a retrospective, population-based nationwide cohort study. The data source is merge from the Birth Certificate Application database (BCA) and the National Health Insurance Research Database in Taiwan. Women aged between 15-45 years who gave birth in Taiwan between 2004 and 2011 were included. Women who were enrolled and with a diagnosis of GDM were assigned to the exposure group. Women who were enrolled without a diagnosis of GDM were assigned to the comparison group. Relative risk for developing T2DM, HTN and HL were analyzed and presented as hazard ratio (HR) by Cox regression analysis and Log-rank regression analysis.
Results: There were total 1,180,477 women being identified by BCA database between 2004-2011. There were 71,611 GDM women and 585,695 non-GDM women included in the final analysis. After adjusting for age, pre-existing cancer, and parity, developing T2DM, HTN and HL were still significantly increased in the GDM group (HR and IQR: 2.83(2.59,3.08), 1.09(1.01,1.06), and 1.29(1.20,1.38) accordingly).
Conclusion: Our findings provide nationwide cohort data that GDM increased risk for developing T2DM, HTN and HL on mothers' health. The GDM complications and risk of cardiovascular diseases later in life need further investigation.

WPCS-22-2
Air pollution exposure and risk of gestational diabetes mellitus in Taiwan, 2006-2016: a nationwide cohort study

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Objective: Air pollution exposure has been linked to various diseases, including gestational diabetes mellitus (GDM). However, a national cohort study is lacking. The objective was to investigate whether pre-pregnancy, 1st trimester, and 2nd trimester exposure to ambient air pollution increases GDM risk.
Methods: Health data came from Health and Welfare Data Science Center of Taiwan. A national population-based cohort of pregnant women was recruited (N=2,215,175). Diagnosis of GDM was defined by ICD codes (N=114,667). Ambient air pollution data came from Taiwan Environmental Protection Administration (EPA): fine particulate matter ($PM_{2.5}$) and gaseous pollutants, including sulfur dioxide (SO_2), carbon monoxide (CO), ozone (O_3), and

nitrogen dioxide (NO_2). Spatiotemporal-estimated air quality data calculated based on Bayesian maximum entropy method were collected. Each subject's residential county and township were reviewed monthly and linked to air quality data based on the corresponding township and month of the year for each subject. The Cox model were used for data analysis.

Results: The increase of $PM_{2.5}$ concentrations significantly increased the risk of GDM during pregnancy or 3 months pre-pregnant (OR=1.14 with 95% CI=1.13-1.15 for 3-month pre-pregnancy; OR=1.13 with 95% CI=1.12-1.14 for 1st trimester; OR=1.10 with 95% CI=1.09-1.11 for 2nd trimester). We also found that the increase of gaseous pollutants (SO_2, CO, O_3, and NO_2) were significantly increased the risk of GDM. SO_2 and CO showed the most robust results (OR=1.17-1.19).

Conclusion: Ambient air pollution exposure, including $PM_{2.5}$ and gaseous pollutants, were significantly associated with increased GDM risk among pre-pregnancy, 1st trimester, and 2nd trimester periods.

WPCS-22-3

Fetal Abdominal Obesity and Adverse Perinatal Outcomes in Older and Obese Pregnant Women with Normal Glucose Tolerance

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Objective: We previously observed increased prevalence of fetal abdominal obesity (FAO) in the older with/without obese women with gestational diabetes mellitus. We investigated whether the increased risk of FAO was also present in the older with/without obese women with normal glucose tolerance (NGT).

Methods: We retrospectively reviewed 6721 NGT subjects, diagnosed by 50-g glucose challenge test (GCT) <140mg/dL or normal subsequent 100-g oral glucose tolerance test if GCT ≥140mg/dL. FAO was investigated ultrasonographically using ratios of gestational age with abdominal circumference, biparietal diameter, and femur length. The NGT subjects were divided into: group 1 (age<35 years and pre-pregnant body mass index (BMI) <25 kg/m^2), group 2 (age<35 & BMI≥25), group 3 (age≥35 & BMI<25), and group 4 (age≥35 &BMI≥25).

Results: FAO ratios of group 3 and 4 were significantly higher than group 1. Relative to group 1, the adjusted odds ratio for FAO in group 3 was 1.42 (95% CI; 1.17-1.73, p<0.05), and in group 4 was and 1.90 (1.15-3.15, p<0.05). The odds ratio for large for gestational age (LGA) at birth, relative to group 1, were 3.06 (1.96-4.77, p<0.005), 1.47 (1.16-1.86, p<0.005), and 2.82 (1.64-4.84, p<0.005) in group 2, 3 and 4, respectively. The odds ratio for primary cesarean delivery in group 3 was 1.33 (1.18-1.51, p<0.005).

Conclusions: Increased risk of FAO at 24-28 GW and the ensuing adverse perinatal outcomes of LGA and primary cesarean delivery were observed in the older with/without obese but not in the younger/non-obese NGT women.

WPCS-22-4

Relationship between pre-pregnancy body mass index and gestational diabetes mellitus in Mongolian women

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Objective: The study aimed to investigate the association between maternal pre-pregnancy body mass index (BMI) and risk for gestational diabetes mellitus (GDM)

Methods: The cross-sectional study involved 91 participants (24-28 weeks pregnant women) who were under care during pregnancy in the Arkhangai and Bayankhongor province's health center between March and April 2022. The study of ethics was approved at a meeting of the Ethics Committee of the Mongolian National University of Medical Sciences (2022/3-02). Structured questionnaires, physical examination, and an OGTT (75gm, oral glucose, capillary**)** were performed. Blood glucose levels were determined at 0, 60, and 120 minutes of the test. OGTT results were considered GDM (ADA, 2022) if the fasting glucose level was ≥5.1mmol/l, the 1-hour result was ≥10.0mmol/l, and the 2-hour result was ≥8.5mmol/l. Pre-pregnancy BMI was classified as normal (<24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), and obese (≥30.0 kg/m^2).

Results: The mean age of participants was 29.32±4.77 (19-43 years). According to pre-pregnancy BMI, 58.2% (n=53), 30.8% (n=28), and 11.0% (n=10) of women were normal, overweight, and obese, respectively. The incidence of GDM was 8.8% (n=8) in total study participants: 3.8% (n=2), 10.7% (n=3), and 30% (n=3) in the normal, overweight, and obese groups, respectively (p=0.025).In regression analysis, women in obese group were more likely to be affected by GDM compared to normal group (OR= 6.5, 95% confidence interval= 1.28-33.15)

Conclusion: In Mongolia, this study found that pre-pregnancy BMI was a risk factor for GDM. Therefore, the optimal BMI before pregnancy is one of the keys to preventing GDM.

WPCS-22-5

Genome-wide association studies for gestational diabetes and glycaemic traits in pregnancy among East Asian women

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This study aimed to uncover novel genetic loci that affected gestational diabetes (GDM) and glycaemic traits in pregnancy among East Asian populations. We performed a meta-analysis of genome-wide association studies (GWASs) in 724 women with GDM and 2,150 without GDM from four sources: 1) 960 Chinese women and 2) 1193 Thai women enrolled in the Hyperglycemia and Adverse Pregnancy Outcome study; 3) 455 Chinese women from the Tianjin's Women and Children Health Centre; and 4) 86 Chinese women with GDM received antenatal treatment and 180 healthy Chinese women enlisted from hospital staff and a community-based health screening program. GDM was diagnosed using the 2013 WHO definition. Within each cohort, ~6.1 million genotyped or imputed SNPs (MAF ≥1%) were tested for the association with GDM using logistic regression, with the adjustments for age, body mass index, and principal components. GWASs for glycaemic traits in pregnancy (fasting, 1-hr, and 2-hr glucose, glucose AUC, fasting c-peptide, HOMA2-IR and HOMA2-β) were conducted in up to 2,468 women, using linear regression adjusted for the same covariates. Results of individual studies were combined by meta-analysis using fixed-effects model. We confirmed 1) the associations of *MTNR1B* locus with GDM risk, fasting and 1-hr glucose, as well as glucose AUC; and 2) the associations of *G6PC2* locus with fasting glucose and HOMA2-β at genome-wide significant levels ($P<5\times10^{-8}$). Moreover, we identified a novel locus for fasting c-peptide at *NDST3* locus ($P=2.3\times10^{-8}$). Our results support that there is a shared genetic basis for hyperglycaemia between the pregnant and non-pregnant state.

WPCS-22-6

Low creatinine levels in early pregnancy are linked to an increased risk of postpartum hyperglycemia in women with GDM

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The progression of GDM to T2DM is an emerging public health issue. This study aimed to investigate whether serum creatinine, a surrogate marker of skeletal muscle mass, was associated with the development of postpartum abnormal glucose metabolism (AGM) in women with GDM. Methods: The medical records of 501 women with GDM who underwent a 75-g, 2-hour oral

glucose tolerance test (OGTT) at 4- 12 weeks postpartum were reviewed. Women were grouped based on quartiles of serum creatinine at the first antenatal visit to estimate the relationship between serum creatinine and the incidence of postpartum AGM. Results: Compared with the highest quartile of creatinine, lower quartiles were significantly associated with a higher risk of postpartum AGM (adjusted odds ratios 3.37 [95% CI 1.77-6.42], 2.42 [95% CI 1.29-4.51] and 2.27 [95% CI 1.23-4.18], respectively). Generalized additive model suggested a linear association between serum creatinine levels and the risk of postpartum AGM for those with serum creatinine levels below 64 μmol/l. Conclusions: Lower serum creatinine levels in early pregnancy were associated with an increased risk of postpartum AGM and poorer β-cell function in women with a recent history of GDM. Further research is needed to understand the mechanisms underlying our findings, as well as the role of skeletal muscle mass or nutritional status in early pregnancy on later glucose metabolism.

WPCS-22-7

Assessment of insulin requirements and relevant factors to determine perinatal outcomes in pregnant women with diabetes.

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【Objective】Changes in body weight, HbA1c and insulin requirements during pregnancy as well as perinatal outcomes in 50 pregnant women with diabetes in our hospital were investigated. These factors were compared with type 1 (T1) versus type 2 (T2) diabetes.【Methods】Although HbA1c at pregnancy was similar between the two groups (6.8 vs. 7.1, NS), BMI was higher in women with T2 (22.7 vs. 28.0, p<0.0001).【Results】The weight gain during pregnancy was significantly higher in T1 (14.9 kg vs. 7.9 kg, p<0.01). HbA1c of women with T1 was not significant, but tends to be higher than that of women with T2 in late pregnancy (6.7 vs. 6.1). While TDD in early pregnancy were similar in the two groups (32.0 vs 25.0 units, ns), those were significantly higher in women with T2 in late pregnancy (47.8 vas 63.0 units, p<0.05). Among perinatal outcomes, the LGA-newborn rate in women with T1 was much higher than in women with T2 (81% vs. 21%). Furthermore, there was a strong correlation between LGA and HbA1c levels late in pregnancy.【Conclusion】It was suggested that an insufficient increase in TDD in response to weight gain resulted in inadequate glycemic control may be the cause of poor perinatal outcomes in women with T1.

WPCS-22-8

Accuracy of Fructosamine for Screening of GDM and Monitoring of Pregnancy outcomes: A Prospective Longitudinal Study

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Background: Gestational diabetes mellitus (GDM) affect pregnancy and perinatal outcomes. An early diagnosis approach and good glycemic control can prevent complications. The Fructosamine is an intermediate glycemic marker for several weeks, appropriate for managing GDM.

This study aimed to assess for accuracy of the fructosamine test for screening and monitoring of GDM.

Methods: A prospective longitudinal study was conducted from December 2021 –December 2022 at a single tertiary center. Fructosamine was performed at the first screening of GDM in all subjects. GDM was checked for blood glucose, fructosamine, and HbA1c monthly until delivery. The cut-point of fructosamine to determine GDM, sensitivity, specificity, and area under the curve was analyzed and compared to standard Carpenter and Coustan criteria. The correlation of fructosamine with blood glucose and HbA1c levels at each time point during monitoring was analyzed.

Result: There were 363 pregnant women enrolled, and 62 pregnant women. Fetal hypoglycemia was found in 2.3% and 10% of non-GDM and GDM subjects, respectively. The cut-point level of fructosamine at 218 umol/L resulted in an area under the curve of 0.66, 73% Sensitivity, and 58% Specificity compared to standard criteria. The correlation coefficient between serum fructosamine and HbA1c were 0.58, 0.66, and 0.44 during each visit until delivery.

Conclusions: This study provided the first longitudinal follow up data of fructosamine starting from the screening period until delivery of pregnant women with GDM. The fructosamine test showed moderate sensitivity and specificity in diagnosing GDM . During monitoring, fructosamine level had a moderate correlation to HbA1c.

WPCS-22-9

Association of Adiponectin rs266729 Gene Polymorphism with Gestational Diabetes Mellitus Risk: an Updated Meta-Analysis

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Objective: To clarify the connection between Gestational Diabetes Mellitus (GDM) susceptibility and Adiponectin (ADIPOQ) rs266729 Gene Polymorphism in general population.

Methods: This Meta-analysis was in accordance with the PRISMA guidelines. The literature was taken from PubMed and Google Scholar, with September 2022 as the latest edition that was computed, and it is limited to English only. Total 4 studies were included in this review. A Review Manager 5.4 was utilized to analyze the data.

Results: 4 studies were incorporated. From the analysis, ADIPOQ rs266729 gene polymorphism was associated with an increase of gestational diabetes mellitus risk (C vs G, OR 95%CI = 1.26 [1.04-1.51] p= 0.02; CC vs CG+GG, OR 95%CI =1.48 [1.10-1.99] p=0.01) and a decrease of gestational diabetes mellitus risk (G vs C, OR 95%CI = 0.80 [0.66-0.96] p=0.02)

Conclusion: There was correlation between ADIPOQ rs266729 gene polymorphism and gestational diabetes mellitus risk in general population. This can be used in precision medicine, such as preconception examinations to determine a person's risk of developing gestational diabetes mellitus

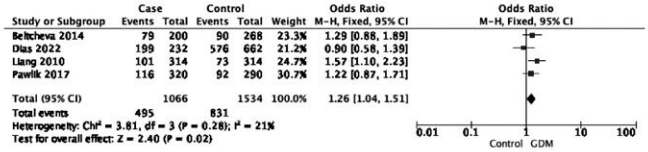

Fig 1. Forest plot of association between ADIPOQ rs266729 gene polymorphism and Gestational Diabetes Mellitus C vs G

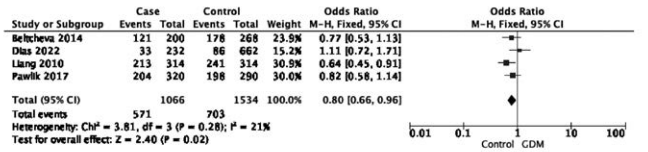

Fig 2. Forest plot of association between ADIPOQ rs266729 gene polymorphism and Gestational Diabetes Mellitus G vs C

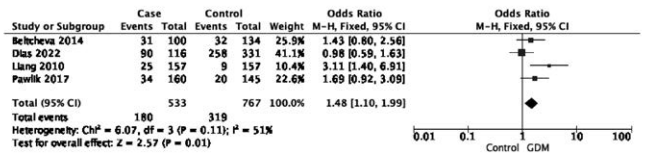

Fig 3. Forest plot of association between ADIPOQ rs266729 gene polymorphism and Gestational Diabetes Mellitus CC vs CG + GG

WPCS-22-10
Linkage of lipocalin-2 with cerebral inflammation in offspring from mother with diabetes.

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A number of human cohort and animal studies suggest that offspring from mother with diabetes (OMD) has an increased risk of both short- and long-term complications, including various neurological issues. However, little is known about its pathogenesis and related factors, and effective treatment is still unknown. Thus, we focused on inflammation in the central nervous system and investigated the factors involved in neuroinflammation. Six- week-old Crl:CD1(ICR) females were injected intraperitoneally with 150 mg/kg of streptozotocin for generating OMD. This OMD model showed learning impairment using accelerated rotarod as we previously reported at the 81st Scientific Sessions of the American Diabetes Association. Citrate buffer was used to generate the control group. After mating them with healthy males, fetal cerebrums were collected at embryonic day 17.5.

Inflammation in OMD cerebrums was confirmed by quantification of Iba1-positive microglial cells, and RNA was extracted from the collected cerebrums for RNA sequencing. 40 differentially expressed genes using the KEGG pathway identified a group of genes Lipocalin-2 (Lcn-2), S100a8, and S100a9 related to the Interleukin 17 (IL-17) pathway. To investigate the distribution of Lcn-2, we next intraperitoneally administered biotinylated Lcn- 2 to pregnant dam at gestational day 17.5 and collect maternal and fetal samples 30 minutes after the administration. Immunohistochemical staining showed that biotin expression was observed in the maternal cortex but not in the fetal one, suggesting that maternally derived Lcn-2 does not reach the fetal cortex. Our results demonstrate that IL-17 signaling in the fetal brain may be involved in learning impairments in OMD.

WPCS-23-1
Endogenous Secretory RAGE is Correlated with Dysregulation of Vascular Calcification In Type 2 Diabetes Patients

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OBJECTIVE

Many studies have report that advanced glycation end-products (AGEs) and the receptor for AGEs (RAGE) system play an important role in the development of diabetic complication. Endogenous secretory RAGE (esRAGE) may act as decoys leading to the neutralization of AGE. Bone morphogenetic protein 4 (BMP4) is known as a promoter vascular calcification, contrary matrix gla protein (MGP) is an inhibitor. This study aims to determine the relationship between esRAGE with MGP/BMP4 ratio, in subjects with minimal, mild, moderate and extensive coronary artery calcification (CAC).

METHODS

A total of 61 type 2 diabetes adult males were enrolled into this cross-sectional study. Serum esRAGE, MGP and BMP4 levels were measured by enzyme-linked immunosorbent assay. Dysregulation of vascular calcification is determined by ratio of MGP and BMP4, while the progression is determined by CAC score, measured by dual slice computed tomography (DSCT).

RESULTS

There is inversely correlation between esRAGE and MGP/BMP4 ratio in mild CAC (score 11-100) group (r=-0.683, p=0.001), whereas in the minimal (score 1-10), moderate (score 101-400) and extensive (score > 400) CAC group, there is no significant correlation.

CONCLUSIONS

In type 2 diabetes, esRAGE plays a protecting role in the early stages of calcification through RAGE-mediated inflammatory inhibition. Optimal plasma esRAGE levels will inhibit the expression of calcification promoter (BMP4), so that MGP as a calcification inhibitor can minimize the occurrence of vascular calcification. Further study is needed to validate that esRAGE and MGP may serve as therapeutics target for intervention in the control of type 2 diabetes.

WPCS-23-2
Time in range in relation to lower extremity atherosclerotic diseasein type 2 diabetes: A cohort study

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Objective: Time in range (TIR) has emerged as a core continuous glucose monitoring (CGM) - derived metric, which was linked to diabetes-related outcomes. However, currently there are few cohort studies in type 2 diabetes and evidences linking TIR to macrovascular complications are limited. We aimed to investigate the association of CGM-derived TIR and other core metrics with the risk of lower extremity atherosclerotic disease (LEAD) among patients with type 2 diabetes.

Methods: A total of 1351 adult patients with type 2 diabetes were prospectively recruited from a single center in Shanghai, China. TIR was obtained from CGM data at baseline. LEAD was measured with color Doppler ultrasonography.

Results: During a median follow-up of 7.4 years, 450 participants developed incident/progressive LEAD. The multivariable-adjusted *HR*s for incident/progressive LEAD across different levels of TIR (> 85%, 71~85%, 51~70%, and ≤50%) were 1.00, 1.15 (95% *CI* 0.87–1.52), 1.37 (95% *CI* 1.04–1.80) and 1.46 (95% *CI* 1.10–1.94) (*P* for trend = 0.004), respectively. With each 10% decrease in TIR, the multivariable-adjusted risk of incident/progressive LEAD increased by 7% (95% *CI* 1.02–1.11). Standard deviation (SD) was independently associated with the risk of incident/progressive LEAD (*HR* 1.12, 95% *CI* 1.01–1.25), whereas the relationships of coefficient of variation (CV), and mean amplitude of glycemic excursions (MAGE) with incident/progressive LEAD did not reach statistical significance (both $P > 0.05$)

Conclusions: TIR was inversely associated with the risk of LEAD among patients with type 2 diabetes.

WPCS-23-3
A Retrospective Study of Glycemic Profiles in Elderly People with Type 2 Diabetes on Hemodialysis

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Objective. We aimed to elucidate glycemic profiles in elderly people with type 2 diabetes undergoing hemodialysis (T2HD).

Methods. 48-hour sensor glucose levels (SGLs) were analyzed on dialysis and non-dialysis days in 116 T2HD using continuous glucose monitoring (CGM), evaluating the difference in clinical parameters and glycemic profiles between elderly group (≥ 65 years) and non-elderly group (< 65 years). Fifty-five people of elderly group (39 males, age 72±6 years, HbA1c 6.3±1.1%, glycated albumin (GA) 22.5±7.4%) and 56 people of non-elderly group (41 males, age 52±9 years, HbA1c 6.7±1.5%, GA 19.8±6.3%) were selected for retrospective analysis.

Results. Thirty people (54.6%) in elderly group and 48 (78.7%) people in non-elderly group were on insulin therapy (p=0.0057). Whereas there was no difference in HbA1c between the two groups, GA was significantly higher in elderly group (p=0.0401). There was no difference in mean SGL and SD of SGL between the two groups, and CV of SGL was significantly higher in elderly group (28.2±7.7% vs 25.3±7.4%, p=0.0439). There was no difference in TIR (70-180 mg/dL), TBR (< 70 mg/dL), TAR (> 180 mg/dL), but TBR (< 54 mg/dL) was significantly higher in elderly group (0.32±0.12[SE]% vs 0.14±0.11[SE]%, p=0.0240). In elderly group, 17 (30.9%) and 15 (27.3%) people had all-cause and hemodialysis-related hypoglycemia, respectively, compared with 19 (31.2%) and 10 (16.4%) people in non-elderly group.

Conclusion. There was no difference in HbA1c and mean SGL between elderly

and non-elderly groups, although the glycemic variability and the time of severe hypoglycemia were significantly higher in elderly group.

WPCS-23-4
Association Between Continuous Glucose Monitoring–Derived Glycemia Risk Index and Albuminuria in Type 2 Diabetes

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Background: The glycemia risk index (GRI) is a new composite metric derived from continuous glucose monitoring (CGM) data to assess the quality of glycemia. This study investigates the association between the GRI and albuminuria.

Methods: Professional CGM data and urinary albumin-to-creatinine ratio (UACR) from 866 individuals with type 2 diabetes were retrospectively reviewed. Albuminuria and macroalbuminuria were defined as one or more UACR measurements ≥30 mg/g and ≥300 mg/g, respectively.

Results: The overall prevalence of albuminuria and macroalbuminuria was 36.6% and 13.9%, respectively. The hyperglycemia component (β = 0.153, p <0.001) and GRI (β = 0.141, p <0.001) correlated positively with the log-transformed UACR, but the hypoglycemia component did not. The prevalence of albuminuria and macroalbuminuria tended to increase with quintile of the hyperglycemia component and the GRI zone (all p <0.001). Multiple logistic regression analyses that adjusted for multiple factors affecting albuminuria revealed that the OR of albuminuria was 1.13 (95% CI: 1.02–1.27, p for trend = 0.027) per increase in the GRI zone (Table 1). The results were similar for risk of macroalbuminuria (OR: 1.42 [95% CI: 1.20–1.69]), and that association remained after adjusting for HbA1c (OR: 1.31 [95% CI: 1.10–1.58]).

Conclusions: GRI is strongly associated with albuminuria and especially with macroalbuminuria in type 2 diabetes.

Table 1. Association between the GRI and risk of albuminuria

	Odds ratio (95% CI)	*P* for trend	*P* for interaction
GRI			
Model 1	1.23 (1.11–1.35)	< 0.001	
Model 2	1.13 (1.02–1.27)	0.027	
Hyperglycemia component			
Model 1	1.15 (1.07–1.22)	<0.001	
Model 2	1.10 (1.02–1.18)	0.018	
Hypoglycemia component			
Model 1	0.88 (0.62–1.25)	0.465	
Model 2	0.93 (0.63–1.37)	0.707	
Subgroups* for GRI			
HbA1c			0.286
≤ 7.5% (n=302)	1.32 (1.04–1.66)	0.020	
> 7.5% (n=561)	1.06 (0.93–1.21)	0.370	
Duration of diabetes			0.192
≤ 10 years (n = 358)	1.22 (1.02–1.47)	0.035	
> 10 years (n = 508)	1.08 (0.95–1.24)	0.235	
HTN			0.407
No (n = 377)	1.20 (0.99–1.46)	0.067	
Yes (n = 489)	1.09 (0.95–1.25)	0.238	
CKD			0.518
No (n = 701)	1.18 (1.05–1.33)	0.006	
Yes (n = 164)	1.09 (0.84–1.42)	0.414	

Model 1: adjusted for age and sex

Model 2: adjusted for model 1 + SBP, BMI, triglycerides, LDL-C, use of ACEi or ARB, use of SGLT2i, CKD, and diabetes duration

ORs represent per 10% increase in the hyperglycemia and hypoglycemia components and per increase in the GRI zone (zone A = 1, zone B = 2, zone C = 3, zone D = 4, zone E = 5).

* Subgroups were analyzed after adjusting for age, sex, SBP, BMI, triglycerides, LDL-C, use of ACEi or ARB, and use of SGLT2i.

ACEi angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *BMI* body mass index, *CKD* chronic kidney disease, *GRI* glycemia risk index, *HTN* hypertension, *LDL-C* low-density lipoprotein cholesterol, *SBP* systolic blood pressure, *SGLT2i* sodium glucose cotransporter-2 inhibitor

WPCS-23-5
Assessment of factors associated with improved glycemic control after isCGM to rtCGM in patients with type 1 diabetes.

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【Objective】The factors associated with improved glycemic control after isCGM to rtCGM in patients with type 1 diabetes were investigated.【Methods】All patients with type 1 diabetes who used the DEXCOM rtCGM device (Terumo Corporation, Tokyo, Japan) at our institution were reviewed, and 23 with type 1 diabetes who switched from isCGM to rtCGM were investigated for this study.【Results】The patients' median HbA1c was 7.2%; this value improved significantly to 6.5% after switching (p=0.016), while the glucose management indicator (GMI) increased from 6.5% to 6.9% (p=0.026). Intriguingly, the percent time below range and coefficient of variation were significantly improved with rtCGM compared to isCGM (3% vs. 9%, p<0.001 and 35.0% vs. 40.8%, p=0.001, respectively). We also found that the discrepancy between HbA1c and GMI among users of isCGM was a key indicator that improved when switching to rtCGM.【Conclusion】If discrepancies are observed between HbA1c and GMI when using isCGM, switching to rtCGM should be considered to improve glycemic control.

WPCS-23-6

Use of Hybrid Closed Loop in Patients with Type 1 Diabetes Mellitus Short-term changes in glycemic control

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【Background】

Hybrid closed-loop (HCL) has been reported to improve glycemic variability in patients with type 1 diabetes. We investigated the short-term effects on glucose fluctuations and glycemic control after starting HCL in Japanese patients with type 1 diabetes using insulin pumps.

【Methods】

We compared HbA1c and glucose fluctuations for 3 months after starting auto-mode in 26 patients with type 1 diabetes (6 men, 48 ± 10 years old) who switched from insulin pump therapy to Minimed 770G at the outpatient clinic. Time in range (TIR), time below range (TBR), time above range (TAR), and daily insulin doses (basal/bolus) were compared. MANOV was used for time-series comparison of each item.

【Results】

HbA1c was changed from 7.4±0.7% at the start of auto-mode to 7.5±0.8% at 3 months. TIR was significantly increased from 65.7±14.1% during 1month before starting, to 70.5±10.5% at 3 months (p=0.018). Similarly, TBR decreased from 4.1±3.6% to 3.0±2.5% at 3 months, and TAR decreased from 29.8±15.0% at start to 26.4±10.9% at 3 months, but these changes were not significant (p=0.113, 0.145, respectively). Total daily insulin dose did not change significantly, basal insulin decreased and bolus insulin increased during 3 months, but not significantly. No severe hypoglycemia was observed after starting the auto-mode.

【Conclusion】

During three months after starting the auto-mode, TIR increased significantly. TAR and TBR also tended to decrease, but were not significant. These results might be partially influenced by the fixed target blood glucose level.

WPCS-23-7

Impact of glycemic variability on all-cause mortality risk in type 2 diabetes patients by continuous glucose monitoring

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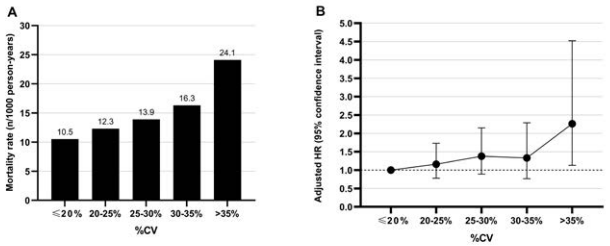
Objective: To investigate the association between short-term glycemic variability (GV) and all-cause mortality in type 2 diabetes with well-controlled glucose profile by continuous glucose monitoring (CGM).

Methods: In this prospective study, 1839 diabetes patients who reached percentage of time in the target glucose range (TIR) of 3.9-10 mmol/L >70%, percentage of time above range (TAR) of 10 mmol/L <25% and percentage of time below range (TBR) of 3.9 mmol/L <4% on CGM were enrolled and were classified into five groups by coefficient of variation for glucose (%CV) level: ≤20%, 20-25%, 25-30%, 30-35%, and >35%. Cox proportional hazard models were used to estimate hazard ratios (HRs) of all-cause mortality risk associated with the different %CV categories.

Results: At baseline, participants had mean age of 60.9 years and mean HbA_{1c} of 7.3%. A total of 165 deaths were identified during a median follow-up of 6.9 years. In multivariate Cox regression analysis, HRs associated with %CV categories were 1.00, 1.16 (95% CI 0.78-1.73), 1.38 (95% CI 0.89-2.15), 1.33 (95% CI 0.77-2.29) and 2.26 (95% CI 1.13-4.52) for all-cause mortality. Meanwhile, compared to patients with %CV≤ 35% (*n*=1773), HR for mortality was 1.93 (95% CI 1.003-3.705, *P*=0.049) for those with %CV>35% (*n*=66). No association of TIR, TAR or TBR with all-cause mortality was found by multivariate Cox regression analysis in all subjects.

Conclusion: Greater %CV was associated with increased risk for all-cause mortality even among patients with seemingly well-controlled glucose status.



WPCS-23-8

Relationship Between Time in Range and Dusk Phenomenon in Outpatients with Type 2 Diabetes Mellitus

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Objective: The dusk phenomenon refers to a spontaneous and transient pre-dinner hyperglycemia that affects glucose fluctuation, and the increasing use of continuous glucose monitoring (CGM) has facilitated its diagnosis. We investigated the frequency of the dusk phenomenon and its relationship with the time in range (TIR) in patients with type 2 diabetes mellitus (T2DM).

Methods: This study involved 102 T2DM patients who underwent CGM for 14 days. CGM-derived metrics and clinical characteristics were evaluated. A consecutive dusk blood glucose difference (pre-dinner glucose minus 2-hour post-lunch glucose) of ≥ 0 or once-only dusk blood glucose difference of < 0 was diagnosed as the clinical dusk phenomenon (CLDP).

Results: We found that the percentage of CLDP was 11.76%. Compared with the non-CLDP group, the CLDP group tended to be younger and have a lower percentage of TIR ($\%TIR^{3.9\text{-}10}$) and higher percentage of time above range ($\%TAR^{>10}$ and $\%TAR^{>13.9}$). Adjusted for confounding factors, the binary logistic regression analysis showed a negative association of CLDP with %TIR. We repeated the correlation analysis based on 70%TIR and found significant differences in HbA1c, FBG, MBG, standard deviation, glucose coefficient of variation, largest amplitude of glycemic excursions, mean amplitude of glycemic excursions, glucose management indicator, and percentage of CLDP between the two subgroups of TIR ≤ 70% and TIR > 70%. The negative association between TIR and CLDP still remained after adjusted.

Conclusion: The CLDP was frequently present in T2DM patients. The TIR was significantly correlated with the CLDP and could serve as an independent negative predictor.

WPCS-23-9

Assessing Glycemic Quality with Glycemic Risk Index (GRI): Could be Better than Time in Range as a Single Metric

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Objective

Glycemic Risk Index (GRI) is a novel composite continuous glucose monitor (CGM) metric of glycemic risk, which weights hypoglycemia more than hyperglycemia and extreme hypo/hyperglycemia more than less extreme hypo/hyperglycemia. This study aimed to validate the effectiveness of GRI for assessing glycemic quality in real clinical practice.

Methods

From an observational cohort comprised of adults with diabetes undergoing CGM, a total of 524 90-day CGM tracings of 194 insulin-treated patients were included in the analysis. GRI was assessed according to standard metrics in an ambulatory glucose profile. A longitudinal analysis was done to compare the effectiveness of GRI and time in range (TIR) reflecting the sequential changes in glycemic quality.

Results

GRI shows a strong correlation not only with TIR (r=0.974) but also with a coefficient of variation (r=0.683). To identify whether GRI differs by hypoglycemia even with a similar TIR, CGM tracings were grouped according to TIR (50–<60%. 60–<70%. 70–<80%. ≥80%). In each TIR group, GRI increased as time below range (TBR) <70mg/dL increased (p<0.001 for all TIR groups). In longitudinal analysis, as TBR <70mg/dL improved, the GRI significantly improved (p=0.003) while TIR did not (p=0.704). Both GRI and TIR improved as Time Above Range (TAR)>180mg/dL improved (p<0.001 for both GRI and TIR).

Conclusion

GRI is effective for assessing glycemic quality in real clinical practice, especially in that GRI reflects hypoglycemia better than TIR alone.

WPCS-24-1

Aryl hydrocarbon receptor deficiency augments dysregulated microangiogenesis and diabetic retinopathy

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Diabetic retinopathy(DR) is a pathophysiologic vasculopathic process with obscure mechanisms and limited effective therapeutic strategies. Aryl hydrocarbon receptor(AhR) is an important regulator of xenobiotic metabolism and an environmental sensor. The aim of the present study was to investigate the role of AhR in the development of DR and elucidate the molecular mechanism of its downregulation. DR was evaluated in diabetes-induced retinal injury in wild type and AhR knockout(AhR-/-) mice. Retinal expression of AhR was determined in human donor and mice eyes by immunofluorescence since AhR activity was examined in diabetes. AhR knockout(AhRKO)mice were used to induce diabetes with streptozotocin, high-fat diet, or genetic double knockout with diabetes spontaneous mutation double knockout for investigating structural, functional, and metabolic abnormalities in vascular and epithelial retina. Structural molecular docking simulation was used to survey the pharmacologic AhR agonists targeting phosphorylated AhR(Tyr245). Compared to diabetic control mice, diabetic AhRKO mice had aggravated alterations in retinal vasculature that amplified hallmark features of DR like vasopermeability, vascular leakage, inflammation, blood-retinal barrier breakdown, capillary degeneration, and neovascularization. AhR agonists effectively inhibited inflammasome formation and promoted AhR activity in human retinal microvascular endothelial cells and pigment epithelial cells. AhR activity and protein expression was downregulated, resulting in a decrease in DNA promoter binding site of PEDF by gene regulation in transcriptional cascade. This was reversed by AhR agonists. Our study identified a novel of DR model that target the protective AhR/PEDF axis can potentially maintain retinal vascular homeostasis, providing opportunities to delay the development of DR.

WPCS-24-2

A Clinical-Genetic Risk Score for Predicting Proliferative Diabetic Retinopathy in Patients with type 2 diabetes

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Objective

Proliferative diabetic retinopathy (PDR), an advanced form of diabetic retinopathy, is a sight-threatening complication of type 2 diabetes (T2DM). We aimed to establish a clinical and genetic predictive risk model for PDR in patients with T2DM.

Methods

We constructed a PDR-polygenic risk score (PRS) using 39 single nucleotide polymorphisms (SNPs) based on our previous findings in the Taiwan–US Diabetic Retinopathy cohort (n=1,007 T2DM, with n=437 PDR cases and n=570 controls with ≥ 8 years DM without DR). The constructed PDR-PRS was combined with a clinical risk model to assess the PRS prediction accuracy in an independent target cohort (n = 3,412 T2DM, with n=576 PDR cases and n=2836 controls).

Results

Significant clinical risk factors detected in the target cohort included age, male, DM duration, HbA1C, and low hemoglobin. The area under the receiver operating characteristic curve (AUC) in the PDR predictive model by clinical risks, and the established PDR-PRS, were 0.797 (95% C.I.:0.772-0.820), and 0.637 (0.608-0.665), respectively. Integrated both clinical and PDR-PRS only slightly increased AUC to 0.801 (95% C.I. 0.776-0.824).

Conclusion

Based on our findings, 5 clinical factors were identified to predict the risk of developing PDR in Asian patients with T2DM. Adding genetic predisposition provides slightly further predictions. Future large-scale studies are needed to increase the power of prediction.

WPCS-24-3

Fenofibrate for diabetic retinopathy

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Objective:

To investigate the effects of fenofibrate on the prevention and progression of diabetic retinopathy (DR).

Methods:

Systematic review and meta-analysis were undertaken under the auspices of the Cochrane Collaboration. Our primary outcome was progression of DR, a composite outcome of; 1) incidence of overt retinopathy for participants who did not have DR at baseline, and/or 2) advancing two or more steps for participants who had any DR at baseline in the Early Treatment Diabetic Retinopathy Study (ETDRS) severity scale.

Results and Conclusion

Two studies were included, both in people with type 2 diabetes: the Action to control cardiovascular risk in diabetes lipid trial (ACCORD-Lipid) and the Fenofibrate intervention and event lowering in diabetes study (FIELD); each with an eye sub-study. The follow-up period was 5 years. Together, they included 15,313 participants (5518 in ACCORD-Lipid and 9795 in FIELD).

In the combined group of people with and without overt retinopathy, fenofibrate resulted in little to no difference in progression of DR (fenofibrate 9.6% [49/512]; placebo 11.8% [59/500], risk ratio [RR] 0.86; 95%CI 0.60 to 1.25; 1 study, 1012 participants). Subgroup analysis in people with overt retinopathy suggested a beneficial effect of fenofibrate (RR 0.21; 95%CI 0.06 to 0.71)". This report is based on a draft and post-peer review version of a Cochrane Review.

WPCS-24-4

The usefulness of the point-of-care nerve conduction device in estimating the severity of diabetic retinopathy.

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[Purpose] The modified Baba classification (MBC) using the DPNcheck, a point-of-care nerve conduction device, was reported to correlate with the severity of diabetic polyneuropathy. We thought that if the DPNcheck could estimate the stage of retinopathy, it would encourage ophthalmologist consultation. We investigated the correlation between the estimated severity in MBC (eMBC) calculated from the results of the DPN check and the severity of retinopathy.

[Methods] Electronic medical records of patients with diabetes who received an ophthalmologist evaluation of diabetic retinopathy and had a DPNCheck were analyzed retrospectively. The retinopathy severity score (RSS) was evaluated using the modified Davis classification: No retinopathy 0 points, simple retinopathy 1 point, pre-proliferative retinopathy 2 points, and proliferative retinopathy 3 points. The eMBC was compared for each RSS and a receiver-operating curve (ROC) analysis was performed to determine the cutoff value of eMBC that could predict RSS.

[Results] Of the 76 individuals with diabetes who had an ophthalmologist evaluation of diabetes retinopathy within 3 months before or after the DPNCheck (56 cases with RSS 0 points, 13 cases with RSS 1 point, and 7 cases with RSS 2-3 points) were analyzed. Univariate analysis showed a weak positive correlation between RSS and eMBC. In ordinal logistic analysis, eMBC correlated with RSS independently of duration of diabetes and HbA1c. eMBC 1.12 and 1.51 were calculated as cutoff values for RSS ≥1 and ≥2 points in ROC analysis.

[Discussion] Prediction of RSS based on eMBC values may encourage patients to visit an ophthalmologist without delay.

WPCS-24-5

Screening of Cardiac autonomic neuropathy in diabetics

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OBJECTIVE

One of the most overlooked complications of diabetes is cardiac autonomic neuropathy. The aim of study was screening of cardiac autonomic neuropathy (CAN) in diabetic patients.

METHODS

Clinical based cross-sectional study was included a 643 diabetic patients. For screening of CAN we used parasympathetic function tests (resting heart rate, deep breathing, standing and valsalva maneuver) and sympathetic function tests (postural hypotension, sustained hand grip) by computer based CAN504 analyzer. Assessment of CAN screening is positive if, 2 or more tests positive or total score more than 4.

RESULTS:

Among diabetic patients 340(52.8%) male and 303(47.2%) female were screened. Diabetic patients' mean age was 52.1±12.1 years old. Resting heart rate test normal and abnormal was 640(99.5%) and 3(0.5%), Deep breathing test normal, borderline and abnormal was 477(74,2%), 99(15.4%) and 67(10.4%), Standing test normal, borderline and abnormal was 229(35.6%), 90(14%) and 320 (49.8%), Valsalva maneuver test normal and borderline was 342(53.2%) and 25(3.9%), Postural hypotension test normal, borderline and abnormal was 448(69.7%), 161(25.1%) and 28(4.3%), Sustained hand grip test normal, borderline and abnormal was 25(3.9%), 43(6.7%) and 487(75.7%), respectively. 276 patients could not perform Valsalva maneuver test. Diabetic patients with positive and negative CAN test was 346(53.9%) and 297(46.1%).

CONCLUSION:

One of two diabetic patients has Cardiac autonomic neuropathy and females are dominant. Among diabetic patients abnormal Sustained handgrip test and could not performed Valsalva maneuver tests are common.

WPCS-24-6

Proportion of Distal Symmetric Polyneuropathy and Association on Quality of Life of Diabetics at Jakarta Health Center

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Objective.

Distal symmetric polyneuropathy is the most common manifestation of peripheral diabetic neuropathy. Quality of life needs to be considered to design, monitor and evaluate the effectiveness of treatment interventions. The aim of this study was to assess the proportion of distal symmetric polyneuropathy and its relationship to quality of life in diabetic patients in Jakarta.

Methods.

Cross-sectional study with an affordable population of diabetes mellitus patients at Jakarta Health Center from September 2022–January 2023. Quality of life was assessed using the EQ-5D-3L instrument. Association between distal symmetric polyneuropathy and quality of life was assessed using a nonpaired t-test and adjusted for confounding variables.

Results.

There were 183 subjects with an average age of 53±8.6 years with duration of diabetes 5±4.8 years. A total of 140 subjects (77.3%) were obese, 123 (67.2%) subjects had HbA1C levels that had not reached control with an average HbA1C level of 8.1±2%. A total of 177 subjects (96.7%) suffered from dyslipidemia with an average total cholesterol level of 207 (43.4) mg/dl, LDL level of 136 (39.3) mg/dl, and HDL level of 48 (10.9) mg/dl .

There was a significant difference in the pain of patients with and without distal symmetric polyneuropathy with an OR value of 2.777 (1.384-5.572) with a p-value of 0.005.

Conclusion.

The proportion of distal symmetric polyneuropathy in this study was 74.9%. Patients with distal symmetric polyneuropathy did not have a lower quality of life, but found significant differences in the pain component when compared to those without distal symmetric polyneuropathy

WPCS-24-7

Exploring the Use of the Norfolk QOL-DN Questionnaire for Diagnosing Diabetic Neuropathy in Taiwanese Diabetes Patients

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Objectives

Although nerve condition velocity (NCV), quantitative sensory testing, pinprick sensation, and vibration sensation are usual exams for diagnosis of diabetes neuropathy (DN), performing these tests on each diabetes patient in Taiwan may not be feasible. We have developed a questionnaire to identify potential DN patients prior to conducting confirmatory tests.

Methods

All the DM participants in this study underwent a comprehensive assessment including a pinprick sensory test, vibration test, and a modified traditional Chinese version of the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (QOL-DN). DN was defined as any abnormal finding in the pinprick or vibration test, as well as NCV.

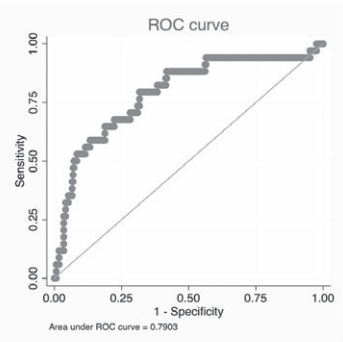
Results

A total of 321 patients were included in this study, of whom 34 (10.6%) were diagnosed with DN. Patients with DN had significantly higher age (66.68±10.84 vs. 60.48±9.86, p<0.001), longer DM duration (18.56±9.50 vs. 12.89±7.17, p<0.001), and higher urine albumin/creatinine ratio (mg/g) [22 (IQR 10-153) vs. 11 (IQR 5-31), p=0.008] than those without DN. The total score of the QOL-DN was significantly higher in patients with DN [5 (IQR 4-8) vs. 9 (IQR 4-20), p=0.002].

The discriminatory capacity of total score of QOL-DN was unsatisfactory with an area under the curve (AUC) of 0.63, but achieved a significant improvement after adding age and DM duration with AUC of 0.79.

Conclusion

DN is strongly associated with age, duration of DM, urine albumin/creatinine ratio, and LDL level. The total score of Norfolk QOL-DN, in combination with age and DM duration, can be used to predict DN with acceptable accuracy.



WPCS-24-8

How does DPN impact patients' burden of illness and the economy? A retrospective studyin Beijing, China

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Objective: Diabetic peripheral neuropathy carries a heavy burden of illness for patients and negatively affects the economy. The objective of this study is to evaluate the cost and quantity of antidiabetic drugs needed in patients with or without DPN, as well as their variation trends inBeijing between 2016 and 2018. **Methods:** This observational cross sectional study used data on diabetic patients with outpatient medication records obtained fro-m Beijing Medical Insurance from 2016 to 2018. The medications, comorbidities, diabetesrelated complications, treatment strategies, and costs of drug treatment were compared betweenDPN patients and non-DPN patients.**Results:** Of the 2853036 diabetic patients included in the study, 375216 (13.15%) had DPN, and 187710 (50.03%) of the DPN patients were women. Compared with non-DPN patients, DPN patients used more mediations (4.7±2.47 vs. 3.77±2.32, p<0.0001, in 2018) to treat related complications and comorbidities (2.03±1.2 vs. 1.71±1.05; 2.68±1.93 vs. 2.06±1.86, p<0.0001, respectively, in 2018). The total annual costs of drug treatment were higher in DPN patients than in non DPN patients (¥12583.25 ± 10671.48 vs. ¥9810.91 ± 9234.14, p<0.0001, in 2018). The usage of DDP4i increased from 2.55% to 6.63% in non-DPN patients and from 4.45% to 10.09% in DPN patients from 2017 to 2018.**Conclusions:** The number of comorbidities, diabetic complications, medications, and annual drug treatment costs was greater in DPN patients than in non-DPN patients.

WPCS-24-9

Thermal Gradient Ring Reveals Thermosensory Changes in Diabetic Peripheral Neuropathy in Mice

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OBJECTIVE: Temperature-related symptoms of DPN have been previously reported to involve the expression and function of temperature-sensitive TRPV1 and TRPA1 channels in rodents. This time, we evaluated using the Thermal Gradient Ring (TGR), which allows mice to move freely and evaluate their natural state.

METHODS: We created streptozotocin type 1 diabetes DPN model mice (DM), and measured and compared non-DM, DM, TRPV1$^{-/-}$ (V1KO), and TRPA1$^{-/-}$ (A1KO) mice in the planter test until the DPN hypoalgesia stage. Changes in TRP channels during the progression of DPN were evaluated using mRNA and protein levels, as well as Ca imaging, and then behavioral experiments were performed using TGR.

RESULTS: In the planter test, DM showed significantly more thermal hypoalgesia than non-DM after 3 weeks of STZ administration. V1KO showed persistent thermal hypoalgesia. In the dorsal root ganglia of DM mice, mRNA expression of TRPV1 and TRPA1 was transiently increased 2 weeks after STZ administration compared with non-DM mice. However, after 5 weeks of STZ administration, the amount decreased to the same level as non-DM. Therefore, we performed a behavioral experiment using TGR 5 weeks after STZ administration. Compared to non-DMs, DMs showed a clear preference for low temperatures, and similar avoidance behaviors in high-temperature regions.

CONCLUSION: Temperature-related symptoms in DPN need investigated by focusing not only on avoidance behaviors, but also behavioral changes based on preference. Analysis with TGR may be suitable for detecting subtle changes in temperature-dependent DPN-related behaviors occurring at the earlier stage of DPN.

WPCS-25-1

Study on the quo of nurses' knowledge, attitude and practice of diabetes foot in Beijing

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Objective: To investigate the current situation of nursing knowledge, attitude, practice of nurses in diabetes foot and to analyze the influencing factors. Methods: A convenience sampling method was adopted to conduct a questionnaire survey to investigate nurses in 5 Class A tertiary hospitals in Beijing in October 2022. A self-developed questionnaire on knowledge,

attitude, practice toward diabetes foot care was distributed for investigation. The questionnaire includes 25 items in three dimensions: knowledge, attitude and behavior. Results: A total of 845 nurses were surveyed. The scores of knowledge, belief, and behavior were (33.5±7.55), (18.93±9.01), and (21.65±7.93), respectively, and the total score was (74.06±16.49). The results of multiple linear regression analysis showed that there were significant differences in whether they are specialist nurses, whether they have received training, whether ever cared diabetes foot and whether ever checked diabetes foot, and they are influencing factors of Class A tertiary hospital nurses' total score of knowledge, attitude, practice about diabetic foot nursing. Conclusion: The level of knowledge, attitude and practice of nurses on diabetes foot nursing is at the middle level in Class A tertiary hospitals in Beijing, which needs to be further improved. The diabetes specialist nurses, nurses who have received relevant training, cared patients of diabetes foot, and had foot examinations for patients of diabetes foot have a high level of diabetes foot nursing knowledge, attitude and practice.

WPCS-25-2
Timolol promotes wound healing and repair in Bama minipigs with diabetic chronic cutaneous ulcers

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Objective To evaluate the wound healing and repair effects of timolol on diabetic chronic cutaneous ulcers (DCUs) in Bama minipigs.
Methods We established DCUs model in Bama minipigs and randomly divided all wounds into the normal saline control group (NSC), timolol low dose group (TLD) and timolol high dose group (THD). Treatment was administered every other day according to the grouping. We calculated the wound healing rate (HR) and recorded the wound healing time (HT) during the treatment. Wound tissues were obtained to evaluate the wound repair conditions.
Results Compared with the NSC group, the HRs were significantly higher in the TLD group and the THD group ($P<0.0001$; $P<0.0001$), and the HTs were significantly shorter in the TLD group and the THD group ($P=0.044$; $P=0.020$). During the treatment, the number of neutrophils and lymphocytes infiltrated in timolol-treated wounds were significantly reduced compared to the NSC group. The thickness of the new epidermis, micro-vessel density, α-SMA positive myofibroblasts, PCNA positive cells and the ratio of type I/III collagen in timolol-treated wounds were significantly increased compared to the NSC group. At the same time, the expressions of VEGF-α, FGF-2, TGF-β1 and TIMP-1 were significantly increased, while the expressions of IL-1β, IL-6, TNF-α, MMP-2 and MMP-9 were significantly decreased in timolol-treated wounds compared to the NSC group.
Conclusions Topical application of timolol promoted the DCUs healing and repair in Bama minipigs, possibly by reducing wound inflammation, promoting angiogenesis, granulation tissue formation, collagen deposition, wound contraction and re-epithelialization, and participating in ECM remodeling.

WPCS-25-3
Timolol for diabetic foot ulcers: A randomized controlled pilot study

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Objective To evaluate the efficacy and safety of timolol in treating diabetic foot ulcers (DFUs) through a randomized controlled study.
Methods According to the inclusion and exclusion criteria, patients with DFUs who attended at the diabetic foot care center of West China Hospital from January 2021 to July 2022 were included and randomly divided into the control group and the timolol group. Standard treatment was applied in the control group, and the timolol group was given 0.5% timolol maleate on the basis of standard treatment. During the treatment, we calculated the wound healing rate (HR), recorded the wound healing time (HT) and adverse reactions.
Results 16 DFUs patients were included in this study, including 8 in each group. There were no statistical differences in baseline data between the control group and the timolol group (all $P>0.05$). The HRs on the D6, D12 and D18 after treatment in the timolol groups were higher than those of the control group at the same time points, but the differences were not statistically significant ($P=0.804$; $P=0.292$; $P=0.078$). The HT in the timolol group was shorter than that in the control group, while the difference was not statistically significant ($P=0.237$). During the treatment, no serious local or systemic adverse reactions occurred in both groups.
Conclusions Topical application of timolol in DFUs showed a trend of promoting ulcer healing, which did not reach statistical difference possibly due to the small sample size. It is necessary to further increase the sample size to confirm this.

WPCS-25-4
High Incidence of Amputation of Diabetic Foot Ulcer in Indonesia' National Referral Hospital: A Clinical Audit

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Objective:
Ministry of Health of Indonesia has instructed Cipto Mangunkusumo General Hospital (RSCM) as the national referral hospital to conduct clinical audit on diabetes with focus on diabetic foot ulcer to improve the quality of care before implementing it to other hospital in the country. Aim of this study was to apply the process of clinical audit to the diabetic foot ulcer for the one year period (July 2021-June 2022).
Method:
We decided six criterias for audit: (1) comprehensive foot exam upon admission; (2) ankle-brachial index examination: (3) comprehensive wound care in the first 24 hour after admission; (4) metabolic control treatment: (5) infection improvement after 5 days of admission; (6) no amputation (mayor or minor). After the criterias were decided, each subject will be graded using code 1 (condition fulfilled); 2 (partially fulfilled, specific condition), and 3 (condition not fulfilled)
Results:
We found 122 subjects with diabetic foot ulcer in the time period. Code 3 in each criterias were as follows (1) 5,6%, (2) 6,6%, (3) 5,7%, (4) 0%, (5) 14,7%, and (6) 41,8%.
Conclusion:
High incidence of amputation was found in diabetic foot ulcer patient in RSCM. Several factors were identified: (1) patients already came with severe infection; (2) delay in referral with inadequate care in previous health facilities; (3) delay in diagnostic procedure; (4) long standing diabetes with poor compliance; (5) multiple co-morbidities especially peripheral artery disease. To avoid patients coming too late, strengthening primary and secondary care in diabetic foot ulcer management is necessary

WPCS-25-5
Increased expression of miR-222-3p in peripheral blood and wound margin tissue of type 2 diabetes foot ulcer patients

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Objective: To investigate the correlations of miR-222-3p expression level in the peripheral blood and wound margin tissue of type 2 diabetes patients (T2DM) with the onset and treatment outcomes of diabetic foot ulcer (DFU) .
Methods:70 newly diagnosed T2DM patients without DFU (T2DM group), 146 T2DM patients with DFU (DFU group), and 70 healthy controls (NC group) were included. MiR-222-3p level in the peripheral blood and wound margin tissue was determined by quantitative real-time PCR, while risk factors for DFU was explored by multivariate logistic regression analysis. The

diagnostic effectiveness of miR-222-3p level on DFU was evaluated using ROC curve analysis.

Results: A significant increase in the level of miR-222-3p was observed in T2DM group compared with NC group ($P < 0.01$), while a markedly increased miR-222-3p level was noted in DFU group compared with T2DM group . Moreover, there was a negative correlation between the levels of miR-222-3p with healing rate of DFU, both in peripheral blood and wound margin tissue ($P < 0.05$). The multivariate logistic regression analysis confirmed that a high expression of miR-222-3p was an independent risk factor for DFU. The ROC curve analysis indicated that the AUC of miR-222-3p for the diagnosis of DFU was 0.803.

Conclusion: The increased expression of miR-222-3p in peripheral blood of T2DM patients is closely related to the occurrence of DFU. MiR-222-3p is a potentially valuable biomarker for diagnosis and prognosis of DFU.

WPCS-25-6

6 years follow-up study of diabetic foot ulcer at the diabetic foot clinic

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Objective

Diabetic foot (DF) is one of common complication of diabetes. The aim of this study was to evaluate diabetic foot ulcer situation at the diabetic foot clinic of EndoMed hospital, Ulaanbaatar, Mongolia.

Methods

We analyzed DIAFI-DATA program where, patients with diabetic foot ulcer (DFU) were registered since January 1, 2017 to March 1, 2023.

Results

Total number of patient visited our center during the last 6 years was 17624 and 1316 subjects screened by foot examination. Patients with DFU were 47 and males were 35(74.5%). By age: <20, 40-60, and >60 years old was 1(2.1%), 13(27.6%) and 33(70.2%); by diabetes duration: 5-10, 10-20 and >20 years was 4(8.5%), 31(65.9%) and 12(25.5%), respectively. Patients with HbA1C <7%, 7-8%, 8-10% and >10% was 7(14.8%), 10(21.2%), 3(6.3%) and 27(57.4%). Neuropathic and neuro-ischaemic ulcer was 20(42.5%) and 27(57.5%). Hospitalized patients due to ulcer, with previous amputations and previous ulceration was 43(91.5%), 12(25.6%) and 13(27.7%). Average time to referral to diabetic foot clinic was 64.47 days and 10 or more days long delay was 37(78.7%). Number of total healed ulcer was 19(40.4%), by wound dressing and by amputation was 12(25.5%) and 7(14.9%). Number of non-healed ulcer was 28(60%), with amputation and wound dressing was 3(6.4%) and 4(8.5%), deceased due to co-morbidity was 2(4.6%) and not seen for 12 months or more was 19(40.4%).

Conclusions

Prevalence of diabetic foot ulcer is 3.7%. Among patients with DFU males are dominant and patients with age >60, diabetes duration 10-20 years, HBA1C >10%, neuro-ischaemic ulcers are common.

WPCS-25-7

Report of 12 months diabetes foot ulcer in 2020 in Cambodia-Korea Diabetes Center

Videm Chea

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Objective: is to document the number of diabetic foot ulcers cases who came to received diabetes foot care in Cambodia Korea diabetes center

Methods: patients with diabetes foot ulcer who come to treat in diabetes foot room in Cambodia-Korea Diabetes Center, from January to December 2020. The data were were entered into a Microsoft Excel™ spreadsheet.

Result: From January to December 2020, clinicians treated 79 patients with a total of 95 diabetic foot ulcers in the diabetes foot room resulting in 322 treatments in 12 months. The average patient age is 59.6y(35-78). The number of female patient is 37(47%). Most of patients are type 2 diabetes (98.6%). Among 95 diabetes foot ulcers, 29(30.5%) are infected at presentation while the average time from diabetes foot ulcer developing until presentation is 5.6weeks. Number of patients who only attend one appointment is 47 (69.1%). Only 20.2% of diabetes foot ulcer is in remission.

Conclusion: Low percentage of diabetes foot ulcers remission by delaying time from diabetes foot ulcer developing until presentation and irregular follow-up. Ongoing patient education should be given at every patient contact and regular follow-up should be emphasized.

Number of patients	79
Total number of DFU treated	95
Total number of dressing appointments provided in 12 months	322
Average patient age	59.6 (35-78)
Gender (female)	37 (47%)
Diabetes Type 2 (%)	98.6
Number of patients who only attend one appointment	47 (69.1%)
Number of DFU infected at presentation	29 (30.5%)
Average time from DFU developing until presentation (weeks)	5.6
Percentage of DFU healed (in remission) (%)	20.2

WPCS-25-8

Collaborative Approach in Managing Diabetes: a Case of Acute Coronary Syndrome in a Diabetic Patient with Foot Ulcer

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Introduction

Longer duration and poorer glycemic control are risk factors for multiple complications of diabetes. Collaborative, patient-centered approach is crucial to manage patient with multiple complications.

Case illustration

A-55-year old female patient with long-standing diabetes and history of three-vessel coronary artery disease, chronic limb-threatening ischemia and chronic kidney disease presented to hospital with acute angina.Initial physical examination showed an ulcer with gangrenous area at fibular side of right foot. Biochemical analysis showed elevated cardiac enzyme and infection markers. The vascular ultrasound confirmed peripheral artery disease in both leg. The patient was diagnosed with non-ST elevation myocardial infarction (NSTEMI) and sepsis due to food ulcer. After optimal pharmacologic treatment of NSTEMI, dispute of what to do next was arising as the patient needed both below-knee amputation and coronary artery bypass graft (CABG) surgery. An-online-collaborative-meeting to discuss this matter was held. Considering the high-risk nature of CABG surgery and ongoing threat of sepsis, we decided that the patient should have below knee amputation prior to CABG surgery. Surgical, anesthetic, rehabilitative, and psychiatric plan were also established

Discussion

Diabetic patients tend to have multiple complications. To decide the priority in managing these complications, several things such as acute condition, high risk surgery, and patient preference should be considered. In this case, as the NSTEMI was treated and infection control is acutely needed, surgical amputation was chosen as priority.

Conclusion
Deciding priority to manage concomitant diabetes complications may not always easy. Collaborative approach is needed to make best shared-decision.

WPCS-26-1
Differences in microvascular complications of diabetes among women and men in China: a cross-sectional study

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Objective: Data were inconsistent regarding the associations between sex and diabetic microvascular complications.
Methods: This cross-sectional study investigated sex differences in diabetes with chronic kidney disease (CKD), diabetic retinopathy (DR), and diabetic peripheral neuropathy (DPN) in patients with type 2 diabetes from primary healthcare in China.
Results: Among 29,877 patients (43.7% men; age: 65.68±7.51 (mean±SD) years; diabetes duration: 7.87±5.28 (mean±SD) years), women had significantly higher prevalence of diabetes with CKD (35.2% vs 33.6%), and lower prevalence of DPN (23.5% vs 24.7%), with no significant differences found between sexes regarding DR (19.1% vs 18.8%) and any microvascular complication (57.0% vs 56.3%). After adjusting for potential confounders, men were less likely to have diabetes with CKD (OR, 95% CI: 0.859 (0.805-0.916)), with no significant associations found between sex and DPN or any microvascular complication. For DR, with significant interaction of sex and age, multivariable analysis showed men were more likely to have DR (OR, 95% CI: 1.214 (1.077-1.369)) among younger adults (age<65 years), and this significant association disappeared among older adults (age≥65 years).
Conclusion: Sex differences in diabetic microvascular complications existed, highlighting the importance of sex-specific intervention on diabetic microvascular complications in China.

WPCS-26-2
Association between the FIB-4 index and the risk of progression of diabetic retinopathy and nephropathy

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Background: The FIB-4 index is widely used as a non-invasive indicator for degree of liver fibrosis. In type 2 diabetes (T2D), the FIB-4 index has been reported to be associated with the risk of progression of diabetic nephropathy, however, its relationship with diabetic retinopathy remains controversy. In this historical cohort study, we examined the association between FIB-4 index and the risk of progression of retinopathy and nephropathy in Japanese patients with T2D.
Methods: Analytic samples were 2,864 patients without proliferative diabetic retinopathy at baseline, 2,303 patients with normo- or microalbuminuria at baseline, and 2,491 patients with an eGFR ≥ 60 mL/min/1.73 m^2 at baseline. Multivariable Cox proportional hazards models were used to estimate hazard ratio (HR) and its 95% confidence interval (CI) for baseline FIB-4 index associated with the progression of diabetic retinopathy, albuminuria, and decline in eGFR to < 60 mL/min/1.73 m^2, respectively.
Results: During the mean follow-up of 6.4-6.9 years, the incidence rate was 22.6, 29.0, and 32.4 per 1000 person-years for retinopathy, albuminuria, and decline in eGFR, respectively. The HR of FIB-4 index (1 unit) for each endpoint was 1.16 (95% CI 1.05-1.30, p=0.006) for retinopathy, 1.18 (1.03-1.36, p=0.002) for albuminuria, and 0.99 (0.88-1.11, p=0.862) for eGFR decline.
Conclusions: The FIB-4 index was significantly associated with the risk of progression of diabetic retinopathy and albuminuria in Japanese patients with T2D.

WPCS-26-3
Effects of switching from a DPP-4 inhibitor to oral semaglutide on glucose metabolism in subjects with type 2 diabetes

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Objective
The oral glucagon-like peptide-1 receptor agonist semaglutide has potent effects on glycemic control, but it is not fully clarified whether switching from a DPP-4 inhibitor (DPP-4i) to semaglutide has merit in real-world clinical settings. We aimed to verify the efficacy and safety of oral semaglutide in subjects with type 2 diabetes (T2D) being treated with a DPP-4i.
Methods
This study is a multicenter, prospective, randomized, open-label, parallel-group trial (jRCT1011210032 in Japan Registry of Clinical Trials). Participants with T2D who had been treated with a DPP-4i for more than 12 weeks and had a glycated hemoglobin (HbA1c) level of 7.0%-9.9% were randomized to continue using their current DPP-4i or switch to oral semaglutide for 24 weeks. The primary endpoint was the change in HbA1c level between the two groups at 24 weeks. Secondary endpoints included change in body weight, metabolic indices, and adverse events.
Results
In total, 174 participants were recruited (DPP-4i group, n=86; semaglutide group, n=88). The overall mean age, HbA1c levels, and body mass index were 63.4±11.5 years, 7.6%±0.5%, and 26.4±4.5 kg/m^2, respectively. There were no significant differences in baseline characteristics between the groups. Patient recruitment was completed in August 2022, and they are currently being followed.
Conclusion
No serious adverse events or illnesses have occurred to date.

WPCS-26-4
5 years diabetes complication and mortality study

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Objective: The aim of our study is to investigate the complications and mortality of diabetes mellitus among patients who admitted to state hospitals.
Methods: A hospital based retrospective study conducted and using electronic medical history data of 113.638 patients admitted at the First central hospital of Mongolia between 2018-2022.
Result: Last 5 years among 72.2% (83) of 115 foot amputation cases, 9.4 % (216) of 2308 stroke cases, 9.0% (177) of 1965 myocardial infarction cases, 3.5% (401) of 11290 diabetic retinopathy cases, hospitalization cause of Covid19 5.6% (181) of 3218 patients and 4.3% (107) of 2845 patients with maxillofacial abscess had diabetes mellitus respectively. During the study 25.9% (235) of the 906 hemodialysis cases and 18.1% (38) of the 209 peritoneal dialysis patients had diabetes. 239 or 10.8% of the total 2216 patients who died in the hospital during the 5 years of study period were people with diabetes mellitus 20.6% of deaths due to Covid19 (43/209), 16.7% of deaths due to kidney disease(10/60), 10.8% of deaths due to sepsis, 10.8% (30/289) due to heart attack, 10.4% (7/67) deaths due to stroke and total 4.9% (12/247) patients had diabetes.

Conclusion: Last 5 years, 7 out of 10 people who had foot amputation in the general hospitals and 1 out of 10 people who had stroke or heart attack had diabetes mellitus. However, 1 out of 10 patients who died in the hospital had diabetes. Covid19, kidney failure and myocardial infarction are the leading

causes of diabetes mortality.

WPCS-26-5

The effectiveness of the advanced system system for optimal care of chronic diseases in primary clinics in Korea

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Objective: This study aimed to evaluate the effects of the advanced system and related services for optimal patient care of chronic diseases in primary clinics in Korea.

Methods

We conducted a community-based clinical trial to treat diabetes and hypertension using an individualized monitoring and education system in primary clinics in Korea. Fourteen participating physicians from nine primary clinics were randomly assigned to the control group (CG), intervention group 1 (IG1), and intervention group 2 (IG2). Nine hundred fifty-five subjects were divided into three groups according to their attending physicians. IG1 and IG2 received individualized goal-setting, education, and counseling using an advanced system for optimal patient care of chronic diseases for six months, compared to CGs who received conventional treatment. For patients in group IG2, additional education or counseling was provided by smart care coordinators (SCCs, experts comprising nurses, nutritionists, and exercise prescribers) upon the doctor's request. We compared six-month changes in continuous variable outcomes between the three groups.

Results

The mean changes of HbA1c levels were -0.16% ± 1.07%, -0.43% ± 1.01%, and -0.74% ± 1.01% in CG, IG1, and IG2, respectively ($p < .001$). There were no statistically significant differences in changes in blood pressure among the three groups of hypertension patients.

Conclusion

Using an advanced system for chronic disease management and receiving additional services from SCCs is an effective and acceptable way to provide optimal patient care for diabetes in primary clinics in Korea.

WPCS-26-6

Heated tobacco product use and risk of developing diabetes: a cohort study

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Objective

To investigate the prospective association between heated tobacco product (HTP) use and risk of diabetes.

Methods

Data were analyzed from a substudy of the Japan Epidemiology Collaboration on Occupational Health Study for adults with no diabetes at baseline (fiscal year 2018 annual health checkup) who attended 2019-2021 annual health checkups (n=27,874). Participants were categorized into five groups: never smokers (n=12,809), past smokers (n=6,685), exclusive HTP users (n=2,939), dual users of cigarettes and HTPs (n=1,597), and exclusive cigarette smokers (n=3,844). Incident diabetes was defined using the American Diabetes Association criteria. Cox proportional hazards regression models were used to investigate the association between HTP use and diabetes, with adjustment for demographic, lifestyle, and health factors.

Results

During a maximum follow-up of 4 years, 1,278 participants developed diabetes. The multivariable adjusted hazard ratios (95% confidence intervals) were 0.96 (0.82, 1.11), 1.38 (1.15, 1.66), 1.26 (0.99, 1.59), 1.48 (1.26, 1.74) for past smokes, exclusive HTP users, dual users, and exclusive cigarette smokers, respectively, as compared with never smokers. Moreover, the risk of diabetes increased with the number of HTPs used per day in exclusive HTP users (P for trend 0<.001). However, no such association was found in dual user, probably due to the small sample size.

Conclusion

HTP use was associated with an increased risk of incident diabetes. This is the first study to evaluate risk of developing diabetes associated with HTP use, providing new evidence on their potential health impact.

WPCS-26-7

Association between primary hyperparathyroidism and incident diabetes

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Objectives:

Hypercalcemia related insulin resistance leads to elevated blood plasma glucose in primary hyperparathyroidism (PHPT) patients**.** We aim to evaluate the risk of diabetes in PHPT patients using a large population-based cohort.

Methods:

We included people who had at least one plasma glucose or HbA1c measurements in any healthcare facilities in Hong Kong Hospital Authority between 2000-2019. Cases with PHPT were identified using a combination of ICD-9 diagnostic codes and laboratory tests. Controls without PHPT were matched to cases by sex, age and diagnosed year. We excluded people with diabetes before baseline and diabetes diagnosed date during 2000-2001 to define a 2-year washout period.

Results:

A total of 16,494 people were included (31.9% men, mean age 64.7 years), consisting of 2,749 PHPT cases and 13,745 controls. During a median time of 5.17 (IQR 2.17, 9.58) years of follow-up, 433 and 2,110 cases of incident diabetes were identified in the PHPT and control group, respectively. The incidence rate of diabetes was 27.60 (95% CI 25.00, 30.30) per 1000 person-years in the PHPT group and 23.90 (95% CI 22.80, 24.90) per 1000 person-years in controls, which increased with increasing age in both groups. The PHPT group had a higher cumulative incidence of diabetes compared with controls throughout the follow-up period (p = 0.007). Crude Cox regression model showed that PHPT was associated with increased risk of incident diabetes as compared to controls (HR 1.15, 95%CI 1.04, 1.28).

Conclusions:

Our population-based analysis suggests that PHPT is associated with increased risk of incident diabetes.

WPCS-26-8

Impact of Liraglutide 3.0 mg on Body Composition of Korean People with Obesity: a Retrospective Observational Study

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Background:

Despite the high prevalence and severe health consequences of obesity, weight loss is difficult to maintain through lifestyle changes alone.

Liraglutide 3.0mg, a glucagon-like peptide-1 (GLP-1) analog, has been approved for weight management for people with BMI ≥ 27 kg/m^2 with weight-related comorbidities (T2DM, hypertension and dyslipidemia) or BMI≥30 kg/m^2 in Korea. Until today, there has been few data of its impact on body composition for Korean population. This study examined for the first time the effect of liraglutide 3.0 mg on weight loss and body composition in a real world setting.

Method:

This was a retrospective, non-interventional medical chart review study collecting based on secondary analysis of an existing data source. Patients had been treated in routine clinical practice of consultation by medical professional, nutritionist and physical trainer and regular assessment was performed. The

primary endpoint was to evaluate the body composition changes such as body weight, fat mass and visceral adipose tissue (VAT).

Results:

For total of 59 patients treated with liraglutide upto dose of 3.0 mg, significant weight loss (6.9%, P-value < 0.001) was observed for mean of 325 days. Significant reduction in total body fat (7.6%, P-value < 0.001) and VAT (13.2%, P-value < 0.001). Significant reduction was also observed in both android fat (12.9%, P-value<0.001)) and gynoid fat (11.3%, P-value<0.001)'

Conclusion:

Use of liraglutide 3.0 mg in routine clinical practice gives clinically meaningful weight loss as well as reduction in visceral adiposity, which is closely linked to increased cardiometabolic risk factors.

WPCS-26-9

Glucose metabolic disorder in acromegaly patients: a retrospective analysis in West China Hospital

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Objective: To investigate the clinical characteristics, insulin sensitivity and islet β-cell function in patients with acromegaly.

Methods: This is a retrospective study enrolled 172 subjects (77males and 95 females, aged 47.2±11.9years) who hospitalized with acromegaly in West China Hospital between Jan. 2018 and Dec.2022.Based on oral glucose tolerant test (OGTT),subjects with acromegaly were divided into three groups: normal glucose tolerance (NGT), impaired glucose glucose regulation (IGR) (or pre-DM) and diabetes mellitus (DM).Data from clinical and laboratory examinations were collected and analyzed retrospectively.

Results:60 cases (34.88%) acromegalic patients complicated with secondary diabetes, while 65 (37.79%) had IGR and 47(27.33%) with NGT. The baseline random GH level of acromegalic subjects with DM ,IGR and NGT were (35. 9 ± 12. 7) ng /ml , (50.1 ± 15.6) ng /ml and (15. 9 ± 9.4) ng /ml respectively(p<0. 001). We found that the prevalence of hypertension and dyslipidemia was higher in patients with hyperglycemia than in acromegalic patients with NGT. The percentage of hypertriglyceridemia in acromegalic patients with DM was significantly higher than that of IGR and NGT (46.7% v.s. 33.8% P < 0. 05, 46.7% v.s.31.9% P< 0. 01, respectively).

Conclusions: There is a marked variation of somatostatin response to glucose load and GH production in patients with acromegaly, leading to changes in insulin secretion and glucose metabolism. Acromegalic patients are more prone to develop hyperglycemia , insulin resistance and β-cell dysfunction. They have a higher prevalence of other metabolic disoders, especially dyslipidemia.

WPCS-26-10

Association between weight change at one year after diabetes diagnosis and incident diabetes remission: a cohort study

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Objective

We aimed to examine the association between weight change at one year after diabetes diagnosis and incidence of diabetes remission.

Methods

We included 38,154 people aged 18-75 years with newly diagnosed type 2 diabetes who participated a territory-wide diabetes risk assessment program in Hong Kong in 2000-2017. We defined diabetes remission as two or more consecutive HbA1c <6.5% measurements at a time interval of at least six months in the absence of glucose-lowering drugs for at least three months. We used Cox regression models to estimate the hazard ratio (HR) for the association between percentage of weight change (%) at one year after diabetes diagnosis and incident diabetes remission.

Results

Among people included in the study, 50.7% (n=19,351) was men and mean (SD) age at diabetes diagnosis was 56.5 (10.0) years. During a median (IQR) follow-up of 7.8 (4.8, 10.5) years, 2,303 people experienced diabetes remission with an incidence rate of 7.7 (95% CI: 7.4, 8.0) per 1,000 person-years. After adjustment for potential confounders, as compared to people with weight change of -5% to 5%, the adjusted HR for diabetes remission was 3.60 (2.98, 4.35) and 2.24 (1.97, 2.54) among people with weight loss of ≥10% and of 5% to 9.9%, respectively; and was 0.79 (0.54, 1.16) and 0.83 (0.68, 1.01) among people with weight gain of ≥10% and of 5% to 9.9%, respectively.

Conclusion

Greater weight loss at one year after diabetes diagnosis was associated with increased likelihood of diabetes remission.

WPCS-27-1

Differential gene expression of a visceral and subcutaneous adipose depot in patients with morbid obesity

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Objective: White adipose tissue is essential for the homeostasis of energy, and it undergoes various cellular and structural remodeling processes. Adipose tissue has different characteristics depending on its depots. Visceral adipose tissue (VAT) is known to negatively impact metabolic disease more than subcutaneous adipose tissue(SAT). However, the difference in gene expression between depots in morbid obesity in Korea is not understood. Therefore, we analyzed the differences between VAT and SAT in patients with morbid obesity.

Methods: Six females with morbid obesity who underwent bariatric surgery were enrolled. We analyzed the gene expression by microarray sequencing between VAT and SAT from the same patient obtained during bariatric surgery.

Results: Median age is 36.5(46-79), and body mass index is 35.22 (32.02-41.21) kg/m2. Unsupervised hierarchical clustering by Pearson correlation in all 12 tissues (6 VAT, 6 SAT) showed two distinct clusters between VAT and SAT. 23633 differentially expressed genes (DEGs) between VAT and SAT were identified. A total of 149 DEGs between VAT and SAT were identified 132 genes were upregulated in VAT, and 17 genes were upregulated in SAT. According to gene set enrichment analysis, VAT was related to inflammatory and immune response pathways, whereas SAT was related to metabolic-related pathways, including bile acid and steroid metabolic processes.

Conclusion: We found a distinct difference between VAT and SAT in patients with morbid obesity. Further studies about the impact of a gene on metabolic health are needed.

WPCS-27-2

Lifestyle behaviors and risk of prediabetes and obesity in middle-aged Japanese

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Objectives: The aim of this longitudinal study was to identify lifestyle behavioral characteristics for the development of prediabetes independent of the development of obesity among middle-aged Japanese population.

Methods: A total of 50,882 non-obese (body mass index [BMI] <25 kg/m^2) adults mean age: 49±3 years) with normoglycemia (HbA1c <5.7% & FPG <5.6 mmol/l) from the Health Insurance Association in Japan were followed between 2011-2019. Cox proportional hazard model was used to identify lifestyle behaviors in the group stratified by the progression of prediabetes (HbA1c 5.7%–6.4% or FPG 5.6–6.9 mmol/l) and obesity (BMI ≥25 kg/m^2). The exposure variables were physical activity, walking speed, waking over 1h/day, eating speed, late dinner, skipping breakfast, nonrestorative sleep, smoking, and heavy alcohol consumption. The covariates were age, sex, family

history of diabetes, hypertension, and dyslipidemia.

Results: The mean follow-up duration was 6.0 years. Behaviours associated with the progression to bothprediabetes and obesity were eating fast (Hazard ratios: 1.41 [95% confidence intervals: 1.28–1.55]) and late dinner (1.12 [1.02–1.24]). Behaviours associated with the progression to obesity without prediabetes were eating fast (1.35 [1.25–1.45]), waking slow (1.18 [1.09–1.27]), nonrestorative sleep (1.13 [1.05–1.21]), and late dinner (1.11 [1.02–1.19]). Behaviours associated with the progression to prediabetes without obesity were waking less 1h/day (1.05 [1.05–1.21]) and waking slow (0.92 [0.89–0.96]).

Conclusions: Lifestyle behavioral characteristics in incident case of pre-diabetes differed between obese-incident and non-incident cases. This suggests the need for more individualized lifestyle interventions for preventing metabolic diseases.

WPCS-27-3

The fluctuation of post-Breakfast blood glucose is associated with metabolic syndrome in type 2 diabetic patients

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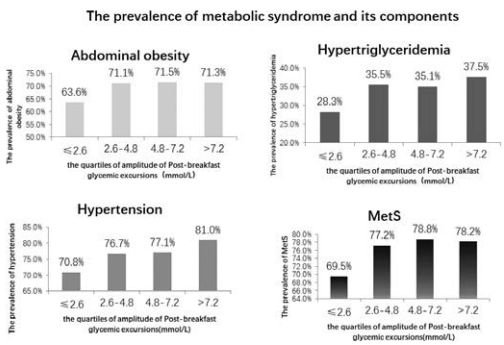
Objective: To investigate the correlation between the fluctuation of post-breakfast blood glucose and the components of metabolic syndrome in patients with type 2 diabetes.

Method:4307 subjects of type 2 diabetes mellitus patients hospitalized were investigated. The amplitude of Post-breakfast glycemic excursions (APBGE) is defined as the absolute value of the difference between 2-hour postprandial blood glucose and fasting blood glucose. Metabolic syndrome(MetS) was defined according to the criteria recommended by the Chinese Diabetes Society. The subjects were divided into four groups according to the quartiles of APBGE: ≤2.6mmol/L, 2.6-4.8mmol/L, 4.8-7.2mmol/L, >7.2mmol/L.

Result: With the increase of APBGE, the prevalence of abdominal obesity (63.6%, 71.1%, 71.5%, 71.3%), hypertension (70.8%, 76.7%, 77.1%, 81%), hypertriglyceridemia (28.3%, 35.5%, 35.1%, 37.5%) increased gradually. The prevalence of MetS increased with the APBGE (69.5%, 77.2%, 78.8%, 78.2%, P<0.01). The prevalence of MetS in the group of APBGE <2.6mmol/L was significantly lower than other three groups (P<0.01). The blood glucose fluctuation after breakfast in MetS group was significantly higher than that of non-MetS group [(5.3±3.3)mmol/L vs (4.8±3.5)mmol/L, P<0.01]. After adjusting for age, gender, duration of diabetes, the risk of MetS in patients with blood glucose fluctuation > 2.6mmol/L after breakfast was 1.41 times higher than that in patients with blood glucose fluctuation ≤2.6mmol/L (95% CI 1.14-1.71, P=0.001).

Conclusion: The fluctuation of post-breakfast blood glucose is associated with abdominal obesity, hypertension,hypertriglyceridemia and MetS in type 2 diabetes mellitus. The fluctuation of post-breakfast blood glucose>2.6mmol/L was an independent risk factor for MetS.



WPCS-27-4

Inducible loss of p53 in skeletal muscle ameliorates insulin resistance in high-fat diet-induced obese mice

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Objective: p53 is a critical protein in tumor suppression and further plays a significant role in energy metabolism. Recent studies have shown that p53 causes insulin resistance in brown adipose tissue, white adipose tissue, and the liver. Previously, we reported that peroxiredoxin2 deficiency exacerbated aging-induced insulin resistance, which was positively correlated with p53 levels in skeletal muscle. Therefore, we examined whether p53 deficiency in skeletal muscle affects high-fat diet-induced insulin resistance in mice.

Methods: Muscle-specific inducible knockout (KO) of p53 was generated by mating $p53^{flox/flox}$ and ACTA1-rtTA, tetO-Cre mice. Eight-week-old male mice were fed with doxycycline containing high-fat diet for 19 weeks. Glucose metabolism was measured using glucose tolerance test, and insulin sensitivity was measured using insulin tolerance test and hyperinsulinemic-euglycemic clamp in KO and wild-type (WT) littermates. In addition, protein phosphorylation of Akt, AS160, and GSK3β, which are markers of the insulin signaling pathway, was confirmed by Western blotting.

Results: High-fat diet induced insulin resistance in both WT and KO mice. Glucose intolerance and insulin resistance were improved in p53 KO mice compared with WT mice. Whole-body glucose turnover and soleus glucose uptake were higher in KO mice than those of WT mice. In addition, the levels of phosphorylated Akt, AS160, and GSK3β were more expressed in skeletal muscle of p53 KO mice.

Conclusion: These results suggest that p53 deficiency in skeletal muscle improves high-fat diet-induced insulin resistance in mice. Thus, skeletal muscle p53 could be a potential therapeutic target for metabolic disease including diabetes.

WPCS-27-5

Skeletal muscle-specific DKK3 overexpression exacerbates insulin resistance in obese mice.

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Objective: Wnt signaling is associated with metabolic diseases such as diabetes. Dickkopf (DKK) family is one of the regulators of Wnt signaling. Among the DKK families, DKK3 is unknown to be involved in glucose metabolism and insulin resistance. Skeleton muscle (SKM) is an insulin sensitivity tissue that plays a vital role in regulating metabolic reactions, such as insulin action. Therefore, we examined whether DKK3 overexpression in SKM affects a high-fat diet (HFD)-induced insulin resistance in mice.

Methods: We produced the SKM-specific inducible DKK3 overexpressed (SKM-iDKK3 TG) mice by Cre-dependent gene expression using ACTA1-rtTA tetO-cre. Mice harboring DKK3 TG without Cre were used as a control. Obesity was induced through an HFD diet for 8 weeks. Insulin sensitivity was measured by a hyperinsulinemic-euglycemic clamp. Insulin signaling pathway markers such as AKT, AS160, and AMPK were identified with western blots.

Results: HFD induced obesity in both SKM-iDKK3 TG and control mice. Body weight, fat mass, and muscle weight were similar between the two groups. The hyperinsulinemic-euglycemic clamp confirmed that the glucose turnover rates and glucose uptake rate in the skeletal muscle were reduced in SKM-iDKK3 TG mice compared with control mice. In addition, the levels of phosphorylated AKT, AS160, and AMPK were lower in SKM-iDKK3 TG than in control mice.

Conclusion: These results imply that the overexpression of DKK3 in skeletal

muscle exacerbates insulin resistance in obese mice. Therefore, DKK3 can be a possible therapeutic target for type 2 diabetes.

WPCS-27-6

Lifestyle factors and BMI change during campus life in Japanese university students with obesity -retrospective study-

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Objective: Concerning the increase of diabetes mellitus in young adults, early interventions for obesity is important. However, evidence-based approaches have not yet been established. We aimed to demonstrate the effective lifestyle changes in normalizing the body mass indices (BMI) in Japanese university students with obesity during their campus life.

Methods: The annual health checkup data of 13,023 students (18-29 years) entering university from 2011 to 2017 were analyzed. On admission, 343 students with obesity (BMI ≥ 25 kg/m2) were divided into three groups in terms of their BMIs between admission and graduation. The decreased group (n=171) consisted of individuals with diminished BMI by more than 1.0; the stable group (n=104) consisted of those with BMI remained within ± 0.99; and the increased group (n=68) consisted of those with increased BMI by more than 1.0. Lifestyle factors including sex, study specialty, residency, diet habits, sleep, and club activities were collected and analyzed to identify the differences between each group.

Results: The frequency of eating out per week was significantly higher and the number of vegetable plates per day was significantly lower in the increased group, compared to the other groups. There were no significant differences associated with factors including sex, study specialty, living with a family member, sleep, and membership of an athletics club.

Conclusion: Our study revealed that the key factors for BMI control were eating out and vegetable intake. Hence, an appropriate education regarding eating habits may be an effective intervention for young adults with obesity.

WPCS-27-7

Association between Zinc-Related Genetic Variants and Risks of Diabetes and Other Metabolic Outcomes in Filipino Adults

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We investigated in this pilot candidate gene studies the potential association between zinc-related single nucleotide polymorphisms (SNPs) and the risks of diabetes and other metabolic outcomes among Filipinos. Using the most recent Philippine nutrition survey data, we first determined the SNPs associated with serum zinc concentration and zinc deficiency risk among ~800 adult respondents in the National Capital Region. Multivariate logistic regressions were performed to investigate the association of zinc-related SNPs with the risks of diabetes, dyslipidemia, hypertension, obesity, and central obesity following an additive genetic model of inheritance. Models were adjusted for sex, age and age-squared, smoking status, and physical activity levels as covariates. We initially identified 14 SNPs that showed significant variations in zinc levels across genotypes, 16 SNPs associated with serum zinc concentration, and 22 SNPs associated with zinc deficiency among study participants. Of these, 15 zinc-related SNPs further demonstrated association with the risks of metabolic disorders and various health indicators. We observed repeated associations as follows: *LINC02669/LOC105376360* rs2165468 with diabetes, dyslipidemia, and hypertension; *FKBP5* rs1360780 with diabetes, hypercholesterolemia, obesity, and central adiposity; *FKBP5* rs9470080 with abnormal lipid profile; *PPIG* rs13382615 with diabetes and hypertension; *PCSK1* rs6234 with low HDL-cholesterol and hypertension; *KNG1* rs10937266 with diabetes and obesity; *KNG1* rs11927941 with hypertriglyceridemia and obesity; *DIO2* rs225012 with hypertension and central adiposity, and; *TMPRSS6* rs1421312 with hypercholesterolemia and obesity. Such findings provide initial evidence to support the roles of underlying genetic variants in the pathophysiology of diabetes and other chronic metabolic conditions, through altered zinc homeostasis, among Filipinos.

WPCS-27-8

Relationship between serum cholinesterase and components of metabolic syndrome in patients with type 2 diabetes

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[Objective] To explore the relationship between serum cholinesterase (CHE) levels and components of metabolic syndrome in patients with type 2 diabetes mellitus (T2DM), and to investigate the significance of CHE detection in this population.

[Methods] A retrospective analysis of clinical data was performed for 1163 T2DM patients. The study population was divided into four groups based on the quartile range of CHE levels: 1st group (CHE ≤ 289U/L, n=289), 2nd group (CHE between 289-347 U/L, n=292), 3rd group (CHE between 347-400 U/L, n=289), and 4th group (CHE > 400 U/L, n=293). Blood glucose, lipid levels, liver and kidney function, and CHE levels were measured, as well as waist circumference and blood pressure. Pearson or Spearman correlation analysis was used to explore the relationship between serum CHE and metabolic syndrome components. Multiple linear regression analysis was used to identify the influencing factors of serum CHE in T2DM patients.

[Results] The metabolic syndrome components in each group had statistical significance (P<0.01). As CHE levels increased, the prevalence of central obesity, fatty liver, hypertriglyceridemia (high TG), and low high-density lipoprotein cholesterol (low HDL-C) increased in a positive correlation. There was no significant difference in the prevalence of hypertension between groups. Regression analysis showed that CHE was an independent risk factor for MS in T2DM patients.

[Conclusion] In patients with T2DM, serum CHE is associated with central obesity, fatty liver, high TG, low HDL, and MS. Serum CHE is an independent risk factor for MS.

WPCS-27-9

The change in the distribution of adiponectin isoforms in abdominal obesity is associated with insulin resistance.

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Objective: Lower levels or ratio of high molecular weight (HMW) adiponectin is well known to cause insulin resistance and metabolic syndrome (MS). However, how the levels of other adiponectin isoforms, such as the middle molecular weight (MMW) and low molecular weight (LMW) isoforms, and their relative ratio to total adiponectin (TA) or other isoforms change in abdominal obesity (AO) has not been determined. Therefore, we investigated the issue.

Methods: We examined the associations between adiponectin-related parameters and AO in a group of 283 subjects with AO and 485 subjects without AO (1st group) randomly selected from among the participants in our previous study. The associations between these parameters and the HOMA-IR in a 2nd group, consisting of the subjects remaining in the 1st group after the exclusion of diabetic subjects, were also examined.

Result: In the 1st group, the HMW/TA ratio was significantly lower among the subjects with AO than among those without AO (P values < 0.0001). On the contrary, the ratios of LMW/TA and LMW/HMW were significantly higher among the subjects with AO (P < 0.001) and tended to be positively associated with MS (P=0.07). In the 2nd group, the HMW/TA ratio was inversely associated with the HOMA-IR; however, the ratios of LMW/TA and LMW/HMW were positively associated with the HOMA-IR (P < 0.01), similar to the

associations with MS.

Conclusion: The current investigation demonstrated that the increased ratio of LMW in AO was associated with MS through its relation to insulin resistance.

WPCS-28-1

The Efficacy of Switching from Basal Bolus Insulin Therapy to Oral Semaglutide plus Basal Insulin Therapy.

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Introduction: We have previously reported that glycemic control could be maintained after conversion from Basal-Bolus insulin Therapy (BBT) with less than 30 units of total prandial insulin doses to Basal insulin Plus GLP-1 receptor agonists (GLP-1RAs) Therapy (BPT) in type 2 diabetic. Here, we aimed to clarify whether oral semaglutide (OS) could control the levels of postprandial blood glucose same as injected GLP-1RAs in the patients treated with BPT and to find the specific characteristics of the well-controlled patients. Methods: In type 2 diabetic in less than 7% of HbA1c with BBT, only prandial insulin were switched into OS 3, 7 and 14 mg every 4 weeks depending on tolerability, gradually. Continuous glucose monitoring (CGM) were performed in each treatment period. Results: Among 22 patients (3 mg; n=22, 7 mg; n=20, 14 mg; n=13), there were no significant differences between each treatment period in fasting plasma glucose (FPG) and Glycated Albumin, and also in mean glucose, SD, MAGE and M value calculated with the data of CGM. Although significant negative correlation between mean glucose, SD, MAGE and M value with C peptide index and fasting C peptide were found only in OS 3 mg period, respectively, significant positive correlation between FPG with mean glucose and M value in every dose of OS period. Conclusion: The current study suggested that BPT with OS could maintain the glycemic control good as well as BBT, and especially the control of FPG might be important for the glycemic control in BPT with OS.

WPCS-28-2

GLP-1RAg related improvements in bronchial asthma and sleep apnea syndrome people

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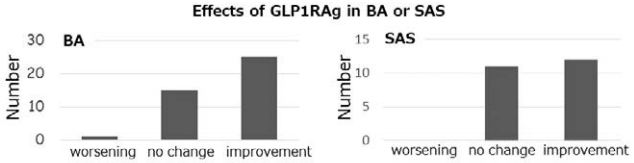
Objective: GLP-1 receptor agonists (GLP-1RAgs), a type 2 diabetes (T2D) drug, not only favorably impacts hyperglycemia but also decreases in body weight and has anti-inflammatory effects. We investigated whether GLP-1RAg is effective in people with bronchial asthma (BA) and sleep apnea syndrome (SAS) who have T2D. Next, we attempted to extract factors contributing to improvement in these diseases in T2D patients treated with GLP-1RAg. Methods: Retrospective analyses were performed on BA or SAS cases with T2D who were prescribed GLP-1RAg from April 1 2019 to January 31 2023. Methods: Asthma score, step down/up of asthma medication, number of attacks, and patient responses were used to divide the patients into 'improvement' and 'non-improvement' groups. Results: A total of 31 patients (9 males, age 63.8±12.4 years, BMI 28.4 ± 5.3 kg/m2, HbA1c 7.3±1.5 %) were included in the analysis of BA and a total of 23 patients (15 males, age 59.0±14.6 years, BMI 32.5±5.9 kg/m2, HbA1c 7.0±1.2 %) in SAS. A comparison of the GLP-1RAg-treated and non-GLP-1RAg-treated groups showed there was significant improvement in BA (p<0.01, -0.363, -0.789) and in SAS (p=0.042, -0.013, -0.734). Although many cases of BA showed a decrease in both body weight and HbA1c with GLP-1RAg treatment, a logistic univariate analysis showed no significant differences in reduction of HbA1c or body weight in BA. It showed significant differences of reduction of HbA1c in SAS. Conclusion: GLP-1RA demonstrated a range of favorable effects in BA or SAS with T2D, especially refractory BA.

Comparison of treatment with or without GLP-1RAg

	BA			SAS		
	P-value	95 % CI		P-value	95 % CI	
Improvement	<0.01	-0.789	-0.363	0.042	-0.734	-0.013
gender	0.101	-0.344	0.031	0.334	-0.384	0.133
age	<0.01	7.664	17.386	0.013	2.381	19.087
Baseline of BMI	0.794	-8.406	6.445	0.039	-6.759	-0.188
Baseline of HbA1c	0.243	-0.2080	0.8129	0.210	-0.289	1.278

t-test



WPCS-28-3

Influence of eating behavior on HbA1c-lowering effects of GLP-1 receptor agonists

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Objective: The relationship between GLP-1RA action on HbA1c and body weight with eating behavior in persons with type 2 diabetes (T2D) receiving GLP-1RA for the first time was evaluated. Methods: The participants received the Dutch Eating Behavior Questionnaire (DEBQ); blood tests and anthropometric measurements were taken before and 3 months after initiation of GLP-1RA. The DEBQ includes 33 questions regarding External, Emotional, and Restrained eating behaviors, i.e., eating prompted by external stimuli such as smell and appearance or social considerations such as time of day, eating prompted by emotions such as anxiety, depression, and boredom, and eating prompted by health consideration, respectively. Results: A total of 61 individuals (age 59.0±13.8 years; the duration of diabetes 13.3±12.7 years; and BMI 29.7±4.9) participated in this study. HbA1c, body weight and % body fat were significantly reduced by GLP-1RA treatment [HbA1c (%), 8.3±1.7 to 7.1±1.3, p<0.001; body weight (kg), 79.3±16.1 to 76.6±18.3, p<0.001; and % body fat (%), 36.2±7.6 to 34.0±8.5, p<0.001], while muscle mass was not affected [muscle mass (kg), 47.4±10.8 to 47.4±10.7, p=0.368]. Macronutrient intake was significantly decreased. The baseline DEBQ scores were as follows: External eating score, 2.97±0.62, Emotional eating score, 2.05±0.86, and Restrained eating score, 2.82±0.64. Change in HbA1c was independently correlated with External feeding score (r^2=0.108, p<0.01). Conclusion: GLP-1RA exerts a greater HbA1c-lowering effect in people with type 2 diabetes prompted to eat by external stimuli such as smell, taste and social factors than anxiety or health considerations.

WPCS-28-4

Practice patterns and outcomes following once weekly semaglutide shortage in Thailand: Theptarin Hospital's experience

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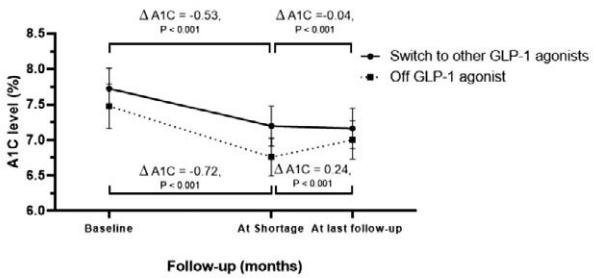
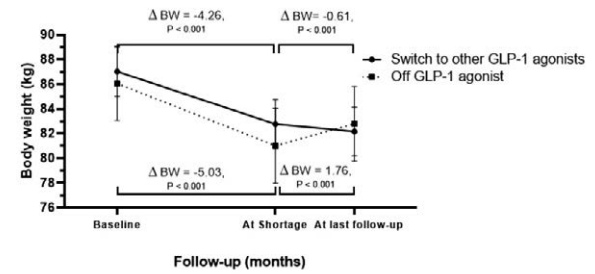
Objective: Worldwide shortage of the once weekly semaglutide injection (Ozempic®) started in early 2022 due to unexpected increase in demand. This study aimed to examine practice patterns and outcomes following semaglutide shortage.

Methods: A retrospective study of patients who initiated once weekly semaglutide injection for at least 1 month from 2020 to 2022 with continuous use during 2022 at Theptarin Hospital, Bangkok was reviewed.

Results: A total of 179 patients was reviewed. The prevalence of off-label semaglutide usage for people without DM was 32.4%. Among analyzed people with T2D (N=65, mean age 58.7 years, BW 86.5 kgs, BMI 32.3 kg/m^2, HbA_{1c} 7.6%), mean HbA_{1c} reduction was 0.5% with weight loss of 4.1 kgs during a median treatment of 9 months. At the time of shortage, 49.2% discontinued the medication without substituting with other GLP-1 RAs, 20.0% substituted with liraglutide, 18.5% with duraglutide, and 12.3% with oral semaglutide. The proportion of patients who could achieve optimal glycemic control decreased from 63.1% to 55.4% at the last follow-up (median duration of analysis at 4 months). 21.9% of the patients who were not prescribed any other GLP-1 RAs experienced weight gain ≥ 3% compared with 9.1% of the patients who substituted with other GLP-1 RAs.

Conclusion: Global shortage of the once weekly semaglutide adversely affected people with T2D. Off-label use for weight loss is also common in Thailand where 2.4 mg of semaglutide is not available for obesity management. Alternative prescriptions should be considered during the shortage period.





WPCS-28-5

Dulaglutide suppresses atherosclerotic lesion formation via inactivation of vascular endothelial cells

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Background:A large-scale clinical study using dulaglutide, one of the GLP-1 receptor agonists, has reported beneficial effects for diabetic macroangiopathy. However, the detailed mechanism remains unclear. In this study, we investigated the effect of dulaglutide on progression of atherosclerosis in apoE-deficient (ApoE-KO) mice.

Methods: High fat diet-fed (HFD) ApoE-KO mice (12 weeks of age) were treated with dulaglutide for 8 weeks. Atherosclerotic lesion formation (ALF) of whole aorta and aortic sinus were evaluated by staining with Oil red O. Macrophage localization and M2 polarization in the lesions were evaluated by immunohistochemical staining and flowcytometry, respectively. Macrophage migration activity was evaluated by the double chamber method using culture media of human aortic endothelial cells (HAECs). Expression of MCP-1, ICAM-1 and VCAM-1 mRNA in HAECs was evaluated by qPCR.

Results:Although dulaglutide did not affect macrophage activity, that suppressed LPS-induced ICAM-1, VCAM-1 and MCP-1 mRNA expression in HAECs. Double chamber method revealed that dulaglutide-treated culture media of HAECs suppressed macrophage migration activity. Dulaglutide suppressed ALF, and localization of macrophages in atherosclerotic plaques was decreased in HFD-fed apoE-KO mice. Expression of ICAM-1, VCAM-1 and MCP-1. and macrophage markers, CD68 and F4/80 mRNA were decreased, and IL-4 mRNA and number of M2 macrophages were increased in aorta of dulaglutide-treated mice.

Conclusion:Dulaglutide did not affect macrophages directly but suppressed macrophage adhesion and infiltration through inactivation of endothelial cells. Moreover, dulaglutide increased IL-4 expression and M2 polarization in atherosclerotic plaques. These finding may indicate one of the mechanisms on dulaglutide-mediated suppression of diabetic macroangiopathy.

WPCS-28-6

Divergence of treatment response with imeglimin: a cluster analysis of randomized, double-blind, controlled trial

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OBJECTIVE

We performed a post-hoc analysis of clinical trial data to investigate whether patients subgroups identified by data-driven clustering respond differently to imeglimin.

METHODS

Data from randomized clinical trials of imeglimin as monotherapy [Ph2b and Ph3 (TIMES-1)] were included in the analysis.

Four coordinates, 1) duration of type 2 diabetes, 2) baseline BMI, 3) baseline HbA1c, and 4) baseline fasting insulin, were applied to form clusters by the non-hierarchical k-means method.

The efficacy of imeglimin were examined for each cluster.

RESULTS

We identified four clusters of patients with diabetes, which had significantly different patient characteristics.

Cluster 1 (n=149) was a group with lower values of all four indices compared to the total patient population before cluster segregation, cluster 2 (n=78) was a group with longer duration of diabetes, cluster 3 (n=59) was a group with higher baseline BMI and higher fasting insulin, and cluster 4 (n=76) was a group with higher baseline HbA1c.

In all four clusters, imeglimin was significantly more effective than placebo in improving HbA1c at all time points evaluated. However, the difference in HbA1c change and effect size (ES) between the imeglimin and placebo groups were varied widely by cluster (Cluster 1: -0.78, ES=1.40, Cluster 2: -0.64, ES=1.18, Cluster 3: -0.91, ES=0.91, Cluster 4: -1.23, ES=1.47).

CONCLUSION

Data-driven clustering of patients with type 2 diabetes allowed us to identify subgroups that respond differently to imeglimin in improving HbA1c.

This new stratification might help to tailor and target the imeglimin treatment to patients who would benefit most.

WPCS-28-7

The effect of imeglimin on glycemic management in Japanese patients with type 2 diabetes

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Imeglimine is a novel oral hypoglycemic agent, exerts hypoglycemic actions by stimulating insulin secretion in a glucose concentration-dependent manner and by improving insulin resistance. We evaluated the effects of imeglimine on glycemic management, insulin secretion, body weight(BW) and composition in Japanese patients with type 2DM.

Patients with inadequate glycemic control(HbA1c>7.0%), treated with diet/exercise or oral antidiabetic drugs(OADs) in our outpatient clinic, were eligible in the study. Height, BW and composition were measured, and calculated body mass index(BMI). Diabetic complications were assessed. HbA1c, glycated albumin(GA), fasting plasma glucose(FPG), and C-peptide(CPR) were measured, and CPR index(CPI: CPR[ng/ml] / glucose[mg/dl] x100) was calculated. Imeglimine 2000mg was administrated without changing the treatment. The change in HbA1c(△HbA1c), GA(△GA) and other measured items after administration were examined with paired *t*-test, and analyzed using simple and multiple stepwise regression analysis. $P<0.05$ was defined as statistically different.

Background of participants was as follows: 11 male and 7 female, 61.4±10.5 y.o, 69.9±17.4kg, 26.2±4.7kg/m^2. OADs(number) were DPP-4i(17), SGLT2i(15), metformin(12), alpha-GI(4) and glinides(3)(overlapped). Evaluation period was 3.3±2.2month. HbA1c, GA, FPG were reduced, and CPI was increased significantly(7.6±0.6→7.2±0.6%, 17.7±2.1→16.1±2.7%, 140.2±19.4→128.7±17.1mg/dl, 1.3±0.5→1.5±0.5, $p<0.05$, respectively). BW and composition were not changed significantly. Neither △HbA1c nor △GA showed significant correlations with each measured items and OADs in single regression analysis. Patients were classified into 4 groups according to BMI and CPI, HbA1c and GA were significantly reduced in BMI<32 and CPI>0.9 group(13 patients, △HbA1c -0.5±0.3%, △GA -2.3±1.2%, $p<0.05$, respectively).

Imeglimine reduced FPG, increased insulin secretion and improved glycemic management without significant changes in BW.

WPCS-28-8

Good timing of insulin intervention to the positive Glutamic acid decarboxylase antibody(GADA) of diabetics?

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Background) After Tokyo Study,in patient with titer >10U/ml of GADA recognized as Slowly progressive insulin dependent diabetes mellitus(SPIDDM) is recommended the speedy insulin administration to prevent and delay the progressive beta cell destruction .On 2023 January,Japan Diabetes Society published the new SPIDDM diagnosis criteria. Object) To asses the pathophysiological analysis in the newly diagnosed GADA positive TID diabetics of our hospital in 2013~2023. Method)About 4 female and 6 male,BMI,HbAic,3hydroxybutyric acid(3HBA),GADA, fasting Cpeptide(CPR)/CPI,24hr- urine CPR and thyroid auto antibody(TAB)were measured. Result)Patients were grouped by the value of GADA as follows: A)2,000<, B)1,000~100, C)100>. All of them were administrated Novorapid 30 MIx insulin 3 times per day as soon as diagnosed. All of data is presented as mean value without unit .In the ( ) numbers presented order is A),B),and C). n:(A) F 1/M 3, B) M 2/F 2, C) M 1/F 1), Age:(63.0,32.2,68.5),BMI:(22.2,21.2,23.6),HbA1c:(12.3,13.2,13.0), 3HBA:(493.697,108), GADA:(2,000<,455.2,17.2),fasting CPR/CPI:(0.78/0.43,0.74/0.39,1.47/0.53), 24hr-UCPR:(56.7,32.6,130), Positive rate of TAB:(2/4, 2/4, 0) Conclusion) On this study, all of newly diagnosed TID with positive GADA did not yet fall in absolutely insulin required state. In the youngest patients with 100~1,000U/ml of GADA group, fasting CPR/CPI, 24hr UCPR was the least values, but 3HBA was the highest in the 3 groups. This data suggests that the speedy and steady insulin administration recommended is the most useful method in the youngest TID diabetics is recognized as SPIDDM to prevent and delay the progressive beta cell destruction. Generally the follow of chronological change of its function is clinically difficult. Further more studies is necessary.

WPCS-28-9

Analysis of skin accumulation of AGEs-associated clinical factors in people with type 2 diabetes

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【Objective】 Skin autofluorescence (SAF) is an indicator for assessment of advanced glycation end-products (AGEs) in subcutaneous tissue. Elevated SAF levels are known to be associated with the development of microangiopathy and macroangiopathy in people with diabetes. However, the clinical parameters associated with SAF levels in people with type 2 diabetes (T2D) have remained unclear. The purpose of this study was to identify clinical determinants of SAF in people with T2D.

【Methods】SAF was measured by AGE Reader®, and clinical parameters including results of physical examination, serum biochemistry data and medications were obtained for 350 Japanese people with T2D. The relationships between levels of SAF and those clinical parameters were statistically evaluated.

【Results】Multivariate regression analysis for the determinants of SAF levels indicated that age, HbA1c, current smoking, duration of diabetes, and hypertension were independently and positively associated with SAF levels, while BMI exhibited a negative correlation. Additional multivariate regression analysis with the identified relevant factors and medications used demonstrated that age, current smoking, hypertension and insulin treatment were independently and positively associated with SAF levels ($p<0.001$, $p=0.031$, $p=0.010$ and $p=0.009$, respectively), whereas BMI was the sole negative factor for SAF levels ($p=0.009$).

【Conclusion】Accumulation of skin AGEs represented by SAF levels was positively associated with age, current smoking, hypertension and insulin use and was inversely associated with BMI in people with T2D. Further longitudinal examination for SAF reduction by adequate nutritional management, smoking cessation and blood pressure control is needed.

WPCS-29-1

Proteasome dysfunction protects mice from immobilization-induced muscle atrophy by suppressing the FoxO1-atrogene axis

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The 26S proteasome is an ATP-dependent protease responsible for the degradation of proteins tagged with polyubiquitin chains. We previously found that obesity impairs proteasome function in the liver, which mediates obesity-induced endoplasmic reticulum (ER) stress and insulin resistance.

To elucidate the role of proteasomes and ER stress in the skeletal muscles with obesity, we generated muscle-specific 20S proteasome assembly chaperone-1 knockout (mPAC1KO) mice by deleting the Psmg1 gene. Eight week-old mPAC1KO mice and wild type (WT) mice were fed a 60% high-fat diet (HFD) or standard diet for 14 weeks.

HFD activated proteasome function by ~8 fold in the skeletal muscles, which was reduced by 50% in mPAC1KO mice. mPAC1KO induced unfolded protein responses in the skeletal muscles, which was restored by HFD. Although the skeletal muscle mass and functions were not different between the genotypes, genes involved in the ubiquitin proteasome complex, immune response, endoplasmic stress, and myogenesis were coordinately upregulated in the skeletal muscles of mPAC1KO mice. Therefore, we established a sarcopenic obesity model by combining HFD and immobilization. mPAC1KO protects skeletal muscle mass reduction by downregulating atrophy-related genes encoding atrogin-1 and MuRF1, together with their upstream Foxo1 and Klf15. In conclusion, obesity elevates proteasome functions in the skeletal muscles. Proteasome dysfunction protects mice from immobilization-induced sarcopenia in obesity. These findings suggest obesity-induced proteasome activation as a possible therapeutic target for sarcopenic obesity.

WPCS-29-2
Variations of Metabolic Risk Factors are Associated with Intrinsic Capacity in Aged Patients with Type 2 DM

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Intrinsic capacity (IC) is defined as the composite of all the physical and mental capacities, that can draw on at any point in their life view and focusing on healthy aging. Long-term variability of blood glucose and metabolic risk factors (blood pressure, lipid parameters, estimated glomerular filtration rate (eGFR) and body weight) is defined as the fluctuations outside the recommended range in serial measures and increased these parameters variability is associated with aspects of frailty. Yet, the association between glucose and metabolic risk factors variabilities and IC in older persons with type 2 diabetes mellitus (T2DM) remains unclear. A total of 1,439 T2DM patients, including 800 female patients, with a mean age of 72.9±5.7, were enrolled. 451(31.3%) patients had abnormal IC score. Compared with patients with normal IC score, patients with abnormal IC were older, female predominant, a longer duration of DM, higher Charlson-Comorbidity Index, lower education level, more likely to be widowed (all $P<0.05$). Patients with abnormal IC had significantly lower mean values of eGFR, and higher HbA1C (all $P<0.05$). As for the variability part, the CVs of body weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, eGFR, and HbA1C had shown statistically significant differences. By using a multiple logistic regression analysis, age, CV (variability) of body weight, SBP, DBP, eGFR, and HbA1c were independent factors associated with IC scores. Conclusion, higher glucose levels and blood pressures long-term variation may be associated with risk of frailty in older adults with T2DM.

WPCS-29-3
Effects of Dietary Patterns on Body Composition and Skeletal Muscle Health in Animal Model of Sarcopenic Obesity

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Sarcopenia has been described as age related decrease of muscle mass and life performances. Sarcopenia is one of the new-developed life threatening diseases in the world. Recently, some studies demonstrated that obesity is associated with the development and progression of sarcopenia. Increasing evidence suggests that obesity plays an important role in certain patients with obesity. However, there is limited known about the effect of sarcopenia in obesity currently, and the paracrine action of obese adipocytes on myocytes in skeletal muscles still need to be further elucidated. Thus, we investigated whether obese adipose tissue exhibited differential cytokines secretion and genes expression, and then cross-talk with skeletal muscle in sarcopenic obesity. Here, we established a co-culture system to achieve cell-to-cell crosstalk and explored the sarcopenia-associating factors or cytokines in both adipocytes and myocytes of skeletal muscles to mimic the microenvironment of sarcopenic obesity. Meanwhile, we also find that possible mechanisms and downstream signaling of interaction between sarcpenia-related myocytes of skeletal muscles and obese adipocytes. This study suggested that crosstalk between myocytes of skeletal muscles and adipocytes is a pathway through the sarcopenia-associating factors and cytokines that might have potential in blocking the vicious cycle in the mechanism of sarcopenic obesity, and regeneration and could be useful for tissue engineering.

WPCS-29-4
Dehydroepiandrosterone sulfate and skeletal muscle disorders in patients with type 2 diabetes

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Objective:We aimed to clarify whether dehydroepiandrosterone sulfate (DHEAS) is associated with the development of skeletal muscle disorders in subjects with type 2 diabetes (T2D).

Methods:

A cross-sectional study was conducted in 362 people with T2D . Laboratory data including serum DHEAS levels, skeletal muscle mass index (SMI), handgrip strength (HS) and gait speed (GS) were examined. Presarcopenia, sarcopenia and dynapenia were classified in accordance with the definitions of the AWGS 2019 criteria and modified algorithm. The relationships between serum DHEAS concentrations and the skeletal muscle-related indices were statistically assessed.

Results:DHEAS was positively associated with HS but not with SMI or GS after clinical confounders adjustment. In addition, multiple logistic regression analysis including DHEAS showed that serum levels of DHEAS were inversely associated with the prevalence of dynapenia but not with the prevalence of presarcopenia or sarcopenia. In addition, habitual exercise with an intensity of 3 Mets or more was inversely associated with the prevalence of sarcopenia and dynapenia.

Conclusion:We demonstrated that serum level of DHEAS was positively associated with HS and inversely associated with prevalence of dynapenia in people with T2D. The results obtained in this study suggested that efficient exercise therapy is essential to preserve skeletal muscle strength.

WPCS-29-5
Factors associated with frailty in hospitalized elderly patients with type 2 diabetes mellitus

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Aging is already a problem in countries all over the world. The impact of aging has led to many health problems, such as frailty and chronic diseases. Frailty is a geriatric syndrome associated with aging and can lead to adverse outcomes such as falls, cognitive impairment, hospitalization, and death. Diabetes mellitus (DM) is also one of the common chronic diseases of the elderly. In order to understand the incidence of frailty and related influencing factors in elderly patients with type 2 diabetes mellitus (T2DM), this study

explored the incidence of frailty and related influencing factors in hospitalized elderly patients with T2DM. A total of 238 patients were collected in a diabetic-specific hospital, with an average age of 68.4 ± 5.6 years, 122 males (51.3%), and 120 (50.4%) were observed with frailty. The duration of disease (p=0.027), marital status (p=0.02), living alone (p=0.05), smoking (p=0.008), exercise (p<0.001), polypharmacy (p<0.001), waist circumference (P=0.009), upper arm circumference (p<0.001), calf circumference (p<0.001), and nutritional status (MNA) (p<0.001) were statistically different between patients with or without frailty. A logistic regression analysis revealed that waist circumference, smoking status, polypharmacy, upper arm circumference, lower leg circumference, MNA and history of falls were major contributors to frailty. Our study indicated that elderly diabetic patients with frailty are affected by multiple factors. Timely detection of relevant risk factors, especially on personal health behaviors and nutritional status, and active intervention were recommended that can effectively reduce the related impact of frailty on elderly diabetes.

WPCS-29-6
Handgrip strength and noncommunicable disease risk among Mongolian adults

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Objective: To study the consequence of measuring handgrip strength in the clinical evaluation of obesityMethods: This cross-sectional study used data from the Mon-Timeline cohort study (N=1180). Bodyweight, height, waist circumference and hand grips strength (HGS, using a digital grip strength dynamometer, Takei Hand Grip Dynamometer 5401-C, Japan) were measured. During the interview, noncommunicable diseases (NCD) such as diabetes, arterial hypertension, stroke, and heart attack questionnaires were administered. To determine the cutoff value of HGS which is an indication of suspected sarcopenia, the 25th percentile of HGS was calculated as 31.8kg for men and 20.5kg for women.Results: Mean age of study participants was 39.3 ± 15.9 and 33.2% (n = 392) were men. The mean HGS of the participants was 40.1 ± 10.4 for men and 24.5 ± 5.6 for women. The HGS was inversely associated with total body fat percentage (r=-0.176) while HGS was positively associated with muscle marker (r=0.573). In the Regression analysis, Odds ratio (OR)s for NCDs were higher in sarcopenic obese people compared to non-sarcopenic obese people. For instance, OR (95% CI) was 4.57 (2.10-9.91), 4.86 (2.26-10.4) and 4.81 (2.30-10.1) for hypertension, diabetes, and stroke in sarcopenic obese people while OR (95% CI) was 3.91 (2.51-6.09), 4.41 (2.11-9.24), 2.73 (1.48-5.01) in obese people respectively. Conclusion: Measuring handgrip strength might beappropriate for the detection of sarcopenia in obesity. The incidence of noncommunicable diseases was more frequent in obese people with suspected sarcopenia than in those without sarcopenia.

WPCS-29-7
Relationship between handgrip strength and triglyceride glucose index in Korean adults based on the KNHANES Survey

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We investigated the association between insulin resistance (IR) and muscle strength via the Triglyceride glucose index (TyG) index and handgrip strength (HGS). We used data from the sixth Korean National Health and Nutrition Examination Survey (KNHANES) to evaluate a total of 10048 subjects aged over 40.

The subjects were stratified into quartiles according to the TyG index. Relative HGS was decreased as the TyG index increased in total subjects. In linear regression analysis, relative HGS showed negative correlation with metabolic parameter and the TyG index in all groups of age and gender.

According to logistic regression analysis after adjusting for multiple risk factors, odds ratio (95% CI) for low muscle strength (defined as the lower 10% on relative HGS) for the highest and lowest quartiles of the TyG index was 2.513 in male and 2.161 in female on total subjects. In group of subjects with mid-age (age between 40 to 64 years old), the prevalence of low muscle strength was positively correlated with increased the TyG index both in male and female. However, in the elderly groups (age over 65 years old), relationships between the increased the TyG index quartiles and prevalence of low muscle strength were not significant in all subjects both in unadjusted and adjusted logistic regression analysis.

In conclusion, the TyG index was independently associated with relative HGS and low muscle strength in mid-aged subject and could have predictive value for further sarcopenia and metabolic disease.

WPCS-29-8
Handgrip strength and muscle mass in relation to cardiac autonomic neuropathy in patients with type 2 diabetes

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Background: No studies have examined the relationship of sarcopenia with cardiac autonomic neuropathy(CAN) in T2DM. Therefore, we examined the relationships of handgrip strength(HGS) and appendicular skeletal muscle mass index(ASMI) with CAN in T2DM. Methods: A total of 666 patients were enrolled. CAN was assessed using five tests according to Ewing's protocol and was defined as the presence of autonomic neuropathy points ≥2.5. Low ASMI was defined as low height-adjusted appendicular muscle mass(men; 7kg/m^2, women; 5.7kg/m^2) using bioelectrical impedance analysis. Low HGS was defined as below 28kg in men and 18kg in women. In addition, HGS was normalized to body weight to account for the proportion of strength relative to body weight(bwt). Results: 17.3% of total patients had low HGS and 14.7% had low ASMI. Bwt-adjusted HGS showed positive correlation with eGFR and negative correlation with age, albuminuria, pulse wave velocity, and hsCRP. The prevalence of CAN gradually increased with decreasing quartiles of bwt-adjusted HGS quartile(p<0.001). The prevalence of CAN was shown decreasing tendency across quartiles of ASMI(p=0.054). The HRs (95% CI) for CAN across quartiles of weight-adjusted HGS were as follows: 1.00 (reference), 0.57 (0.18, 1.85), 0.25 (0.07, 0.88), 0.11 (0.03, 0.45)(p=0.01). On the other hand, the HRs (95% CI) for CAN across quartiles of ASMI were as follows: 1.00 (reference), 0.76 (0.23, 2.5), 0.99 (0.31, 3.15), 0.28 (0.08, 0.92) (p=0.11). Conclusions: Lower HGS may be significantly associated with CAN in patients with T2DM. In addition, lower HGS rather than lower ASM may be an independent risk factor for CAN.

WPCS-29-9
A Simple Formula for Evaluating the Appendicular Skeletal Muscle Mass in patient with Diabetes

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Background and aims: Dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA) methods are often used to evaluate skeletal muscle mass, however, they require the use of specific equipment and are difficult to implement at all facilities. The purpose of this study was to devise a simple formula for evaluating skeletal muscle mass.

Materials and methods: We carried out a retrospective study on diabetic patients who admitted to Kansai Electric Power Hospital between 2017 and 2022. The inclusion criteria for selecting study subjects were those who had performed skeletal muscle mass measurement by the BIA method and 24-hour creatinine excretion (24hCre) measurement by 24-hour urine collection. We created a regression equation that the appendicular skeletal muscle mass (ASM) obtained by the BIA method as the objective variable and 24hCre, age, sex, and height as the explanatory variables, to examine a method for estimating the ASM.

Results: A total of 336 subjects (209 males, 127 females: 65.0±12.6 years old) were identified. A significant positive correlation was found between ASM obtained from BIA and 24hCre (p<0.001). In addition, a regression equation for estimating ASM was obtained by performing multiple regression analysis

using ASM obtained from BIA as the objective variable and 24hCre, age, sex, and height as explanatory variables [ASM=0.0045*24hCre-0.0183*Age-1.3132*Sex(male=1,female=2)+0.2727*Height-26.5945]. There was high correlation between the ASM obtained from the calculation formula and from the BIA ($p<0.001$).

Conclusion: Our data suggest that the simple formula might be applied as a practical method of quantifying ASM in Japanese patients with diabetes.

WPCS-29-10

Effect of cadmium exposure on the risk of sarcopenic obesity: A propensity score-matched cohort study

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This propensity score-matched cohort study investigated the effects of blood cadmium (Cd) levels (<1.2 mg/dL vs. ≥1.2 mg/dL) on incident sarcopenic obesity (SO) in a cohort matched for age, sex, and body mass index (BMI). Body composition was assessed by multifrequency bioelectrical impedance analysis and was categorized into three groups: metabolically healthy obesity (MHO), adiposity obesity (AO), and SO. Among 186 participants (mean age, 51 ± 7 years; male-to-female ratio, 1.0:1.3), 45.7% and 54.3% had MHO and AO at baseline, respectively. During the 14-year follow-up, the incidence of MHO, AO, and SO was 24.7%, 72.0%, and 3.2%. Baseline adiposity, female, age 60-69 years, and blood Cd ≥1.2 mg/dL were associated with SO at follow-up ($p<0.05$). In the inverse probability of treatment weighting Cox regression analysis, female and BMI were risk factors for AO. In addition to sex and BMI, age, and high blood Cd (adjusted hazard ratio=1.63, 95% confidence interval=1.06-2.50, p=0.025) were independent risk factors for SO.

WPCS-30-1

Beneficial effects of Fruit intake in Korean Patients with Diabetes Mellitus

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Objective

The importance of medical nutrition therapy (MNT) with goals of promoting and supporting healthy eating patterns, addressing individual nutrition needs, maintaining the pleasure of eating is recognized as one of the cornerstones in the treatment type 2 diabetes mellitus (T2DM). Despite the well-recognized health benefits of fresh fruit consumption, substantial uncertainties remain about its potential effects on glycemic control in patients with T2DM.

Methods

We examined the association of fresh fruit consumption and glycemic control in patients with T2DM using data from the 7th Korea National Health and Nutrition Examination Survey. Study samples were divided 460 patients into 3 groups based on the weekly fruit consumption frequency for the analysis.

Results

Patient with highest fruit intake were older compared to the other two groups and women were more likely to consume fruits. Fruit consumption was positively correlated with better HbA1c levels in these patients. Currents smokers and weekly alcohol intake also showed negative correlation according to the fruit intake tertiles. On the other hand, DM duration, proportion of patient with insulin treatment, baseline BMI and lipid profiles were not significantly different among three groups. From the Cox regression analysis, patients with highest tertile of fruit intake were 3.63 times more likely to be in good glycemic control, defined as HbA1c < 7%.

Conclusion

In this study, we observed a significant beneficial impact of fruit consumption on glycemic control in Korean patients with T2DM.

WPCS-30-2

Association between antidiabetic drugs and the incidence of atrial fibrillation in patients with type 2 diabetes

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Objective: Although diabetes is a risk factor for atrial fibrillation (AF), studies on the AF risk according to the antidiabetic drugs are lacking. This study evaluated the effects of antidiabetic drugs on the AF incidence in Korean patients with type 2 diabetes.

Research Design & Methods: We included 2,515,468 patients with type 2 diabetes from the Korean National Insurance Service database without a history of AF, who underwent health check-ups between 2009 and 2012. Newly diagnosed AF incidence was recorded until December 2018 according to the main antidiabetic drug combinations used in the real world.

Results: Of the patients included (mean age, 62 ± 11 years; 60% men), 89,125 were newly diagnosed with AF. Metformin (MET) alone (hazard ratio [HR] 0.959, 95% CI 0.935–0.985) and MET combination therapy (HR < 1) significantly decreased the risk of AF. The antidiabetic drugs consistently showing a protective effect against AF incidence were MET (HR 0.977, 95% CI 0.964–0.99) and thiazolidinedione (TZD; HR 0.926, 95% CI 0.898–0.956), even after adjusting for various factors. Moreover, this protective effect was more remarkable with MET and TZD combination therapy (HR 0.802, 95% CI 0.754–0.853) than with the other drug combinations. In the subgroup analysis, the preventive effect of MET and TZD treatment against AF remained consistent, regardless of the age, sex, duration, and diabetes severity.

Conclusion: The combination therapy of MET and TZD is the most effective antidiabetic drug for preventing AF in patients with type 2 diabetes.

WPCS-30-3

Ten-year cost-effectiveness of Risk Assessment and Management Programme – Diabetes Mellitus in Hong Kong primary care

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Objective

To evaluate the cost-effectiveness of the multidisciplinary Risk Assessment and Management Programme – Diabetes Mellitus (RAMP-DM) for patients with type 2 diabetes managed in Hong Kong primary care over ten years.

Methods

A population-based cohort study which included patients with type 2 diabetes managed in public primary care setting between August 2009 and September 2010 was conducted. Patients received routine care and participated in RAMP-DM were one-to-one matched with patients received routine care only by propensity score. The cost-effectiveness of RAMP-DM was assessed by incremental cost-effectiveness ratio (ICER), i.e. RAMP-DM cost divided by number of complication and all-cause mortality event avoided. Direct medical cost incurred by healthcare service utilization were also compared between groups.

Results

36,746 patients (18,373 patients in each treatment group) were included. RAMP-DM participants were observed to have lower cumulative incidence of any complication (27.0% vs. 39.0%) and mortality (16.1% vs. 32.3%) compared with patients received routine care only over ten years. The ten-year cost for delivering RAMP-DM services was HK$2,568 (US$329) per patient. The ICER of RAMP-DM was HK$20,544 (US$2,634) and HK$15,408 (US$1,975) to prevent one complication and mortality event, respectively. The total direct medical cost incurred by healthcare service utilization was HK$82,236 (US$10,543) less in RAMP-DM participants (HK$182,751 [US$23,430]) compared with patients managed in routine care only (HK$264,986 [US$33,973]) in a ten-year period.

Conclusion

Addition of RAMP-DM to routine care was a cost-saving approach to manage patients with type 2 diabetes in primary care. RAMP-DM was recommended to be integrated into routine care.

WPCS-30-4

Nomogram for Predicting 5-year Diabetes Remission after Roux-en-Y Gastric Bypass Surgery in Obese Chinese Patients

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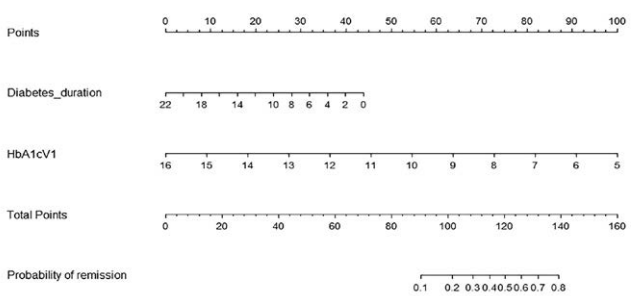
Objective: Establish a new tool for predicting long-term diabetes remission (DR) with a nomogram.

Methods: 105 individuals with complete preoperative information and undergoing Roux-en-Y gastric bypass (RYGB) were enrolled in this retrospective study. DR criteria after bariatric surgery was defined according to the 2009 ADA guideline. 15 individuals were lost to 5-year follow-up. Thus, 90 individuals were available and seen at the end of follow-up. The baseline and 5-year data of these 90 individuals were analyzed. Multivariate logistic regression analysis was performed to identify independent predictors for long-term DR and these predictors were used to create a nomogram. Discriminative accuracy of the nomogram and the other four models, ABCD, DiaRem, Advanced DiaRem and Diabetter was compared by calculating their areas under curve respectively and using DeLong method.

Results: Preoperative glycated hemoglobin (A1C) and diabetes duration were identified as independent influential factors that could be combined for precise prediction of long-term complete DR. We created a nomogram by using these 2 factors. The area under the curve was 0.78 (95% confidence interval 0.67–0.89). The Hosmer-Lemeshow X^2 value of nomogram was 3.86 (P=0.87) and indicated consistency between predicted and observed remission. Discriminative accuracy of the nomogram in predicting long-term DR was significantly better than the ABCD model (P<0.01) and comparable to DiaRem, Advanced-DiaRem and Diabetter models (P>0.05) .

Conclusions: Our nomogram was a novel and useful tool for accurate prediction of long-term DR after RYGB.



WPCS-30-5

The glucose lowering drugs and glycemic control in inpatients with Diabetes Mellitus in Central Hospital of MNUMS

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Absract

Objectives: The aim of this study was to describe clinical practice in terms of type 2 diabetes mellitus (T2DM) disease treatment patterns and glycemic control in Mongolia.

Methods: We reviewed data of patients with diabetes mellitus who admitted to Central Hospital of Mongolian National University of Medical Sciences from November 2021 to December 2022. Glycated hemoglobin A1c (HbA1c) was used to evaluate glycemic control as defined good (HbA1c<7.5%) and poor (HbA1c>7.5%).

Results: A total of 386 patients' data was reviewed. The male patients were 46.2% (n=179) and mean age was 56.35±11.95 years, mean duration of diabetes was 9.64 years (1-43) and 94.0% (n=386) of them had type 2 diabetes. Among all patients, 79% were given glucose lowering drugs and others (21%) were being treated with insulin. Regarding to types of oral glycemic drugs, 47.0% (n=182) was biguanide, 11.1% (n=52) was sulfonylurea, 27.3% (n=106) was incretin based and 2.8% (n=11) sodium-glucose cotransporter 2 inhibitor drugs (SGLT-2). In the study, 30% of all patients did not get tested HbA1c for the last year. Moreover, 60% of patients who had tested HbA1c have poor glycemic control (HbA1c>7.5%).

Conclusion: Although novel drugs have been using in Mongolia in recent years for the treatment of diabetes mellitus, approximately 60% of people with DM had poor glycemic control. Therefore, we need to increase the practical use of clinical guidelines and to improve the management and follow-up of patients with diabetes.

WPCS-30-6

Age-dependant and sex-specific differences in cardiovascular diseases risks among adults with diabetes in China

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Objective: Data were inconsistent regarding sex and cardiovascular diseases (CVDs) risks among adults with diabetes.

Methods: This cross-sectional study investigated sex differences in the attainment of the targets for CVDs risk factors, including hemoglobin A1c (HbA1c<7%), blood pressure (BP<130/80 mmHg), low-density lipoprotein-cholesterol (LDLc<2.6 mmol/L) and body mass index (BMI<24 kg/m^2) in China. Age-adjusted targets for HbA1c (<7.5%) and BP (<140/90 mmHg) were used for those over 65 years old.

Results: Among 29,877 patients, women had significantly higher rates of the attainment of the targets for HbA1c (53.1% vs 48.2%), age-adjusted HbA1c (61.6% vs 57.2%), and BMI (35.6% vs 33.1%), with a significantly lower rate of the attainment of LDLc target (28.9% vs 39.0%). No significant differences were found between sexes regarding BP target attainment (13.3% vs 13.7%), while a significantly lower rate of the attainment of age-adjusted BP target was found in women (22.9% vs 26.3%). After adjusting for confounders, compared with women, men were less likely to reach the attainment of the targets for HbA1c (OR, 95%CI: 0.817, 0.770-0.866), age-adjusted HbA1c (0.818, 0.770-0.869), and BMI (0.753, 0.702-0.807). Men were more likely to reach the attainment of LDLc target, with significant interaction between different age groups (<65 years: 1.759,1.600-1.934; ≥65 years: 1.552, 1.436-1.676). For age-adjusted BP, men were more likely to reach the target in those over 65 years (1.228, 1.132-1.332), with no significant sex-differences in those under 65 years.

Conclusion: Sex differences in quality of diabetes care existed, highlighting the importance of sex-specific intervention on CVDs risks in China.

WPCS-30-7
Effect of DPP-4 Inhibitors on severity of atherothrombotic stroke in older patients with type2 diabetes

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【Introduction】
Several studies have demonstrated that DPP-4 inhibitors improve endothelial function in patients with T2D in the clinical setting. This suggests that DPP-4 inhibitors may reduce severity of atherothrombotic stroke. In our study, we aimed to evaluate the effect of DPP-4 inhibitors on severity of atherothrombotic stroke in older patients with T2D.
【Methods】
This cross-sectional study was performed using data from the Medical Data Vision administrative claims database. The severity at admission was defined as a Modified Ranking Scale (mRS) of 3 or higher. We performed multivariate analysis with severe atherothrombotic stroke as the objective variable, and calculated ORs. The explanatory variables used in the multivariate analysis were administration of antidiabetic agents (yes/no), clinical characteristics of patients.
【Results】
We included 1,057 atherothrombotic stroke patients with T2D aged 65 years or older. Of the eligible patients, 265(25.1%) had severe atherothrombotic stroke. The severity of atherothrombotic stroke was increased by age/10yers (OR: 1.79, 95%CI: 1.48-2.16), whereas decreased by DPP-4 inhibitor use (OR: 0.61, 95%CI: 0.44-0.86).
【Conclusion】
Our study suggests that DPP-4 inhibitors may reduce the severity of atherothrombotic stroke in older patients with T2D. Early treatment with DPP-4 inhibitors may help prevent a more severe atherothrombotic stroke and preserve patients' quality of life.

WPCS-30-8
THE EFFECT OF IMPLEMENTING HEALTH PROTOCOLS DURING THE COVID-19 PANDEMIC ON GLYCEMIC CONTROL IN T2DM

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Objective: The aim of the study is to find out the effect of implementing health protocols during the COVID 19 pandemic on glycemic control in type 2 DM patients.
Methods: This research is a nested cohort design where the sample is selected by consecutive sampling at the metabolic endocrine outpatient clinic in Dr. M. Djamil General Hospital from August 2020 to January 2021. We compared the glycemic parameters before and during health protocols.
Results: On 28 patients, 53.6% were women and 46.4% were men. There were significant increases from before to during health protocols in HbA1c (1.88% to 2.42%), body weight (69.69 kg to 71.76 kg), BMI (26.91 to 27.76), FPG (151.54 mg/dl to 174.25 mg/dl). There were change in PPG (221.43 mg/dl to 232.25 mg/dl), LDL (117.68 mg/dl to 114.79 mg/dl), HDL (55.5 mg/dl to 50.75 mg/dl), cholesterol total (180.71 mg/dl to 175.21 mg/dl), triglyceride (134.79 mg/dl to 137.41 mg/dl), systolic BP (136.39 mmHg to 136.68 mmHg), and diastolic BP (78.21 mmHg to 77.71 mmHg), but not statistically significant.
Conclusion: There are glycemic control deteriorations in T2DM patients due to the application of health protocols during the COVID-19 pandemic, including an increase in HbA1c, fasting blood glucose, and BMI.
Keywords: diabetes mellitus, glycemic control, COVID-19, health protocols

WPCS-30-9
Relationship between blood glucose by CGM and HbA1c and antidiabetic drugs in patients with type 2 diabetes

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Background: HbA1c levels and the use of insulin secretagogue antidiabetic drugs are associated with time below range (TBR, % time of blood glucose level < 70 mg/dL) measured by the continuous glucose monitoring (CGM) in patients with type 2 diabetes (T2D). In this cross-sectional study, we examined the relationship between TBR or time above range (TAR, % time of blood glucose level >180 mg/dL) and HbA1c and the use of antidiabetic drugs among patients with T2D.

Methods: CGM with Medtronic CGMS-Gold® or Abbott's FreeStyle Libre Pro® was performed on 107 patients (61 men, 64±14 years old) with T2D using antidiabetic drugs. Multivariable regression analysis was used to examine the relationship between TAR or TBR and HbA1c, with age, sex, body mass index, duration of diabetes, and individual antidiabetic drugs as covariates. Similar analysis was performed in the relationship between TAR or TBR and each antidiabetic drug.

Results: The mean HbA1c was 8.2±1.4% and 73% of the patients were insulin-users. The mean TAR and TBR were 33.2±22.5% and 4.3±7.2%, respectively. Multivariable regression analysis showed that HbA1c was significantly associated with TAR (β=10.8, $p<0.01$) but not TBR. The insulin use was significantly associated with TAR (β=17.4, $p<0.01$) and the α-glucosidase inhibitor (α-GI) use was associated with TBR (β=-4.03, $p=0.04$).

Conclusions: TAR increased as HbA1c increased and no association was shown between TBR and HbA1c. It seems to be difficult to predict TBR from HbA1c level. The positive association between insulin use and TAR may be due to reversal of causality.

WPEC-01-1
Development of Nursing Support Guidelines for End-of-Life Care in Diabetic Patients

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【Purpose】
The purpose of this study was to create "Nursing Support Guidelines for End-of-Life Care in Diabetic Patients".
【Methods】
We carefully reviewed 33 papers on end-of-life care for diabetic patients in Japan and overseas, and clarified the direction of nursing care by the qualitative integration method (KJ method). Based on the symbols derived from the data analysis, the draft of "Nursing Support Guidelines for End-of-Life Care in Diabetic Patients" were created. Focus group interviews were conducted for further refinement, having focused on the five Donabedian quality of care criteria: validity, feasibility, timing, contribution to the advancement of healthcare, and effectiveness.
【Results】
The six symbols were derived, and a theory concerning the structure was derived, which required two of them like wheels of vehicle: "Support for maintaining one's health until death: Avoiding acute complications through foot care and adjustment of medication" and "Support for maintaining peace and dignity until death: Symptom control and an empowerment approach focused on the needs of the patients and their families". Based on a theory concerning the structure, the draft was revised by the expert panel to fit the clinical situation.
【Conclusion】
The provisional version has been created, and will be validated.

WPEC-01-3

The effects of ABC control of electronic medical records-linked diabetes self-management system in real clinical setting

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Aims/Introduction

This study evaluated the effect of a mobile diabetes management program called "iCareD" which was designed to minimize the workload of the healthcare team with integrating the program into the hospital electronic medical records (EMR) system.

Materials and methods

In this retrospective observational study, we recruited 308 patients. We categorized these patients into based on their compliance to use the "iCareD" at home; compliance was determined through self-monitored blood glucose inputs and message subscription rates. We analyzed changes in the ABC (A: Alc, B: Blood pressure, C: Cholesterol (LDL-C; Low Density Lipoprotein cholesterol)) levels from the baseline to 12 months thereafter based on the patients' "iCareD" usage patterns.

Results

The patients comprised of 92 (30 %) non-users, 170 (55 %) poor-compliance users, and 46 (15 %) good-compliance users; their ABC target achievement rate showed prominent changes in good compliance groups from baseline to 12 months (10.9 % vs. 23.9 % *p <0.05),* while poor-compliance users and non-users were not significantly different (13.5% vs 18.8% p = 0.106; 20.7 % vs 14.1% p= 0.201, respectively).

Conclusions

"iCareD" involves minimal input from the healthcare team and can improve the ABC levels of diabetic patients by supporting patients' self-care in real clinical settings.

WPEC-01-4

Prognostic significance of glucose, lipid and insulin resistance parameters on incident CKD in Chinese patients with T2D

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Objective

Dyslipidaemia, hyperglycaemia and insulin resistance (IR) are closely related and implicated in chronic kidney disease (CKD) in type 2 diabetes (T2D). We examined the prognostic significance of triglycerides to high-density lipoprotein cholesterol ratio (TG/HDLc), fasting C-peptide to plasma glucose ratio (CP/FPG) and HOMA2-IR for incident CKD.

Methods

In 5230 patients with T2D consecutively enrolled to the Hong Kong Diabetes Register in 1995-2012 observed till 2019, we measured fasting CP in stored samples at baseline to derive HOMA2-IR. We used Cox regression to examine risk factors for CKD (ICD-9) and used time-dependent receiver operating characteristics (ROC) analysis to evaluate the prognostic value of HOMA2-IR, TG/HDLc and CP/FPG for CKD at different timepoints of follow-up period.

Results

In 4058 patients free of CKD at baseline (mean age: 53.11 ± 12.86 years, median (IQR) diabetes duration of 5 (1-11) years), during a follow-up period of 12.9 (6.8-16.4) years, 1658 (40.9%) developed CKD. Per 1-unit increase of log2 transformed TG/HDLc, CP/FPG and HOMA2-IR were associated with increased risk of CKD with adjusted hazard ratios (95%CI) of 1.12 (1.06-1.18), 1.07 (1.00-1.16) and 1.06 (0.96-1.16) respectively. TG/HDLc demonstrated the highest AUC (0.560) for predicting 13-year survival for CKD with an optimal cut-off of 2.57, while CP/FPG and HOMA2-IR achieved the highest AUC at 20-year follow-up period (0.671 and 0.686) with optimal cut-offs of 121.92 and 1.5 respectively.

Conclusion

In Chinese patients with T2D, dyslipidemia, hyperglycemia and IR were independently associated with CKD with HOMA2-IR showing the greatest prognostic value during a 20-year follow-up period.

WPEC-01-5

Excessive daytime napping independently associated with decreased insulin sensitivity

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Background In recent years, daytime napping for more than one hour has been reported to be a risk factor for the development of diabetes, but the mechanism is unclear. In this study, we investigated the relationship between nap time and insulin sensitivity and secretion.

Methods and Results We analyzed 436 subjects enrolled in the HSCAA Study, a prospective cohort study of patients with at least one risk factor for atherosclerosis, and confirmed napping with an actigraph, and excluded those who were diagnosed diabetes. The subjects were divided into two groups: a short nap group (<1 hour) and a long nap group (≥1 hour), and the relationship between the insulin sensitivity (QUICKI, Matsuda index) and the insulin secretion (Disposition index) calculated from the results of 75g oral glucose tolerance test. Insulin sensitivity was significantly lower in the long nap group compared to the short nap group (QUICKI:$p<0.01$, Matsuda index:$p<0.05$), and the long nap group was an independent associated factor for decreased insulin sensitivity in multivariate analysis that took patient background into account(QUICKI:$\beta=-0.154$, $p<0.05$, Matsuda index:$\beta=-0.158$, $p<0.05$). On the other hand, the long nap group showed no significant association with the index of insulin secretion. Furthermore, in a subanalysis of the nocturnal sleep duration, the long nap group was significantly associated with decreased insulin sensitivity only in the short nocturnal sleep duration group(<6 hours).

Conclusion Napping for more than 1 hour is a factor associated with decreased insulin sensitivity, independent of autonomic dysfunction.

WPEC-01-6

HbA1c and Systolic Blood Pressure Variation to Predict All-cause Mortality in Patients with Type 2 Diabetes Mellitus

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Objective: HbA1c variation was known to be an independent predictor of all-cause mortality in patients with type 2 diabetes mellitus (T2DM). Similar association was also reported in blood pressure (BP) variation. However, few of the studies report the combined effect of HbA1c and BP variation on all-cause mortality. This study aimed to investigate the associated risk between HbA1c and systolic blood pressure (SBP) variation and all-cause mortality in patients with T2DM.

Methods:Using the Diabetes Shared Care Program database of China Medical University hospital, patients with T2DM who had at least three HbA1c, SBP measurements within 12-24 months during 2002-2007 were included. Coefficient of variation (CV) was used to evaluate variation. The 75th percentile of HbA1c-CV and SBP-CV were set as a cutoff to define high and low variation. Hazard ratios (HRs) for all-cause mortality during 2007-2016 were estimated using Cox proportional hazard models.

Results: A total of 2744 patients were included, of whom 769 died during the 11.7 observation years. The associated risk (HRs) of all-cause mortality were 1.22 [1.01- 1.48], P = 0.044, for low HbA1c-CV & high SBP-CV; 1.28 [1.04-1.57], P = 0.020, for high HbA1c-CV & low SBP-CV; and 1.68 [1.31-2.17], P

< 0.001, for high HbA1c-CV & high SBP-CV.
Conclusion:Both HbA1c and SBP variation were significant predictors of all-cause mortality in patients with T2DM. The combined effect of variation was higher than either alone. In addition to achieving HbA1c and BP targets, low HbA1c and BP variation were also important components in our clinical diabetes care.

Table Hazard ratios of all-cause mortality by categories of variation in HbA1c and systolic blood pressure

	Unadjusted model		Adjusted model 1		Adjusted model 2	
Variables	HR [95%C.I.]	p-value	HR [95%C.I.]	p-value	HR [95%C.I.]	p-value
HbA1c-CV & SBP-CV						
low HbA1c-CV & low SBP-CV	1.00[ref.]		1.00[ref.]		1.00[ref.]	
low HbA1c-CV & high SBP-CV	1.35 [1.12-1.63]	0.002	1.20 [0.99-1.46]	0.059	1.22 [1.01-1.48]	0.044
high HbA1c-CV & low SBP-CV	1.26 [1.04-1.53]	0.017	1.41 [1.15-1.72]	<0.001	1.28 [1.04-1.57]	0.020
high HbA1c-CV & high SBP-CV	1.93 [1.52-2.46]	<0.001	1.88 [1.47-2.41]	<0.001	1.68 [1.31-2.17]	<0.001

Adjusted model 1: adjusted for multiple confounders
Adjusted model 2: adjusted for confounders in model 1 plus mean HbA1c and mean SBP

WPEC-01-7
Diabetes fact sheet Mongolia

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Objective
National diabetes registration is important for data source for fact sheet. First web based, diabetes registration of Mongolia was begin in December, 2015 by the supporting grant to the Mongolian Diabetes Association from the Novo Nordisk A/S Denmark. The aim of this study was to make a Diabetes fact sheet Mongolia, using diabetes registration online data source.

Methods
Web based diabetes registration data from 2016-2022, provided by 26 medical centers of Mongolia were used. Urban 12 and rural 14 medical centers were participated out of 42.

Results
Web based diabetes registration was collected 12225(6281 male, 5944 female) diabetic patients' information. Among registered diabetic patients T1DM, T2DM, GDM and Other type of DM was 3.3%(411), 95.6%(11839), 0.5%(63) and 0.5%(66), respectively. Prevalence of hypertention was 40.9%. Prevalence of macrovascular complications such as stroke, myocardial infarction and peripheral artery disease was 2.1%, 1.7% and 0.9%, respectively. Prevalence of diabetic eye disease: retinopathy, cataract and blindness were 8.6%, 2.8%, and 0.1%, respectively. Prevalence of diabetic kidney disease: microalbuminuria, macroalbuminuria, kidney failure, heamodialysis and kidney transplantation 6.2%, 2.6%, 1.3%, 0.3% and 0.03%, respectively. Prevalence of diabetic peripheral and vegetative neuropathy was 17.0% and 1.1%, respectively. Prevalence of diabetic foot complications: foot ulcer, toe amputation, foot amputation, below knee and above knee amputation was 0.9%, 0.2%, 0.02%, 0.1% and 0.1%, respectively.

Conclusion
Making, presenting and publishing of diabetes fact sheet is important for management of diabetes. National diabetes registration is necessary in Mongolia. Thanks to Novo Nordisk for the implementation of the online database system.

WPEC-01-8
Evaluation of PHR app with Gamification Theory and Wearable Devices

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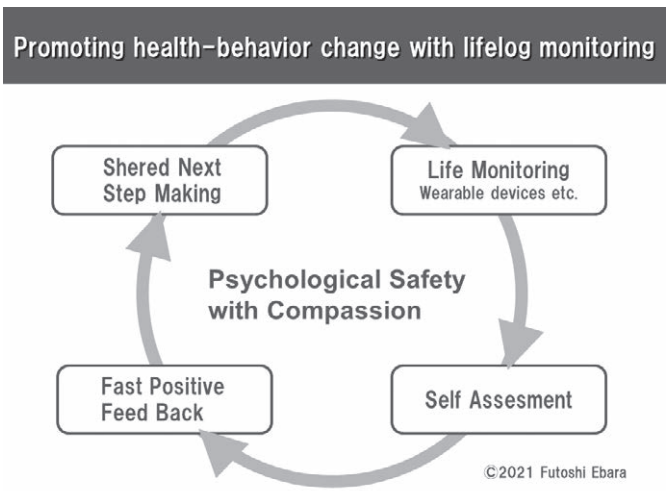
Background
PHR apps are useful in managing diabetes patients. On the other hand, patients often drop out due to security and usability issues caused by the use of smartphones.
This study will evaluate the efficacy, and intervention characteristics of PHR app with gamification theory and wearable devices to promote continuity and health-behavior change.

Method
The subjects were 30 patients with type 2 diabetes attending an outpatient clinic. The PHR APP for promoting health-behavior change strategy was implemented with 7 items based on gamification theory. Patients were briefed on the use of the APP. Satisfaction were surveyed for each of the seven items by portfolio analysis before and 24 weeks after the survey. Continuity and improvement levels were assessed by access frequency, medication adherence, and glycemic control .

Result
Twenty-seven cases were analyzed.
Information from the subject was quantified in a diary-style lifelog, which was shared and feed back to be used for the following goal setting.
The seven items implemented were classified into four categories by portfolio analysis.
group1 = Most important (feature superiority of the app)
"Quantified by wearable device" and "calendar sharing by lifelog."
group2 = Important (evaluated as expected)
"Customization of achievement items" and "device-independent"
group3 = Improvement needed (possibility of promoting health-behavior)
"Medication adherence" and "immediate feedback"
group4 = untouched
"Competition"

Conclusion
This study could demonstrate the effectiveness of using gamification theory to use the PHR app for the efficacy of health-behavior change interventions. Further validation is needed for preventive interventions with diverse population.



WPEC-01-9
Electronic consultations of a framework for improving endocrinology and metabolism medical care in Western China

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Objective: To summarize and analyze the development of electronic consultations (E-consults) in a national medical center in western China. Limited studies are conducted during COVID-19 epidemic period.
Methods: A retrospective analysis was performed for E-consults cases of endocrine and metabolic diseases at West China Hospital of Sichuan University(WCHSU) from January 1 to December 31, 2022. The geographical

distribution of applicant institutions, disease composition, waiting for time, and effectiveness of e-consults were analyzed.

Results: A total of 114 E-consults patients with endocrine and metabolic diseases from 46 hospitals were included in the present study. Among them, the top three types were pituitary-adrenal diseases in 54 cases (47.37%, 54/114), glycolipid metabolism disorders in 27cases (23.68%, 27/114), and water-electrolyte and acid-base balance disorders in 15 cases (13.16%, 15/114). The waiting time for e-consultation was 29 patients (25.44%, 29/114) in 24 hours, 54 (47.37%, 54/114) in 48 hours, and 78 (68.42%, 78/114) in 72 hours. Among the 114 cases, 21 cases (18.42%, 21/114) were recommended for referral, of whom 16 cases were transferred to inpatient department, and 5 cases were transferred to outpatient clinic. The average referral time after e-consults was approximately 72 hours, with the shortest referral period being 26 hours.

Conclusion: E-consults conducted at WCHSU were effective and conducive to sharing high-quality medical resources and improving the professionalism of physicians in different hospitals in China. We agree that a more rigorous investigation of e-consults is warranted to incorporate them into clinical practice for future medical care.

WPEC-02-1

Changes of serum creatinine and adverse outcomes after post-contrast acute kidney injury

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Objective: To investigate the changes of serum creatinine (SCr) and adverse outcomes after post-contrast acute kidney injury(PC-AKI).

Methods: Diabetics who used contrast media(CM) from 2010 to 2020 at our institution were included. Participants were identified according to the following two schemes. Scheme 1 (n=5911), SCr was detected before and after using CM within 72 hours, Scheme 2 (n=81), SCr was detected within 24 hours before using CM and every 24 hours in three days after that. The baseline of SCr in patients with PC-AKI occurred in each stage, dialysis rate and mortality of patients with non-PC-AKI and PC-AKI, and mortality in different PC-AKI stages were compared.

Results: The baseline of SCr occuring PC-AKI within 3 days was higher than that in 4-7 days (P<0.05).The value continuously increased from 177.00 [150.50, 215.25] umol/l to 344.00 [333.00, 468.00] umol/l on the second and third day after PC-AKI. Furthermore, there was a statistical difference in the second day after PC-AKI compared to the first day (P<0.05). The dialysis and mortality in PC-AKI group were significantly higher than that in non-PC-AKI group (P<0.01). The in-hospital mortality gradually increased among the three groups of PC-AKI, and the rate in stage3 of CIN was higher than that in stage1 groups (*P*<0.01).

Conclusion: The possibility of delayed PC-AKI after using CM should be alarmed, despite the low basic SCr value. For those with elevated SCr in the first day after PC-AKI, SCr should be continuously detected in following two days to prevent its skyrocketing increase and adverse events.

WPEC-02-2

A utility of the uptake of loss and the vitamins supplying drink of blood vitamins by the haemodialysis

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【Aim】Nutritional management to limit potassium becomes important, and, for treatment of DKD and CKD and ESKD, an intake of vegetables and the fruit is limited.A report that some vitamins are wanting by the removal of vitamins with the dialyzator appears.When we drank vitamins supplying drink (125ml) this time, we were and compared serum vitamins value about the haemodialysis.

【Method】

We did drawing blood of before haemodialysis therapy and two times first when we did not drink vitamins supplying drink.We did drawing blood of before haemodialysis therapy of the next day and two times after having drunk vitamins supplying drink (125ml) next on 14th from the next day.

We compared serum vitamins level (A,B6, B12, folic acid, C), Hcy value, hs-CRP value.

【Rresults】

When we drank vitamins supplying drink, we showed the increase that serum vitamins (A, B6, B12, folic acid, C) were significant (p <0.01).

As for Hcy value, hs-CRP value, the significant difference was not found in uptake and the non-uptake time.

【Discussion】

The internal vitamins are less than a reference value conspicuously after having done haemodialysis in particular.

A utility with the avoidance of potential lack was suggested by continuing vitamins supplementation drink.

WPEC-02-3

Effect of nutrition education intervention on glycaemic control of individuals with type 2 diabetes mellitus

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Nutrition education is extensively used in improving the glycaemic control for better clinical management. Current study was conducted with the objective assessing the effect of nutrition education package on glycaemic control of individuals with type 2 diabetes mellitus (T2DM). Sixty (n=60) T2DM patients were randomly allocated either to receive the nutrition education programme (NEP) or general education programme (GEP). GEP consisted of 03 educational sessions on dietary management using plate model, foot care, physical activity, stress management and one group dietary counseling session. NEP offered three structured counseling sessions, cooking sessions and interactive discussion sessions in addition to the GEP. Dietary booklet, cooking recipe booklet and clinical chart were provided to the individuals of the NEP. Both groups were followed up to 16 weeks on the respective programme. Information on general lifestyle, disease and medication history was obtained using a general lifestyle questionnaire. Anthropometry, blood pressure, fasting plasma glucose and glycated haemoglobin concentration (HbA1c), dietary intake and physical activity level were assessed at the baseline (t=0 weeks) and end (t=16 weeks) of each study phase. T2DM followed the NEP, showed significant reductions in their body weight, waist circumference, fasting plasma glucose and HbA1c concentrations compared to the baseline and control group. Improvements in dietary intake and engagement in physical activities and accompanied reductions in the body fatness may have contributed to the favorable glycaemic control of T2DM following the NEP. Therefore, it can be concluded that NEP was effective in improving the glycaemic control of T2DM compared to the GEP.

WPEC-02-4

Study on the effects of Medical Nutrition Therapy for patients with Type 2 Diabetes

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Patient education is an essential component of diabetes care. Diabetes self-management education aims to empower the person with diabetes with knowledge, skills and the motivation necessary for performing appropriate self-care.

Individualized Medical Nutrition Therapy (MNT) implemented in collaboration

with the individual with diabetes is essential because a variety of nutrition interventions are effective.
Strong evidence supports the effectiveness of MNT provided by registered dietitian nutritionist (RDNs) on HbA1c with decreases up to 2.0% at 3 months, and with ongoing MNT support, decreases were maintained or improved long-term and also supported the positive influence of MNT on medication use and quality of life. RDNs serve as facilitators for lifestyle modification to prevent diabetes, coaches for diabetes self-management and supporters for diabetes complication management.
Yet, very few patients receive structured education, even though structured self-management education is recommended for all people with T2DM.
This study aims to probe the effects of nutritional education of the patients with Type 2 diabetes
Among patients who received diabetes education, we would like to present the results of observing blood glucose changes before and after nutrition education (3 months after education) without changing medications.

Table. Changes in laboratory data according to before and after dietitian's intervention

	n	Dietitian's intervention		t-value	p-value[1]
		Before	After		
		M± SD			
Fasting blood sugar	45	157.96 ± 37.99	143.67 ± 36.08	2.26	0.029*
HbA1C	44	8.24 ± 1.02	7.67 ± 1.01	5.40	<0.001***
Total cholesterol	44	159.50 ± 37.62	145.80 ± 34.12	3.90	<0.001**
Triglyceride	43	148.47 ± 102.96	130.56 ± 64.17	1.88	0.068
HDL_cholesterol	43	50.86 ± 17.56	51.72 ± 18.07	-0.64	0.524
LDL_Cholesterol	43	86.81 ± 24.34	77.88 ± 20.32	3.06	0.004**

[1]By paired t-test
*$p<0.05$, **$p<0.01$, ***$p<0.001$

WPEC-02-5
DIABETES AND HEALTHY PLATE DIET

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Objective
The diabetes plate meal method is the easiest way to create healthy meals that can help manage blood sugar. The aim of study was to compare blood glucose level before and after healthy plate diet lunch.

Methods
Cross sectional study included 194 patients: 74 (38%) males and 120 (62%) females with type 2 diabetes mellitus. Before and 2 hours after healthy plate diet lunch blood glucose level was measured. Paired T test was calculated.

Results
Type 2 diabetes mellitus patients' mean age was 54.5±12.2 years old, fasting blood glucose mean level mean was 11.9±5.4 mmol/l and postprandial glucose mean level was 11.4±4.7 mmol/l. Before and after healthy plate lunch blood glucose levels was non significantly different by paired T test(p=0.112)

Conclusions:
Healthy plate diet is helpful for better control of postprandial glucose of diabetic patients.

WPEC-02-6
Effect of Diabetes Self-Management Education (DSME) Program in Type 2 Diabetes Mellitus: Retrospective Real-World Study

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Objective: To study the real-world effect of diabetes self-management education (DSME) program on the clinical parameters for patients with type 2 diabetes mellitus (T2DM).

Methods: This is a retrospective observational real-world study at an Indonesian private hospital specialized diabetes clinic (SDC). Patients with T2DM with at least baseline and one other HbA1c, systolic and diastolic blood pressure (SBP; DBP), body mass index (BMI) and low-density lipoprotein (LDL) were included. Patients receiving DSME program was compared to those receiving targeted education by the attending physician (NDSME). Outcomes observed were change in HbA1c, SBP, DBP, BMI and LDL.

Results: A total of 172 and 61 patients were included as NDSME and DSME group, respectively. The baseline median for HbA1c is higher in the DSME group (8.9% [2.65] vs 7.8% [2.35], p=0.03). No significant difference found in the primary and secondary outcome both numerically or categorically in achieving targets. If anything, median reduction is slightly greater in the DSME group for HbA1c (-0.5% [1.75] vs -0.4% [1.85], p=0.58), LDL (-13.0 mg/dL [64.0] vs -12.0 mg/dL [58.0], p=0.40), and SBP (-3.0 mmHg [17.0] vs 0.0 mmHg [14.0], p=0.26). Further, Cohen's d effect size value suggested low practical significance for HbA1c (0.08), LDL (0.49) and DBP (0.27) and high practical significance for BMI (0.92) and SBP (0.91).

Conclusion: In an SDC, a comprehensive education program gives relatively similar clinical benefit in comparison to targeted education approach by the attending physician in managing T2DM. However, a larger real-world study would be needed to confirm the outcome.

WPEC-02-7
Making a brochure to use for efficacious education for type 1 diabetes patients

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Medications and devices for diabetes are varied and advanced. Basic knowledge and the latest information is required for type 1 diabetes (T1) patients. We made the brochure that contained 11 issues visually shown. After the IRB approval, we showed it to 60 T1 patients (male25, female 35), and requested them to fill out the checklist that asked whether they had ever been given the information or not. We also interviewed and gave them the specific information to compensate for their insufficient knowledge at the same time. 28 patients answered that the article described about "preparation for disasters" was useful. 24 answered "sick day rule", 16 answered "pregnancy and delivery" was useful. As a corollary, we newly prescribed glucagon nasal powder (Baqsimi®) for 4 patients, 2 decided to use continuous glucose monitoring (Dexcom G6®), and 2 started continuous subcutaneous insulin infusion. Because the population of T1 is relatively small, it is difficult for them to reach wide, deep, and the newest knowledge in the busy, crowded, and time-limited ambulatory system in Japan. We had developed the brochure specific for T1 to communicate, and to utilize the checklist to grasp their circumstances in a short period. We were able to provide practical knowledge and noticed patients' needs efficiently by using this brochure as a tool. It also made the opportunities to propose new treatments and devices to improve their quality of life.

WPEC-02-8
The oral hygiene educational intervention in patients with type 2 diabetes mellitus

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Objective: To investigate oral health educational intervention in patients with type 2 diabetes mellitus
Methods: This study was conducted as quasi-experimental design on 60 patients with type 2 diabetes referring to a diabetes center of Sukhbaatar Health center of Ulaanbaatar selected systematic sampling, who were assigned to two groups of control (N = 30) and intervention (N = 30). The data collection tool

was Oral Health Hygiene questionnaire and dental assessment which was completed by both groups before the intervention. Then, the intervention group received of oral hygiene practice educational program based in 1 months. The control group received only routine care which included a monthly visit by a doctor, diabetes educators, a dietitian, and a nurse for less than 20 min. The data were analyzed through SPSS version 25 software.

Results: The mean age was 52.36 ± 3.30 in the intervention groups and control groups 51.42 ±4.0 years of diabetic patients. Two months after the intervention, awareness of the patient's oral hygiene-related knowledge score and habits had a significantly increased in the intervention group ($p < 0.05$) and more increased females was significantly higher than that of males. In control groups oral health-related behaviors, such as brushing time 2 minutes, use of fluoridated toothpaste, and mouth rinsing after eating, resulted increased after oral hygiene educational intervention.

Conclusion: This study suggested that, in addition to diabetes health care and self-care practices, and oral hygiene education. The oral hygiene education can lead to positive attitudes to oral health in diabetic patients.

WPEC-02-9

The diabetes team is problem oriented to improve the safe insulin injection skills of non endocrine nurses

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Objective To explore the effect of problem oriented application of diabetes special nursing team in improving the safe insulin injection of non endocrine nurses.

Methods 372 non endocrinology nurses in our hospital were selected by random sampling, and the problems in the process of insulin injection education among non endocrinology diabetes liaison nurses were collected based on the problem orientation. The causes were analyzed, and the knowledge of safe insulin injection was investigated. At the same time, 38 nursing units in the hospital were assessed for safe insulin injection operation, and corresponding improvement plans were formulated and implemented according to the analysis results, Check the implementation and effect of the plan during implementation.

Results The flow and guidance path of insulin injection education were developed, and the injection education kit and other measures were developed. 372 questionnaires were all recovered, with 100% effective rate. Non-endocrine nurses lacked knowledge of insulin injection safety; The qualified rate of theoretical knowledge before training is 72.2%, the qualified rate of operational skills is 84.6%, and the qualified rate of theoretical knowledge after training is 88.8%; The qualification rate of operation skills before training is 95.53%.

Conclusion Non-endocrine department nurses lack relevant knowledge about safe injection of insulin. After receiving the training on safe injection of insulin, their theoretical knowledge and operational ability have increased, thus ensuring the safety of insulin use, improving the standardization of insulin pen injection, and ensuring the correctness of insulin use of non-endocrine department nurses.

WPEC-02-10

Effects of Mobile eHealth Literacy on Self-care Behaviors in Taiwanese Patients with Type 2 Diabetes

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To validate the associations between clinical characteristics, mobile eHealth literacy, self-efficacy, and self-care behaviors in Taiwanese type 2 diabetes (T2DM) patients. Overall, 250 patients with T2DM were recruited from the outpatient departments of a single medical center in northern Taiwan through convenience sampling. Data regarding personal clinical characteristics, mobile eHealth literacy, self-efficacy, and self-care behaviors were collected. The diabetes self-care behaviors scale included items pertaining to diet management, exercise, adversity prevention, blood sugar monitoring, and medication adherence. The mean age was 52.6±11.2 years and males were predominant (68%). The average points of the self-care behaviors scale were 61.2±11.5 (total of 72 points). The results showed a significant positive association between each item of the self-care behaviors scale and age, mobile eHealth literacy, and self-efficacy. However, the most significant association between items of self-care behaviors scale and age (blood sugar monitoring), mobile eHealth literacy (diet management), and self-efficacy (diet management) were different. In summary, first, our study elucidates the association between mobile eHealth literacy and items of self-care behaviors. Second, our data also amplifies the correlation between clinical characteristics, self-efficacy, and self-care behaviors as in previous studies. Enhancing mobile eHealth literacy and self-efficacy is important to improve self-care behaviors and may subsequently influence glycemic control in type 2 diabetes patients.

WPEC-03-1

Outcome of intensive treatment for obesity at our hospital

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Ehime University Graduate School of Medicine

Since 2006 at our hospital, lifestyle modification, such as diet and exercise, for obese patients has been provided through a team approach with a physician, dietician, nurse, physical therapist and psychologist. From 2016, a surgeon and anesthesiologist were added to the team for metabolic/bariatric surgery. The aims of this study are to clarify the effectiveness and problems of lifestyle modification, and to clarify the characteristics of patients who transferred for surgical treatment. The intake energy is (resting energy expenditure + exercise energy) x 0.9. The regular exercise is more than 5000 steps per day. Until now, 150 obese patients (mean age of 50 years and mean BMI of 36) have received medical management, and the mean BMI significantly decreased by 1.2 over 3 months. Thirty patients (20%) have transferred for surgical treatment. Seventeen patients had diabetes with a BMI of 31-48 and HbA1c 8-9% despite intensive therapy. The complete (HbA1c < 6 % without diabetic medication) and partial (HbA1c < 6.5 % with some medication) remission of diabetes was achieved in 70 % and 30 %, respectively. Serum C-peptide levels were significant higher in patients with the complete remission of diabetes than that in patients with the partial remission. In conclusion, diabetic patients need a lower BMI for metabolic / bariatric surgery compared with non-diabetic patients, and baseline serum C-peptide level has a major influence on outcome.

WPEC-03-2

The Role of Urokinase Plasminogen Activator on Irisin and Insulin Resistance During Exercise

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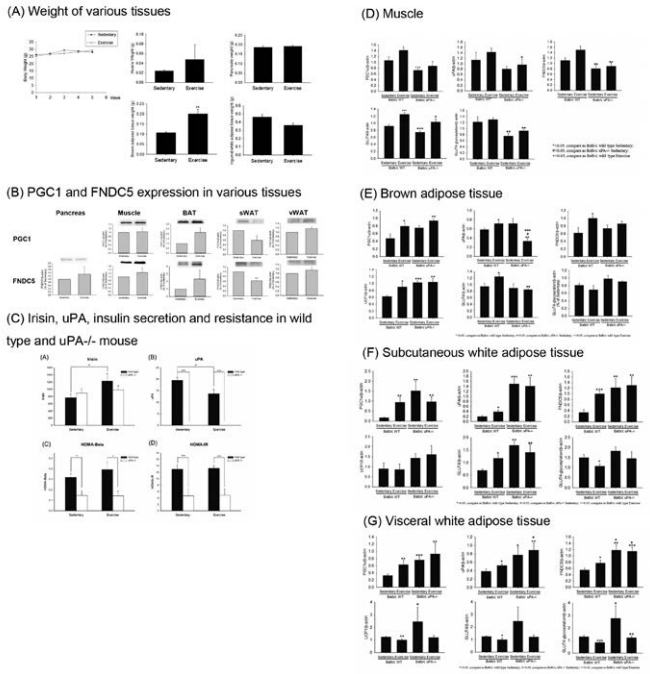
Objective: Urokinase plasminogen activator (uPA) was associated with the development of type 2 diabetes mellitus in our previous study. Irisin, a novel myokine secreting from muscle during exercise, improves insulin resistance and browns white adipose tissue. In the present study, we explored the role of uPA on muscle and adipose tissues during exercise.

Methods: Wild type and uPA knockout (uPA-/-) BALB/c mice were divided into sedentary and exercise groups. In exercise group, the mice ran on a motorized treadmill for four weeks. The femoral muscle, brown adipose tissue (BAT), subcutaneous and visceral white adipose tissues (sWAT, vWAT) of each group were harvested after euthanization.

Results: In the exercise group, the weight of muscle and BAT in wild type mice increased significantly. In addition, the expressions of PGC-1α and FNDC5 increased in BAT and decreased in sWAT in exercise group. Serum irisin levels significantly increased after exercise in wild type mice, but not in uPA-/- mice. In muscle, the amplified amounts of the PGC-1α, FNDC5, and GLUT4 expression in uPA-/- mice were fewer than that in wild type mice. Similarly, the same results also showed in BAT, sWAT and vWAT in uPA-/- mice.

Conclusion: The uPA may contribute to myokine, irisin, improving insulin resistance in skeletal muscle and adipose tissues during exercise. However, the real mechanism needs further study in the future.



WPEC-03-3
THE EFFECTIVENESS OF DIABETIC FOOT EXERCISE USING SPONGE AND PLASTIC BALL IN INCREASING FEET SENSITIVITY

Abd. Gani Baeda, Abd. Gani Baeda
University of Sembilanbelas November

Aims: compare the effectiveness of diabetic foot exercises using sponge media and plastic balls in increasing foot sensitivity in type 2 diabetics. Methods: with a quasi-experimental method approach consisting of pre and post test control groups. design. Sampling by purposive sampling consisting of 30 respondents according to the specified criteria. A total of 15 respondents in the foot exercise intervention group using a sponge and 15 respondents in the foot exercise intervention group using a plastic ball. Data collection used 10 g monofilament to measure foot sensitivity. Monofilament was used at 10 point locations on the left and right feet. Examinations were carried out before and after diabetic foot exercises, with a scale of 0-10.

Data collection was presented in univariate, bivariate, and multivariate analysis. Results: Foot sensitivity in the sponge group averaged 4.87 on the right foot and 4.73 on the left foot, while the ball group on the right foot averaged 4.47 and the left foot was 3.67. There was an increase in foot sensitivity in the sponge group after being given the intervention, on the right foot p = 0.001 and the left foot p = 0.001, while the ball group had an increase in sensitivity on the right foot p = 0.023 and the left foot statistically there was no change with p = 0060 but Clinically there is increased sensitivity. Conclusion: Foot exercises using a sponge are more effective in increasing the sensitivity of the feet

Keywords : Diabetic Foot Exercise Sponge Plastic ball, Sensitivity

WPEC-03-4
Study on the effect of high interval exercise in pre-diabetic population

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[Abstract] Objective: In order to delay the progression of prediabetes, to evaluate the correlation between high interval exercise and the progression of diabetes by guiding the application of high interval exercise in people with prediabetes, and to evaluate the comparative study before and after the intervention of HBA1c after exercise

Methods: In this study, a total of 280 patients with prediabetes who underwent physical examination from October 2021 to October 2022 were selected as the research objects, 140 cases were randomly selected as the experimental group and the rest as the control group. The experimental group received high intermittent exercise intervention. The control group was not subjected to exercise intervention, and both groups were reexamined for glycosylated hemoglobin 6 months later.

Results: After the implementation of high intermittent exercise intervention, the HBA1c of the experimental group decreased by 1.5% on average, while the HBA1c of the control group did not change significantly. The difference was statistically significant.

Conclusion: High interval exercise is beneficial to prediabetes

WPEC-03-5
A study of obesity risk in relation to diet habits and frequency of physical activity

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Study aim: To study the association between diet habits, frequency of physical activity and obesity risk

Materials and methods: In this cross-sectional study, we used data (N=2004, mean age of 41.1 ± 13.6 and 29.2% (N=586) males) from the Mon-Timeline cohort study, which is a multidisciplinary, prospective, population-based cohort study in Mongolia. Food consumption of 6 food groups was studied using a 24-hour diet diary to assess the ratio of 6 groups which recommended in the "Ger recommendations". Physical activity was assessed with the questionnaire developed by WHO. When body mass index (BMI) above 30 kg/m^2 is considered as obesity.

Results: Of the total calories, 44.7% were grains, 29.2% were meat and protein products, 9.3% were fats, 7.1% were dairy products, 6.6% were vegetables, and 3.1% were fruits. In terms of gender, women consumed more fruit and milk than men. Of all the participants, 51% of those involved did not engage in regular physical activity or sports at all, and the proportion of people who do moderate intense physical activity for more than 150 minutes a week according to WHO was very low at 16.7%. In the multivariate Regression analysis, the risk of obesity (OR, 95% CI) was higher in people who do not follow the diet recommendations such as consume less fruits (OR=1.47, 1.25-1.73) and vegetables (OR=1.25, 1.08-1.44) and people who do not exercise regularly (OR=1.56, 1.19-2.03) respectively.

Conclusions: Unhealthy diet and lack of physical activity might be the main risk of obesity among Mongolians.

WPEC-03-6

Impact of Metabolic-Bariatric Surgery on glycemic and metabolic outcomes in an Asian cohort: a 10-year follow-up study

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Objective

Metabolic-bariatric surgery (MBS) has been shown to produce sustained weight loss in persons with obesity. However, data on it's long-term glycemic and metabolic effects is limited, especially in Asian populations, which have a higher prevalence of Type 2 Diabetes (T2D).

We aim to report the long-term effect of MBS on glycemic and metabolic outcomes in Asian populations.

Methods

Demographics and biochemical parameters of patients who had MBS from 2008-2011 were obtained from a web-based data repository at a tertiary centre in Singapore. T2D remission was defined as HbA1c ≤6% without T2D medications.

Results

Our study included ninety-one patients, of which 61.5% underwent sleeve gastrectomy and 38.5% underwent gastric bypass. Baseline weight was 119.4±29.1 kg, with weight loss of 29.5 kg (24.5%), 27.8 kg (23.3%) and 26.1 kg (21.5%) at 2, 5, and 10 years respectively. Thirty-six patients (39.5%) had T2D prior to MBS. Among those with pre-existing T2D, HbA1c decreased from 8.11% to 5.90% at 2 years, 6.34% at 5 years and 6.67% at 10 years post-operatively. Average number of T2D medications used decreased from 1.72 to 0.17, 0.58 and 0.86 at 2, 5, and 10 years respectively. Of the twenty-nine (80.6%) patients who achieved T2D remission at 2 years, twenty-one patients (58.3%) maintained remission after 10 years. Five non-T2D patients (9.1%) developed newly-diagnosed T2D 10 years post-surgery. Use of anti-hypertensive and lipid-lowering medications also decreased over 10 years.

Conclusion

MBS is effective in achieving sustained weight loss, glycemic and metabolic improvement over 10 years in this Asian population.

WPEC-03-8

What is the image of diabetes in healthcare workers in Japan? (Survey of questionnaire)

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Diabetes support Team "Isu I-ssu"

[Objective]

There are few reports on stigma/advocacy targeting healthcare professionals. We investigated the real-world situation.

[Methods]

We administered a questionnaire on the perception of diabetes to healthcare professionals and non-healthcare workers.

[Results]

There were 1,193 responses (healthcare workers 559 / non healthcare workers 590 / others 44). (1) Interest of diabetes: P<0.001. (2) Resistance to diabetes: P=0.23. (3) Change of disease's name: P=0.90. The open-question responses are as follows: "I am familiar with the term 'diabetes'. There is no need to change it now"; "The pathology of type 1 diabetes is different from that of type 2 diabetes. I would like a different name for the disease"; "I would like the disease to have a name that conveys its seriousness to people"; "The name of the disease should be changed if it affects people with diabetes"; and "The word 'urine' has a negative connotation."

[Conclusion]

Although the healthcare professionals were more concerned about diabetes than the non-healthcare professionals were, there were no significant differences between their responses to the other questions. In Japan, the term "sugar urine disease" called by Japanese is so prevalent that many people do not feel uncomfortable with it. We recommend establishing a diabetes support team led by a Certified diabetes care and education specialist and actively supporting educational activities for the public, including children, and education at universities and nursing schools. Appropriate advocacy can change attitudes toward diabetes, leading to a stigma-free society.

WPEC-03-9

Stigma and psychological burden faced by people with type 1 diabetes who don't disclose their feelings to friends

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<Background>

Given the stigma around type 1 diabetes (T1D), some individuals with T1D do not disclose their diagnosis. It is important to ensure that people with T1D do not bear the burden of T1D alone.

<Objective>

To investigate the frequency and clinical/psychological background of individuals who do not express their feelings about T1D to their close friends and family.

<Methods>

A single-center, cross-sectional survey was conducted among adults having T1D. All participants completed self-administered questionnaires which included Diabetes Stigma Assessment Scale (DSAS-1), Problem Areas in Diabetes Scale-5 (PAID-5), General Anxiety disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9), Rosenberg Self-esteem scale, General Self-efficacy scale, and questions regarding the presence or absence of severe hypoglycemia and retinopathy, educational background, and marital status. Participants' age, duration of T1D, and HbA1c were obtained from their medical records. Logistic regression analysis was used to analyze the data.

<Results>

Of the 396 participants (106 men, mean age 48±13 (SD) years, duration 27±13 years), 131 (33%) did not talk to close friends, and had higher scores on DSAS-1 (p<0.0001), PAID-5 (p<0.01), GAD-7 (p<0.05), and PHQ-9 (p<0.05). Additionally, 47 (12%) did not talk to family members, and had higher scores on DSAS-1 (p<0.05) and PHQ-9 (p<0.0005)and marital status (p<0.05).

<Conclusion>

One in three adults with T1D was unable to share their feelings regarding their condition with their close friends. These people face a significant psychological burden. Therefore, reducing social stigma and healthcare professionals must listen to patients' feelings to establish person-centered collaborative care.

WPEC-04-1

Relationships between Autonomous Motivation for Diet and Quality of Life in People with Type 2 Diabetes

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Objective

The goals of diabetes treatment are to prevent or delay complications and optimize quality of life (QOL); dietary self-care activities are essential to achieve such goals. However, engaging in dietary self-care activities can also

impair QOL. Some studies based on self-determination theory have shown that autonomous motivation for health behaviors positively affects QOL. However, no studies exist regarding the impact of autonomous motivation for dietary self-care activities on QOL for people with type 2 diabetes.

Methods
This study is cross-sectional, with a questionnaire. We recruited participants with type 2 diabetes over 18 years old at a university hospital from August 2022 to January 2023. Using structural equation modeling, we investigated relationships between autonomous motivation and competence for, and implementation levels of dietary self-care activities, respectively, as well as overall and diabetes-dependent QOL.

Results
Complete responses were obtained from 223 participants. Results showed that autonomous motivation for dietary self-care activities was related to overall QOL through competence for and/or implementation levels of dietary self-care activities but not to diabetes-dependent QOL. There was no direct impact from autonomous motivation on QOL.

Conclusion
The lack of significant direct impact from autonomous motivation on QOL may be because of possible higher autonomous motivation in those who thought diabetes had a greater impact on their lives. Healthcare providers should support people with type 2 diabetes to increase their autonomous motivation for dietary self-care activities and confirm changes in their competence and frequency of dietary self-care activities to improve their QOL.

WPEC-04-2
Effectiveness of Combination Use of a Lifestyle Improvement Support App and a Wearable Device in People with T2DM

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Objective: Despite the availability of various therapeutic agents for type 2 diabetes mellitus (T2DM), about half of patients do not achieve their glycemic control targets in Japan. In recent years, apps and wearable devices supporting diabetes treatment have rapidly spread. However, evidence of their impact, especially in combination, is limited. This is the first study to explore the effectiveness of combination use of a lifestyle improvement support app (TOMOCO™ Mitsubishi Tanabe Pharma Co.) and a wearable device (Fitbit) to improve glycemic control in Japanese people with T2DM with insufficient glycemic control (jRCT1070220007).
Methods: In this single-arm, exploratory study, the participants used TOMOCO™ and Fitbit in addition to conventional diet/exercise and anti-diabetic drug therapy for 12 weeks, and were provided feedback/advice based on TOMOCO™ and Fitbit records from health care providers (Figure). The primary endpoint was the change in HbA1c and major secondary endpoint was the change in body weight.
Results: Of 61 patients enrolled, 59 completed the study (HbA1c: 7.57 ± 0.42%, Body weight: 69.12 ± 13.36 kg; at baseline). At the end of the observation period, HbA1c was significantly decreased (-0.41 ± 0.41%; range -1.9 to 0.7, $p<0.001$) and body weight was also reduced (-0.88 ± 1.58 kg; range -5.7 to 2.1, $p<0.001$), and the trend was consistent across the pre-specified patient background.
Conclusion: Combination use of a lifestyle improvement support app and a wearable device with conventional therapy may be effective for glycemic control in people with T2DM.

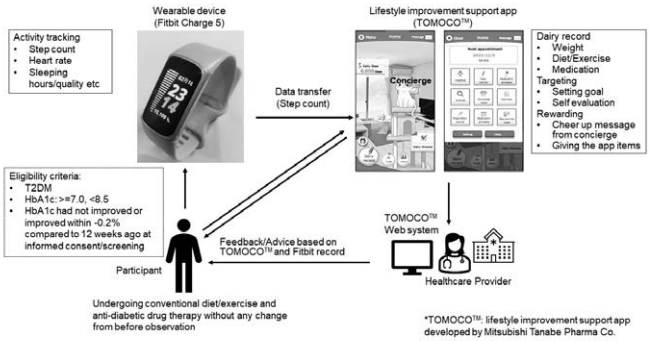

Figure) Combination use of a lifestyle improvement support app and a wearable device

WPEC-04-3
Association between self-care and depression in pediatric patients with type 1 diabetes during the COVID-19 pandemic.

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Objective
To determine the association between type 1 diabetes self-care behaviors and depression in children whose diabetes camps were cancelled due to the COVID-19 pandemic.

Methods
A self-administered questionnaire using attributes, change in care environment, diabetes self-care scale, and depressive scale was administered to 218 children with type 1 diabetes in August 2022.

Results
Data from 74 respondents from 15 camps nationwide were analyzed. The mean age was 13.5 years, age of onset was 5.8 years, HbA1c level was 7.9 mg/dl, and the number of camps attended was 3.8. There was no change in HbA1c, frequency of hypoglycemia or hyperglycemia, exercise time, or eating out during the corona pandemic.However, 63.5% of the children reported that they spent more time playing games. Scores on the self-care scale were above 80% for independence in treatment behaviors and daily living and blood glucose measurement, but scores for food intake and blood glucose control and consultation with a health care provider or teacher were low at 50%.Depression scale scores were significantly higher in the depressed group, and there was a significant negative correlation between total depression scale scores and total self-care scale scores ($r=-652$, $p<0.01$). The children felt isolated because they could not meet their peers due to the cancellation of the camp.

Conclusion
Although the children were able to maintain diabetic self-care, the cancellation of the camp increased their sense of isolation. The need for face-to-face camps as a place to interact with peers and exchange information was suggested.

WPEC-04-4
An observational study on diabetes distress among adults living with diabetes mellitus in Japan

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Objective. The objective of this study is to clarify mechanism concerning change of diabetes distress and its coping strategies by general treatment for two years among adults living with diabetes.
Methods. A self-reported questionnaire on diabetes distress and its coping strategies and self-efficacy was administered to adults living with diabetes (Phase 1). We selected the participants who had diabetes distress at Phase 1 and

continued general treatment of diabetes for two years. Eighty-seven participants answered the questionnaire at Phase 2 (two years after Phase 1).
Results. There was a significant decrease of feelings about diabetes distress from Phase 1 to Phase 2. There was a marginally significant decrease of threat to diabetes and a marginally significant increase of HbA1c from Phase 1 to Phase 2. The participants were categorized into four groups based on the changes of feeling of diabetes distress and HbA1c from Phase 1 to Phase 2. The participants categorized as the group of increase of feeling about diabetes distress and HbA1c from phase 1 to phase 2 showed marginally significant decrease of self-acceptance, keeping to an adequate diet and exercising as coping strategies from Phase 1 and Phase 2. The participants categorized as the group of decrease of feelings about diabetes distress and HbA1c from phase 1 to phase 2 showed marginally significant decrease of constant behavioral demands and treatment as thoughts of diabetes distress.
Conclusion. Coping strategies on self-acceptance, diet, and exercise may be important to take care of diabetes distress and glycemic control.

WPEC-04-5
COMPARISON OF CHRONOLOGICAL AND BIOLOGICAL AGE OF TYPE 2 DIABETIC PATIENTS

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Objective
Studies have relieved a biological age different to the chronological age (printed on passport). Some people's age much faster than others and aging advances at different rates according to factors like health, fitness, diet and life style. The aim of study was to compare chronological and biological age of type 2 diabetic (T2DM) patients.

Material and Methods
Cross sectional study included 131 patients: 76(58%) males and 55(42%) females with T2DM, admitted in hospital. Physical examination, blood glucose and HbA1C were determined. Body composition (body mass index, body fat, body muscle, body age and visceral fat) was measured by Xiaomi-XMTZC05.

Results:
T2DM patients' mean age was 48.5±12.1 years old, body weight 84.5±15.3 kg, height 166.9±9.2 cm, body mass index (BMI) 31.1±9.7 kg/m^2, body fat(BF) 39.3±12.1%, body muscle (BM) 41.1±14.9%, body age 58.6±13.0 years old, visceral fat(VF) 12.1±3.6%, metabolic rate (MR) 1694±292.2 kcal, fasting blood glucose (FBG) 12.11±4.0 mmol/l and mean HbA1C was 9.8±2.4%, respectively. Mean body age and mean passport age was different (58.6±13.0 years old vs 48.5±12.1 years old; $p<0.001$) in T2DM patients.

Conclusions:
Biological age is much older than chronological age in T2DM patients.

WPEC-04-6
Association of psychosocial characteristics on quality of life in patients newly diagnosed with type 2 diabetes

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This study aimed to examine the relative association of positive and negative psychosocial characteristics with quality of life in patients newly diagnosed with type 2 diabetes. A cross-sectional design was employed. Totally, 195 participants aged between 20 and 64 years old and diagnosed type 2 diabetes more than five months but less than 18 months were recruited by convenience sampling from three outpatient clinics in Taiwan. Demographic and disease characteristics, positive psychological characteristics (optimism, gratitude, resilience), negative psychological characteristics (self-stigma, Type D personality with subscales of negative affectivity and social inhibition) and quality of life were collected by self-report questionnaires. The HbA1c and body mass index were collected from medical record of participants. Multiple regressions were conducted to analyze the significant psychological characteristics associated with quality of life. Results showed that HbA1c levels (r = -0.172), negative affectivity (r = -0.441), social inhibition (r = -0.275), self-stigma (r = -0.372), optimism (r = 0.299), gratitude (r = 0.168) and resilience (r = 0.340) were significantly associated with quality of life. Multiple regression analysis indicated that HbA1c levels (β = -.184), negative emotion of Type D personality (β = -.326), and self-stigma (β = -.236) were significantly associated with quality of life. Findings of this study supported that negative psychological characteristics are more crucial than positive psychological characteristics to associate with quality of life. Early assessing the negative psychological characteristics and provide needed intervention to improve quality of life is needed for patients newly diagnosed with type 2 diabetes.

WPEC-04-7
CENTRAL OBESITY IN TYPE 2 DIABETIC PATIENTS

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Objective
Type 2 diabetes is strongly related to overweight and obesity. Central obesity (intra-abdominal) is observed in the majority of patients with type 2 diabetes (T2DM). The aim of study was to evaluate the central obesity of T2DM inpatients.
Materials and methods
Cross sectional study included 131 patients (male 76/58%, female 55/42%). with T2DM admitted in hospital. Physical examination (height, weight, waist circumference and blood pressure), blood glucose and HbA1c were determined. Body composition (body mass index, body fat, body muscle and body age) was measured. Central obesity was determined by Asian and European criteria of waist circumference.
Results
T2DM patients mean age was 48.5±12.1years old, body weight 84.5±15.3kg, height ±12.4cm, body mass index (BMI) 31.1±9.7kg/m^2, body fat (BF) 39.3±6.2%, body muscle (BM) 41.1±14.9%, body age 58.6±13.0 years old, visceral fat (VF) 12.1±3.6%, metabolic rate (MR) 1784±392.2kcal, fasting blood glucose (FBG) 8.9±3.9mmol/l and mean HbA1C was 9.8±2.4%. Male patients' mean WC was 106.5±12.8cm and VF was 13.9±3.4% but female patients' mean WC was 100.5±9.5cm and VF was 9.6±2.1%. Among T2DM patients: males with WC <94cm, 95-102cm and >102cm was 9.3%, 31.5% and 59.3%, respectively; females with WC <80cm, 81-88cm and >88cm was 20%, 0% and 80%, respectively.
CONCLUSION:
Among T2DM patients central obesity was determined 94% in male and 80% in female by Asian criteria, but 59.3% in male and 80% in female by European criteria.

WPEC-04-8
Pathways of Character strengths, diabetes distress, self-management behaviors to quality of life in patients with T2DM

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Objective In the 21st century, diabetes is one of the fastest growing chronic diseases worldwide. Although factors including diabetes distress and self-management behaviors were found to associate with quality of life, the possible pathway among these were not well studied. Furthermore, positive psychological states such as character strengths' use on association with quality of life were less evaluated. The aim of this study was to examine a hypothetical model linking diabetes distress, character strengths use in self-management behaviors, and self-management behaviors to quality of life in patients with type 2 diabetes.
Methods A cross-sectional study design was applied and 343 participants diagnosed with type 2 diabetes were recruited. Path analyses and bootstrap analyses were applied to test hypothesized pathways among variables.
Results After controlling gender, type of treatment, age, HbA1C, and duration of diabetes, self-management behaviors were positively and significantly

associated with quality of life (β = 0.161, p < 0.001). Diabetes distress was significantly and negatively associated with quality of life (β = -0.536, p < 0.001). Character strengths use in self-management behaviors had significant indirect effect (β = 0.126) on quality of life.

Conclusion Diabetes distress was more crucial than self-management behaviors and character strength use, which contributed to quality of life. Character strengths use in self-management seemed more connected with self-management behaviors than with quality of life. Accordingly, nurses led strength-based intervention could further be used to enhance character strength use in self-management behaviors, and eventually improve the quality of life in patients with type 2 diabetes.

WPEC-04-9

Development and validation of the Chinese Brief Version of Spiritual Need Scale for Patients with Chronic Diseases

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Spirituality is one of the main factors associated with good health outcomes among patients with chronic diseases. A reliable and valid instrument to measure spirituality is essential to identify the spiritual needs of an individual and to evaluate the effect of spiritual care. The study developed and examined the brief Chinese version psychometric properties of the spiritual need scale in patients with chronic diseases (SNCD). This was a cross-sectional study among 272 patients with chronic diseases who were recruited in the three outpatient diabetes clinics in Taiwan. A well-trained nurse applied standardized procedure to interview the patients when they visited clinics. The psychometric testing of the spiritual need scale for patients with chronic disease included construct validity with confirmatory factor analysis, validity and internal consistency reliability. The results of the confirmatory factor analysis supported the five-factor model as an acceptable model fit. Five subscales (related to beliefs/religion, transcendence, connected with others, meaning derived from living, and peaceful mind) were extracted from an exploratory factor analysis. The five subscales accounted for 77.26% of the variance. The evidence based on concurrent validity was supported by a significant correlation between the social support scale (r=. 519) and the PAID-C(r= -.166). Cronbach's α value (0.93) demonstrated internal item consistency of the SNCD. This preliminary 13-item and 5-factor constructed SNCD demonstrated a valid and reliable instrument to assess the spiritual needs of patients with chronic diseases in Taiwan. Furthermore, it is a manageable tool for chronic diseases nursing practitioners to gage their patients' spiritual needs.

WPEC-04-10

Establishment of the risk prediction model of hypoglycemia fear in patients with type 2 diabetes mellitus

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Objectives onstruct the risk prediction model of fear of hypoglycemia (FoP) in T2DM-patients, to provide evidence evaluation and coping FoP T2DM-patients.

Methods Type 140 patients withT2DM hospitalized in the department of Endocrinology of our hospital from February to July 2022 were selected with convenience sampling .general information questionnaire,Fear of Hypoglycemia Scale-15,CHFSII-WS,Self-Rating Anxiety Scale,Self-rating Depression Scale,According to whether they had FoP or not, they were divided into two groups: non-FoP group (N = 70) and FoP group (N = 70),Logistic regression analysis used establish the risk prediction model, and the area under the ROC curve was used to test the prediction effect of the model.

Results the incidence of FoP was 60.45% inT2DM-patients,the monofactor analysis showed Whether knowing the manifestation of hypoglycemia, whether know hypoglycemia-treat , rate of hypoglycemia in half-a-year, the most serious degree of hypoglycemia, whether having hypoglycemia at night, whether participat the health education about hypoglycemia are the influencing factors of FoP in T2DM-patients the early risk hypoglycemic prediction models Inclusion half-a-year the hypoglycaemia happened > once-a-month (OR=1.000), the most severe hypoglycaemia was Heavy-hypoglycaemia (OR= 6.40), Model formula Z = 25.375-19.922 ×half-a-year hypoglycaemia happened > once-a-month ×Heavy-hypoglycaemia. half-a-year the hypoglycaemia happened > once-a-month the area under the ROC curve was 0.852,sensitivity was 0.818, the Heavy-hypoglycaemiaarea under the ROC curve was 0.801.

Conclusion The model can effectively predict the occurrence of FoP in T2DM, and it can provide reference for medical staff to take preventive nursing intervention on FoP in early .

WPEC-05-1

Telephone encouraging in-person consultations at medical institutions in the Prevention program for diabetic nephropathy

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The purpose of this study is to determine whether telephone-based recommendations for consultations for those who have not yet undergone treatment and those who have suspended treatment in the Diabetic Nephropathy Aggravation Prevention Program contribute to improving the consultation rate at medical institutions and the rate of continued consultations. Twenty-six municipalities nationwide were assigned to an intervention group and a control group; a cluster randomized controlled trial was conducted.

A total of 8,271 subjects (4,189 in the intervention group and 4,082 in the control group) were selected and mailed letters recommending medical examinations. In the intervention group, public health nurses and registered dietitians called 2,927 people for whom phone numbers were available using the call manual prepared by the research group (1,398 people were successfully contacted, 626 people twice). Receipts and medical checkup data of 7,760 subjects (16.1% who had not received treatment and 83.9% who had discontinued treatment) were extracted from the KDB system and analyzed. The consultation rate was significantly lower in the intervention group (21.3%) than in the control group (24.8%) and the continuous consultation rate was even lower in the intervention group (11.6%) than in the control group (13.0%). Telephone-based recommendations for consultation clearly do not increase the consultation rate or the continuous consultation rate. Other methods such as SNS and those that provide incentives for medical examinations might be helpful.

WPEC-05-2

Self-care Nonadherence among Diabetes Patients in Home Health Care Settings

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Objective

There are many examples of diabetes patients who struggle in non-adherence situations. This work was aimed at providing an example of self-care nonadherence of a diabetes patient in the home health care setting.

Methods

Here, self-care nonadherence is discussed from the viewpoint of three aspects—the physician, patient, and situation—in the case of an 80-year-old woman with diabetes (blood glucose: 230-400, hemoglobin A1c: 9.00-11.0,

blood pressure: 120-140) who was transferred from an outpatient clinic to home care.

Results

The patient showed some cognitive impairment in the outpatient setting and was transferred to home health care. Later, her daughter, the key person, came to live with the patient. However, the living arrangement between the two failed, with the patient being deprived of daily activities such as cooking meals. The patient showed progressive cognitive decline and worsening of diabetes and was moved to a nursing home.

Conclusion

In terms of adherence difficulties, physicians were unable to develop a close relationship with the key person. From the patient's perspective, she was deprived of her independence by the key person. Regarding the situational perspective, the patient distrusted diabetes drug management and health care providers. I am acutely aware that from the perspective of ambivalence and socioeconomic context the relationship between the physician and the key person was inappropriate.

Items for screening social needs

Living place	Does the individual have a stable living place?
Meals	Can the individual get enough meals for financial reasons?
Means of transportation	Is the individual's means of transportation to commute to the hospital secure?
Lifelines	Has the individual had his/her gas, electricity, and water cut off?
Child-rearing support	Has the individual's work or education been interrupted owing to lack of support?
Employment	Does the individual have work?
Education	Did the individual have high school education or higher?
Economic status	Does the individual have trouble paying for daily expenses?
Personal safety	Has the individual ever been physically or emotionally abused?
Need for support	Does the individual need any type of help?

WPEC-05-3
DIABETES VISITS IN ENDOCRINE CLINIC

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Objective

The aim of study was to determine the proportion of visits of people with diabetes mellitus in outpatient department of Endocrinology, metabolism and diabetes specialized clinic.

Method

We analyzed one year outpatient registration of Endomed - Endocrinology, metabolism and diabetes specialized clinic, Ulaanbaatar, Mongolia. We used international classification disease 10 (ICD10) for registration of morbidity.

Results:

A total 4330 outpatient visits were registered. First and follow up visits were 60.3% (2611) and 39.7% (1719), respectively. Among them women were 68.9% (2986). The mean age of the patients was 42.4±13.7 years old. Visits due to diabetes mellitus were 34.2% (1480), thyroid disease 30.0% (1297), obesity 3.4% (148), pituitary disorders 0.7% (29), adrenal disease 0.1% (6), dyslipidemia 0.2% (9), vitamin D deficiency 0.1%(5), other endocrine disease 0.3%(13) and non-endocrine disease was 31% (1343) by the ICD10. Among the diabetes visit T2DM, T1DM, Prediabetes, GDM and Other type DM was 85.8% (1270), 4.1% (60), 7.6% (112), 2.3% (34) and 0.3% (4), respectively.

Conclusions:

1of 3 visits of endocrine clinic is due to diabetes mellitus. Type 2 diabetes mellitus is common among the diabetes visits.

WPEC-05-4
A qualitative study on the roles and challenges for the prevention of diabetes in the Filipino community health workers

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Background: Given the rising of diabetes prevalence, high healthcare resource constraints in the Philippines. Operating at the level of barangays, the smallest political unit, volunteer Barangay health workers (BHWs) play important roles as community health workers in the Philippines where the shortage of health professionals is felt more acutely.

Objectives: This study aimed to describe how BHWs perceive their role and the challenges related to the prevention of diabetes.

Methods: Data were collected from 25 participants through semi-structured interview. The thematic analysis by Braun and Clarke was performed. The institutional review boards of Kobe University's Graduate School of Health Sciences, Japan (approval number 1016) and University of the Philippines Manila (approval number UPMREB 2021-0704-01) approved this study.

Results: The mean age was 50.3 ± 9.5 years, 92.0% were women, and the mean experiences as BHWs were 9.4 ± 7.7 years. A total of seven major themes and 22 sub-themes were identified. The roles of the BHWs for the prevention of diabetes included "screening for diabetes", "symptom control for patients with diabetes", and "promoting healthy behaviors". The challenges against to the prevention of diabetes included "insufficient awareness of preventative behaviors", "economic burden for medical checkup", "lack of resources for managing diabetes", and "difficulty of access to medical care facilities".

Conclusion: BHWs could be in a unique position as the bridge between patients and health professionals for the prevention of diabetes. The findings are meaningful to develop the health care system for the prevention of diabetes in the Philippines.

WPEC-05-5
Oral Health Knowledge and Habits among adults with Type 2 Diabetes

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Objective: To determine oral health knowledge in and habits among adults with Type 2 Diabetes

Method:A cross-sectional study was conducted 60 adults' patients with type 2 diabetes from Diabetes Sukhbaatar Health center Ulaanbaatar, Mongolia received dental examinations using the Oral Health Hygiene questionnaire, glycated hemoglobin, blood pressure and anthropometric measurements. Statistical analyses were performed using the SPSS23 software.

Results: The men 43.6% , more than half of the participant's women 56.7%, the mean age was 52.36 ± 4.30 years. 31.7% of the adults had a family history of diabetes and 38.16 % current smoker, 12% ex-smokers, 49.8% non-smokers. The total adults' 34% were taking antihypertensive medication. Mean Oral Health Knowledge score was females (33.1 ± 1.8) was significantly higher than that of males (12.2 ± 2.1). The participants 71.3% brushed their teeth twice or more a day, and 24.8% performed once a day. Women (76.4%, were more likely to fear dentists or dental treatment than men (23.6%).Patients with HbA1c ≥ 7% suggesting poor control of diabetes were 2.73 times more likely to exhibit periodontal disease.

Conclusion: The study results recommended oral health education and follow-up during controlling, monitoring for T2DM patients.

WPEC-05-6

Adherence to recommended self-care behaviors and its related factors among Taiwanese patients with type 2 diabetes

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Objective:
The aim of this study is to investigate relationships between the degree of adherence to recommended self-care behaviors and its related factors among patients with diabetes.
Methods:
A cross-sectional evaluation was performed in adult outpatients aged 40 years and older with type 2 diabetes who had received both dietitian-led nutrition education and nurse-led diabetes education sessions for more than one year. Adherence of five diabetes self-care behaviors were assessed by using the Diabetes Self-Care Behavior (DSCB) questionnaire, and their influencing factors of each behaviors were investigated by using the Factors Affecting Diabetes Self Care (FADSC) questionnaire. Odds ratios derived from logistic regression analysis were used to identify predictive factors that resulted in adherence to self-care behaviors and its related factors.
Results:
A total of 201 patients was completed in this study and the average age was 60.2±12.1 years old. The most regularly self-care behavior was taking medications (87%). Patients who exercised regularly more had lower A1C levels (OR=0.32), healthier body mass index (BMI) (OR=0.49) and fewer chronic complications (OR=0.43). From the results of the influencing factors, we found that patients who had better understanding of health education had more self-care behavior such as following medication use (OR=1.61) and checking feet regularly (OR=1.26). Patients with fewer environmental barriers were more likely to follow self-care behaviors (all but checking feet). Those patients who experienced fewer complications of diabetes had better quality of life.
Conclusion:
Promoting self-care behaviors in diabetic patients contributes to better disease control and quality of life.

WPEC-05-7

Introducing AI-assisted diagnosis of diabetic retinopathy to improve the quality and efficiency of care for diabetic

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In Taiwan, about 3.5 out of every 10 diabetics over the age of 40 have retinopathy. Affected by COVIDE-19, the willingness of diabetics to undergo ophthalmic mydriatic retinal examination has decreased, and the examination rate of our hospital in 2020 was 36.16%, which decreased by 1.6% after the outbreak of the epidemic. In order to achieve early detection of lesions and timely treatment, the goal is to increase the fundus examination rate of diabetics by 40%.
The use of pupil dilation-free fundus photography equipment is performed by Certified Diabetes Educator who have completed the instrument training. Diabetics can go directly to the Diabetes Clinic to complete the examination after the same-day consultation, and the Certified Diabetes Educator uses AI-assisted analysis of the results to explain to the patient the necessity of referring for an eye examination.
In 2021, the fundus photography inspection rate in our hospital will be 28.6%, and in 2022, the fundus photography inspection rate will be 42.36%, reaching the planned target value.
The "AI fundus examination" through the software and hardware integration solution not only provides safe, simple and acceptable examination methods for diabetics under the influence of the COVIDE-19 epidemic, but also assists medical staff with non-ophthalmic specialties to initially and quickly screen patients with possible vision lesions. Effectively refer people with high-risk eye diseases to ophthalmology for follow-up treatment.

WPEC-05-8

Making a new style of peer education by online-meeting for type 1 diabetes patients

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Because of the lower prevalence of type 1 diabetes (T1) in Japan compared to Western countries, T1 patients seek opportunities of peer education. Under the COVID-19 pandemic, they have lost the chances of meeting with peers. We decided to hold online meetings for them. To protect their privacy, we provided the information of these meetings at patients' regular visits to our clinic. The participants were limited to T1 patients, their family, and our staff. We received identified email from them and sent the invitation URL. The meetings were held in the evening on Saturdays by using Zoom®. The participants chose to show their real name or nickname. 19 T1 patients (male 5, female 14) participated to the latest meeting. Average age was 57 years old, 15 were using intermittently scanned continuous glucose monitoring (isCGM), and 3 were using continuous subcutaneous insulin infusion (CSII) pumps. The diabetologist gave a small lecture about how to use CGM, and hybrid closed loop (HbCL) system. One of the patients gave a speech about her nearly 50 year history of life with T1 and resent years with CGM. After that, participants discussed with one another. One of the participants decided to start hbCL. Holding online meetings was somewhat technically challenging for the medical staff, but it still enabled new young T1 who usually would not have access to peer education, to participate.

WPEC-05-9

Psychometrics Properties of the Indonesian Version of the Audit of Diabetes-Dependent Quality of Life (ADDQoL-19)

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Objective: Diabetes mellitus (DM) is a chronic condition that has a major impact on reducing quality of life of people with diabetes. The Audit of Diabetes-Dependent Quality of Life (ADDQoL) is an extensively used individualized diabetes-specific quality of life measure. The aim of this study is to evaluate the psychometric properties of the Indonesian version of ADDQoL.
Methods: A total of 228 outpatients with type 2 DM were recruited from one hospital and one primary health care unit. Confirmatory Factor Analysis (CFA), internal consistency, test-retest reliability and known group comparison were analyzed in order to determine the psychometric properties
Results: the CFA test showed that ADDQoL-19 has a moderately fitting one factor structure, $\chi^2/df = 2.320$ ($\chi^2= 352.5$, df=152), Normal Fit Index (NFI)=0.755, Comparative Fit Index (CFI)=0.839, Tucker-Lewis Coefficient (TLI)=0.799, and Root Mean Square Error of Approximation (RMSEA)=0.078. All domains had factor loading values >0.4 except for two domains, namely 'holiday' (0.337) and 'working life' (0.221). Test-retest reliability (ICC=0.860; 95% CI=0.676–0.936) and internal consistency (Cronbach's alpha=0.894) were satisfactory. In terms of known group validity, the results showed that respondents who required insulin and had diabetes with complications had lower AWI and diabetes-dependent QoL scores than those who did not ($p<0.001$).
Conclusions: The Indonesian version of ADDQoL showed high internal consistency, good reliability, and acceptable validity.

WPEC-05-10

Estimated cost of CGMS for T1DM patients in Mongolia

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OBJECTIVE
Over 1.2 million children and adolescents have type 1 diabetes. In IDF

Diabetes Atlas 10th Edition 2021 reports, Mongolia has 185 children and adolescence (0-19 years old) with type 1 diabetes. The most accurate 14-day continues glucose monitoring system (CGMS) to help reduce time spent in hypoglycemia and improve overall glucose control. Aim of this study was to estimate cost of CGMS for type 1 diabetic patients around a year in Mongolia.

METHODS

We analyzed only 14-day continues glucose monitoring system (CGMS) costs by 200 type 1 diabetic patients per year and economic burden for patients in Mongolia based on real market price by levels of care structure such as comprehensive care.

RESULT

Comprehensive level of care: demanded 520.000 USD per year for 200 type 1 patients for continues glucose monitoring system (CGMS) for accurate control of blood glucose. There of 0% from state budget or health insurance and 100% from patients' pocket.

CONCLUSION

Estimated economic burden is very high by comprehensive level of care with continues glucose monitoring system (CGMS) for type 1 diabetic patients in Mongolia. It is necessary to decrease economic burden of family which type 1 diabetic patients by increasing state budget or improving health insurance system.