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2022 International Congress of Diabetes and Metabolism

6 ~ 8 October 2022
Swiss Grand Hotel, Seoul, Korea

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2022 International Congress of Diabetes and Metabolism

October 6 ~ 8, 2022
Swiss Grand Hotel, Seoul, Korea

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Program at a Glance

Time / Room	Convention Hall A 4F	Convention Hall B 4F	Convention Hall C 4F
1st day (Thursday 6 October, 2022)			
15:00~17:00	Research group on beta cell biology and islet transplantation & genetics joint session	KDA & KVBM joint session	Research group on diabetic neuropathy session
17:00~18:00	Sponsored session 1	Sponsored session 2	Sponsored session 3
18:00~	Welcome reception (Cocktail party) / *Triangle Foyer, Hotel, 2F*		
2nd day (Friday 7 October, 2022)			
08:20~08:50	Breakfast symposium 1 *Grand Ballroom A, Hotel, 2F*	Breakfast symposium 2 *Grand Ballroom B, Hotel, 2F*	
08:50~09:00	Break		
09:00~11:00	Clinical diabetes and therapeutics 1	Translational research 1	Diabetes complications 1
11:00~11:20	Coffee break		
11:20~11:30	Opening address		
11:30~12:10	Plenary lecture 1		
12:10~12:30	Break (Poster viewing)		
12:30~14:00	Luncheon symposium 1	Luncheon symposium 2	Luncheon symposium 3
14:00~15:00			
15:00~15:40	Plenary lecture 2		
15:40~16:00	Coffee break		
16:00~18:00	Clinical diabetes and therapeutics 2	Education and integrated care 2 (K)	KDA & KRS joint session
18:00~	Dinner (Congress Banquet Ceremony) / *Grand Ballroom, Hotel, 2F*		
3rd day (Saturday 8 October, 2022)			
08:20~08:50	Breakfast symposium 3 *Grand Ballroom A, Hotel, 2F*	Breakfast symposium 4 *Grand Ballroom B, Hotel, 2F*	
08:50~09:00	Break		
09:00~11:00	Clinical diabetes and therapeutics 3	Diabetes care and education (K)	Diabetes complications 2
11:00~11:20	Coffee break		
11:20~12:00	Plenary lecture 3		
12:00~12:20	Break (Poster viewing)		
12:20~13:30	Luncheon symposium 5	Luncheon symposium 6	Luncheon symposium 7
13:30~15:30	Clinical diabetes and therapeutics 4	Education and integrated Care 3	Clinical diabetes and therapeutics 5
15:30~16:30	Sponsored session 4	Sponsored session 5	Sponsored session 6
16:30~			Closing ceremony

Program at a Glance

Time / Room	Emerald Hall A 3F	Emerald Hall B 3F	Diamond Hall 3F	Meeting room (Crane, Swan, White heron, Flamingo), Hotel, 2F
1st day (Thursday 6 October, 2022)				
15:00~17:00	Research group on diabetic nephropathy session	Basic research hot topic session	Research group on fatty liver disease session	
17:00~18:00				
18:00~	Welcome reception (Cocktail party) / *Triangle Foyer, Hotel, 2F*			
2nd day (Friday 7 October, 2022)				
08:20~08:50				
08:50~09:00				
09:00~11:00	Epidemiology and genetics 1	Basic research 1	Education and integrated care 1 (K)	
11:00~11:20	Coffee break			
11:20~11:30				
11:30~12:10				
12:10~12:30	Break (Poster viewing)			
12:30~14:00	Luncheon symposium 4			
14:00~15:00			Diabetes and metabolism journal session	Oral presentation 1~4
15:00~15:40				
15:40~16:00	Coffee break			
16:00~18:00	Epidemiology and genetics 2	Committee of clinical practice guideline session (K)	Committee of media-public relation session (K)	Committee of the health insurance and legislation session (K) *Flamingo, Hotel, 2F*
18:00~	Dinner (Congress Banquet Ceremony) / *Grand Ballroom, Hotel, 2F*			
3rd day (Saturday 8 October, 2022)				
08:20~08:50				
08:50~09:00				
09:00~11:00	Committee of international liaison session	Translational research 2		
11:00~11:20	Coffee break			
11:20~12:00				
12:00~12:20	Break (Poster viewing)			
12:20~13:30	Luncheon symposium 8			
13:30~15:30	Epidemiology and genetics 3	Basic research 2		
15:30~16:30				Oral presentation 5~8
16:30~				

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PL1

Towards precision medicine in diabetes: using genetics to understand disease heterogeneity

Jose C. Florez
Massachusetts General Hospital, Harvard Medical School, USA

Diabetes is a heterogeneous disease. Any form of hyperglycemia that is not autoimmune or monogenic in origin is labeled as "type 2 diabetes", which thereby comprises a diverse group of pathophysiological entities that are ill-defined. Similarly, treatment approaches are typically algorithmic, and based on comorbidities, side effect profiles or cost rather than the underlying pathogenic processes that caused the hyperglycemic derangement in a given individual. Thus, there is an urgent need to define the specific mechanisms that give rise to diabetes, as a way to classify its various subtypes and implement better tailored preventive and therapeutic strategies. Current approaches to subclassify diabetes include clustering methods that leverage either phenotypic or genetic features. We now have the ability to query various axes of biology in a high-throughput manner. These approaches are converging and beginning to define subgroups of people whose path to hyperglycemia reflect a predominant pathophysiological process - reflecting beta-cell dysfunction, obesity, lipodystrophy-like insulin resistance, and others. They are being expanded to non-European populations and tested for an impact on relevant health outcomes including therapeutic drug response. Models used in this fashion must be reproducible, interpretable, and actionable; when implemented in public health, they must also be sustainable and equitable.

PL2

CNS control of glucose homeostasis

Min-Seon Kim
Asan Medical Center, University of Ulsan College of Medicine, Korea

In mid-19th century, Dr. Claude Bernard firstly suggested the involvement of the central nervous system (CNS) in the regulation of glucose metabolism and this concept has been ignored for more than a century in the research field of glucose metabolism. However, thanks to genetic animal models and recent progress in neuroscience, it has now become clear that the CNS is indeed vital for maintaining glucose homeostasis. To maintain glucose homeostasis, the specific populations of neurons in the hypothalamus and brainstem sense the fluctuations in the blood concentrations of glucose as well as in hormones such as insulin, leptin, glucagon-like peptide 1, glucagon, etc. Those information is integrated and transmitted to multiple brain areas and eventually modulates various processes of glucose metabolism (i.e. hepatic glucose production, glucose uptake in the brown adipose tissue and skeletal muscle, pancreatic insulin and glucagon secretion, renal glucose reabsorption, etc.). Errors in these processes could lead to hyperglycemia/diabetes or impaired recovery of hypoglycemia. In addition to neurons, emerging evidence indicate a considerable contribution of non-neuronal CNS cell glia (astrocytes, microglia, macrophages, and tanycytes) to the maintenance of normoglycemia. In my talk, I will present an overview of the CNS control of glucose metabolism and then our recent findings indicating that specific signaling pathways in hypothalamic neurons and immune cells critically affect systemic glucose metabolism.

PL3

Preventing type 2 diabetes: back to the future

Vanita R. Aroda
Brigham and Women's Hospital, Harvard Medical School, USA

The burden of the wide spectrum of complications related to type 2 diabetes continues to increase significantly worldwide, and in large part is due to the increased prevalence of obesity and type 2 diabetes, the changing demographics of people with/at risk of type 2 diabetes, and the gaps in implementing evidence-based approaches to preventing/delaying type 2 diabetes. Individuals at increased risk of type 2 diabetes are also at increased cardiometabolic risk, and thus, screening for and treatment of modifiable risk factors during this stage are recommended. Minimizing exposure and progression of hyperglycemia is associated with significant reduction in diabetes-related morbidity and mortality. Evidence-based intervention to prevent/delay the progression to type 2 diabetes includes intensive lifestyle intervention and pharmacotherapy. Guidelines and recommended standards of care have been updated to reflect person-centered care goals in individuals at increased risk of type 2 diabetes, and include weight loss or prevention of weight gain, minimizing progression of hyperglycemia, and attention to cardiovascular risk and associated comorbidities. Advances in both the current medical model and in the socioecological approach to obesity and type 2 diabetes hold promise for curbing the epidemics of obesity and type 2 diabetes.

S1-1

Youth-onset type 2 diabetes: definition and natural history in Korea

Nam Hoon Kim
Korea University, Korea

The prevalence of young-onset (diagnosis at age <40 years) type 2 diabetes mellitus (T2DM) is increasing globally. Young-onset T2DM has a common pathophysiology of glucose dysregulation as in late-onset T2DM. However, it presents a greater association with obesity and a more rapid decline in β-cell function than late-onset T2DM. Accumulating evidence indicates that disease progression in young-onset T2DM is rapid, resulting in early and frequent development of microvascular and macrovascular complications, as well as premature death. Improper management and low adherence to medical therapy are important issues in young-onset T2DM. I will discuss the epidemiology, disease entity, natural history and clinical issues associated with young-onset T2DM in Korea.

S1-2

Differences between adult-onset and youth-onset type 2 diabetes - genetic perspectives

Soo Heon Kwak
Seoul National University, Korea

Youth-onset type 2 diabetes (T2D) is expected to have strong genetic predisposition. A recent genome-wide association study identified seven common variants that were associated with risk of youth-onset T2D, most of which overlapped with genetic risk factors for adult-onset T2D. In addition, for validated common variants of T2D, effect sizes were larger for youth-onset T2D compared to adult-onset T2D. Targeted sequencing study showed that 2.8% of the youth-onset T2D cohort harbored genetic variant of monogenic diabetes. To gain further insight into the genetic architecture and biology of youth-onset T2D, we analyzed whole exome sequence data of youth-onset T2D cases and ancestry matched adult controls. We identified (a) known monogenic diabetes mutations in 2.1% of individuals; (b) four genome-wide significant common variant associations; (c) three exome-wide significant ($P < 2.5 \times 10^{-6}$) rare variant gene-level associations (*HNF1A, MC4R, ATX2NL*); and (d) an enrichment of gene-level associations in gene sets for obesity (driven by *MC4R, ATXN2L, GHRL, HESX1*) and β-cell function (*HNF1A, GCK, RFX6, ABCC8, SLC30A8, SIX3, PAM*). Many associations were shared between youth-onset and traditional adult-onset T2D, but most of these had effect sizes much larger within youth-onset cases. The strongest rare and the strongest common variants contributed more to youth-onset T2D heritability than they did to adult-onset T2D heritability, but the relative increase was larger for rare variants (6.9-fold) than for common variants (3.0-fold). We could identify 3.7% of youth-onset cases with relative risk (RR)>5 (additional 4.7% with RR>3) due to variants in these genes, and these cases showed phenotypic differences depending on the variants they carried. These data paint a picture of youth-onset T2D as a disease intermediate in extremity between monogenic diabetes and adult-onset T2D, in which genetic heterogeneity might in the future be used to sub-classify patients for different treatment strategies.

S1-3

Treatment options and current guidelines of care

Tatsuhiko Urakami
Nihon University, Japan

Principle of treatment in youth-onset type 2 diabetes is dietary and exercise management. Successful treatment is cessation of excessive body

weight gain with normal linear growth, control of emotional conditions, and improvement of hyperglycemia.
In dietary management, a relatively modest diet regimen is recommended, i.e., caloric restriction of 5-10% of the energy requirement for age-matched healthy children with an adequate composition of energy source. Overly restricted food intake impairs childhood physical development and is likely to lead to patient withdrawal from the regimen with time. Patients' family are encouraged to modify a dietary habit with reduced carbohydrate, sugar, and total and saturated fat intake, increased fiber intake. In exercise management, participation in at least 60 minutes of moderate to vigorous physical activity daily with muscle and bone strength training 3 days a week is recommended.
While some patients fail to improve hyperglycemia through dietary and exercise management, and eventually require pharmacological treatment. If the youth is metabolically stable - HbA1c >7.0%, <8.5%- metformin is the treatment of first choice. In a case with ketosis or HbA1c ≥8.5%, insulin will be required initially with once-a-day basal insulin (0.25-0.5 units/kg). Transition to metformin only can usually be achieved over 2-6 weeks by decreasing the insulin dose and the metformin is increased. The goal of initial treatment should be to attain an HbA1c of <7.0%. If this glycemic goal is not attained, addition of a second agent should be considered. However, antidiabetic drugs approved for use in pediatric patients are limited in most countries. Therefore, it is expecting that the efficacy and safety of various antidiabetic drugs, including GLP-1 receptor agonists and SGLT2 inhibitors used in adult patients, will be evaluated for use of pediatric population worldwide.

S1-4

Long-term complications in youth-onset type 2 diabetes

Petter Bjornstad
University of Colorado, USA

Youth have emerged as an important population with increased risk for type 2 diabetes (T2D) complications. Although youth-onset T2D is reported in all racial and ethnic groups, people of color and indigenous ancestry are disproportionately affected. The rising frequency, earlier onset, and greater severity of childhood obesity in recent decades combined with sedentary lifestyle and an increasing frequency of intrauterine exposure to diabetes are important drivers of this epidemic. Other environmental determinants may also play a role, particularly in disadvantaged populations, in which access to healthcare is limited, hazardous environmental exposures are more common, and healthy lifestyle choices are often inaccessible. Individuals who develop T2D during childhood and adolescence often display a more aggressive clinical course than those with type 1 diabetes of normal weight or those who develop T2D in adulthood. Among those with youth-onset T2D, the intermediate complications of diabetes often appear in late childhood or early adulthood, and the end-stage complications, including kidney failure, in mid-life. Understanding the mechanisms responsible for the appearance of youth-onset T2D and its more aggressive clinical course are key to its successful management and prevention. In this lecture, we will explore the impact of youth-onset T2D on the key micro- and macrovascular complications of diabetes, with a primary focus on the development and progression of diabetic kidney disease (DKD) because of its frequent occurrence and aggressive course in this population. Additionally, we will examine recent findings involving mechanisms which offer possible explanations for the more aggressive clinical phenotype observed in these patients and discuss various diabetes management strategies and the challenges associated with implementing these strategies.

S2-1

Two-dimensional study of drug timing to reconvert glucocorticoids into striated muscle boosters and counteract metabolic dysfunction

Mattia Quattrocelli
University of Cincinnati, USA

Glucocorticoids are pleiotropic regulators of energy metabolism, but little is known about the striated muscle-autonomous effects of exogenous glucocorticoids. Here we investigate the extent to which two complementary time dimensions impact glucocorticoid pharmacology in heart and muscle. In the first dimension, we investigated the impact of circadian time of intake. Glucocorticoid signaling follows circadian oscillations, but the extent to which the circadian clock gates glucocorticoid effects in cardiomyocytes and myocytes is unknown. In mice with either normal or failing hearts, we found that the glucocorticoid prednisone improved cardiac content of NAD^+ and ATP with light-phase dosing (ZT0), while the effects were blocked by dark-phase dosing (ZT12). This correlated with time-specific effects on upregulation of *Nampt* (NAD^+ biogenesis) and *Ppargc1a* (PGC1alpha, mitochondrial biogenesis). These effects were cardiomyocyte-autonomous and clock-dependent, as shown by inducible cardiomyocyte-restricted inducible ablation of either the glucocorticoid receptor or the clock factor BMAL1. In skeletal muscle, we found analogous clock-dependent effects on mitochondrial health and aerobic exercise tolerance, which were dependent on myocyte-autonomous PGC1-alpha. In the second dimension, we investigated the impact of frequency of intake. We discovered that once-weekly intermittence reverses the metabolic stress induced by once-daily dosing in normal and dietary obesity conditions. Using adiponectin-KO mice and adipose-specific inducible GR-KO mice, we found that intermittent glucocorticoids promoted a regimen-specific upregulation of adiponectin production and adiponectin-dependent response in muscle. Furthermore, circadian-restricted intermittent prednisone rescued NAD^+ content, glucose-fueled respiration and diastolic function in heart of diabetic db/db mutant mice. Finally, in aging 24-month-old mice, circadian-restricted glucocorticoid intermittence increased mitochondrial respiration, NAD^+ and phosphocreatine/ATP content in striated muscles. This correlated with decrease in intramyocellular lipid accumulation and a functional rejuvenation of both cardiac and skeletal muscles in treated aging mice. In summary, our study identifies two complementary timing dimensions to leverage glucocorticoid chrono-pharmacology as pro-ergogenic booster against metabolic dysfunction.

S2-2

Mitochondrial plasticity and skeletal muscle fitness

Zhenji Gan
Nanjing University, China

Skeletal muscle is the major tissues of glucose and fatty acid consumption that heavily rely on mitochondrial metabolism, and, as such, mitochondrial function in skeletal muscle is a critical determinant of systemic metabolic homeostasis. Our long-term goal is to understand the regulatory networks involved in the control of mitochondrial remodeling that define muscle fitness and their potential for therapeutic development. We have unveiled a regulatory circuit that orchestrates muscle mitochondrial function and contractile machinery during adaption of skeletal muscle to physiological and pathophysiological stimuli. In addition, mitochondrial quality in skeletal muscle is crucial for maintaining energy homeostasis during the adaptive response to metabolic stresses. However, how muscle mitochondrial quality is controled and its physiological impacts remain unclear. Our recent work reveals a pivotal role of LONP1-dependent mitochondrial protein quality-control in safeguarding mitochondrial function and preserving skeletal muscle mass and strength, and unravel an intriguing link between mitochondrial protein quality and muscle mass maintenance during muscle disuse. Moreover, we also demonstrated that mitochondrial proteostasis imbalance elicits an UPR^{mt} in skeletal muscle that communicates with adipose tissue and liver, conferring leanness by promoting favorable metabolic remodeling in adipose tissue and liver, linking muscle UPR^{mt} to systemic metabolic homeostasis.

S2-3

TAZ links exercise to mitochondrial biogenesis and insulin sensitivity

Jeong-Ho Hong
Korea University, Korea

Mitochondria are energy-generating organelles and mitochondrial biogenesis is stimulated to meet energy requirements in response to extracellular stimuli, including exercise. However, the molecular mechanisms underlying mitochondrial biogenesis remain unknown. This study demonstrates that transcriptional coactivator with PDZ-binding motif (TAZ) stimulates mitochondrial biogenesis in skeletal muscle. In muscle-specific TAZ-knockout (mKO) mice, mitochondrial biogenesis, respiratory metabolism, and exercise ability were decreased compared to wild-type mice. Mechanistically, TAZ stimulates the translation of mitochondrial transcription factor A via Ras homolog enriched in brain (Rheb)/Rheb like 1 (Rhebl1)-mTOR axis.

TAZ stimulates Rhebl1 expression via TEA domain family transcription factor. Physiologically, mKO mice do not stimulate exercise-induced mitochondrial biogenesis. In terms of insulin signaling, TAZ upregulates IRS1 and stimulates Akt- and Glut4-mediated glucose uptake in muscle cells. mKO mice shows significantly decreased Irs1 expression and insulin sensitivity. Collectively, this study suggests that TAZ is a novel stimulator for mitochondrial biogenesis and insulin signaling and plays an important role in exercise-induced muscle adaptation.

S2-4

Tracing metabolic flux in vivo using stable isotope tracers: effects of exercise training and obesity

Il-Young Kim
Gachon University, Korea

Living organisms are in a constant state of turnover of virtually all body constituents (e.g., metabolites, proteins, lipids, etc.) at varying rates to accomplish dynamic homeostasis. That is, biomolecules are constantly synthesized, broken down, oxidized, exchanged, and/or converted to different compounds. Despite this dynamic nature, metabolic status has been typically examined with tools for static, snapshot information ("statomics") such as abundance of mRNA, protein, and metabolites and/or (in)activation of molecular signaling, often leading to erroneous conclusions on the actual metabolic status. Over the past century, stable, nonradioactive isotope tracers have been widely used to provide critical information on metabolic dynamics of specific biomolecules *in vivo* in both animals and humans. In this talk, I will cover 1) basic model structures of tracer methodology with emphasis on stable isotope tracers that enables quantitative assessments of metabolic flux using ^{13}C, ^{15}N or ^{2}H labeled tracers regarding carbohydrate, lipid, and amino acid/protein kinetics and 2) its applications to the current metabolic research in my lab with examples of metabolic study that uncover dynamic changes in glucose kinetics and glucogenesis from various precursor including lactate, alanine, glycerol, and glutamine in relation to endurance exercise training and/or obesity.

S3-1

Diabetic cardiomyopathy: translating mechanistic insights into practice

Chan Joo Lee
Yonsei University, Korea

The prevalence of diabetes has more than doubled in 20 years and is a major risk factor for the development and progression of cardiovascular disease. The prevalence of heart failure is also increasing with the aging of the population, and it is known that the prognosis of heart failure patients with diabetes is quite poor compared to those without diabetes. Although there are no clear causes of heart failure, such as coronary artery disease and valve disease, diabetes is the cause of heart failure in some patients. However, some researchers question whether a disease called diabetic cardiomyopathy actually exists. Despite these questions, several epidemiological and basic studies provide evidence supporting the association between diabetes and heart failure. Hyperglycemia and insulin resistance change the myocardial metabolism to beta-oxidation and cause cell damage due to free fatty acids, decrease mitochondrial function and generate reactive oxygen species, and alter cellular calcium homeostasis, thereby impairing myocardial function. In addition, advanced glycation end products cause myocardial thickening and fibrosis. This series of processes causes a decrease in the diastolic and systolic functions of the heart, leading to clinical manifestations of heart failure. Despite the clear evidence mentioned above, there are no clinical guidelines for the diagnosis and treatment of diabetic cardiomyopathy. Traditionally, strict control of blood sugar is effective in reducing microvascular complications caused by diabetes, and is important for improving the clinical prognosis and quality of life of diabetic patients. Recent research results of new diabetes drugs show a clear improvement in heart failure beyond the glycemic control effect of diabetes drugs, drawing attention as a new treatment for heart failure. This is evidence that diabetes has a significant effect on heart failure. This presentation will explore the scientific evidence supporting diabetic cardiomyopathy and discuss potential future treatments.

S3-2

Heart failure in type 2 diabetes: current perspectives on screening and diagnosis

Javed Butler
Baylor Scott and White Research Institute, USA

S3-3

The role of SGLT2 inhibitors in cardiorenal syndrome: to diabetes and beyond

Mark Cooper
Monash University, Australia

SGLT2 inhibitors have now been used in clinical practice in type 2 diabetes for at least 10 years and are recommended in many international guidelines for the treatment of type 2 diabetes. Initially the focus was on these drugs' ability to reduce glucose but further advantages of this class of glucose lowering drugs have now been identified. These agents which block the major sodium-glucose transporter SGLT2 in the kidney promote glycosuria and natriuresis. This leads to calories sodium and water excretion in the urine resulting in weight loss, reduction in blood pressure and polyuria. In addition, these agents influence tubuloglomerular feedback as a result of altered delivery of sodium and chloride to the macula densa. These actions are presumed at least in part to explain the renal and cardiac benefits that have been seen in the various major clinical trials with these agents. Since many of these actions are glucose independent the renal and cardiac benefits including preservation of GFR, reduced albuminuria and decreased heart failure have been seen not only in diabetic but also non-diabetic subjects.

S3-4

An integrated approach to managing heart failure in patients with diabetes

Eun-Jung Rhee
Sungkyunkwan University, Korea

Heart failure is one of the mostly increasing cardiovascular complications in patients with diabetes and the prevalence is gradually increasing. Heart failure could result from ischemic heart disease and cardiomyopathy that results from the damage of cardiomyocytes. The mechanism of cardiomyopathy in patients with diabetes is not clearly known and even not known if it exists. Recent development of SGLT2 inhibitors as the glucose-lowering agent increases the interests in heart failure in patients with diabetes. In this talk, I'd like to review current epidemiology, pathophysiology and treatment of heart failure in patients with diabetes.

S4-1

Adiposity, body shape, and risk of diabetes: insights from genetic analyses in the China Kadoorie Biobank

Robin Walters
University of Oxford, UK

China Kadoorie Biobank (CKB) is a population-based prospective cohort of >512,000 adults recruited in 2004-2008 from 10 geographically diverse regions across China. In addition to detailed baseline data from questionnaire and physical measurements, incident disease events are captured through electronic linkage to death and disease registries and to the national health insurance system. Genotyping has been completed for >100,000 participants, including >10,000 with type 2 diabetes (T2D).
The importance of adiposity in the aetiology of type 2 diabetes (T2D) is well established, but the biological mechanisms underlying the observed associations remain poorly understood. Furthermore, there are substantial differences between populations of different ancestries in the patterns of body fat distribution and in the relationship of body fat to T2D risk. Mendelian randomisation (MR) analyses to establish causality of adiposity traits for T2D in non-European ancestry populations are hampered by the absence of strong genetic instruments.

We have conducted GWAS in CKB and UK Biobank for 8 adiposity and fat distribution traits, which we have used to construct genetics scores. Compared to scores derived from each biobank separately, scores from trans-ancestry meta-analysis give a marked improvement (up to 80%) in variance explained in CKB and other East Asian cohorts. We have used these genetic instruments to perform MR in both biobanks, to test the causal relationship between adiposity traits and T2D risk. Univariate MR results are broadly in line with observational estimates. However, when using multivariate MR to identify independent effects of these highly correlated traits, we find that waist circumference has the strongest causal association with T2D, while body mass index makes only a limited independent contribution and increasing hip circumference has a protective effect. These findings emphasise the importance of the location of body fat in determining how it impacts on T2D risk.

S4-2

Contribution of common and rare variants in metabolic traits in East Asians

Young Jin Kim
National Institute of Health, Korea

Metabolic traits are heritable intermediate phenotypes widely-used in assessing the risk of various diseases. We conducted a large-scale genome-wide association analysis of nine medically-relevant metabolic traits (including glycemic, lipid, liver enzyme levels) in 125,872 Korean subjects genotyped with the Korea Biobank Array (KBA). The common variant component of this study was extended through meta-analysis with GWAS data from Biobank Japan (N=162,255). We identified 144 novel signals (MAF≥1%), of which 57.0% were replicated (at nominal significance and with consistent genetic effect) in European subjects from UK Biobank. Additionally, 89 significant associations (66 variants) attributable to rare (MAF <1%) protein altering variants were discovered in the Korean data set, 94.4% of them co-incident to common variant signals for the same trait, adding to allelic series at these loci. Although these rare variants had limited contribution to overall trait variance, absolute effect sizes of these variants were on an average five times larger than the co-incident common variant signals, leading, in carriers, to substantial loss of predictive accuracy from polygenic predictions of disease risk derived from common variants alone. For example, a protective rare allele influencing type 2 diabetes (T2D) risk (I349F at *SLC30A8*; MAF=0.6%) was associated with decreased T2D prevalence (14.2% to 7.3%) in individuals in the top decile of a fasting plasma glucose (FPG) genetic risk score (GRS). Integration of information from FPG-GRS, T2D-GRS, and the I349F variant captured groups with up to 16-fold variation in T2D prevalence compared to the median group (40-60% GRS group). This study highlights the need to consider the joint contribution of both common and rare variants on inherited risk of metabolic traits and related diseases.

S4-3

Large scale human exome sequencing identifies novel therapeutic targets for obesity

Luca A. Lotta
Regeneron Genetics Center, USA

This lecture describes the use of human exome sequencing in a multi-ancestry study of >640,000 individuals to identify GPR75 as a new therapeutic target for obesity.

S4-4

Polygenic risk, lifestyle, and cardiometabolic disease

Jae-Seung Yun
The Catholic University of Korea, Korea

Over the past decade, substantial progress has been made in identifying the alleles that increase the risk of common diseases and these efforts have produced and made it possible to improve polygenic risk scores (PRS). PRS is a marker that can be used to reflect an individual's genetic risk and can explain the inter-individual variance in genetic liability for disease and pertinent quantitative qualities by encoding the genetic burden of a particular disease or trait as a single score. Recent advances in computation, well-profiled biobank creation, statistical method upgrades, and large-scale GWAS have led to the development of PRS, which can be used to simultaneously apply to several diseases. PRS is particularly appropriate for use in screening methods or the treatment of illnesses for which there are efficient preventive therapies. PRSs have the potential to enhance disease risk prediction and diagnostic refinement; predict progression and recurrence of disease; deploy precision therapeutics, and improve the efficiency of population-level screening. PRSs provide the opportunity to estimate risk trajectories across a lifetime, rather than for 5 or 10 years, as is the case for most clinical risk scores. Both genetic and environmental risk factors are important to a varying extent depending on the biomedical domain, so it only makes sense to model both classes of risk factors together. Coupling these in genetic epidemiology studies empowers our dissection of causes from correlations or consequences of the disease. In clinical risk prediction, there is always a balance between performance and practicality. Throughout the life course, we should maximize the amount of information that can reasonably be gathered and design risk prediction models that are flexible enough to extract useful information out of both complete and incomplete data. In this lecture, we will discuss the clinical utility of PGS, the relationship between polygenic risk and lifestyle, the limitations of PGS, and its future direction.

S5-1

Endoplasmic reticulum stress in pancreatic β-cells induces incretin desensitization and β-cell dysfunction via ATF4

Jaemin Lee
DGIST, Korea

Pancreatic β-cell dysfunction and eventual loss are key steps in the progression of type 2 diabetes (T2D). Endoplasmic reticulum (ER) stress responses, especially those mediated by the PERK-ATF4 pathway, have been implicated in promoting these β-cell pathologies. However, the exact molecular events surrounding the role of the PERK-ATF4 pathway in β-cell dysfunction remain unknown. Here, we report our discovery that ATF4 promotes the expression of PDE4D, which disrupts β-cell function via a downregulation of cAMP signaling. We found that β-cell-specific transgenic expression of ATF4 led to early β-cell dysfunction and loss, phenotypes resembling accelerated T2D. Expression of ATF4, rather than CHOP, promoted PDE4D expression, reduced cAMP signaling, and attenuated responses to incretins and elevated glucose. Furthermore, we found that β-cells of leptin receptor-deficient diabetic (*db/db*) mice expressed increased levels of ATF4 and PDE4D, accompanying impaired β-cell function. Finally, we found that inhibiting PDE4D activity with selective pharmacological inhibitors improved β-cell function in both *db/db* mice and β-cell-specific ATF4 transgenic mice. In summary, our results indicate that ER stress causes β-cell failure via ATF4-mediated PDE4D production, suggesting PDE4D as a therapeutic target for protecting β-cell function during the progression of T2D.

S5-2

Therapeutic modulation of antioxidant system for damaged β-cell

Jun Sung Moon
Yeungnam University, Korea

In type 2 diabetes, metabolic stress has a negative impact on pancreatic β-cell function and survival (T2D). Although the pathogenesis of metabolic stress is complex, an imbalance in redox homeostasis causes abnormal tissue damage and β-cell death due to low endogenous antioxidant expression levels in β-cells. We have been tracking the CD36-initiated redoxosome changes in reactive oxygen species (ROS) production and intracellular signal changes in β-cells in diabetic milieu. In addition, we suggested how these signal changes could be therapeutic targets for protection from oxidative stress. Previous studies showed aberrant non-receptor tyrosine kinase (c-Abl) signaling caused by chronic oxidative stress is involved in the progression of β-cell loss in diabetes. We found these changes are closely related to ferroptotic-like cell death, and the oxidative stress-driven GSH depletion and degradation of GPX4 are attributed to lipid peroxidation of cellular membrane resulting in ferroptosis. When we use non-ATP com-

petitive c-Abl kinase inhibitor, selectively preserves β-cell function. In this lecture, I will touch how we modulate these old and new targets under diabetic conditions.

S5-3

Spatial and transcriptional heterogeneity of pancreatic beta cell neogenesis revealed by a time-resolved reporter system

Shugo Sasaki
Osaka University, Japan

Aims: While pancreatic beta cells have been shown to originate from endocrine progenitors in ductal regions, it remains unclear precisely where beta cells emerge from and which transcripts define newborn beta cells. We therefore investigated characteristics of newborn beta cells extracted by a time-resolved reporter system.
Methods: We established a mouse model, 'Ins1-GFP; Timer', which provides spatial information during beta cell neogenesis with high temporal resolution. Single-cell RNA-sequencing (scRNA-seq) was performed on mouse beta cells sorted by fluorescent reporter to uncover transcriptomic profiles of newborn beta cells. scRNA-seq of human embryonic stem cell (hESC)-derived beta-like cells was also performed to compare newborn beta cell features between mouse and human.
Results: Fluorescence imaging of Ins1-GFP; Timer mouse pancreas successfully dissected newly generated beta cells as green fluorescence-dominant cells. This reporter system revealed that, as expected, some newborn beta cells arise close to the ducts (βduct); unexpectedly, the others arise away from the ducts and adjacent to blood vessels (βvessel). Single-cell transcriptomic analyses demonstrated five distinct populations among newborn beta cells, confirming spatial heterogeneity of beta cell neogenesis such as high probability of glucagon-positive βduct, musculoaponeurotic fibrosarcoma oncogene family B (MafB)-positive βduct and musculoaponeurotic fibrosarcoma oncogene family A (MafA)-positive βvessel cells. Comparative analysis with scRNA-seq data of mouse newborn beta cells and hESC-derived beta-like cells uncovered transcriptional similarity between mouse and human beta cell neogenesis including microsomal glutathione S-transferase 1 (MGST1)- and synaptotagmin 13 (SYT13)-highly-expressing state.
Conclusions: The combination of time-resolved histological imaging with single-cell transcriptional mapping demonstrated novel features of spatial and transcriptional heterogeneity in beta cell neogenesis, which will lead to a better understanding of beta cell differentiation for future cell therapy.

S5-4

The significance of mRNA modifications in the regulation of islet biology

Rohit N. Kulkarni
Harvard Medical School, USA

The regulation of islet cell biology is critical for optimal glucose homeostasis in mammals with implications for metabolic disorders including diabetes and obesity. While a majority of studies have focused on investigating the expression and modifications in proteins that regulate the function and growth of metabolic cells the significance of mRNA modifications is not fully explored. This presentation will center on discussing the role of N6-methyladenosine (m6A) as the most common internal mRNA modification that can impact protein turnover and hence regulate cellular processes in metabolic cells. The relevance of the m6A landscape in islet cells in both type 1 and type 2 diabetes will be discussed with complementary studies in human islets and the human β-cell line, EndoC-βH. In summary data will be presented to argue for a hitherto unidentified role for RNA methylation in the regulation of β-cell biology with therapeutic implications for all forms of diabetes.

S6-1

Diabetes education strategy for vulnerable elderly patients

Hae Soon Hwang
Gyeonggi Provincial Medical Center, Paju Hospital, Korea

The elderly people who are vulnerable suffer from diabetes, high blood pressure, in severe cases, cardiovascular disease.
Many of them often have functional health problems such as hand tremors, chewing discomfort due to tooth extraction, nutritional imbalances, joint issues, self-care, and more.
Above all, mental and functional health problems are mostly associated with uneducated or under-educated, hearing loss, and memory loss, and are required training on food exchange tables, blood glucose measurements, self-insulin injections multiple times, not just once.
For example, a nurse may explain the diabetic consumables prescription reimbursement process to a patient and instruct them to create an email address for continuous blood glucose monitoring. Sometimes these tasks are handled by nurses on behalf of patients.
In addition, to help patients understand, pictures are inserted in the training material and distributed to patients, and 1st, 2nd, and 3rd phases to facilitate understanding by conducting education several times.
In P hospital for 3 years, 59% of the diabetes education patients were over 65 years old, and I would like to share our experience through specific cases among them.

S6-2

Exercise recommendations in older adults with diabetes

Seung Jae Jeong
Samsung Medical Center, Korea

As the human body ages, not only the maximum heart rate, cardiopulmonary function, but also the nerve function decreases. For elderly diabetics, regular exercise lowers risk factors for cardiovascular disease, increases muscle strength, and improves insulin sensitivity by improving cardiopulmonary function. However, injuries to joints due to aging and fractures due to falls are things to be careful about when exercising. Therefore, there may be a difference from the exercise methods of young diabetics in terms of balance exercise that can enhance the sense of balance, stretching that can enhance flexibility, and increasing limited exercise intensity. Therefore, it is a safe and efficient exercise method only when elderly diabetics know the exact type, intensity, time, and frequency of exercise that suits them.
Moreover, elderly diabetics have a high incidence of complications. If you have complications such as autonomic neuropathy, peripheral vascular disorder, and retinal disease, it is important to know the precautions for complications accurately and exercise. Accurate exercise methods are needed to prevent aging through regular exercise that can control blood sugar and reduce the risk of cardiovascular disease, as well as to improve the quality of life by improving activities of daily living (ADL).

S6-3

The application of medical nutrition therapy in older adults with diabetes

Meera Kweon
Seoul National University Hospital, Korea

Diabetes is a highly prevalent health condition in the aging population. Older adults with diabetes are distinct from younger adults with diabetes, leading to differences in therapeutic approach.
Lifestyle management in older adults should be tailored to frailty status. Diabetes in the aging population is associated with reduced muscle strength, poor muscle quality and accelerated loss of muscle mass, which may result in sarcopenia.
Nutrition therapy for older adults with diabetes should include meeting the nutritional needs for patients while considering their age, evaluating their fluid intake, avoiding significant weight loss, and being sensitive to individual preferences and long standing food habits while advocating good nutrition.
Inadequate nutritional intake, particularly inadequate protein intake, can increase the risk of sarcopenia and frailty in older adults. Management of frailty in diabetes includes optimal nutrition with adequate protein intake combined with an exercise program that includes aerobic, weight-bearing, and resistance training.

The goals and methods of diabetes management should be individualized according to the results of these assessments. In the treatment of vulnerable elderly patients with diabetes, hypoglycemia or overtreatment should be avoided. Diabetes educators should provide comprehensive geriatric assessment, personalized diabetes education.
In this lecture, we are going to deal with the nutritional management of older adults with diabetes, especially elderly patients with dysphagia.

S6-4

Psychosocial support for the older adults with diabetes

Jee Hyun Lee
Gangnam Severance Hospital, Korea

Diabetes management in older adults requires a comprehensive assessment of the physical, cognitive, emotional, and social status or function of each older adult with diabetes based on an understanding of the life cycle characteristics of old age. The characteristics of old age lead to various deficiencies in the above various aspects of the older adults, which may negatively affect the independent daily life of the older adults as well as self-management of diabetes. Therefore, diabetes educators need to identify the deficiencies of older adults with diabetes and support them in meeting these. It is necessary for diabetes educators to dispel misunderstandings and prejudices about older adults with diabetes and to educate and support them so that they can self-manage diabetes by actively using the patient's strengths. Additionally, family care and community care must be combined for diabetes management. Supporting families that function appropriately and effectively as caregivers as well as linking with community resources is important. Social resources not only relieve the burden of care on the family and help the family not burn out, but are also very necessary for the older adults who lack family resources or have no family to manage diabetes in the community.

S7-1

Current status of antidiabetic agents usage in Korea, and the future?

Jin Hwa Kim
Chosun University, Korea

The global prevalence of diabetes, especially type 2 diabetes, has reached epidemic proportions in the last few decades. The International Diabetes Federation reported in November 2019 that the number of adult diabetic patients reached 436 million worldwide, 90% of whom had type 2 diabetes. Type 2 diabetes is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control. There has been an increase in the range of new antidiabetic agents used to treat type 2 diabetes. In the treatment of diabetes, it is important to pay attention to the patients' comorbidities and prevent diabetic complications. There are many factors, such as efficacy, safety and economics, involved in the selection of antidiabetic agents for diabetes patients. Because type 2 diabetes is a progressive disease in many patients, maintenance of glycemic targets with monotherapy is often possible for only a few years, after which combination therapy is necessary. Traditional recommendations have been to use stepwise addition of medications to metformin to maintain A1C at target. The advantage of this is to provide a clear assessment of the positive and negative effects of new drugs and reduce potential side effects and expense. However, there are data to support initial combination therapy for more rapid attainment of glycemic goals and later combination therapy for longer durability of glycemic effect.
In this presentation, I will discuss the current status of antidiabetic agents usage in Korea, and the future. I believe that the present discussion provides valuable implications for the treatment of type 2 diabetes in Korea.

S7-2

Comparative effectiveness for second-line therapy - GRADE trial

Rodica Pop-Busui
University of Michigan, USA

S7-3

TriMaster trial: implications for precision medicine

Ewan Pearson
University of Dundee, UK

Unless patients are high risk for cardiovascular or renal disease, current guidelines suggest multiple treatment options for the treatment of hyperglycaemia as add on to metformin. The guidelines suggest we individualise treatment yet there is very little evidence as to who responds best to what drug, and who has side effects. The Trimaster study is the first study specifically set up to investigate what is the best drug for an individual, and importantly what is the preferred drug by an individual. The Trimaster study was a 3-way crossover study of Sitagliptin, Pioglitazone and Canagliflozin with HbA1c, weight and patient reported side effects captured at the end of each 4 month treatment block. The results will be presented in detail, but in brief, show that approximately one third of patients preferred each of the drugs. Two hypotheses were confirmed - that those with a high BMI respond better (in terms of HbA1c) to Pioglitazone than Sitagliptin with the opposite seen for those with a low BMI; and those with a normal eGFR (>90 ml/min) respond better to Canagliflozin than to Sitagliptin, whereas those with a eGFR 60-90 ml/min respond better to Sitagliptin than to Canagliflozin. The implications of the Trimaster and other studies of phenotypic determinants of response to diabetes treatment is discussed, with consideration of how these findings can be incorporated into clinical care.

S7-4

Quadruple oral combination therapy for type 2 diabetes - is it reasonable?

Woo Je Lee
University of Ulsan, Korea

Type 2 diabetes (T2D) is a progressive disease that is characterized by a deterioration in pancreatic beta cell function and aggravation of insulin resistance. As the disease progresses, several patients with T2D are eventually unable to adequately achieve or maintain glycemic control. The American Diabetes Association and the Korean Diabetes Association have recommended injectable therapies, including glucagon-like peptide 1 receptor agonist (GLP-1 RA) and insulin, if the HbA1c level exceeds the target despite the use of two to three oral hypoglycemic agents. However, refusal to inject oneself and the fear of weight gain or hypoglycemia may hinder compliance to insulin therapy. Although GLP-1 RA is more convenient and has a lower risk of hypoglycemia than insulin, patients still experience inconvenience upon administration as it is an injectable therapy. Currently, several pharmacotherapies, more than five classes of oral hypoglycemic agents (OHAs) are available for glycemic control in T2D, and these agents act via different mechanisms. Therefore, quadruple oral therapy is an available option for management of T2D. In this talk, I will introduce some recent publications, including real-world studies and randomized controlled trials on the efficacy and the safety of quadruple oral combination therapy. By reviewing recent studies, I will discuss the possible combinations and the clinical usefulness of quadruple oral therapy as a viable option in patients with T2D.

S8-1

Microvascular complications and self management

Hye-Ryoung Yun
Jeonbuk National University Hospital, Korea

Microvascular complications of diabetes are those long-term complications that affect small blood vessels. These typically include diabetic retinopathy,

nephropathy, and neuropathy. Those microvascular complications affect the quality and duration of life for diabetes patients. Prevention is the optimal approach to managing the microvascular complications of diabetes. Near-normal glycemic control, implemented early in the diabetes, has been shown to effectively delay or prevent the development of microvascular complications. The three main approaches to preventing retinopathy are intensive glycemic, blood pressure and serum lipid control. Whereas, higher levels of HbA1c were associated with an increased incidence and progression of retinopathy. Many people with diabetic peripheral neuropathy may be asymptomatic. If the patient is not recognized and does not practice preventive foot care, the patient is at risk of injury to the numb foot. A comprehensive foot assessment should be performed at least annually to identify risk factors for ulcers and amputations. Patients should also be educated on appropriate footwear selection. The early recognition and appropriate management of microvascular complications in the patient with diabetes is important. Multifactor interventions, including structured patient self-management education and optimize control of hyperglycemia, hypertension, dyslipidemia and smoking cessation, are the basis of good management to improve microvascular health.

S8-2

Macrovascular complications and self management

Miae Yoon
Korea University Anam Hospital, Korea

The macrovascular complications of diabetes include cardiovascular disease, cerebrovascular disease, and peripheral vascular disease and these are mostly caused by atherosclerosis. Atherosclerosis causes blood vessels to narrow, blocking blood flow. Smoking, high blood pressure, dyslipidemia, hyperglycemia, and obesity are considered as main risk factors and those are also often found in diabetes patients. As such, diabetes patients have four times higher risk of developing atherosclerosis than those without diabetes.
Cardiovascular is the leading cause of death for diabetics and diabetes have 2-5 times higher risk of developing it than people without diabetes. Screening test may be considered for diabetics who have non-typical symptoms, associated vascular symptoms or signs.
Diabetes is the most common cause of non-hypertensive amputation, which is due to large blood vessel or small blood vessel disease in the lower extremities. The main symptoms and signs of peripheral vascular disease include intermittent disruption and limb ischemia. However, since the risk of developing asymptomatic peripheral vascular disease is 3-4 times higher for diabetic patients than that of people without diabetes, it is required for asymptomatic patients to do lower extremity examinations as well as additional audits as needed in order for early diagnosis.
Stroke is three times more likely to occur in diabetics than people who does not have diabetes. Also, stroke patients with diabetes show a more serious prognosis than those without diabetes.
Macrovascular complications are more likely to occur in diabetics than in people without diabetes. Therefore, it is very important to prevent in advance and diagnose as early as possible so it can be well managed.

S8-3

Acute diabetes complications and self management

Young Jin Choi
Kyung Hee University Hospital at Gangdong, Korea

What are some of the acute complications that require first aid in diabetics? Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic syndrome (HHS) related to hyperglycemia symptoms as well as hypoglycemia are acute complications. DKA and HHS are acute complications characterized by decreased extracellular fluid due to hyperglycemia in the absence of insulin, followed by electrolyte abnormalities and ketoacidemia (in the case of DKA). Infection, insulin interruption, and myocardial infarction are leading factors, so you must check them, and you must visit the hospital as soon as possible because professional treatment is required along with immediate measures.

S8-4

Diabetic foot and self management

Wonkyung Lee
Soonchunhyang University Bucheon Hospital, Korea

One of the significant complications of diabetes, diabetic foot is caused by poor blood circulation, weakening of microvessels, and decreased sensation due to peripheral nerve damage. As the diabetic foot is one of the major causes of lower limb amputation worldwide, it is recognized as a fearful complication for diabetic patients. However, the management of diabetic foot is mostly focused on treatment and more attention and education for diabetic patients are needed for the prevention of the disease. Feet check-up and management done in the hospital and diabetes clinic is not enough to prevent the possible diabetic foot. It is important to find out efficient ways to educate patients to manage themselves to prevent and care for the diabetic foot.

S9-1

Sex differences in the risk, pathophysiology & complication of type 2 diabetes

Eun Roh
Hallym University, Korea

Sex hormones have a great impact on insulin sensitivity, body composition, energy metabolism, and cardiometabolic risk. Age dependency is evident in both sexes in age-specific prevalence of diabetes. Type 2 diabetes is more prevalent at lower age and body mass index in men. However, obesity, the most prominent risk factor, is more common in women after the age of 45, and it contributes the prevalence patterns of type 2 diabetes. In normal metabolic condition, women are more insulin sensitive than men. When glucose tolerance deteriorates, insulin sensitivity in women is reduced more than in men. In type 2 diabetes, the impairment of insulin sensitivity and insulin secretion is substantial and similar in both sexes. This trend partly explain why women show better insulin sensitivity and overall more favorable cardiometabolic risk profiles, than males if normoglycemic. With age, sex differences in body composition and fat deposition clearly contribute to sex-dimorphic diabetes risk. In men, a decline in the circulating level of testosterone according to age deteriorates muscle mass and function, consequently leading to visceral obesity, whereas in postmenopausal women, the lack of estrogen leads directly to visceral fat accumulation. The shifting of body composition and the imbalance between visceral and lower extremity subcutaneous fat seems to have greater importance on the incidence of diabetes especially in postmenopausal women. In terms of energy metabolism, women display lower resting energy expenditure, which declines more rapidly with ageing compared with men. Menopause is associated with decrease of total energy expenditure due to the loss of estrogen effects on the hypothalamus via increased release of orexigenic hormones. Hyperglycemia modifies the beneficial effects of estrogen and the activity of estrogen receptors of protecting against cardiovascular complications. Indeed, women with diabetes have greater increases of the development of cardiovascular diseases than diabetic men. More research regarding sexual dimorphism in pathophysiological mechanisms of type 2 diabetes and its complications could contribute to more personalized diabetes care in the future.

S9-2

Cardiovascular disease risk in women with diabetes

Eun Young Lee
The Catholic University of Korea, Korea

Cardiovascular disease (CVD) is the leading cause of death for both women and men, and it is well known that the risk of CVD increases with diabetes. Previous studies have shown the relative risk for CVD in women with diabetes, compared with women without diabetes, is greater than that in men with diabetes. Epidemiologic data and physiologic mechanisms that potentially contribute to the sex differences in diabetes-related risk of CVD have been extensively studied. However, most of the conclusions were driven by sex-related differences in relative risk without consideration of absolute risk. The heterogeneity between studies should also be considered. Moreover, it remains unclear whether sex differences in the risk of CVD exist at any level of glycemia or diabetes duration. Recently, a few studies have shown both the absolute and relative risk of CVD in women and men with

diabetes. This lecture will focus on how sex influences the diabetes-associated risk of CVD in women and men from the perspective of both absolute and relative risk. The proposed mechanisms affecting the sex differences will be briefly summarized.

S9-3

Gestational diabetes and its implications across the life span

Ravi Retnakaran
University of Toronto, Canada

Gestational diabetes mellitus (GDM) has long been recognized as a medical complication of pregnancy that also identifies women who are at risk of developing type 2 diabetes (T2DM) in the future. In recent years, a series of studies has led to the recognition that women who develop GDM actually have chronic cardiometabolic dysfunction that not only exists during and after gestation but even precedes the pregnancy in which GDM was diagnosed. Moreover, this patient population has an elevated lifetime risk of not only T2DM and its complications (include retinal, renal and liver disease outcomes) but also cardiovascular disease. This vascular risk appears to be determined by cumulative exposure across the lifespan to an adverse cardiovascular risk factor burden that first emerges before the index pregnancy. Thus, despite its clinical presentation in pregnancy, the diagnosis of GDM carries important implications across the life span of a woman. In this talk, we will consider these life course implications and the challenges and opportunities that they may present for optimizing women's health.

S9-4

Sex differences of COVID-19-related outcomes in diabetes

Mi Kyung Kim
Keimyung University, Korea

Sex dimorphism differently influences physiological or pathophysiological processes in males and females. These sex differences impact the pathogenesis of numerous diseases, including metabolic disorders such as diabetes, and are associated with various factors, including sex steroid hormone, fetal/neonatal programming, and epigenetic modifications. Clinical and experimental observations have reported the protective actions of endogenous estrogens, mainly through estrogen receptor α activation in various tissues. Therefore, conditions that lose a protective role of endogenous estrogens in women, including menopause, premature ovarian insufficiency, increased incidence of metabolic disorders, and an increased risk of type 2 diabetes compared to premenopausal women. In addition, there are gaps in drug response and complications depending on sex.
By Aug 27, 2022, about 600 million people have confirmed COVID-19 cases. Since then, many risk factors have been presented for COVID-19. Commonly reported variables for an adverse outcome from COVID-19 comprised patient characteristics: age>75, male sex, severe obesity, and active cancer. Such as, a male is considered one of the risk factors for COVID-19 -related morbidity and mortality. This sex disparity of COVID-19-related morbidity and mortality is likely explained by a combination of biological sex differences such as differences in chromosomes, reproductive organs, and related sex steroids and gender-specific factors such as differential behaviors and activities by social and cultural/traditional roles. Diabetes is a risk factor for the poor prognosis of COVID-19. This session will review whether sex differences are associated with COVID-19-related outcomes in diabetes.

S10-1

Diagnosis of adult-onset type 1 diabetes

Sang-Man Jin
Sungkyunkwan University, Korea

Accurate classification of diabetes is important for choice of insulin regimen, use of adjuvant therapies, and the decision to introduce newer technologies soon after diagnosis. Nevertheless, diagnosis of adult-onset type 1 diabetes remains challenging, resulting in frequent misclassification.
Because the formal definition of type 1 diabetes is conceptual, a working definition could be suggested for practical purpose: 1) A random C-peptide levels <200 pmol/l, which generally defines severe insulin deficiency, and 2) progression to insulin therapy in three years, which strongly predict eventual progression into severe insulin deficiency. It is also useful to consider that most people with type 1 diabetes develops severe insulin deficiency in 3-5 years from diagnosis, with a two phased decline in the C-peptide levels.
Another issue in the diagnosis of adult-onset type 1 diabetes is the belief that adult-onset type 1 diabetes would have mild feature, as an intermediate between type 1 and type 2 diabetes. Recently, a genetically stratified survival analysis from UK Biobank clearly showed that >40% of patients with autoimmune diabetes are diagnosed after 30 years of age, and that whatever age it presents, type 1 diabetes is associated with rapid requirement for insulin and risk of ketoacidosis, suggesting that it is not a milder phenotype if diagnosed later in life.
At least in part, the discrepancy between this observation and the common conception from the studies on latent autoimmune diabetes of adult (LADA) is likely to be explained by the low positive predictive value of GAD antibody in adults with diabetes. Although it remains controversial whether LADA is a discrete subtype of type 1 diabetes, it has been demonstrated that diabetes with fluctuating or low-titer GAD antibody has a similar disease progression with type 2 diabetes, in East Asian populations as well.

S10-2

Update on continuous glucose monitoring and connected insulin pens in type 1 diabetes

Jee Hee Yoo
Yonsei Wonju University, Korea

Achieving target glycated hemoglobin (HbA1c) while minimizing hypoglycemia has always been a challenge for diabetes treated with insulin. However, technological advances including continuous glucose monitoring (CGM), connected insulin pens (CIPs), insulin pumps, and automated insulin delivery (AID) algorithms combined with virtual platforms have made it possible to achieve the optimal control of diabetes using insulin.
With the steady improvement in sensor accuracy, duration of wear, and smaller size, the use of CGM is expanding widely. The CIP is a new technology with a function that displays the last dose of insulin and timing and has reminder alerts that integrate with a smart app. Today, with greater advances in the technology of the CIP, it integrates with CGM and even integrates with mobile apps to help users to calculate bolus doses easily with a bolus calculator, and finally, all the data are submitted to a virtual platform. The display of injection timing with insulin on board (IOB) helps to prevent insulin stacking. Alerts for injection reminders help to avoid injection omission. CIP also helps health care providers (HCPs) to make better decisions in diabetes management by engaging diabetes with correct insulin use information. Unfortunately, there are only a few clinical trials evaluating the effectiveness of these CIPs. Further studies of randomized clinical trials are needed.

S10-3

Highlights from the international consensus meeting on recommendations for the use of Automated Insulin Delivery (AID) technologies in clinical practice

Revital Nimri
Schneider Children's Medical Center of Israel, Israel

In recent years we have witnessed tremendous advances in AID technologies (also called artificial pancreas or closed loop system). Numerous randomized controlled trials and real-world studies have shown that the use of AID systems is safe and effective in helping people with T1D achieve their long-term glycemic goals while reducing hypoglycemia risk. This improvement in glycemic outcomes was demonstrated across all age groups, in all genders and regardless of diabetes duration, initial treatment or baseline HbA1c. Thus, AID systems have recently become an integral part of diabetes management.
However, recommendations for using AID systems in clinical settings have been lacking. Such guided recommendations are critical for AID success and acceptance. All clinicians working with people with diabetes need to become familiar with the available systems in order to eliminate disparities in diabetes quality of care. The consensus recommendations provide much-needed guidance for clinicians who are interested in utilizing AIDs.
The recommendations were developed by a large group of developers, researchers, and clinicians with recognized expertise in AID as well as indi-

viduals with diabetes. The meeting was hosted by the 14th Annual Conference of Advanced Technologies & Treatments for Diabetes. The consensus recommendations cover all relevant aspects of using this technology, including clinical evidence, target populations, initiating AID, clinical application, education and training, reporting AID data, psychological issues and the future of AID.
The presentation will include highlights from the consensus including a summary of the clinical evidence supporting the efficacy and safety of AID systems. Presents graded evidence-based recommendations for people with diabetes who can be considered for AID. Presents general recommendations for initiating AID use such as setting up the AID system etc. In addition, will discuss essential elements that should be considered in providing education, training and follow-up to individuals who are initiating AID. Will focus on the clinical recommendations for AID use such as treatment of hypoglycemia events, exercise management, meals treatment, sick days and more.

S10-4
Adjunctive therapies for type 1 diabetes

Jae Hyun Bae
Korea University, Korea

Insulin therapy is a cornerstone of the management of type 1 diabetes (T1D). However, it is often difficult to achieve glycemic goals in people with T1D owing to varying insulin demands, the risk of hypo- and hyperglycemia, and undesirable weight gain. Furthermore, insulin replacement per se has little effect on pathogenic mechanisms of T1D and the risk of cardiovascular (CV) disease. Several drugs, to date, including metformin, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), and sodium-glucose cotransporter (SGLT) 2 inhibitors, have been studied to compensate for these unfulfilled needs. Metformin has insulin-sensitizing properties but has shown inconsistent results in glucometabolic and cardiovascular perspectives. In adults with T1D and increased CV risk, metformin did not reduce the progression of atherosclerosis and glycated hemoglobin (HbA1c) levels. Glucagon-like peptide-1 has pleiotropic effects, suggesting that GLP-1 RAs may be beneficial to improving glycemia and ameliorating the decline in β-cell function. In adults with T1D, long-acting GLP-1 RA (liraglutide), not short-acting GLP-1 RA (exenatide), reduced HbA1c levels, body weight, and total daily insulin dose. However, it also increased rates of hypoglycemia and ketosis. The combination of liraglutide and anti-interleukin-21 preserved β-cell function in adults with recently diagnosed T1D. Given the effects on CV risk factors, including weight reduction, GLP-1 RAs may have a role for people with T1D and overweight or obesity. SGLT2 and SGLT1/2 inhibitors improve hyperglycemia with an insulin-independent mechanism and have shown clear cardiorenal benefits in people with or without diabetes. In clinical trials in people with T1D, these drugs reduced HbA1c levels, improved time in range, decreased insulin dose, and reduced body weight but also increased the risk of diabetic ketoacidosis. When using SGLT2 inhibitors, careful patient selection, proper insulin dose adjustment, and frequent monitoring are required. Since current evidence on adjunctive therapies for T1D is limited, further studies are needed.

S11-1
Current status of diabetes education in Korea & diabetes education fact - nursing

Junghwa Lee
Kyung Hee University Hospital at Gangdong, Korea

The World Health Organization (WHO) said in its previous press release "Diabetes and Human Rights" that diabetics have the right to education and information on diabetes to improve their quality of life. In the case of Korea, the Korea Diabetes Association (KDA) proposed a self-management education recommendation in 1999 and the Ministry of Health and Welfare has been able to calculate diabetes education costs as non-payment since June 2003. However, despite the importance of diabetes education, there is no research on the actual situation or current situation of diabetes education.
Therefore, in this lecture, we will examine the actual status of diabetes education from the perspective of diabetes education nurses.

S11-2
Diabetes education fact - nutrition

Min Young Noh
Seoul St. Mary Hospital, Korea

Until now, the effect of nutritional treatment on blood sugar management in diabetic patients has been confirmed in many studies, and thus dietitians are included as essential educators in multidisciplinary education for diabetic patients in Korea. However, many difficulties and problems have been raised in the field of nutrition education for diabetic patients due to realistic problems in manpower and fees, and changes in the hospital environment caused by the recent COVID-19 pandemic. Therefore, in this session, we will conduct a survey of nutritionists interested in diabetes nutrition education to understand the current status of diabetes nutrition education and think about the direction of progress.

S11-3
Diabetes education fact - social work

Donghee Yang
Ilsan Paik Hospital, Korea

The purpose of this study is to examine the current status of diabetes education implemented by social workers in a rapidly changing medical environment. Through this, we intend to identify limitations and seek future directions for development.

S11-4
Diabetes education fact - exercise

Hye Young Lee
Asan Medical Center, Korea

Exercise is very important part of diabetes care. Currently, exercise education is essential to diabetes education in Korea, but only a few hospitals provide exercise education in the actual field. The purpose of this study is to examine the current state of exercise education for diabetic patients in Korea. I would like to find out and introduce systems such as who, how, and what materials are used for exercise education. Furthermore, I will suggest how the system to provide better exercise education to diabetic patients should be developed.

S12-1
Sarcopenia in Korea: prevalence and clinical aspects

Kyoung Min Kim
Yonsei University, Korea

Sarcopenia is commonly defined by a combination of low muscle mass with low muscle strength or impaired performance. Although muscle mass is not specifically a predictor of muscle strength or physi-cal performance, it is significantly correlated with these parameters. Therefore, the accurate measurement of muscle mass is a crucial step for classifying sarcopenic subjects. Appendicular lean mass (ALM), which is a sum of the muscle mass of both arms and legs, is generally used for the muscle mass index. However, muscle mass is fundamentally correlated with body size, indicating that subjects with a larger body size may have larger muscle mass. Therefore, when evaluating the adequacy of muscle mass, the absolute level of ALM has been used after adjusting for body size in different ways, namely using height squared (ALM/ht2), weight (ALM/wt), or body mass index (ALM/BMI). Among those indices, ALM/ht2 was first suggested by Baumgartner et al. However, because this index is positively correlated with BMI, it has the limitation that subjects with a greater BMI due to a larger amount of fat are less likely to be classified as having sarcopenia. In 2002, a weight-adjusted muscle mass index was proposed by Janssen et al. This weight-adjusted model was subsequently modified as ALM/wt. More recently, another muscle mass index, the ALM/ BMI index, was introduced by the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project in 2014 and the use of this index is growing. However, among these parameters, the most appropriate method with the highest predictive value for identifying sub-

jects who are at higher risk of weakness and slowness remains still uncertain. Moreover, the prevalence of sarcopenia varies considerably depending on the method used. Therefore, there is a need to elucidate which operational definition is ideal for identifying sarcopenic subjects at high risk. Large-scale prospective studies to address this issue are urgently warranted.

S12-2

Sarcopenia as a potential cause and consequence of T2DM and interventions to improve musculoskeletal and metabolic health

David Scott
Deakin University, Australia

'Sarcopenia' describes the age-related progressive decline in skeletal muscle composition and functional capacity which is a major public health concern given its associations with increased risk for disability, institutionalization and early mortality in older adults. A potentially underappreciated outcome of sarcopenia may be deleterious effects on cardiometabolic health, including increasing risk for type 2 diabetes mellitus (T2DM). Muscle composition changes such as declines in muscle volume and increasing fat infiltration may contribute to development and progression of T2DM through altered glucose disposal and increased inflammation. Furthermore, reduced functional capacity can result in older adults' achieving lower amounts of physical activity and increasing sedentary time, both of which are strong predictors of insulin resistance. The relationship between sarcopenia and T2DM also appears to be bidirectional; T2DM characteristics including insulin resistance, inflammation, advanced glycation end-product accumulation and oxidative stress negatively affect skeletal muscle composition and function through impairments in protein metabolism, vascular and mitochondrial dysfunction, and cell death. Indeed, despite having similar or greater muscle mass, older adults with T2DM generally demonstrate poorer physical function than those without T2DM, suggesting that poor metabolic health leads to compromised muscle quality.
There are currently no approve pharmacological treatments for sarcopenia and so lifestyle modifications, particularly progressive resistance training and appropriate protein intake, remain the frontline therapy. Resistance training has also been demonstrated to be effective for improving metabolic health and so is likely to have additional benefit in individuals with both T2DM and sarcopenia. However, there is limited evidence on the feasibility, acceptability and effectiveness of exercise and nutrition interventions for older adults with comorbid T2DM and sarcopenia. This presentation will examine the bidirectional relationship between T2DM and sarcopenia and describe novel strategies for managing these conditions in older adults.

S12-3

How to evaluate sarcopenia in patients with type 2 diabetes

Jiyeon Baek
University of Ulsan, Korea

Sarcopenia is the progressive loss of muscle mass and function, and it is an age-related phenotype; the concept of this geriatric syndrome is similar to that of physical. Sarcopenia is closely related to risk of falls, functional decline, institutionalization, and mortality. Thus, defining and diagnosing sarcopenia and providing early intervention are important with the aging of the current global population. The definition of sarcopenia has been revised from simply having low muscle mass to having low muscle strength or physical performance in addition to decreased muscle mass. However, there is still no universal consensus in the operational definition of sarcopenia. Herein, we will discuss the operational definition of sarcopenia and how to evaluate sarcopenia in patients with type 2 diabetes.

S12-4

Effects of anti-diabetic drugs on sarcopenia: best treatment options for elderly patients with type 2 diabetes mellitus and sarcopenia

Eugene Han
Keimyung University, Korea

Sarcopenia, which is defined as age-related loss of muscle mass, strength, and function, has become a serious medical issue in aging societies. It is known that sarcopenia is significantly associated with an increased risk of cardiovascular events or mortality in patients with metabolic phenotypes such as type 2 diabetes (T2D). This close association between sarcopenia and cardiovascular events or mortality can probably be explained by the fact that patients with sarcopenia, especially those with chronic medical illnesses, are inevitably subject to increased risk due to decreased physical ability and functional impairment preventing exercise. Sodium glucose co-transporter 2 inhibitor, thiazolidinediones, glucacon like peptide 1 receptor agonist have been known for reducing cardiovascular disease in patients with T2D. However, the effects of those drugs in sarcopenia has not been elucidated. In this presentation, available scientific evidences for the anti-diabetic drugs on patients with T2D and sarcopenia will be summarized.

S13-1

Metabolomics profiling provides potential novel biomarkers for the impact of diet quality on cardiometabolic disease risk

Clemens Wittenbecher
Chalmers University of Technology, Sweden

Increasing dietary unsaturated fat intake at the expense of saturated fats is recommended for cardiometabolic disease prevention. However, the standard cardiometabolic risk markers do not fully reflect the metabolic benefits of improved dietary fat composition, and well-powered randomized controlled trials on hard endpoints are lacking. Here, we demonstrate that deep lipidomics profiling-based multi-lipid metabolite score accurately reflects the dietary fat quality and predicts cardiometabolic disease risk. We identify lipid metabolites affected by unsaturated-for-saturated fat substitution through deep lipidomics profiling in the 16-week Dietary Intervention and VAScular function (DIVAS) study. Then- we combine the dietary fat quality-responsive lipid metabolites in DIVAS in a multi-lipid metabolite score (MLS) and reconstruct the score in an independent study population. The DIVAS healthy fat diet-induced difference in this MLS is associated with a substantial reduction of cardiovascular disease (32% fewer cases) and type 2 diabetes (26% fewer cases) incidence in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam cohort. These MLS-based risk reduction estimates are more substantial than similar extrapolations with standard surrogate biomarkers and consistent with the limited evidence from high-quality trials on clinical endpoints. Finally, we show that the higher diabetes risk with an adverse pre-intervention multi-lipid metabolite score can be mitigated through a diabetes-protective healthy Mediterranean diet intervention using data from the Prevención con Dieta Mediterránea (PREDIMED) trial. The effect modification by a Mediterranean diet intervention suggests potential applications of lipidomics-based multi-biomarker panels for targeting precise dietary prevention approaches.

S13-2

Lipidome in non-alcoholic fatty liver disease: pathways, metabolic models, and biomarkers

Matej Orešič
Örebro University, Sweden

Nonalcoholic fatty liver disease (NAFLD) is a progressive liver disease that is strongly associated with type 2 diabetes. Accurate, non-invasive diagnostic tests to delineate the different stages: degree of steatosis, grade of nonalcoholic steatohepatitis (NASH) and stage fibrosis represent an unmet medical need. In our previous studies, we successfully identified specific serum molecular lipid signatures which associate with the amount of liver fat as well as with NASH.
Here we report underlying associations between clinical data, lipidomic profiles, metabolic profiles and clinical outcomes, including downstream

identification of potential biomarkers for various stages of the disease.
We leverage several statistical and machine-learning approaches to analyze clinical, lipidomic and metabolomic profiles of individuals from the European NAFLD Registry. We interrogate data on patients representing the full spectrum of NAFLD (n=627), across 3 clinical perspectives: steatosis, NASH, and fibrosis. We found that steatosis grade was strongly associated with (1) an increase of triglycerides with low carbon number and double bond count as well as (2) a decrease of specific phospholipids, including lysophosphatidylcholines. We identified that progression from F2 to F3 fibrosis coincides with a key pathophysiological transition point in disease natural history.
Analysis of circulating metabolites provides important insights into the metabolic changes during NAFLD progression, revealing metabolic signatures across the NAFLD spectrum and features that are specific to NAFL, NASH, and fibrosis. The F2-F3 transition marks a critical metabolic transition point in NAFLD pathogenesis, with the data pointing to the pathophysiological importance of metabolic stress and specifically oxidative stress.

S13-3

Organokines & other potential biomarkers for cardiometabolic disorders

Kyung Mook Choi
Korea University, Korea

Previous studies have shown that chronic cardiometabolic disorders, such as sarcopenic obesity, metabolic syndrome, type 2 diabetes, cardiovascular disease, and nonalcoholic fatty liver disease (NAFLD), are closely interlinked. As the socioeconomic burden of these disorders has significantly grown in elderly population, novel approach for early detection and treatment for cardiometabolic disorders are required. Adipose tissue, skeletal muscle, and liver are now recognized as endocrine organs that produce and secrete adipokines, myokines, and hepatokines. These organokines are pivotal organizers that regulate inflammation, energy and metabolic homeostasis as well as neuroendocrine axis through endocrine, paracrine, and autocrine pathways. Furthermore, these organokines including adipokines, myokines, and hepatokines interact with each other and crosstalk with distant target organs. Organokines might be classified according to their pro-inflammatory and anti-inflammatory effects. Pro-inflammatory organokines induce obesity-related metabolic dysfunction and insulin resistance that result in type 2 diabetes and cardiovascular disease, whereas anti-inflammatory organokines provide protection against the harmful impact of pro-inflammatory organokines.
In the present lecture, I would like to provide a comprehensive overview of organokines and other potential biomarkers for cardiometabolic disorders. This will include the roles of novel organokines through pathophysiological mechanisms in sarcopenic obesity, metabolic syndrome, type 2 diabetes, cardiovascular disease, NAFLD, and neurodegenerative disorders.

S13-4

Potential molecular transducer of exercise-induced cardiac adaptation

Jin Han
Inje University, Korea

The heart is the primary pump that circulates blood through the entire cardiovascular system, serving many important functions in the body. Exercise training provides favorable anatomical and physiological changes that reduce the risk of heart disease and failure. Compared with pathological cardiac hypertrophy, exercise-induced physiological cardiac hypertrophy leads to an improvement in heart function. Exercise-induced cardiac remodeling is associated with gene regulatory mechanisms and cellular signaling pathways underlying cellular, molecular, and metabolic adaptations. We found that aerobic exercise training decreased cereblon (CRBN), a substrate recognition protein in the E3-ligase ubiquitin complex. The binding target of CRBN varies according to tissues and cells, and the protein regulates various biological functions by regulating tissue-specific targets. As new endogenous targets of CRBN have been identified over the past decade, the physiological and pathological functions of CRBN and its potential as a therapeutic target in various diseases have greatly expanded. Here, I will present a cellular and molecular signaling pathway of CRBN to understand the exercise-induced cardiac adaptation.

S14-1

Effects of tirzepatide versus insulin glargine on kidney outcomes in participants with type 2 diabetes: a post-hoc analysis from the SURPASS-4 trial

Hiddo Lambers Heerspink
University Medical Center Groningen, Netherlands

Background: Tirzepatide, a dual GIP/GLP-1 receptor agonist, reduced glycated haemoglobin (HbA1c) levels, weight, and blood pressure more than titrated daily insulin glargine in people inadequately controlled on oral diabetes treatments with type 2 diabetes and high cardiovascular risk (SURPASS-4). In exploratory analyses, we compared effects of tirzepatide and insulin glargine on kidney parameters and outcomes.
Methods: SURPASS-4 was an open-label, parallel-group, phase 3 study at 187 sites in 14 countries. Participants were ≥18 years with type 2 diabetes treated with any combination of metformin, sulfonylurea, or sodium-glucose co-transporter-2 inhibitor, and with baseline HbA1c of 7.5-10.5% (58-91 mmol/mol), body mass index of 25 kg/m^2 or greater, and established cardiovascular disease or high risk of cardiovascular events. Randomisation was 1:1:1:3 to once-per-week tirzepatide (5, 10, or 15 mg) or titrated insulin glargine (100 U/mL). The study included up to 104 weeks of treatment, with a median treatment duration of 85 weeks. Rate of estimated glomerular filtration rate (eGFR) decline and urine albumin-creatinine ratio (UACR) were compared between combined tirzepatide and insulin glargine treatment groups. A composite kidney endpoint was defined as eGFR decline ≥40% from baseline, end-stage kidney disease, death due to kidney failure, or new-onset macroalbuminuria.
Results: Between Nov 20, 2018, and Dec 30, 2019, 3045 people were screened with 2002 randomised to study drug. Of the 2002 people randomised, 1995 received at least one dose of tirzepatide or insulin glargine. At baseline, participants had a mean (SD) eGFR of 81.3 (21.11) mL/min per 1.73 m^2 and median (IQR) UACR of 15.0 (5.0, 55.8) mg/g. The mean (SE) rate of eGFR decline was -1.4 (0.2) mL/min per 1.73 m^2 per year in the combined tirzepatide group and -3.6 (0.2) mL/min per 1.73 m^2 per year in the insulin group (between group difference: 2.2 [95% CI 1.6, 2.8]). Tirzepatide compared to insulin glargine reduced the annual rate of eGFR decline by more in participants with eGFR <60 mL/min per 1.73 m^2 than in those with eGFR ≥60 mL/min per 1.73 m^2 (between group difference: 3.7 [95% CI 2.4, 5.1]). UACR increased over time with insulin glargine (36.9% [95% CI 26.0, 48.7]) but not with tirzepatide (-6.8% [-14.1, 1.1]) (between group difference -31.9% [95% CI -37.7, -25.7]). Participants who received tirzepatide showed a significantly lower occurrence of the composite kidney endpoint compared to insulin glargine (HR 0.58 [95% CI 0.43, 0.80]).
Conclusion: In people with type 2 diabetes and high cardiovascular risk, tirzepatide meaningfully slowed eGFR decline and reduced UACR relative to insulin.

S14-2

The strong on top of the strong: cagrilintide and semaglutide combination for obesity

Jae-Han Jeon
Kyungpook National University, Korea

Cagrilintide is a long-acting lipidated long-acting amylin analogue, investigated for weight management. This analogue harbor non-selective agonistic effects on native amylin and calcitonin receptors. Native amylin is secreted simultaneously with insulin by the pancreas to defer gastric emptying and interrupt glucagon release after food intake. This hormone can also reduce energy intake, regulate appetite, induce satiety and satiation.
The weight loss effect of semaglutide is widely known and has been proved by multiple studies. Semaglutide has been demonstrated to reduce appetite, induce satiety, and improve control of eating behaviors and food choices, consequentially tapering off ad libitum energy intake.
In a recent clinical trial, the combined therapy of cagrilintide and semaglutide 2.4 mg showed positive effects on body weight reduction with an acceptable safety profile in individuals with obesity (BMI 27-39.9 kg/m^2). This combined therapy is a promising pharmacological option for weight management.

S14-3

"When they go low, we go high" _ GLP-1/Glucagon dual agonist

Seungjae Baek
Hanmi Pharmaceutical, Korea

MK-6024/HM 12525A contains a synthetic, modified oxyntomodulin (OXM) peptide that displays in-vitro potency as a dual agonist at both human GLP-1 and GCG receptors. The dual agonist properties of MK-6024/HM 12525A distinguish it from existing GLP-1 receptor agonists and give this therapy the potential for displaying increased efficacy for inducing weight loss.
The presenter will present the safety and efficacy of MK-6024/HM12525A in with class II/III obesity and type 2 diabetes.

S14-4

The novel GIP, GLP-1, and glucagon triple receptor agonist LY3437943: from discovery to clinical proof-of-concept

Tamer Coskun
Eli Lilly and Company, USA

With an increasing prevalence of obesity, there is a need for new therapies to improve body weight management and metabolic health. Multi-receptor agonists in development may provide approaches to fulfill this unmet medical need. LY3437943 is a novel, unimolecular triple agonist peptide at the glucagon receptor (GCGR), glucose-dependent insulinotropic polypeptide receptor (GIPR), and glucagon-like peptide-1 receptor (GLP-1R). *In vitro*, LY3437943 shows balanced GCGR and GLP-1R activity, but more GIPR activity. In obese mice, administration of LY3437943 decreased body weight and improved glycemic control. Body weight loss could be attributed to a combination of energy expenditure, primarily mediated by GCGR, and food intake, driven primarily by GLP-1R and GIPR. In a randomized, double-blind, placebo-controlled, Phase 1 proof-of-concept study, we assessed the safety and tolerability of multiple ascending doses of LY in patients with type 2 diabetes (T2D). Vital signs, laboratory data and adverse events (AEs) were monitored to assess safety and tolerability. Efficacy was assessed by monitoring change in glycated hemoglobin (HbA_{1c}) and body weight at week 12. The most common treatment-emergent AEs were gastrointestinal (nausea and diarrhea), which were mostly mild in severity. By week 12, mean HbA_{1c} decreased from baseline in all groups, with higher doses of LY showing statistically significant baseline-adjusted decreases of up to 1.90%. Dose-dependent decreases in mean baseline-adjusted body weight of up to 8.65 kg were observed with LY.
In conclusion, LY3437943 showed a safety and tolerability profile similar to other incretins. Its pharmacokinetic profile supported once-weekly dosing. Promising glycemic and body weight loss efficacy within these studies highlights the potential for LY to provide additional benefit versus existing therapies in treatment of T2D and obesity.

S15-1

Driving force and policy implication in the transition of cardiometabolic status and diet quality in Korean adults

Min-Jeong Shin
Korea University, Korea

In order to help prevent cardiometabolic disease burdens, a comprehensive investigation of the trends in overall diet quality and identification of possible contributing factors would be useful. The aim of this study was to investigate the trends and independent associations of age, period, and birth cohort with diet quality and cardiometabolic risk factors among Korean adults. Serial cross-sectional and age-period-cohort analyses were conducted of nationally representative 24-hour dietary recall data from the Korea National Health and Nutrition Examination Survey 2007-2018. The study population included 65 416 Korean adults aged 19 to 79 years. In 2007-2018, the age-standardized mean KHEI score increased, which was associated with reduced sodium intake and increased whole grain, dairy, and protein-rich food intakes. Controlling for age and period effects, the highest KHEI score was observed among the birth cohorts of 1960-1964 (53.6) and decreased in subsequent cohorts (45.5 in the 1990-1999 birth cohort). Similar cohort effects in cardiometabolic risk factors were observed, showing the lowest waist circumference, blood pressure, and total cholesterol levels among the birth cohorts of the 1960s and 1970s and higher levels among more recent birth cohorts (1990-1999 vs 1960-1964). At most ages, periods, and birth cohorts, the mean KHEI score was consistently higher in adults living in urban areas and among high-income and educational levels. Despite the improvement in the diet quality of Korean adults from 2007 to 2018, inequalities in diet among age, birth cohort, and socioeconomic subgroups persisted, which suggests that more intense interventions may be needed to target the susceptible groups. In this presentation, the Driving Force-Pressure-State-Exposure-Effect-Action (DPSEEA) framework used to explain the observed trends of cardiometabolic risks and diet quality by mapping potential determinants and to address policy implications would be discussed.

S15-2

Investigate the role of dietary patterns and behaviors of optimal health - what and when should we eat?

YoonJu Song
The Catholic University of Korea, Korea

Compared to conventional nutritional guidelines of healthy dietary pattern and behaviors, individual approaches based on a refined phenotyping have been paid attention. In this regard, inter-individual variability in the response to diet and meal planning based on the circadian rhythm warrant investigation. Dietary intake is a major determinant of blood glucose levels and postprandial glucose response are usually targeted in clinical practice by counting carbohydrate amount in diet or glycemic index of food items. However, recent studies using continuous glucose monitoring have reported high interpersonal variability in postprandial glucose response for the same meals, which are linked with multiple person-specific clinical factors. The carbohydrate intake of the Korean population is still considerably high compared with that in Western population. The interpersonal variability in high carbohydrate diets may lead to the progression of obesity or cardiometabolic disease. In addition, a recent study showed that distributing carbohydrate intake through the day into multiple meals and snack was associated with individuals' postprandial blood glucose. Meal patterns including meal timing and frequency have been extensively reviewed in recent literatures along with popularity of intermittent fasting. Modifying the meal timing can lead to better cardiovascular outcomes and key mechanism is based on optimization of circadian rhythms, which control many aspects of physiological function on a 24-hour cycle. According to a recent study of young adults with delayed sleep-wake cycle, confining eating window started eating before noon improved glycemic response and lipid metabolism. Beyond diet, meal planning including meal and sleep timing should be provided as additional aspect of individualized nutritional guidelines.

S15-3

Precision nutrition in the prevention and management of diabetes

Frank B. Hu
Harvard T.H. Chan School of Public Health, USA

Recent advances in powerful tools such as genomics, metabolomics, and gut microbiome have offered new opportunities as well as challenges in the application of precision nutrition for the prevention and management of type 2 diabetes (T2D). The integration of such technologies into epidemiological studies, referred to as "systems epidemiology", can enhance our understanding of biological mechanisms underlying diet and human health. This approach can also enable us to achieve better assessment of diet and nutritional status in free-living populations by identifying novel biomarkers of dietary intakes. Nutritional genomics has identified genetic variants that influence intakes and metabolism of specific nutrients and predict individuals' variability in response to dietary interventions. Metabolomics has revealed metabolomic fingerprints of food and nutrient consumption and has uncovered new metabolic pathways that are potentially modified by diet. In addition, dietary interventions have been shown to alter abundance, composition, and activity of gut microbiota that are relevant for food metabolism and glycemic control. By integrating these technologies with big data analytics, precision nutrition has the potential to provide personalized nutrition guidance to achieve more effective T2D prevention and management. Despite recent advances, major challenges still exist, including non-replication of study results, difficulty in translation of research findings into practice, and high cost. Although commercial companies have

promoted personalized nutrition assessment and genetic testing, there is little evidence on the benefits of these approaches for improving diet and preventing disease. Therefore, it is essential to balance the investment in precision nutrition, which targets individual characteristics, with public health nutrition, which aims to improve the health of populations.

S16-1

Impact of COVID-19 and associated preventive strategy on cardiometabolic risk

Soo Lim
Seoul National University, Korea

Severe acute respiratory syndrome coronavirus 2 has been spreading worldwide since. Early studies have shown that underlying diabetes is common among patients with COVID-19. The potential inter-relationships between diabetes and COVID-19 have been reported substantially. It is important to note that glycaemic deterioration is a typical complication of COVID-19. In addition, an integrated analysis showed that patients with severe COVID-19 have a highly impaired interferon type I response, indicating an impaired inflammatory process. Evidence also proposed that virally induced inflammation increases insulin resistance. For example, in coronavirus-induced pneumonia, inflammatory cells increase, leading to acute lung injury. This large burden of inflammatory cells can affect the functions of skeletal muscle and liver, the major insulin-responsive organs.
The molecular pathogenesis of SARS-CoV-2 is also related to inflammation and oxidative stress, which can contribute to development of T2D. Pro-inflammatory cytokines with type 1 T-helper cells are known to increase insulin resistance particularly in people with obesity.
The medications for treating COVID-19 can also affect glucose metabolism pharmacologically or through the modulation of inflammation and the immune system. Chloroquine and hydroxychloroquine have glucose-lowering efficacy by increasing insulin sensitivity. Camostat mesylate, a serine protease inhibitor, reduced the incidence of new-onset diabetes in patients with chronic pancreatitis. IL-6 receptor inhibitors had beneficial effects on insulin resistance in patients with rheumatoid arthritis. In contrast, protease inhibitors such as lopinavir and ritonavir have been reported to increase the risk of new-onset diabetes. Apparently, it seems it is necessary to carefully observe the long-term effects of these drugs for the future.
In conclusion, the COVID-19 global pandemic causes substantial health hazards, especially T2D. COVID-19 increases the risk of T2D and metabolic syndrome. These data suggest that active monitoring for metabolic dysregulation is needed in people who have recovered from COVID-19.

S16-2

New-onset diabetes after COVID-19 infection: it ain't over till it's over!

Yu Mi Kang
Harvard Medical School, USA

During the early phase of the coronavirus disease 2019 (COVID-19) pandemic, numerous studies have suggested the association between preexisting diabetes and poor COVID-19-related outcomes. As our battle with the pandemic is extended, however, a markedly increased incidence of type 1 and 2 diabetes is also being observed after the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.
This finding is consistent with our previous experience with other viral infections and acute illnesses leading to diabetes with a caveat: the mechanisms through which SARS-CoV-2 infection makes hosts susceptible to diabetes mellitus involves more complicated pathophysiology. For example, SARS-CoV-2 often induces an overwhelming inflammatory response, and corticosteroid use in severe cases often leads to steroid-induced hyperglycemia, both of which place hosts at significant risk of metabolic derangement. Lastly, the direct and indirect influences of SARS-CoV-2 on pancreatic beta-cells have been suggested as important pathophysiology. These findings warrant both mechanistic studies as well as prospective studies to identify the long-term metabolic effect of COVID-19 in a susceptible population.

S16-3

Efficacy and safety of dapagliflozin in patients with and without type 2 diabetes hospitalized with COVID-19 - results from the DARE-19 global randomized controlled trial

Mikhail Kosiborod
Saint Luke's Mid America Heart Institute, USA

Background: DARE-19 was an investigator-initiated, collaborative, international, multicenter, randomized, double blind, placebo-controlled trial testing whether dapagliflozin can reduce cardiovascular, kidney, respiratory complications or death, and improve recovery, in hospitalized COVID-19 patients.
COVID-19 leads to multiorgan failure, especially in high-risk patients. Dapagliflozin, a sodium-glucose cotransporter 2 inhibitor (SGLT2i), has significant cardio- and reno-protective benefits in cardiometabolic disease, and may provide organ protection in COVID-19 patients by impacting processes dysregulated during acute illness.
Methods: Eligible adults with ≥1 risk factor for COVID-19 complications (hypertension, type 2 diabetes, heart failure, chronic kidney disease or atherosclerotic cardiovascular) were randomized 1:1 to dapagliflozin 10 mg or placebo for 30 days. Dual primary endpoints included time to new or worsened organ dysfunction, or death; and a hierarchical composite of clinical recovery.
Results: Between April 22, 2020 and January 1, 2021, 1250 patients underwent randomisation, 625 in each group. 312 patients (49.9%) of patients in the dapagliflozin group and 324 patients (51.8%) in the placebo group had type 2 diabetes. Organ dysfunction or death occurred in 70 patients (11.2%) in the dapagliflozin group, and 86 (13.8%) in the placebo group (hazard ratio 0.80; 95% confidence interval [CI] 0.58-1.10; P=0.17). In total, 548 patients (87.7%) in the dapagliflozin group and 532 (85.1%) in the placebo group experienced clinical status improvement (win ratio, 1.09; 95%CI 0.97-1.22; P=0.14). There were 41 deaths (6.6%) in the dapagliflozin group, and 54 (8.6%) in placebo (hazard ratio, 0.77; 95%CI 0.52-1.16). Serious AEs were reported in 65 (10.6%) of 613 dapagliflozin-treated and 82 (13.3%) of 616 placebo-treated patients.
Conclusions: In patients with cardiometabolic risk factors hospitalized with COVID-19, treatment with dapagliflozin did not result in a statistically significant risk reduction in organ dysfunction or death, or improvement in clinical recovery. Numerically fewer patients treated with dapagliflozin experienced organ failure and death. Dapagliflozin was well-tolerated, with no new safety issues identified.

S16-4

Prescription of glucose-lowering therapies and risk of COVID-19 mortality in people with type 2 diabetes: from nationwide observational studies worldwide

Sun Ok Song
National Health Insurance Service Ilsan Hospital, Korea

Type 2 diabetes has been found to be one of the most significant and prevalent risk factors for the mortality of COVID-19. People with type 2 diabetes have a twice higher risk of COVID-19 mortality than those without. Hyperglycemia, which makes it more susceptible to a dysregulated inflammatory response, increases the risk of COVID-19-related mortality. It has been hypothesized that some blood glucose-regulating medications may improve COVID-19-related outcomes in patients with type 2 diabetes. However, we have not yet had sufficient time to collect data from evidence to prove this hypothesis from randomized control studies so far. In this session, I would like to introduce whether anti-T2DM medication use is associated with the risk of COVID-19-related mortality from studies conducted with large nationwide data.

S17-1

Burden of diabetes in youth: what we know and don't know and why we should care

Dana Dabelea
University of Colorado, USA

The prevalence and incidence of both type 1(T1D) and type 2 diabetes (T2D) in youth have been rising over the past decades. In the U.S, the SEARCH study aimed to address major knowledge gaps in the understanding of pe-

diatric diabetes. Age, sex and race/ethnicity-adjusted T1D increased on average by 1.8%/year (P=0.03), with the greatest increase among Hispanic youth. T2D rates also increased by 4.8%/year on average (P<0.001), with the largest increases in American Indian (8.9% per year) and Black youth (6.3% per year). Projections suggest that, by 2050, the number of youth with T1D age < 20 years will increase in the U.S. more than threefold, and numbers of youth with T2D will quadruple.
In addition, SEARCH has documented that many youth with diabetes are at risk for acute and chronic complications. Most studies worldwide have found that the prevalence of diabetes comorbidities, complications and mortality are higher in young people diagnosed with T2D compared to those diagnosed with T1D. In SEARCH, where risk factors for complications were directly compared among carefully-phenotyped participants, the prevalence of at least one complication or comorbidity in youth with T1D was approximately 1 out of 3, whereas for T2D, the prevalence was approximately 3 out of 4 participants. Mortality also appears to be more common in young-onset T2D compared to T1D.
Given these findings, early monitoring for early vascular complications is necessary, as is effective treatment of these complications and/or their risk factors. In addition, glycemic control and obesity are modifiable risk factors. Identifying and addressing barriers to receiving care are essential, particularly in the young adult population when many life transitions are occurring.

S17-2

IDF Diabetes Atlas, 10th edition: global regional and country-level diabetes prevalence estimates for 2021 and projections for 2045

Edward J. Boyko
University of Washington, Seattle, WA, USA

Aims: The aims of this talk will be to provide global, regional, and country-level estimates of diabetes prevalence and health expenditures for 2021 and projections for 2045.
Methods: A total of 219 data sources meeting pre-established quality criteria reporting research conducted between 2005 and 2020 and representing 215 countries and territories were identified. For countries without data meeting quality criteria, estimates were extrapolated from countries with similar economies, ethnicity, geography, and language. Logistic regression was used to generate smoothed age-specific diabetes prevalence estimates. Diabetes-related health expenditures were estimated using an attributable fraction method. The 2021 diabetes prevalence estimates were applied to population estimates for 2045 to project future prevalence.
Results: The global diabetes prevalence in persons between the ages of 20-79 years in 2021 was estimated to be 10.5% (536.6 million people), rising to 12.2% (783.2 million) in 2045. Diabetes prevalence was similar in men and women and was highest in those aged 75-79 years. The countries with the highest number of persons with diabetes in 2021 were in descending order China, India, and Pakistan. The countries with the highest prevalence of diabetes in 2021 were in descending order Pakistan, French Polynesia, and Kuwait. Prevalence (in 2021) was estimated to be higher in urban (12.1%) than rural (8.3%) areas, and in high-income (11.1%) compared to low-income countries (5.5%). The greatest relative increase in the prevalence of diabetes between 2021 and 2045 is expected to occur in middle-income countries (21.1%) compared to high- (12.2%) and low-income (11.9%) countries. Global diabetes-related health expenditures were estimated at 966 billion USD in 2021. These are projected to reach 1.05 trillion USD by 2045.
Conclusions: Just over half a billion people are living with diabetes worldwide which means that over 10.5% of the world's adult population now have this condition.

S17-3

Current status of adult type 1 diabetes and insulin-treated type 2 diabetes in Korea

Jae Hyeon Kim
Sungkyunkwan University, Korea

Type 1 diabetes (T1D) may develop at any age, even in the elderly. In Western populations, almost 40% of patients with T1D were estimated to develop the disease after age 30. In Asian countries such as Korea and Japan, the prevalence of T1D in adult two-fold higher than that of children. In addition, atypical T1D (slowly progressive T1D) was higher in people aged 40 years or older than in younger age groups. The prevalence of metabolic syndrome in patients with T1D in Korea was almost 55%.
In the real-world, T1D and type 2 diabetes (T2D) with insulin treatment might be associated with increased risk of cardiovascular events and/or early mortality although previous randomized controlled trials (RCTs) that compared insulin to other regimens demonstrated no significant increase in these outcomes in insulin groups. In Korea, recent epidemiologic studies showed that T1D had increased risks of incident cardiovascular disease (CVD), premature mortality and the risk for end stage renal disease (ESRD) development from chronic kidney disease (CKD) compared T2D. In addition, insulin treated T2D also showed increased risks of incident CVDs and premature mortality compared to T2D without insulin treatment. These results suggest that optimal glycemic control should be achieved in T1D and insulin treated T2D in Korea. Recent RCT in Samsung Medical Center (SMC) showed that real-time continuous glucose monitoring (rt-CGM) with structured individualized education increased 15.3% of time in range (TIR) compared to rt-CGM alone. Recently, more than 50% of T1D have been achieved target A1C using the continuous glucose monitoring with intensive education for insulin treatment in Samsung Medical Center. In this lecture, I will introduce current status of adult type 1 diabetes and insulin treated type 2 diabetes in Korea.

S17-4

Current status of type 2 diabetes and complications in Korea

Dae Jung Kim
Ajou University, Korea

In South Korea, the prevalence of diabetes has increased, but the incidence of diabetes has decreased. However, in young adults, the incidence of diabetes has increased. In addition, the proportion of obesity in young-onset diabetes has also increased dramatically. In older adults, although the incidence rate of diabetes in older adults has decreased, ~34% of newly diagnosed cases of diabetes are adults aged ≥65 years, which should not be overlooked.
Glycemic control improved in diabetes, but the awareness and comprehensive management of diabetes are still low.
During the last decade, the prevalence of diabetic neuropathy decline, while a rising trend was seen in diabetic retinopathy and diabetic nephropathy.
The prevalence of major cardiovascular complications, including ischemic heart disease, stroke, and myocardial infarction, tend to be declined among people with diabetes. However, a rising trend was seen in heart failure hospitalization and peripheral artery disease. Mortality rate in people with diabetes has steadily decreased in the last 10 years in Korea. Cancers and cardiovascular diseases are most important causes of death in people with diabetes.
Thus, we need a better implementation of evidence-based policies and integrated health systems strategies that improve management of diabetes and prevention of diabetic complications in all age groups.

S18-1

Dynamic remodeling of adipose tissue for survival

Jae Bum Kim
Seoul National University, Korea

In mammals, white adipose tissues are largely divided into visceral epididymal adipose tissue (EAT) and subcutaneous inguinal adipose tissue (IAT) with distinct metabolic properties. Although emerging evidence suggests that subpopulations of adipose stem cells (ASCs) in EAT and IAT would be important to explain fat depot differences, ASCs of two fat depots have not been comparatively investigated. Using single-cell RNA-sequencing with lean and obese mice, adoptive transplantation, and lymph node dissection, we characterized heterogeneous ASCs in two fat depots and examined the effects of intrinsic and tissue micro-environmental factors on distinct ASC features. We demonstrated that ASC clusters in EAT and IAT would exhibit different molecular features with three adipogenic stages and these features appeared to be conserved in human ASCs. Transplantation experiments with EAT and IAT ASCs into two fat depots revealed that intrinsic features of ASCs primarily determined adipogenic potential. Collectively, our data broaden the understandings of ASCs with new insights into the origin of white fat depot differences.

S18-2

Brown adipose tissue and systemic lipoprotein metabolism

Jörg Heeren
University Medical Center Hamburg-Eppendorf (UKE), Germany

The remarkable capacity of energy combustion by thermogenic brown adipocytes represents a valuable therapeutic target for treating obesity, dyslipidemia and atherosclerosis. Adaptive thermogenesis is an energy-demanding process mediated by cold-activated beige and brown adipocytes, which requires increased uptake of dietary carbohydrates and lipids for maintaining caloric balance. The canonical lipid uptake pathway involves the hydrolysis of triglyceride-rich lipoproteins (TRL) by active lipoprotein lipase and the subsequent fatty acid uptake by active adipocytes. In addition to fatty acid uptake, we have shown whole TRL particle internalization into active brown adipose tissue (BAT). These lipoproteins subsequently follow the endosomal/lysosomal pathway, where they undergo lysosomal acid lipase (LAL)-mediated processing. Endothelial cell-specific LAL-deficiency results in impaired thermogenic capacity as consequence of reduced recruitment of brown and brite/beige adipocytes. Mechanistically, TRL processing by LAL induces proliferation of endothelial cells and adipocyte precursors via beta-oxidation-dependent production of reactive oxygen species, which in turn stimulates hypoxia-inducible factor-1 alpha-dependent proliferative responses. Furthermore, we investigated the regulation as well as the molecular processes of lipid disposal into activated BAT, using pharmacological and genetic interventions in mice. We found that short-term BAT activation by cold exposure or beta-3-adrenergic receptor agonism triggers insulin secretion, a process depending on fatty acid release by white adipose tissue. At the end, we showed that both insulin release and brown adipocytes insulin sensitivity is essential for the replenishment of endogenous energy stores and efficient adaptive thermogenesis. These data demonstrate that both catabolic and anabolic processes are important for energy balance and function of BAT.

S18-3

Adipose tissue and metabolic health

John Yoon
University of California, Davis, USA

Adipose tissue plays a key role in the pathogenesis of metabolic disorders such as obesity and type 2 diabetes. White adipose tissue stores excess energy as lipid and secretes various hormones and cytokines, while its dysfunction contributes to inflammation and insulin resistance in type 2 diabetes. Brown adipose tissue burns energy and has been linked to better cardiometabolic health including lower odds of developing diabetes, dyslipidemia, and coronary artery disease. Activating brown adipose tissue by cold exposure enhances glucose uptake, insulin sensitivity, and mobilization of lipids from the periphery. Therefore, remodeling white adipose tissue or manipulating brown adipose tissue activity offers a potential strategy for achieving metabolic benefits and improving energy balance. This makes it essential to elucidate the mechanisms of adipose tissue thermogenesis and the cellular signaling pathways involved therein. We recently identified new genetic regulators of adipocyte thermogenesis and have characterized knockout mouse models for their metabolic phenotypes with respect to thermogenesis, energy balance, and glucose homeostasis. In separate efforts, we have employed animal models to examine genes mutated in cystic fibrosis and mitochondrial disorders for possible connections between their adipose tissue roles and the impact on systemic metabolism. Our findings can serve as the groundwork for further studies of adipose tissue in the context of metabolic disease pathogenesis and therapy development.

S18-4

Metabolic flux in brown adipose tissue and its regulation by nutrient sensing pathways

Su Myung Jung
Sungkyunkwan University, Korea

Brown adipose tissue (BAT)'s abilities to consume a variety of circulating nutrients and dissipate the stored energy as heat have made it an attractive therapeutic target against metabolic diseases including T2D. However, the question of how BAT metabolizes these nutrients remains unclear. Here, using transcriptomics, metabolomics and stable isotope tracing in mice, we comprehensively elucidated glucose utilization in BAT. While glucose has long-been thought of as a major thermogenic fuel (i.e. through glycolysis and TCA), our data suggests glucose feeds into many biosynthesis pathways (*de novo* fatty acids, glycerol-lipids and nucleotides) that support BAT functioning. By studying nutrient-sensing mTOR pathways, we recently reported signaling mechanisms by which BAT nutrient utilization is regulated. Conditionally deleting the essential mTORC2 subunit Rictor in BAT reprograms metabolism to promote lipid uptake, lipolysis, and thermogenesis at the expense of glucose utilization. Interestingly, mice lacking Rictor only in BAT are protected against obesity and hepatic steatosis reflecting the strong influence that BAT can have over systemic metabolic homeostasis. Unexpectedly, mTORC2 loss triggers lipid catabolism, not by impairing classic mTORC2-AKT signaling, but by promoting SIRT6-dependent FoxO1 deacetylation independently of AKT. I will present these findings and discuss our ongoing efforts to understand how BAT contributes to systems-level metabolic homeostasis.

CS1-1

Diabetes mellitus and cause-specific mortality: a population-based study

Sen Li
Beijing University of Chinese Medicine, China

Background: To investigate whether diabetes contributes to mortality for major types of diseases.
Methods: Six National Health and Nutrition Examination Survey data cycles (1999 to 2000, 2001 to 2002, 2003 to 2004, 2005 to 2006, 2007 to 2008, and 2009 to 2010) and their linked mortality files were used. A population of 15,513 participants was included according to the availability of diabetes and mortality status.
Results: Participants with diabetes tended to have higher all-cause mortality and mortality due to cardiovascular disease, cancer, chronic lower respiratory diseases, cerebrovascular disease, influenza and pneumonia, and kidney disease. Confounder-adjusted Cox proportional hazard models showed that both diagnosed diabetes category (yes or no) and diabetes status (diabetes, prediabetes, or no diabetes) were associated with all-cause mortality and with mortality due to cardiovascular disease, chronic lower respiratory diseases, influenza and pneumonia, and kidney disease. No associations were found for cancer-, accidents-, or Alzheimer's disease-related mortality.
Conclusion: The current study's findings provide epidemiological evidence that diagnosed diabetes at the baseline is associated with increased mortality risk due to cardiovascular disease, chronic lower respiratory diseases, influenza and pneumonia, and kidney disease, but not with cancer or Alzheimer's disease.

CS1-2

Time to reach target HbA1c is associated with long-term durable glycemic control and risk of diabetic complications in patients with newly diagnosed type 2 diabetes: a 6-year observational study

Kyoung Jin Kim
Korea University, Korea

The aim of this study was to evaluate the impact of early glycemic control on the prevention of future diabetic complications beyond glycemic durability in a real-world clinical setting. In a longitudinal observational cohort, 194 patients with T2DM newly diagnosed between January 2011 and March 2013 were followed up over 6 years. Patients were classified according to the time needed to reach the target HbA1c (<7.0%): <3, 3 to 6 (early achievement group), and ≥6 months (late achievement group). Risks of microvascular complications including diabetic retinopathy, nephropathy, and neuropathy as well as macrovascular events including ischemic heart disease, ischemic stroke, and peripheral arterial disease were assessed by multivariable Cox proportional hazards analysis. During a median follow-up of 6.53 years, 66 microvascular and 14 macrovascular events occurred. Maintenance of durable glycemic control over 6 years was more likely in the early achievement groups than in the late achievement group (34.5%, 30.0%, and 16.1% in <3, 3 to 6, and ≥6 months, respectively, P=0.039). Early target HbA1c achievement was associated with lower risk of composite diabetic complications (adjusted hazard ratio [HR, 0.47; 95% confidence interval [CI], 0.26 to 0.86 in <3 months group) (adjusted HR, 0.50; 95% CI, 0.23 to 1.10 in 3 to 6 months group, in reference to ≥6 months group). Similar trends were maintained for risks of microvascular and macrovascular complications, although statistical significance was not reached for macrovascular complications. Early target HbA1c achievement was associated with long-term durable glycemic control and reduced risk of diabetic complications in newly diagnosed T2DM.

CS1-3

Ipragliflozin, an SGLT2 inhibitor, ameliorates high-fat diet-induced metabolic changes by upregulating energy expenditure through activation of the AMPK/SIRT1 pathway

Minyoung Lee
Yonsei University, Korea

Background: Sodium-glucose co-transporter 2 (SGLT2) inhibitors are a new class of antidiabetic drugs that exhibit multiple extraglycemic effects. However, there are conflicting results regarding the effects of SGLT2 inhibition on energy expenditure and thermogenesis. Therefore, we investigated the effect of ipragliflozin (a selective SGLT2 inhibitor) on energy metabolism.
Methods: Six-week-old male 129S6/Sv mice with a high propensity for adipose tissue browning were randomly assigned to three groups: normal chow control, 60% high-fat diet (HFD)-fed control, and 60% HFD-fed ipragliflozin-treated groups. The administration of diet and medication was continued for 16 weeks.
Results: The HFD-fed mice became obese and developed hepatic steatosis and adipose tissue hypertrophy, but their random glucose levels were within the normal ranges; these features are similar to the metabolic features of a prediabetic condition. Ipragliflozin treatment markedly attenuated HFD-induced hepatic steatosis and reduced the size of hypertrophied adipocytes to that of smaller adipocytes. In the ipragliflozin treatment group, uncoupling protein 1 (Ucp1) and other thermogenesis-related genes were significantly upregulated in the visceral and subcutaneous adipose tissue, and fatty acid oxidation was increased in the brown adipose tissue. These effects were associated with a significant reduction in the insulin-to-glucagon ratio and the activation of the AMP-activated protein kinase (AMPK)/sirtuin 1 (SIRT1) pathway in the liver and adipose tissue.
Conclusion: SGLT2 inhibition by ipragliflozin showed beneficial metabolic effects in 129S6/Sv mice with HFD-induced obesity that mimics prediabetic conditions. Our data suggest that SGLT2 inhibitors, through their upregulation of energy expenditure, may have therapeutic potential in prediabetic obesity.

CS1-4

Magnetic resonance-based assessments better capture pathophysiologic profiles and progression in nonalcoholic fatty liver disease

Seung Joon Choi
Gachon University, Korea

Background: Several noninvasive tools are available for the assessment of nonalcoholic fatty liver disease (NAFLD) including clinical and blood biomarkers, transient elastography (TE), and magnetic resonance imaging (MRI) techniques, such as proton density fat fraction (MRI-PDFF) and magnetic resonance elastography (MRE). In the present study, we aimed to evaluate whether magnetic resonance (MR)-based examinations better discriminate the pathophysiologic features and fibrosis progression in NAFLD than other noninvasive methods.
Methods: A total of 133 subjects (31 healthy volunteers and 102 patients with NAFLD) were subjected to clinical and noninvasive NAFLD evaluation, with additional liver biopsy in some patients (n=54).
Results: MRI-PDFF correlated far better with hepatic fat measured by MR spectroscopy (r=0.978, P<0.001) than with the TE controlled attenuation parameter (CAP) (r=0.727, P<0.001). In addition, MRI-PDFF showed stronger correlations with various pathophysiologic parameters for cellular injury, glucose and lipid metabolism, and inflammation than the TE-CAP. The MRI-PDFF and TE-CAP cutoff levels associated with abnormal elevation of serum alanine aminotransferase were 9.9% and 270 dB/m, respectively. The MRE liver stiffness measurement showed stronger correlations with liver enzymes, platelets, complement component 3, several clinical fibrosis scores, and the enhanced liver fibrosis (ELF) score than the TE-LSM. In an analysis of only biopsied patients, MRE performed better in discriminating advanced fibrosis with a cutoff value of 3.9 kPa than the TE (cutoff 8.1kPa) and ELF test (cutoff 9.2 kPa).
Conclusion: Our results suggest that MRI-based assessment of NAFLD is the best non-invasive tool that captures the histologic, pathophysiologic and metabolic features of the disease.

CS1-5

Effect of sarcopenia and body shape on cardiovascular disease according to obesity phenotypes

Wankyo Chung
Seoul National University, Korea

Background: This study aimed to assess the effects of sarcopenia and A Body Shape Index (ABSI) on cardiovascular disease (CVD) risk according to obesity phenotypes.
Methods: We used data from the National Health and Nutrition Examination Survey 1999 to 2012. A total of 25,270 adults were included and

classified into the following groups: metabolically healthy normal weight (MHNW), metabolically healthy overweight/obese (MHO), metabolically unhealthy normal weight (MUNW), and metabolically unhealthy overweight/obese (MUO). Sarcopenia was defined as the appendicular skeletal mass index <7 kg/m^2 in men and <5.5 kg/m^2 in women. A multivariate logistic regression analysis was performed to evaluate the odds ratio (OR) of sarcopenia and ABSI for CVD events according to the obesity phenotype.
Results: The MHNW participants with sarcopenia had higher risk for CVD than those without sarcopenia (OR, 2.69; 95% confidence interval [CI], 1.56 to 4.64). In the analysis with MHNW participants without sarcopenia as a reference, the participants with sarcopenia showed a higher OR for CVD than those without sarcopenia in both MHO (OR in participants without sarcopenia, 3.31; 95% CI, 1.94 to 5.64) (OR in participants with sarcopenia, 8.59; 95% CI, 2.63 to 28.04) and MUO participants (OR in participants without sarcopenia, 5.11; 95% CI, 3.21 to 8.15) (OR in participants with sarcopenia, 8.12; 95% CI, 4.04 to 16.32). Participants within the second and third tertiles of ABSI had higher ORs for CVDs than the counterpart of obesity phenotypes within the first tertile.
Conclusion: These results suggest that clinical approaches that consider muscle and body shape are required.

CS1-6

The effects of exercise and restriction of sugar-sweetened beverages on muscle function and autophagy regulation in high-fat high-sucrose-fed obesity mice

Wook Song
Seoul National University, Korea

Background: Autophagy maintains muscle mass and healthy skeletal muscles. Several recent studies have associated sugar-sweetened beverage (SSB) consumption with diseases. We investigated whether muscle dysfunction due to obesity could be restored by SSB restriction (SR) alone or in combination with exercise (EX) training.
Methods: Obese mice were subjected to SR combined with treadmill EX. Intraperitoneal glucose tolerance test, grip strength test, hanging time test, and body composition analysis were performed. Triglyceride (TG) and total cholesterol (TC) serum concentrations and TG concentrations in quadriceps muscles were analyzed. Western blot and reverse transcription-quantitative polymerase chain reaction helped analyze autophagy-related protein and mRNA expression, respectively.
Results: SR alone had no significant effect on fasting blood glucose levels, glucose tolerance, and muscle function. However, it had effect on serum TC, serum TG, and BCL2 interacting protein 3 expression. SR+EX improved glucose tolerance and muscle function and increased serum TC utilization than SR alone. SR+EX reduced P62 levels, increased glucose transporter type 4 and peroxisome proliferator-activated receptor γ coactivator-1α protein expression, and improved grip strength relative to the high-fat and high-sucrose liquid (HFHS) group, and this was not observed in the HFHS+EX group.
Conclusion: SR induced mitophagy-related protein expression in quadriceps, without affecting muscle function. And, the combination of SR and EX activated mitophagy-related proteins and improved muscle function.

CS2-1

Nonpharmacological therapy vs. pharmacological therapy

Suk Chon
Kyung Hee University, Korea

All the treatment guidelines for type 2 diabetes around the world recommend comprehensive lifestyle modification as the 1st line therapy for all patients as soon as they are diagnosed with type 2 diabetes. The ADA guidelines recommend LSM for overweight and obese patients to lose and maintain body weight by 5% or more and include at least 150 minutes of moderate to high-intensity exercise per week. Similarly, in Korea, LSM is recommended as the first-line treatment, but the specific method is not provided.
Type 2 diabetes has a progressive nature, and at the center of it lies an increase in insulin resistance before onset and progressive beta cell dysfunction. Therefore, for the treatment of diabetic patients, active intensification of therapeutic agents and adding of drugs with various mechanisms are inevitable according to the progress of diabetes. However, despite these various drug treatments or even multiple insulin treatments, glycemic control is often difficult, and most of the reason is because it is difficult to maintain active lifestyle modifications.
LSM, which is recommended as an essential element of primary treatment, is known to be capable of remission of diabetes according to its method and intensity level compared to drug treatment. In this session, I'd like to review the effects of intensive lifestyle intervention as an 1st line therapy for diabetes that have been studied until recently and suggest a method to be applied in Korea.

CS2-2

Metformin monotherapy vs. initial combination therapy

Jong Han Choi
Konkuk University, Korea

For sixty years after its introduction as anti-diabetic medication, metformin remains a milestone in the treatment of type 2 diabetes mellitus (T2DM). From the UKPDS onward, all international guidelines for standard of care in diabetes have recommended metformin as first-line treatment and stepwise therapy adding other drugs one by one to achieve the glycemic target for patients with T2DM. Recently, there is strong evidence showing that early combination treatment with metformin and vildagliptin improves glycemic durability compared with stepwise therapy with metformin even in newly diagnosed patients with T2DM. Accordingly, initial combination therapy has been proposed as a novel strategy to achieve glycemic goals earlier. However, there is still insufficient evidence on the efficacy and harm of early combination therapy with other anti-diabetic drugs. It is also inconclusive which patients are more effective in applying early combination therapy. Here, we will share the evidence from the systematic review and network meta-analysis of randomized controlled trials that reported the efficacy and safety outcomes of metformin monotherapy and initial combination therapy with various anti-diabetic drugs. We will also discuss optimal therapeutic strategies in newly diagnosed patients with T2DM.

CS2-3

Insulin-based vs. oral combination therapy

Jong Suk Park
Yonsei University, Korea

The glucotoxicity generated by hyperglycemia is commonly thought to be the fundamental acquired factor causing continuous decline of β-cell function in type 2 diabetes. The rapid normalization of glucose levels in patients with newly diagnosed T2DM through intensive treatment leads to eliminate the deleterious effects of hyperglycemia and rescue injured β cells, avoiding irreversible loss of β-cell secretory function and β-cell mass that leads to the worsening of diabetes. Several small size and observational studies have found that the early normalization of glucose in patients with newly diagnosed T2DM via intensive insulin treatment (IIT) can lead to drug-free glycemic remission.
Also a RCT with comparative treatment methods and a meta-analysis showed that early IIT in newly diagnosed patients with T2DM produces favorable outcomes for glycemic control and β-cell recovery in terms of long-term efficacy over 1 year. Furthermore a recent RCT conducted by Chon et al. suggested that outpatient clinic-based early IIT to ensure euglycemia in patients with newly diagnosed T2DM might be an effective initial therapeutic option for greater improvements in short- and long-term β-cell function and long-term glycemic control.
Whether these benefits are derived from the effects of insulin or the rapid elimination of glucotoxicity still remains unclear. Additionally, there is a lack of sufficient evidence from RCTs regarding the effects of early IIT.
In this lecture, I will show the published studies of Insulin-based vs. oral combination therapy in Initial treatment strategies in patients with newly diagnosed type 2 diabetes mellites and discuss which treatment is more appropriate as an initial treatment for patients newly diagnosed with type 2 diabetes.

CS2-4

Treatment strategies based on the sub-classification of adult-onset diabetes mellitus

Bo Kyung Koo
Seoul National University, Korea

Type 2 diabetes is defined through a broad definition based on insulin resistance and insulin deficiency, and there have been efforts to classify type 2 diabetes into subtypes according to degree of insulin resistance and insulin deficiency, presence or absence of obesity or onset-age, etc. Suggested subclassifications based on clinical parameters reveal heterogenous metabolomic features and diversity in diabetic complication risk. Identification of subclass of type 2 diabetes might improve clinical outcomes through precision medicine and get insights on its pathogenesis.

CS3-1

Diabetes fact sheet in Korea

Hyuk-Sang Kwon
The Catholic University of Korea, Korea

Korean Diabetes Association published 'Diabetes Fact Sheet in Korea' for the first time among various medical societies in 2012. Diabetes Fact Sheet in Korea 2022 will provide the prevalence of diabetes and pre-diabetes, estimated population, and distribution by age, as in previous years. In addition, data on diabetes management level, diabetes complications and various comorbidities, and diabetes drug treatment status will be included. This year marks the 10th anniversary, and through this session, we want to discuss on the importance and clinical meaning of this representative epidemiological data and unmet need in the preparation of this kind of 'Fact Sheet' data together with related societies.

CS3-2

Korea hypertension fact sheet

Hyeon Chang Kim
Yonsei University, Korea

CS3-3

Dyslipidemia fact sheet in Korea

In-Kyung Jeong
Kyung Hee University, Korea

The Korean Society of Lipid and Atherosclerosis (KSoLA) is a nonprofit organization founded in 2001 by the merger of the Korean Society of Lipid and the Korean Association for the Study of Atherosclerosis. The mission of our society is to prevent and cure atherosclerosis, and to improve public awareness regarding the seriousness of atherosclerosis and its risk factors. To fulfill this mission, we have analyzed the status of dyslipidemia based on data from the 2007-2020 Korea National Health and Nutrition Examination Survey (KNHANES). Recently we launch the 4th edition of the Dyslipidemia Fact Sheet, which we have been publishing since 2015. More than 1 in 4 Korean adults are living with hypercholesterolemia. The prevalence of hypercholesterolemia in adults has more than doubled from 2007 to 2020. More than 2 in 5 adults in Korea have dyslipidemia, which is a serious cause of mortality and morbidity due to cardiovascular disease. It places a heavy burden on the affected individuals and our society. In this edition, the definition of hypo-HDL-cholesterolemia for women (less than 50 mg/dL) was added in the analysis of the prevalence of dyslipidemia.
Diabetes, high blood pressure, hyperlipidemia, and obesity are linked to each other based on the pathological mechanism of insulin resistance. Therefore, when conducting an epidemiological investigation of these diseases, it is necessary to organize them well with a unified definition. We will discuss about it in this session.

CS3-4

Obesity fact sheet

Jang Won Son
The Catholic University of Korea, Korea

Since 2015, the Korean Society for the Study of Obesity has annually updated the Obesity Fact Sheets, based on representative data from the National Health Insurance Service, to report the national obesity status and its impacts. The 2021 Obesity Fact Sheet presents trends in obesity and abdominal obesity prevalence among Korean adults from 2009 to 2019 according to age and sex, and risk of major comorbidities, such as type 2 diabetes mellitus, cardiovascular diseases, and cancers. This study sought to analyze differences in obesity prevalence and comorbidity risk by different age groups to understand age-specific differences and to develop targeted interventions for those subgroups.
Recently, we are analyzing the life expectancy and healthy life expectancy according to the degree of obesity and the genetic architecture of obesity in Korean population through bio-big data analysis.
In addition, we evaluate the prevalence of rare genetic diseases of obesity based on the 2019-2020 rare disease annual data.
This fact sheet is intended to improve obesity care and provide a valuable resource for establishing national health policies in Korea.

CS3-5

Noncommunicable diseases (NCD) statistics based on Korea National Health and Nutrition Examination Survey (KNHANES)

Kyungwon Oh
Korea Disease Control and Prevention Agency, Korea

The Korea National Health and Nutrition Examination Survey (KNHANES) was initiated in 1998 to provide evidence for the development and evaluation of health policies and programs. The Korea Disease Control and Prevention Agency (KDCA) is responsible for the KNHANES and has conducted it as a series of surveys. The survey consists of standardized physical examinations in mobile examination centers, and laboratory tests on blood and urine specimens, and dietary interviews conducted in participants' homes in a nationally representative sample of about 10,000 persons each year. Examination sample weights, accounting for the differential selection probabilities and adjusting for nonresponse and noncoverage, were used to estimate prevalence. Findings from this survey will be used to determine the prevalence of major noncommunicable diseases (NCD) and risk factors for diseases. The age-adjusted prevalence of obesity in men (19 years and over) increased from 35.1% in 2011 to 48.0% in 2020 and hypercholesterolemia prevalence doubled both men (10.6% in 2011, 20.2% in 2020) and women (12.0% in 2011, 18.8% in 2020). The age-adjusted prevalence of hypertension and diabetes show no a statistically significant trends. In health risk factors, the age-adjusted prevalence of smoking declined, however physical inactivity, heavy drinking, and fat intake showed increasing trends. The increased trends of NCD and health risk factors may have contributed to the burden of NCD and mortality, and continuous monitoring is needed to improve lifestyle and manage NCD. The KDCA publishes summary statistics, current issues, in-depth reports along with the annual report ("Health Statistics") to meet different data needs, and microdata are publicly available through the KNHANES website (http://knhanes.kdca.go.kr). In addition, KDCA support or collaborate with the publication of fact sheets by related academic societies, and need to continue discussion data and analytical considerations (combination of survey cycle, estimation, weighting procedures, etc.) to improve the accuracy and comparability with academic societies.

CS3-6

National statistics of NCD using the NHIS database

Jong Heon Park
National Health Insurance Service, Korea

NHIS, as a single insurer, take responsibility for operation of National Health Insurance (NHI) scheme, such as eligibility review of the insured, imposition and collection of contributions, insurance benefit, and negotiation of medical fee schedule with healthcare service providers.
The Korean National Health Insurance Big Data (NHID) features a whole population cohort which can be used for research purposes. National Health Insurance Big Data is made out of many resources. Database of

beneficiary, contributions, medical service utilization, health screening service, long-term care service is integrated into NHID through individual ID linkage.
National Health Insurance Big Data can be used in various areas. NHIS supports for research that contributes to evidence-based policies and provides customized health service and so on.
NHIS created a public research DB, only after a de-identification process, to improve the accessibility of data, and provides big data and support for research that contributes to evidence-based policies, relates to issues of public concern, and improves data availability, conducted by a professional societies or public institutions.
NHIS provides a various health services, such as one-stop service which includes an annual physical diagnosis, an assessment of potential health risks and a customized treatment plan to counteract any health risks, monitoring indicators for the prevention of cardiovascular disease, and a health map service for an adequate allocation of healthcare resources and design an effective system.

CS4-1

Overview of special estimate cases system of incurable diseases

Kyungwon Lee
National Health Insurance Service, Korea

The Special Estimate Care System in Korea lowers co-payment rates for severe diseases (cancer, cardiovascular/cerebrovascular diseases, severe burn injury, severe trauma, etc.), rare and incurable disease, tuberculosis, and latent tuberculosis infection. This system has been playing an important role as safety net since 2009 by reducing excessive financial burden caused by care for severe disease. By related laws, the special estimate care system is applied to covered items by National Health Insurance (NHI).
The typical co-payment rate is 20% for inpatient care, and 30% to 60% for outpatient care, however, when registered as a special estimate case, 0% to 10% co-payment applies to both inpatient and outpatient care. As for incurable disease, if patients are registered as special estimates system of National Health Insurance Service (NHIS) according to the diagnosis of medical specialists, they just need to pay 10% of total cost of healthcare benefit which is covered by NHI.
In this lecture, definition, criteria, and procedures for designating incurable disease by NHIS will be introduced briefly.

CS4-2

Type 1 diabetes mellitus - why it should be treated as a severe incurable diseases

Dughyun Choi
Soonchunhyang University, Korea

Severe incurable diseases in Korea are a group of diseases designated by the Korean government, which are difficult to cure and eventually cause fatal outcomes like death or permanent disabilities to the patients unless treated and managed well. Severe intractable diseases include chronic renal failure patients undergoing dialysis, organ transplant patients, seropositive rheumatoid arthritis patients, etc. The Korean government manages these disease groups and is implementing a policy to reduce the out-of-pocket costs of patients who fall under the disease group. Type 1 diabetes is a severe endocrine metabolic disease accompanied by permanent damage to the pancreas, which results in patients with type 1 diabetes can only survive through lifelong insulin treatment. Nevertheless, type 1 diabetes is not recognized as a severe incurable disease, and type 1 diabetes patients and their families are suffering from acute and chronic diabetes complications that occur throughout their lives, as well as excessive medical expenses. In this session, I would like to discuss from a doctor's point of view why type 1 diabetes should be classified as a serious incurable disease.

CS5-1

The current recommendation of SGLT2 inhibitor in clinical practice guidelines

Nan Hee Kim
Korea University, Korea

Diabetic kidney disease (DKD) is a major burden of patients with diabetes, increasing morbidity and mortality. Despite the standard treatment of hyperglycemia and hypertension, the prevalence and incidence of end stage renal disease (ESRD) due to diabetes is steadily increasing. However, the introduction of SGLT2 inhibitor could be a game changer for DKD treatment. There have been large, randomized placebo-controlled cardiovascular and renal outcome trials with SGLT2 inhibitors, most of which have shown clear beneficial effects on the prevention of renal function deterioration and the development of ESRD. Therefore, clinical practice guidelines recommend SGLT2 inhibitors for the treatment of people with type 2 diabetes who have kidney disease or are at high risk. Here, I summarize major findings of the key clinical trials of SGLT2 inhibitors and present how they are reflected in current practice guidelines.

CS5-2

Nephrologist's view of sodium-glucose co-transporter-2 inhibitors and chronic kidney disease (in Asians)

Behram A. Khan
The National Kidney Foundation Singapore, Singapore

Chronic Kidney Disease (CKD) is on the rise in several countries with a shift of demographics to an older population and rise of Diabetes Mellitus (DM) and Hypertension. For the past nearly 2 decades, CKD progression has been retarded with Renal Angitotension Aldosterone System Inhibitors (RAASi). The recent data on sodium-glucose co-transporter-2 inhibitors (SGLT2i) has been very promising to reduce the residual risk of CKD progression which was unaddressed by RAASi usage alone. CKD is a Cardiovascular Risk Equivalent and the data also translates to better cardiovascular endpoints, as well as mortality related to these adverse events. SGLT2i have been identified by several international guidelines to be part of effective management of CKD, DM and related cardiovascular risk reduction. CKD stages based on estimate Glomerular Filtration Rate (eGFR) and albuminuria, are both essential for proper diagnosis and risk stratification. Early diagnosis of CKD with introduction of SGLT2i is essential to reduce progression of CKD and delay the onset of End Stage Renal Disease, which requires dialysis or transplantation. SGLT2i have been shown to be useful in these respects in both diabetic and non-diabetic patients. In the Asia Pacific region, we are also seeing an aging population, increase DM/HTN and CKD rates. It is vital to review SGLT2i indications of usage, protocols of their addition to previous standard of care and addressing common concerns that practitioners may have to comfortably prescribe them.

CS5-3

SGLT2 inhibitor: beyond glucose lowering effect, cardiometabolic renal axis

Daisuke Yabe
Gifu University, Japan

The interplay between metabolic disorders, cardiovascular disease (CVD) and kidney dysfunction, termed cardio-renal-metabolic (CRM) disease has been illuminated by preclinical and clinical studies on sodium-glucose co-transporter-2 (SGLT2) inhibitors which has been gaining much attention for the management of type 2 diabetes (T2D), heart failure (HF) and chronic kidney disease (CKD). T2D confers increased risk for heart failure, which-although well known-has only recently come into focus for treatment, and may differ by ethnicity, whereas atherosclerotic heart disease is a well-established complication of T2D. Many people with T2D also have CKD, with a higher risk in Asians than their Western counterparts. Furthermore, CVD increases the risk of CKD and vice versa, with heart failure, notably, present in approximately half of CKD patients. Molecular mechanisms involved in CRM disease include hyperglycaemia, insulin resistance, hyperactivity of the renin-angiotensin-aldosterone system, production of advanced glycation end-products, oxidative stress, lipotoxicity, endoplasmic reticulum stress, calcium-handling abnormalities, mitochondrial malfunction and deficient energy production, and chronic inflammation. We'd

like to discuss mechanisms underlying beyond glucose-lowering effects of SGLT2 inhibitors on CRM disease at molecular and physiological levels.

RS1-1

Human genetics as a model for target validation: finding new therapies for diabetes

Anna L. Gloyn
Stanford University, USA

Large-scale genetic studies have now uncovered hundreds of regions of our genomes which influence our risk for developing diabetes. Signals which are due to coding variants offer a short cut to understand disease biology as they identify the protein which is involved. This presentation will highlight an example of how human genetics can deliver novel mechanisms for islet-cell dysfunction and provide opportunities for precision medicine for diabetes.

RS1-2

Genetics of diabetes and beta-cell function in East Asians

Soo Heon Kwak
Seoul National University, Korea

Recent epidemiologic study revealed that Korean people with type 2 diabetes (T2D) already have impaired insulin secretion as well as insulin resistance 10 years before the onset of diabetes. Those who developed T2D were characterized by impaired β-cell compensation with abrupt decrease in insulin secretion during the last two years before the development of diabetes. The retrograde trajectory of disposition index was different according to the baseline subgroups of insulin secretion and insulin sensitivity. Recent large scale genome-wide association study highlighted that genetic risk factor for T2D are substantially shared between East Asians and European. However, there were notable differences between the two ancestries including 1) less attenuation of effect size after adjusting for BMI, 2) presence of variants that were associated with lipodystrophy-like phenotype, 3) presence of East Asian specific variant with higher effect size. Genetic studies identified that coding variants that are specific to East Asians, such as rs2233580 in PAX4, and rs3765467 in GLPR1R play important role in the pathogenesis of T2D by modulating beta-cell function. Polygenic risk score for T2D seems to predict rate of decline in beta-cell function in those without diabetes in East Asians. In the presentation, I will underscore East Asian specific genetic risk factors for T2D and beta-cell function.

RS1-3

TIGER: the gene expression regulatory variation landscape of human pancreatic islets

Josep M Mercader
Broad Institute of MIT & Harvard, USA

Genome-wide association studies (GWASs) identified hundreds of signals associated with type 2 diabetes (T2D). To gain insight into their underlying molecular mechanisms, we have created the translational human pancreatic islet genotype tissue-expression resource (TIGER), aggregating >500 human islet genomic datasets from five cohorts in the Horizon 2020 consortium T2DSystems. We impute genotypes using four reference panels and meta-analyze cohorts to improve the coverage of expression quantitative trait loci (eQTL) and develop a method to combine allele-specific expression across samples (cASE). We identify >1 million islet eQTLs, 53 of which colocalize with T2D signals. Among them, a low-frequency allele that reduces T2D risk by half increases CCND2 expression. We identify eight cASE colocalizations, among which we found a T2D-associated SLC30A8 variant. We make all data available through the TIGER portal (http://tiger.bsc.es), which represents a comprehensive human islet genomic data resource to elucidate how genetic variation affects islet function and translates into therapeutic insight and precision medicine for T2D.

RS1-4

Characterizing the process of loss of β-cell identity by mouse model for early diabetes

Joonyub Lee
The Catholic University of Korea, Korea

Loss of β-cell identity is thought to be an early event of functional β-cell mass decrease during the development of type 2 diabetes. However, the mechanism how β-cells lose their identity has been poorly understood. In this talk, I would like to share some data characterizing the process of loss of β-cell identity by using mouse model generated by knocking out Prmt1 in adult β-cells (Prmt1 βiKO). This model recapitulates early and progressive diabetic phenotype. Importantly, β-cells in Prmt1 βiKO mouse were functionally immature and the protein level of mature β-cell markers were decreased. Single cell transcriptomic analysis of Prmt1 βiKO β-cells revealed groups of β-cell subpopulations that serially ranged from transcriptomic normal β-cells to the stressed β-cells and immature β-cells. Stressed β-cells were increased in mRNA expression of both Insulin and ER stress-related genes whereas immature β-cell population were decreased in mRNA expression of insulin, insulin biosynthesis gene and β-cell transcription factors. Metabolic challenge in βiKO mice resulted in robust 'loss of identity' in β-cells with profound proteomic and transcriptomic change. Pseudotemporal analysis revealed a biological meaningful wave of transcriptomic changes. Single cell transcriptomic analysis of Prmt1 βiKO β-cells revealed groups of β-cell subpopulations that serially ranged from transcriptomic normal β-cells to the stressed β-cells-immature β-cells. Stressed β-cells were increased in mRNA expression of both Insulin and ER stress-related genes whereas immature β-cell population were decreased in mRNA expression of insulin and β-cell transcription factors. These results can provide a new insight into how β-cells lose their identity in type 2 diabetes.

RS2-1

Diabetic neuropathy: what does the future hold?

Ralf Baron
Universitätsklinikum Schleswig-Holstein, Germany

Diabetic painful neuropathy represents a major medical problem and treatment has been unsatisfactory. A hypothetical concept was proposed in which pain is analysed on the basis of underlying mechanisms and sensory abnormalities. If a systematic clinical examination of the patient and a precise phenotypic characterization is combined with a selection of drugs acting at those particular mechanisms, it should ultimately be possible to design optimal treatments for the individual patient.
Several international consortia (German Research Network on Neuropathic Pain, IMI-Europain, Neuropain) established a large data-base that includes epidemiological and clinical data as well as standardized symptom questionnaires and quantitative sensory testing. More than 2000 patients with different neuropathic pain states including painful diabetic neuropathy have been examined. Furthermore, epidemiological and clinical data on the symptomatology of thousands of patients from a cross sectional survey (pain*DETECT*, pain*PREDICT*) are available.
Using a subgroup analysis different somatosensory profiles could be identified that might be indicative of the underlying pathophysiological mechanism. Several recent clinical trials using this sensory profile-based classification could identify a differential treatment effect in subgroups of patients. Consequently, cohorts in clinical trials of diabetic painful neuropathy should be stratified and potentially enriched with patients who likely respond to the study drug based on the sensory profile. This approach has the potential to minimize pathophysiological heterogeneity within the groups under study and to increase the power to detect a positive treatment result. In clinical proof-of-concept trials the study population can be enriched prospectively on the basis of "a priori" defined entry criteria. This enrichment with patients who potentially require a specific treatment will increase the likelihood for positive trial outcomes.

RS2-2

Nerve and brain in diabetic peripheral neuropathy

Chong Hwa Kim
Sejong General Hospital, Korea

Diabetic peripheral neuropathy (DPN) is concomitantly affect both the PNS

and CNS. Several studies showed pathological alterations in spinal cord and brain structures in patients with DPN. Neuronal injury in DPN has been well recognized within the peripheral nervous system for over a century. DPN directly targets dorsal root ganglion sensory neurons. This neuron-specific concept, supported by accumulating evidence, might account for important features of DPN, such as its early sensory neuron degeneration. Diabetic sensory neurons develop neuronal atrophy alongside a series of messenger ribonucleic acid (RNA) changes related to declines in structural proteins, increases in heat shock protein, increases in the receptor for advanced glycation end-products, declines in growth factor signaling and other changes.
And also DPN had the demonstration of significant structural abnormalities in the brain. we need to understand why there is a reduction in somatosensory peripheral grey matter volume. What are the potential mechanisms for this? It might be possible that these patients may have abnormal regional blood perfusion or a reduction in neuronal activity because of altered peripheral and long-tract neuronal function. The involvement of CNS in DPN has opened a whole new area for further research and has a great potential for the development of new treatments for DPN.

RS2-3

Relationship between lipids and diabetic neuropathy: a new potential therapeutic target?

Ho Chan Cho
Keimyung University, Korea

Diabetes is the chronic disorder and diabetic polyneuropathy (DPN) is the most frequent type 2 diabetes complication and is associated with poor outcomes. The pathophysiology of DPN includes several factors such as metabolic, vascular, autoimmune, oxidative stress and neurohormonal growth-factor deficiency. Hyperlipidemia is known to be associated with the development of neuropathy. Some studies showed plasma TG were associated with progressive DPN and LDL particle size as a marker of atherogenic dyslipidemia appeared to be an independent risk factor for DPN. Furthermore, the mechanism linking lipids to DPN include that peripheral nerves are affected by insulin resistance, free fatty acid mediate insulin resistance and dysfunction in peripheral nerves, imbalance of mitochondrial bioenergetics further mediates neuropathy, and oxidized lipids may promote DPN. Therefore, there are a number of experimental and clinical studies about a mechanistic link between lipid metabolism and peripheral nerve dysfunction and cholesterol and triglyceride-lowering pharmacotherapy have shown reduced rates of progression of diabetic neuropathy. Future studies need to investigate the effects and mechanisms of lipid-lowering therapy on the progression and severity of DPN in larger group.

RS3-1

Emerging targets of diabetic kidney disease

Mark Cooper
Monash University, Australia

Diabetic kidney disease (DKD) occurs as a result of multiple factors which have been increasingly defined over the last 2 decades. Many research groups have identified pathways that are implicated in the susceptibility and progression of DKD. Oxidative stress, fibrosis and inflammation have all been considered to play a role in. this disorder which appears to damage numerous cell populations in the kidney with a major focus being on the podocyte with the diabetic glomerulus. This has led to investigation of numerous targets to develop drugs which afford renoprotection in diabetes. Some of the promising targets and potential drugs that act on these specific proteins will be reviewed.

RS3-2

Mechanistic insight toward understanding the therapeutic effect of finerenone in diabetic kidney disease

Wonsuk Choi
Chonnam National University, Korea

In two recent trials (FIDELIO-DKD and FIGARO-DKD), the addition of finerenone, a novel selective, nonsteroidal mineralocorticoid receptor antagonist (MRA), to the maximum tolerated inhibition of the renin-angiotensin system slowed the progression of kidney disease in a variety of patients with type 2 diabetes and chronic kidney disease (CKD). Several biological pathways that can be accomplished by MR antagonism can be used to explain these positive effects of finerenone. The activation of inflammatory and fibrotic pathways in the kidney is caused by MR activation in non-epithelial cells, and it has negative effects on podocytes and mesangial cells. In preclinical models of diabetic kidney disease (DKD), MRA decreases albuminuria, renal fibrosis, glomerular lesions, and inflammation. It is interesting to note that finerenone improved albuminuria in CKD and T2DM patients who were already taking a sodium-glucose cotransporter-2 inhibitor (SGLT2i) at baseline, and the benefits on kidney outcomes were constant regardless of SGLT2i use. The progression of DKD may be slowed by SGLT2i and finerenone together, according to current mechanistic findings. According to a single-cell transcriptome analysis, patients with DKD have variable levels of renal expression for the gene *NR3C2*, which encodes the MR, and *SLC5A2*, which encodes SGLT2. *NR3C2* was detected in all the kidney cell types and kidney compartments examined, whereas *SLC5A2* was mostly expressed in the proximal convoluted tubule. These results imply that finerenone and SGLT2i might function in different cell types, and that using them together might thus have additional clinical benefits. In conclusion, finerenone has renoprotective benefits in DKD patients by lowering renal fibrosis and inflammation.

RS3-3

Targeting nox in aging and diabetes

Jin Joo Cha
Korea University, Korea

The main characteristics of aging kidney are age dependent glomerulosclerosis, tubular atrophy and interstitial fibrosis; therefore, aging is now considered as an independent risk of chronic kidney disease. The changes can be accelerated in the presence of increased inflammatory processes and oxidative stress, which are common findings in diabetic mellitus. Moreover, Aging process itself is a risk factor for altered glucose metabolism and insulin resistance. Diabetes with serious complications has been steadily increasing in older patients. NADPH oxidases (Nox) are a major source of ROS in the vasculature and are key players in mediating redox signaling under physiological and pathophysiological conditions. Nox-mediated ROS signaling pathways are known to involved in regulation of age-associated vascular changes. Experimental animal model of aging showed Nox1,2,4 significantly increases during aging and also in diabetic aging model, the changes tend to be more accentuated. Nox inhibition improves insulin resistance and systemic oxidative stress in aging mice. Nox inhibition in streptozotocin induced diabetic model in aging mice, although did not show systemic improvement of insulin resistance, showed significant decrease in urinary 8 isoprostane excretion, and MCP-1, collagen IV expressions in the kidney, which may indicate that nox inhibition may have a protective effect in aging diabetic kidney disease.

RS3-4

Role of the lysosomal transcription factor TFEB in podocyte injury in diabetic kidney disease

Mako Yasuda-Yamahara
Shiga University, Japan

Diabetic kidney disease (DKD) is the leading cause of end-stage renal disease, and there is a need to develop new therapeutic strategies. Podocytes are essential for the glomerular filtration barrier function, and they do not typically proliferate. Therefore, the autophagy-lysosome system, an intracellular catabolic mechanism, is thought to be important in protecting podocytes during the progression of DKD. TFEB, a transcription factor that regulates lysosome biogenesis, and stress and starvation condi-

tions enhance nuclear translocation of TFEB and activate it. While, TFEB is negatively regulated by mTORC1 (mechanistic target of rapamycin). We hypothesis that the nuclear translocation of TFEB may be suppressed by hyperactivation of mTORC1 under diabetic condition, and this may be involved in the pathogenesis of podocyte injury in DKD.
We evaluated the mTORC1 activity and TFEB expression in podocytes of diabetic model mice. In podocytes from 20-week-old db/db mice, there was hyperactivation of mTORC1 and suppression of TFEB nuclear translocation. In the cultured podocytes isolated from podocyte-specific TCS1-deficient mice, an inhibitor of mTORC1, mTORC1 was hyperactivated and TFEB nuclear translocation were suppressed compared to those in the podocytes isolated from wild-type mice. In addition, TNFα-induced cell death were exacerbated in TSC1-deficient podocytes, which were attenuated by co-incubation with rapamycin, an mTORC1 inhibitor. Furthermore, we established both constitutively TFEB-active and constitutively TFEB-inactive podocytes by gene mutations of TFEB at the mTORC1 phosphorylation site. Cell apoptosis induced by palmitic acid were significantly decreased in the TFEB-active podocytes compared to TFEB-inactive podocytes.
These results suggest that TFEB activity may suppressed by mTORC1 hyperactivation in podocytes, which may lead to the podocyte susceptibility and loss under diabetes. TFEB activation may be a promising therapeutic option against podocyte injury in DKD.

RS4-1

Macrophages as a source of fibrosis biomarkers for non-alcoholic fatty liver disease

Sachiyo Yoshio
National Center for Global Health and Medicine, Japan

Non-alcoholic fatty liver disease/steatohepatitis (NAFLD/NASH) is becoming a leading cause of liver disease worldwide. Liver fibrosis and cirrhosis is one of the most impactful risk factors of hepatocellular carcinoma (HCC), thus associating with long-term prognosis in patients with NAFLD. Liver macrophage plays key roles in the regulation of inflammation and fibrosis by interacting hepatic stellate cells and other immune cells. An increase of portal macrophages is the earliest change at the stage of steatosis before inflammation or fibrosis and predict disease progression in patients with NAFLD. These reports raise the possibility that the abundance of activated macrophage in the liver is the phenomenon accompanying the progressive nature of NAFLD. In human NAFLD study, CCR2 is highly expressed in monocyte-derived macrophages and CCR2+ macrophages are increased in patients with NAFLD. CCL2 and other chemokines promote the infiltration of CCR2+ monocytes into the damaged liver. Experimental mouse models of NASH showed that the infiltration of CCR2+ monocytes is a critical pathogenic event promoting steatohepatitis and subsequently fibrosis progression. In addition, exercise improved steatohepatitis and liver fibrosis with the decreased number of liver-infiltrated macrophages. Macrophage-related biomarkers could be feasible for diagnosing liver inflammation and fibrosis, or the stratification of patients according to the risk of fibrosis progression. In the NAFLD liver, IL-34 is produced from activated fibroblasts and YKL-40 and sSiglec-7 are from macrophages, respectively. I would like to show that serum levels of IL-34, YKL-40 and soluble Siglec-7 are closely associated with liver fibrosis and could serve as diagnostic biomarkers in patients with NAFLD/NASH.

RS4-2

Recent issues in MAFLD

Wah Kheong Chan
University of Malaya, Malaysia

Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of liver conditions characterized by excess accumulation of fat in the liver. For a strict definition, excessive alcohol intake and other causes of chronic liver disease must be excluded. Majority of cases of NAFLD are related to overnutrition, and NAFLD is considered as the liver manifestation of the metabolic syndrome. However, the term NAFLD does not attribute the disease to its underlying etiology, and it is not in line with the reality that more than one cause of chronic liver disease can and often exist in the same patient. Furthermore, the term NAFLD is seen as trivializing to the disease and stigmatizing for some. Because of these issues, the term metabolic dysfunction-associated fatty liver disease (MAFLD) has been proposed. MAFLD is diagnosed in a person who has fatty liver and is overweight or obese, has type 2 diabetes mellitus or has at least 2 other metabolic risk abnormalities. The non-overlapping patients between NAFLD and MAFLD appear to be one of the key considerations in the on-going nomenclature debate. The MAFLD only group represents an important group at risk of more severe liver disease, but the diagnosis can be obscured by the NAFLD term and its definition, while the NAFLD only group appears to be a low-risk group. Overall, the MAFLD term and its definition has better clinical utility. While the new term has been accepted by international and national organizations, patient group and various stakeholders, there has been objections from some parties who felt that there should have been more engagement and who are concerned about potential issues in terms of disease awareness, ongoing clinical trial, and uncertainties in the definition of metabolic dysregulation. At the time of preparing this abstract, the MAFLD term and its definition has not been universally accepted.

RS4-3

Diabetes is the strongest risk factor of hepatic fibrosis in lean patients with non-alcoholic fatty liver disease

Dae Won Jun
Hanyang University, Korea

Lean patients with NAFLD were older, more likely to be female, and had lower body mass index and waist circumference. In addition, lean patients with NAFLD showed lower alanine transaminase and triglyceride levels and higher high- density cholesterol levels than non- lean patients.
Lean patients with NAFLD who have a lower number of metabolic risks showed a non- negligible prevalence of diabetes similar to that in non-lean patients with NAFLD. The presence of diabetes is the most specific predictive (but not necessarily causative) factor for hepatic fibrosis in lean patients with NAFLD.

RS4-4

GLP1/GLP2 receptor dual agonist to treat NASH: targeting the gut-liver axis and microbiome

Yong-ho Lee
Yonsei University, Korea

Non-alcoholic fatty liver disease (NAFLD) has become one of the most common metabolic liver diseases worldwide with an estimated prevalence ranging from 25% to 45% in Asian as well as western countries. NAFLD is defined as accumulation of lipids, mainly triglycerides, in ≥5% of hepatocytes with no evidence of excessive alcohol consumption or other secondary causes. The spectrum of NAFLD ranges from simple steatosis, a non-progressive disease entity with absence of hepatic inflammation and fibrosis, to non-alcoholic steatohepatitis (NASH), the most progressive and severe condition which can develop into cirrhosis, hepatocellular carcinoma and liver-related mortality. The absence of an effective pharmacological therapy for NASH is a major interest for research into novel therapeutic approaches for this condition. The current targets for NASH therapeutics include the modulation of nuclear transcription factors; agents that target lipogenesis, lipotoxicity, cell death and oxidative stress; and the modulation of cellular energy homeostasis, metabolism and the inflammatory or fibrotic pathways. Novel therapeutic agents are being developed in each of these pathways, and several have shown promise in early phase trials but not been approved by FDA yet due to the failure in phase 3 trials. Here, I will summarize pathophysiologic mechanisms of NASH and several therapeutic approaches for the treatment of NASH including our recent data using glucagon-like peptide (GLP)-1/GLP-2 receptor dual agonists.

SP1-1

Targeting endothelial dysfunction in diabetes

Huang Yu
City University of Hong Kong, China

Healthy vascular endothelium is the critical player in maintaining vascular homeostasis through releasing several vaso-protective substances called endothelium-derived relaxing factors (EDRFs) such as nitric oxide. By contrast, loss of EDRFs in diseased endothelial cells unmasks the vaso-harmful impact of endothelium-derived contracting factors (EDCFs) such as vaso-constrictive prostanopids. Such disrupted balance between EDRFs and EDCFs in endothelium is referred to endothelial dysfunction, an important initial pathological event that triggers pathogenesis of vascular diseases in diabetes. Increased production of reactive oxygen species (ROS) or raised oxidative stress in the vascular wall is probably the key factor to inactivate nitric oxide within endothelial cells. Understanding and targeting the sources of ROS is effective to increase the bioavailability of endothelium-derived nitric oxide, thus improving endothelial function in cardio-metabolic diseases. For example, a number of drugs clinically used to treat cardiovascular and metabolic diseases are able to reduce vascular oxidative stress so as to augment endothelial function in arteries from animals of diseases and from patients.

SP1-2

New insights on cardio-renal protective mechanism of SGLT2 inhibitors: ketones and inflammasome

Yong-ho Lee
Yonsei University, Korea

Sodium-glucose transporter 2 (SGLT2) carries glucose across apical membranes of polarized epithelial cells against concentration gradients, driven by Na+ gradients. SGLT2 is mainly expressed in the kidney and responsible for most glucose reabsorption in the convoluted proximal tubules. SGLT2 inhibitors are widely used as anti-diabetic drugs. Recently, SGLT2 inhibitors significantly reduce cardiovascular events in humans with type 2 diabetes (T2D); however, the underlying mechanism remains unclear.
Activation of the NLR family, pyrin domain-containing 3 (NLRP3) inflammasome and subsequent interleukin (IL)-1β release induces atherosclerosis and heart failure. Here we show the effect of SGLT2 inhibitor empagliflozin on NLRP3 inflammasome activity. Patients with T2D and high cardiovascular risk receive SGLT2 inhibitor or sulfonylurea for 30 days, with NLRP3 inflammasome activation analyzed in macrophages. While the SGLT2 inhibitor's glucose lowering capacity is similar to sulfonylurea, it shows a greater reduction in IL-1β secretion compared to sulfonylurea accompanied by increased serumβ-hydroxybutyrate (BHB) and decreased serum insulin. Ex vivo experiments with macrophages verify the inhibitory effects of high BHB and low insulin levels on NLRP3 inflammasome activation. In conclusion, SGLT2 inhibitor attenuates NLRP3 inflammasome activation, which might help to explain its cardioprotective effects.

SP1-3

Key role of Drp1-KLF4 engagement on vascular smooth muscle cell function

Kyung-Sun Heo
Chungnam National University, Korea

Vascular smooth muscle cell (VSMC) phenotypic switching plays a critical role in the progression of cardiovascular diseases, such as atherosclerosis and restenosis. Upon pathological conditions, VSMCs can transform from a contractile into a synthetic phenotype, increasing cell proliferation and migration. Emerging studies has been demonstrated the unprecedented insights into the molecular reprogramming of VSMCs to other cell phenotypes using innovative technologies including cell lineage tracing, single-cell RNA sequencing, and human genomics in experimental and clinical atherosclerosis. It has been recognized that a small subset of contractile VSMCs would undergo a fate switch to transitional and multi-potential cells to adopt plaque-destabilizing cell condition by inducing inflammation and ossification, or plaque-stabilizing cell states by regulating collagen matrix deposition. Today, I will introduce several candidate mediators and possible therapeutic targets of such VSMC fate and state changes in atherosclerosis development.

SP1-4

Cerebrovascular recovery mechanism via neurovascular signaling

Won Jong Oh
Korea Brain Research Institute, Korea

Brain vascular damages featured in various types of strokes and traumatic brain injury are common causes of death and even survivors have severe lasting disabilities. To facilitate functional recovery following those vascular defects, proper vascular remodeling such as reactivation of the angiogenic process and reconstruction of the blood-brain barrier (BBB) is necessary. However, it is still largely unknown how the cerebrovascular remodeling is coordinated with multiple neurovascular unit components and what underlying mechanism regulates the complicated processes. Last decades, the traditional axon guidance molecules have been revealed as key players in vascular development beyond their well-characterized guidance roles in the nervous systems. Previously, one such molecule, Semaphorin 3E (Sema3E), and its receptor Plexin-D1 pair are known to control vascular development via vascular endothelial growth factor (VEGF) signaling. This work leads us to investigate whether Sema3E-Plexin-D1 signaling is also involved in cerebrovascular remodeling after diverse vascular injuries. In the ischemic stroke mouse model, Sema3E was rapidly induced in the neurons around the peri-infarction areas, followed by Plexin-D1 expression in the reactivated angiogenic vessels. Plexin-D1 ablation caused worsened neurological symptoms, underdeveloped vasculature, leaky BBB permeability, and reduced blood flow recovery. Interestingly, the overall vascular impairments were caused by aberrantly increased VEGF signaling, thus the chemical inhibition of VEGF signaling during vascular remodeling facilitated functional recovery followed by ischemic insults. These findings demonstrate that the reactivation of Sema3E-Plexin-D1 signaling between neurons and endothelial cells is critical for proper cerebrovascular remodeling by dampening VEGF signaling in the injured brain. For the therapeutic purpose, it will be of interest to uncover the mediator molecules switching between the two signaling pathways in the future.

SP2-1

Single-cell fate decision in development and diseases

Ik Soo Kim
Gachon University, Korea

My lab's research goal is to understand how cells decide their fate to be specific cell types. This knowledge will foster us to utilize cell-fate decision mechanisms to modulate cell states in various biological systems involving development and disease. With recent technological advances in genomics and single-cell research, we are unraveling heterogeneous cell states in biological systems and demonstrating cell's origin (where each cell comes from) and cell's destination (where each cell progress into). Recently, we combined single-cell transcriptomics and genetic recording to characterize embryoid bodies (EBs), a heterogeneous mixture of three germ layers, differentiation. We mapped transcriptional states along a time course and model cell fate trajectories and branch points as cells progress to distinct germ layers. To validate this inferential model, we proposed an innovative inducible genetic recording technique that leverages recombination to generate cell-specific, timestamp barcodes in a narrow temporal window. We validated trajectory architecture and key branch points, including early specification of a primordial germ cell (PGC)-like lineage from preimplantation epiblast-like cells. We will further identify a temporally defined role of epigenetic regulation of cell fate decisions. To this end, we are developing new single cell technologies recording cell state in molecular level and tracing innate or acquired cell barcodes in developing cells. Our study provides a high-resolution lineage map for developmental or disease model systems, insights into epigenetic determinants of fate specification, and a strategy for lineage mapping of differentiation processes.

SP2-2

Single-cell analysis of mouse pancreatic islet for study of progressive β-cell failure

Kyun Hoo Kim
KAIST, Korea

Type 2 diabetes (T2D) develops when pancreatic β-cells fail to meet in-

creased demand for insulin secretion caused by metabolic stress. Loss of functional β-cell mass is considered as one of major features of T2D, and it is important to maintain mature β-cell identity for preserving functional β-cell mass. Recent studies propose that β-cell dedifferentiation can decrease functional β-cell mass, thereby leading to β-cell failure. However, molecular mechanisms underlying β-cell dedifferentiation remain largely unknown. Due to heterogeneity of β-cells, it is hard to capture transcriptomic features in subtypes of β-cell using conventional bulk RNA-sequencing (RNA-seq) of whole islets. In contrast, single-cell RNA-seq (scRNA-seq) enables transcriptomic profiling of heterogenous β-cells and characterization of differential responses of β-cells to metabolic stress. Here, we investigate features and molecular mechanisms of β-cell dedifferentiation by performing scRNA-seq of pancreatic islets from mouse model for β-cell failure. By analyzing time-course scRNA-seq data, we were able to delineate how β-cells behave in response to chronic metabolic stress and loss of identity occurs during progression of β-cell failure.

SP2-3

Dissecting cellular heterogeneity and plasticity in adipose tissues

Jong Kyoung Kim
POSTECH, Korea

Cell-to-cell variability in gene expression exists even in a homogeneous population of cells. Dissecting such cellular heterogeneity within a biological system is a prerequisite for understanding how a biological system is developed, homeostatically regulated, and responds to external perturbations. Single-cell RNA sequencing (scRNA-seq) allows the quantitative and unbiased characterization of cellular heterogeneity by providing genome-wide molecular profiles from tens of thousands of individual cells. In this talk, I demonstrate how scRNA-seq can be used to dissect cellular heterogeneity and plasticity of adipose tissues in homeostasis and stress.

SP2-4

A study on the relationship between type 2 diabetes mellitus and periodontitis through single cell transcriptome analysis

Yun Hak Kim
Pusan National University, Korea

Diabetes mellitus (DM) is a multifaceted metabolic disease and the global burden of it continuously increased. Periodontitis (PD), which is one of the diabetic complications, is a common chronic inflammatory disease caused by destruction of the supporting structures of the teeth. Epidemiologic studies have suggested the existence of a two-way relationship between PD and DM. DM increased the risk for PD, and periodontal inflammation has negative impacts on glycemic control. However, the underlying mechanisms of the bidirectional relationship are not completely understood. Here, we report single cell transcriptomes of peripheral blood mononuclear cells (PBMCs) from 27 samples (11 healthy donors, 10 PD patients, 6 periodontitis with diabetes patients (PDDM)). We extracted differentially expressed genes and its' biological pathways for each cell types. In addition, we found intercellular inflammatory networks of cell types. The highest number of differentially expressed genes were found in classical monocyte and CD16 high NK cell. Several immune reactions were activated and the antigen presentation molecules were up-regulated in both PD and PDDM. The cytotoxicity of CD16 high NK cell was highest in PD, but was lower than normal in PDDM. The exhaustion increased only in PDDM. In the intercellular network analysis, tumor necrosis factor (TNF) pathway was observed in both PD and PDDM. TNF has diverse effects on various cell types according to TNF receptors. TNF contributed to the production of anti-inflammatory and inflammatory mediators. We also found that the resistin, which is a well-known inflammatory molecule, intracellular network gradually increased in the order of normal, PD, and PDDM. In conclusion, these data provide insight of transcriptomic changes and molecular interactions of circulating immune cells in PD and PDDM.

SP3-1

Monitoring of retinopathy progression from diabetologists' perspective

Jae-Seung Yun
The Catholic University of Korea, Korea

Systematic screening program for diabetic retinopathy (DR) is one of the most important preventive strategies to control the development and progression of DR. The current guidelines suggest annual or biannual DR screening examinations for patients with type 2 diabetes without DR. However, several challenges remain for systematic monitoring and timely intervention for DR. The sub-optimal awareness of primary care physicians, lack of evidence for individualization of retinal screening cycles, limited access to DR screening and coverage in poor/intermediate-resource settings, and sustainability of DR screening programs are challenges to be addressed. Current DR screening programs require manual grading of DR which is not sustainable in the long run, even in high-resource settings. Therefore, scaling up and expanding to meet the growing diabetes epidemic is challenging. AI-based technology, including deep-learning systems, is gaining popularity in ophthalmology, particularly for DR screening for diagnosing and staging of DR. In this lecture, we will review studies on the proper screening interval of DR, individualized screening programs, and we will also discuss the challenges and solutions for DR screening.

SP3-2

Management of diabetic metabolic status from retinal specialists' perspective

Yong-Kyu Kim
Hallym University, Korea

Diabetic retinopathy is a leading cause of vision loss in adults worldwide. The benefits of achieving 'tight control' early in the course of diabetes are well established, based on the landmark studies such as Diabetes Control and Complications Trial (DCCT) for type 1 diabetes, and the UK Prospective Diabetes Study (UKPDS) for type 2 diabetes.
In this presentation, we will summarize the survey results from the members of the Korean Retina Society on how they perceive the importance of metabolic treatment in diabetic patients. In addition, we will review on 'point of no return', a certain point in time when glycemic control cannot prevent diabetic retinopathy progression anymore; 'metabolic memory', an enduring effect of early intensive glycemic control; and 'glucose variability' which is not reflected in HbA1c that measures mean blood glucose, and development and progression of diabetic retinopathy.

SP3-3

Clinical evidence of medical treatments for patients with diabetic retinopathy

Min Kyung Lee
Myongji Hospital, Korea

Diabetic retinopathy (DR) may lead to vision-threatening damage to the retina, eventually leading to blindness; it is the most common and severe ocular complication. DR may be asymptomatic until an advanced stage and then it is often too late for effective treatment. Therefore, early detection and timely intervention are the keys to avoiding blindness due to DR. Poor glycemic control, uncontrolled hypertension, dyslipidemia, nephropathy, male sex, and obesity are associated with worsening diabetic retinopathy. The management options include strict control of the systemic conditions, intravitreal pharmacotherapy, and laser photocoagulation. Medical treatment involves controlling glucose, lipid blood levels and hypertension treatment.
The usefulness of strict glycemic control was clearly seen in clinical trials like the UKPDS and DCCT. By improving their blood glucose and blood pressure control a person with diabetes can slow down the progression of DR. Based on the FIELD study, the fenofibrate-administered group showed a significant reduction of relative risk in need for laser treatment for DME and PDR. When it comes to the ACCORD-Eye study, the progression of DR was significantly reduced in the fenofibrate-statin-administered group compared to that in the only statin administered group. Fenofibrate seems to be a good option for type 2 diabetic patients (with or without dyslipemia) with a wide range of DR stages (from mild to severe nonproliferative

DR). RAS inhibitors reduce the risk of DR, and increase the possibility of DR regression. ACE inhibitors might be better than ARBs for treating DR, and might exert the most beneficial effect on DR of all widely used antihypertensive drug classes. Efficacy of SGLT2 inhibitor on DR has been evaluated in animal model-based studies. Dapagliflozin decreased the retinal capillary flow and prevented vascular hyperemia, and further clinical studies should be evaluated.

SP3-4

Updates in pathogenesis and future treatments of diabetic retinopathy

Junyeop Lee
University of Ulsan, Korea

Diabetic retinopathy (DR) is a chronic and progressive microvascular complication that remains an important cause of visual loss in working-age people. To delay the progression of DR, laser photocoagulation and intraocular injections of anti-vascular endothelial growth factor drugs have been widely used as major treatment strategies. Although DR is an irreversible neurovascular disease, there is currently no preventative treatment option targeting or reversing the early changes in diabetes. This presentation shows updates in the pathogenesis of DR in terms of endothelial-pericyte interactions. We will suggest a new treatment direction based on novel pathogenesis. Meanwhile, several medical treatments for hyperglycemia have been developed and used to treat patients with diabetes. Although the use of new drugs has been on the rise in recent years, it has not been known how these new drugs affect the progression and treatment response in DR. In this respect, this presentation will propose future directions for practical collaborations between diabetologists and retinal specialists.

SS1-1

Where are we in type 2 diabetes management from oral to injection?

Sung Hee Choi
Seoul National University, Korea

T2D treatment is needed to reduce the risk chronic complications of diabetes and yet many patients do not achieve current HbA1c targets with the available treatment options. Global guidelines show approaches to T2D treatment from glucose lowering to cardiovascular outcome safety in patients. Importantly, obesity management in T2D is increasing. "Patient centric approach" considering CV and renal comorbidities, impact on weight loss, efficacy, hypoglycaemia. Thus, GLP1 agonist based therapy provides multiple options for glucose lowering effect & metabolic benefits.

SS1-2

Innovations in the GLP-1 RA landscape

Juris Meier
Augusta Clinic Bochum, Germany

Incretin based therapies have been introduced to the treatment of type 2 diabetes almost 15 years ago. Since then, they have been established in all national and international Type 2 diabetes guidelined because of their marked glucose-lowering potential and weight loss as well as their cardioprotective effects.
Until recently, GLP-1 receptor agonists have been available as long-acting and short-acting injectable agents. The strongest glucose- and weight-lowering effects have been demonstrated with once weekly s.c. semaglutide.
The co-formulation of semaglutide with SNAC, an oral absorption enhancer, has now allowed for the oral administration of semaglutide. Indeed, robust glucose- and weight lowering effects have been demonstrated with once daily oral semaglutide.
Future developments in this field include peptide co-agonists as well as small molecule GLP-1 receptor agonists.

SS2-1

Diabetes and chronic complication care and management from SGLT2i

Changhee Jung
University of Ulsan, Korea

The goal of type 2 diabetes management is not just normalizing the glucose level but preventing and/or delaying its chronic cardio-metabolic complications associated with type 2 diabetes. Before the era of SGLT2 inhibitor and GLP-1 receptor agonists, we have faced several challenges in preventing these cardio-metabolic complications just by reducing hyperglycemia. Among these various cardio-metabolic complications, chronic kidney disease (CKD) and heart failure (HF) have been major burden in subjects with type 2 diabetes. These two complications are interrelated with each other and pose the affected subjects to worse prognosis such as increased future cardiovascular events and mortality.
In this session, let me address the interaction between CKD and HF. In addition, I'd like to focus on the role of SGLT2 inhibitor in the management of these complications by introducing the dapagliflozin's clinical trials whose primary outcomes were 3-point MACE, CKD and HF (DECLARE, DAPA-CKD, and DAPA-HF).

SS2-2

Cardiometabolic benefit beyond glycemic control for T2D

Sang Youl Rhee
Kyung Hee University, Korea

The recent management goal of people with diabetes is not to simply control blood glucose, but to prioritize the prevention of complications through the integrated evaluation and management of accompanying risk factors. From this point of view, recently released anti-diabetic medications play a very important role in improving the risk of various diabetic complications including cardiovascular disease, and their use continues to expand. In this presentation, I would like to communicate with the audience by preparing an in-depth review focusing on cardiorenal benefits beyond simple glycemic control of SGLT2 inhibitors.

SS2-3

Overcoming therapeutic inertia: achieving optimal targets

Jun Hwa Hong
Eulji University, Korea

Cardiovascular disease (CVD) remains the leading cause of death in patients with type 2 diabetes (T2D). Older age, prior heart failure (HF) and CV events, peripheral artery disease, and kidney complications can identify a subgroup of patients with T2D at high risk of mortality who are likely to achieve the greatest benefit from newer glucose-lowering agents. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors can reduce CV risk in patients with T2D, and are recommended by the American Diabetes Association to reduce the risk of hospitalization of heart failure and chronic kidney disease. SGLT2 Inhibitors combined with DPP4i or GLP-1 RAs reduce risk of MACE in Patients With ASCVD with additive glycemic control, while only SGLT2 Inhibitors demonstrate effects on hHF and progression of kidney disease. Dapagliflozin addresses the cardiorenal burden, beyond glycemic control, across the spectrum of patients with T2D.
In this session, we will discuss about the benefits in cardiovascular disease and CKD with SGLT-2 inhibitors.

SS3-1

Efficacy and safety of evogliptin in patients with type 2 diabetes and non-alcoholic fatty liver disease

Ji Hye Huh
Hallym University, Korea

Background & Aims: The effect of dipeptidylpepdiase-4 inhibitor on non-alcoholic fatty liver disease (NAFLD) has not been elucidated. We investigated the efficacy of evogliptin, a novel, selective DPP-4 inhibitor, compared to that of pioglitazone for treating patients with type 2 diabetes (T2D) complicated by NAFLD.
Methods: This was a 24-week, double-blind, active-controlled, randomized, parallel, phase IV clinical trial that evaluated the efficacy and safety of evogliptin (5 mg/day) versus pioglitazone (15 mg/day) in T2D patients who were drug naïve or on metformin. NAFLD was assessed by ultrasound at baseline, and changes of liver fat content were measured using magnetic resonance imaging-derived proton density fat fraction (MRI-PDFF).
Results: Both evogliptin and pioglitazone treatment decreased liver fat content as assessed by MRI-PDFF. Pioglitazone-treated participants showed a greater reduction in liver fat content compared with evogliptin-treated participants (-6.02±1.04 % vs. -1.69±0.98%; p=0.0047). Glycemic and liver enzymes were decreased in both groups (median change from baseline: HbA1c -0.31% vs. -0.48%, AST -2.0 IU/L vs. -12.0 IU/L, ALT -6.0 IU/L vs. -22.0 IU/L for evogliptin and pioglitazone). Pioglitazone increased body weight (median change of 2.50 kg), while the evogliptin group showed less of a change in body weight (median change of 0.30 kg)
Conclusions: In summary, this 24-week trial demonstrated that evogliptin was safe and showed a trend in reducing liver fat for patients with T2D and NAFLD. Our results also showed a clinically comparable change in glycemic control with evogliptin therapy compared with pioglitazone treatment. We believe that the solid evidence in this study provides rationale for future prospective studies focusing on the effect of DPP-4 inhibitors in treatment of NALFD. Further large and long-term studies are needed to confirm the potential of evogliptin as a treatment strategy for NAFLD.

SS3-2

Cardiovascular outcome from big data study

Sangmo Hong
Hanyang University, Korea

Several medications to treat diabetes have been discovering. In the beginning, the purpose of the antidiabetic medication was focused on glycaemic

control. However, there was an issue of muraglitazar (PPARα/γ agonist), which could be increased the risk of cardiovascular events. Therefore, regulatory organization such as FDA recommended to ensure the cardiovascular safety of antidiabetic drugs. From the SAVOR-TIMI 53 study, the newly developed antidiabetic medications performed a clinical trial of cardiovascular safety. Among the antidiabetic medications, dipeptidyl peptidase-4 (DPP-4) inhibitors have a potency of cardioprotective effect. Incretin has a role of not only reducing left ventricular size but enhanced BNP action based on the several non-clinical trials. However, most of the DPP-4 inhibitors did not demonstrate the significant reduction of cardiovascular events in clinical trials.
Evogliptin, which is a novel DPP-4, was released to the market in 2016. There was an animal study that it prohibits calcification in aortic valve, so a clinical trial is in progress to identify whether the use of evogliptin can improve aortic heart valve calcification. Meanwhile, the retrospective cohort observational studies were conducted to investigate that the cardiovascular safety of evogliptin compared to glimepiride or other oral antidiabetic drugs (OADs) as a second line or third line therapy to overlook the cardiovascular safety. In this lecture, the recent results of retrospective cohort studies of evogliptin will be reviewed.

SS4-1
EASD/ESC symposium: new perspectives on heart function and failure in diabetes

Javed Butler
Baylor Scott and White Research Institute, USA

SS4-2
New insights for prevention of microvascular complications

Christoph Wanner
University Hospital Würzburg, Germany

Prevention of progression of kidney disease first requires the identification of patients early on with measurement of eGFR and determination of UACR. Patients with very high albuminuria progress with more than 5 ml/min per year glomerular filtration loss towards kidney replacement therapy. This loss of filtration can be prevented by a strategy including RAS blockade, SGLT2 inhibition and nonsteroidal mineralocorticoid receptor antagonism. The new KDIGO guideline update (Kidney International October 2022) outlines a comprehensive care including dietary intervention with low salt, blood pressure targets and cardiovascular protection. The feasibility of this guideline directed kidney and heart risk factor management will be discussed in detail.

SS5-1
Optimal personalized treatment of T2DM based on recent evidence

Young Min Cho
Seoul National University, Korea

Patients with type 2 diabetes have different characteristics with regard to insulin secretion and insulin action as well as diabetes-related complications. Therefore, in order to decrease hyperglycemia and reduce the risk of complications, it is necessary to adopt personalized approach. In general, metformin is the first-line agent to treat type 2 diabetes. If metformin fails, another drug is usually added on it. But, which drug is the best add-on is yet clear. Studies on the best drug to choose after metformin failure in the treatment of type 2 diabetes have been under way.
The GRADE is the first comprehensive long-term comparative effectiveness study to compare the glucose-lowering effect and safety of using insulin, sulfonylurea, GLP-1 receptor agonist, and DPP-4 inhibitor as a second drug after metformin for patients with relatively new-onset type 2 diabetes. The primary end-point was the time it takes for HbA1c to reach 7% or more after using the drug. Microvascular and macrovascular complications, adverse effects, tolerability, quality of life, and cost-effectiveness were also evaluated according to treatment options.
The TriMASTER is a randomized, double-blind, crossover trial comparing the glucose-lowering effect of pioglitazone, sitagliptin, and canagliflozin in 3-way crossover administration for 16 weeks each in patients with inadequate glycemic control with metformin alone or metformin plus sulfonylurea. The primary endpoint is HbA1c after 16 weeks of therapy and secondary endpoints are participant-reported preference between the three treatment arms, tolerability and safety.
By reviewing the preliminary results of these two studies, strategies to approach individualized treatment for type 2 diabetes will be discussed.

SS5-2
New issues of SGLT-2 inhibitors

Seung-Hwan Lee
The Catholic University of Korea, Korea

SGLT2i has proven Cardio-Renal benefit through many large-scale RCTs and it is recommended for patients with ASCVD (atherosclerotic cardiovascular disease), HF (heart failure), and CKD (chronic kidney disease) in the guidelines. It is also well known that SGLT2i is expected to significantly reduce the risk of HF in patients with/without T2DM, HF patients. Type 2 diabetes is one of the largest risk factors for NAFLD (non-alcoholic fatty liver disease). Now, interest of SGLT2i's benefit in NAFLD with type 2 diabetes patients is rising beyond the cardio-renal benefit. Among diabetes drugs, SGLT2i is a drug that promotes the prevention and treatment of NAFLD by lowering body weight and intrahepatic fat. This lecture will deal with the meta-analysis of various RCT studies of SGLT2i in NAFLD patients with type 2 diabetes, long-term effect of empagliflozin on ALT, and long-term study of ipragliflozin on the pathogenesis of NAFLD diagnosed by liver biopsy. Recently, the concept of MAFLD (metabolic dysfunction-related fatty liver disease) which is an extended meaning in NAFLD, has emerged. We will look at the concept of a new terminology, changes of parameters related to MAFLD improvement in patients treated with SGLT2i.

SS5-3
2022 ADA/ENDO hot topic: should obesity be a primary target for type 2 diabetes?

So Hun Kim
Inha University, Korea

The benefits of weight control in the prevention and management of type 2 diabetes have been well known. However, obesity was not considered to be the primary treatment goal for patients with type 2 diabetes. During the ADA and ENDO 2022 scientific sessions, there has been debates held on whether there should be a paradigm shift to obesity as the primary target of management and related presentations on this topic. In this lecture, I will review current evidence supporting weight reduction as a primary goal for type 2 diabetes, and the opposing claims and the most recent joint ADA/EASD guideline for the management of glycemia in type 2 diabetes.

SS6-1
SGLT2 inhibitor: beyond the glucose-lowering effect

Soo Lim
Seoul National University, Korea

The final goal in the management of patients with type 2 diabetes (T2D) is reduction in cardiovascular (CV) complications and total mortality. Various factors including hyperglycemia contribute to these complications and mortality directly and indirectly. In recent years, large-scale CV outcome trials with new antidiabetic medications, such as dipeptidyl peptidase-4 (DPP4) inhibitors, glucagon-like peptide-1 (GLP1) receptor agonists, and sodium glucose cotransporter-2 (SGLT2) inhibitors, have been completed. Most clinical trials with DPP4 inhibitors have shown no inferiority compared with placebo treatments in terms of CV safety. However, they did not show benefits in terms of adverse CV events or mortality. Four large-scale CV outcome trials with SGLT2 inhibitors showed significant results: empagliflozin proved to be superior in preventing CV and all-cause mortality, and canagliflozin proved to be superior in preventing CV mortality but not all-cause mortality. So far, controlling cardiometabolic risk factors such as

hemodynamic changes and weight loss by SGLT2 inhibitors are suggested to be the main mechanisms for these results. However, the risk benefit profile for these new drugs will need further elucidation, and more studies are warranted to reveal the possible mechanisms. Therefore, it would be crucial to dissect the mechanism how SGLT2 inhibitors induce cardiorenal and metabolic benefits.

SS6-2

Efficacy and safety of SGLT2 inhibitor for Korean T2DM patients

Suk Chon

Kyung Hee University, Korea

The preferred first-line therapy in patients with T2DM is metformin and several other therapies are available as add-on treatments for those who do not respond adequately to metformin alone, among them sulfonylureas, thiazolidinedione, DPP-4 inhibitors, GLP-1 receptor agonists and sodium-glucose cotransporter (SGLT)-2 inhibitors.

Enavogliflozin is a novel SGLT-2 selective inhibitor currently under clinical development. ENHANCE-M study (add on to metformin) and ENHANCE-D study (add on to metformin and gemigliptin) were a multicenter, double-blind, randomized, phase 3 study, conducted in 24 sites and 28 sites, respectively. Korean type 2 diabetic patients were randomized to receive enavogliflozin 0.3 mg/day or dapagliflozin 10 mg/day for both studies in addition to ongoing therapy for 24 weeks. The primary objective of the study was to prove non-inferiority of enavogliflozin to dapagliflozin in terms of hemoglobin A1c (HbA1c) change at Week 24.

In ENHANCE-M study, adjusted mean change of HbA1c at Week 24 was -0.80% with enavogliflozin and -0.75% with dapagliflozin (difference: -0.04%; 95% CI: -0.21%, 0.12%). Percentages of patients achieving HbA1c <7.0% were 61% and 62%, respectively. In ENHANCE-D study, adjusted mean change of HbA1c at Week 24 was -0.92% with enavogliflozin and -0.86% with dapagliflozin (difference: -0.06%; 95% CI: -0.19%, 0.06%). Proportions of patients achieving HbA1c < 7.0% at Week 24 in enavogliflozin and dapagliflozin groups were, respectively, 66.39% and 62.60% (odds ratio=1.17, 95% CI: 0.66; 2.09).

Enavogliflozin significantly improved glycemic control in Korean patients with T2DM and was non-inferior to dapagliflozin 10 mg in both studies, suggesting enavogliflozin as a viable treatment option for patients who have inadequate glycemic control on metformin alone and metformin and gemigliptin.

BS1

How to find the optimal combination therapy for patients with type 2 diabetes

Hwi Seung Kim
Chung-Ang University, Korea

Type 2 diabetes is a complex metabolic and cardiovascular disorder with multiple pathophysiologic abnormalities. For sustainable glycemic control, the combination of anti-diabetic drugs with complementary mechanisms of action at an early stage is important. Early optimal glycemic control showed a legacy effect on diabetic complications, inducing a shift from a stepwise approach to early combination therapy. Dipeptidyl peptidase-4 inhibitor is complementary and even synergistic when combined with metformin and sodium-glucose cotransporter-2 inhibitor. Dual therapy with dipeptidyl peptidase-4 inhibitor and metformin as well as dipeptidyl peptidase-4 inhibitor and sodium-glucose cotransporter-2 inhibitor was more effective than either drug alone in glycemic control. The addition of sodium-glucose cotransporter-2 inhibitor to metformin and dipeptidyl peptidase-4 inhibitor resulted in a significant lowering of glycated hemoglobin compared to placebo. Dipeptidyl peptidase-4 inhibitor has been suggested to moderate the risk of genital tract infections, thereby making this combination favorable. The optimal combination therapy may be different for each individual with type 2 diabetes depending on the patient's characteristics and comorbidities. Dipeptidyl peptidase-4 inhibitor is still a good option for many type 2 diabetics especially in combination therapy due to its efficacy and safety.

BS2

10 years of improvement in type 2 diabetes patient care

Clifford J. Bailey
Aston University, UK

Guidelines for the management of type 2 diabetes have evolved over the past 10 years; they have moved from a gluco-centric focus through a more flexible patient-centred approach to accommodate cardio-renal aspects.
Dipeptidyl peptidase-4 (DPP4) inhibitors have established a reputation for safe and efficacious use as add-on to metformin, particularly offering low risk of hypoglycaemia and avoidance of weight gain.
The DPP4 inhibitor linagliptin is used extensively worldwide and is conveniently used without need for dose adjustment in patients with chronic kidney disease.
Utility of linagliptin has also been confirmed in large trials that have measured cardiovascular outcomes.

BS3

Efficacy and safety of combination treatment with SGLT2 inhibitor and DPP4 inhibitor

Changhee Jung
University of Ulsan, Korea

Because the pathogenesis of T2DM is complex and involves multiple metabolic defects, the use of combination therapy with antidiabetes drugs with different mechanisms of action has the advantage of preventing compensatory mechanisms and has the potential of producing an additive reduction in HbA_{1c}.
The sodium glucose cotransporter 2 (SGLT2) inhibitors and dipeptidyl peptidase-4 (DPP4) inhibitors are very useful in that they rarely cause common adverse effects of other oral hypoglycemic agents, such as weight gain and hypoglycemia. SGLT2 inhibitors reduce hyperglycemia by increasing urinary glucose excretion independent of insulin secretion or action. DPP4 inhibitors, which inhibit the breakdown of active incretin hormones, improve glucose homeostasis by increasing insulin secretion and decreasing glucagon secretion in a glucose-dependent manner. In this regard, the combination of these two drugs could be effective and safe for the treatment of hyperglycemia in patients with suboptimally controlled type 2 diabetes.
In this lecture, let me deal with the benefits of combined treatment with saxagliptin and dapagliflozin in terms of their glucose lowering efficacy and safety.

BS4

The simple solution for injectable patients' compliance and glycemic control

Mi-Kyung Kim
Inje University, Korea

Glycemic control is crucial because dysglycemia increases the risk of micro- and macrovascular complications. However, glycemic control in adults with diabetes initiating second-line glucose-lowering therapy is sub-optimal. Especially, many patients have HbA1c above target despite of their FPG (being) at target, so-called 'residual hyperglycemia'. If patients on basal insulin remain with their HbA1c uncontrolled, combination with GLP-1 RA is recommended in regard of their complementary mechanism and effect. For iGlarLixi which is a fixed-ratio combination of iGlargine and Lixisenatide proved its additional effect in lowering HbA1c in basal insulin uncontrolled patients. In SOLIMIX study, greater proportions of iGlarLixi patients achieved HbA1c <7 % without weight gain and hypoglycemia compared to PREMIX. The latest SOLI-simplify and SOLI-complex studies showed better persistence with comparable HbA1c reduction of iGlarLixi compared to existing complex treatment(Basal Bolus or PREMIX). Finally, compared to long-acting GLP-1 RA, short-acting GLP-1 RA combination would be recommended in addition to basal insulin, especially if a patient has residual hyperglycemia due to its strength in PPG lowering effect versus long acting GLP-1. In addition, in the latest CV RWE study, iGlarLixi showed better CV and microvascular complication outcomes vs. iDegLira. In conclusion, for patients sub-optimally controlled with basal insulin, treatment should be advanced without delay to reduce their complication. In that case, regarding PPG control, patient satisfaction and prevention of complication, iGlarLixi could be a preferred option.

LS1

Management of CRM and role of SGLT2i in clinical practice: perspective

Mi Kyung Kim
Keimyung University, Korea

The prevalence of diabetes is increasing globally, and diabetes complication is also increasing. Type 2 diabetes (T2D) is a significant risk factor for cardiovascular disease (CVD), and 32.2 % of T2DM have CVD. In addition, CVD is the most common cause of death in T2D. As well as CVD, diabetic kidney disease is also a major cause of end-stage renal disease and reduces life expectancy. Like this, the systemic effect of T2D contributes to heart and kidney disease progression. Therefore, early intervention is essential for preventing cardiorenal complications for T2D. Recently, sodium-glucose co-transport (SGLT) 2 inhibitor showed a beneficial effect on the heart and kidney and a glucose-lowering effect. Therefore, this session will review the management of the cardiorenal metabolic system in patients with diabetes and the role of an SGLT2 inhibitor in clinical practice.

LS2

Effects of patient-driven lifestyle modification using is CGM in patients with type 2 diabetes

Young Min Cho
Seoul National University, Korea

To investigate the effects of patient-driven lifestyle modification using intermittently scanned continuous glucose monitoring (isCGM) in patients with type 2 diabetes mellitus (T2D). We conducted a 12-week, open-label, randomized controlled trial. A total of 126 participants were 1:1 randomized to either the intervention group (structured education + isCGM) or the control group (standard care with blood glucose monitoring). The Self-Evaluation Of Unhealthy foods by Looking at the postprandial glucose (SEOUL) algorithm was developed and applied to aid structured education by guiding patients to follow healthy eating behavior depending on the postprandial glycemic response. The primary endpoint was the change in HbA1c level from baseline. Implementation of the SEOUL algorithm with isCGM was associated with a greater improvement in HbA1c than standard care (risk-adjusted difference, -0.50%, 95% CI, -0.74 to -0.26%, P<0.001). Participants in the intervention group had a greater reduction in fasting blood glucose and body weight (-16.5 mg/dL, 95% CI, -30.0 to -3.0 mg/dL, P=0.017; -1.5 kg, 95% CI, -2.7 to -0.3 kg, P=0.013, respectively). No severe

hyperglycemia or hypoglycemia was reported in either group of patients. In conclusion, patient-driven lifestyle modification primarily focused on eating behavior using isCGM effectively lowered HbA1c levels in patients with T2D.

LS3

The new wave of incretin therapy

Juris Meier
Augusta Clinic Bochum, Germany

Despite numerous innovations in the treatment of type 2 diabetes, a considerable proportion of patients still fail to reach their glycaemic targets. As a consequence, type 2 diabetes is still associated with a marked increase in cardiovascular mortality and morbidity.
The GLP-1 receptor agonists have now demonstrated not only strong reductions in glucose levels and body weight, but also reduction of cardiovascular events and mortality.
Until now, GLP-1 receptor agonists have been available as short- or long acting injectable treatments, with once weekly s.c. semaglutide showing the greatest efficacy.
More recently, an oral version of semaglutide has been developed that is suitable for once daily oral administration.
The availability on an oral once daily and a s.c. once weekly version of semaglutide will allow physicians to individualize treatment to the personal needs of each patient.

LS4

What's new; TZD in Korea?

Gyuri Kim
Sungkyunkwan University, Korea

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease characterized by insulin resistance and progressive beta-cell dysfunction. With the recent increase in the proportion of T2DM patients with obesity in Korea by up to 50%, oral hypoglycemic agents targeting insulin resistance can be an important option for T2DM. Thiazolidinediones (TZDs) activate peroxisome proliferator-activated receptor-γ, which primarily effects insulin sensitivity. In addition, TZDs have been shown to preserve pancreatic β-cell function and effectively lower glucose levels. Proactive and IRIS trials have shown TZDs improved cardiovascular risk and favorable safety outcomes. Lobeglitazone, a novel TZD, was developed and approved for the treatment of T2DM in Korea in 2013 with a comparable efficacy and safety profile to pioglitazone. In this session, I will discuss the efficacy of lobeglitazone in improving glucose levels, non-alcoholic fatty liver disease, and albuminuria in patients with T2DM. Furthermore, I will present the recently published DISCOVERY and REFIND studies for lobeglitazone.

LS5

Optimal clinical approach for the management of diabetes and chronic complications with SGLT2 inhibitors

Mark Cooper
Monash University, Australia

SGLT2 inhibitors have been shown in diabetes to lower plasma glucose levels, induce modest weight loss and decrease blood pressure. Furthermore, seminal clinical trials have demonstrated reduced cardiovascular events, primarily heart failure as well as attenuating progression of renal disease as reflected by reduced albuminuria and retardation of the decline in GFR. This has led to widespread use of these agents, often as first or second line agents as recommended in national and international guidelines. SGLT2 can be used with many other glucose lowering agents including insulin and are increasingly prescribed as fixed combinations with drugs such as DPPIV inhibitors and metformin.
Thus, SGLT inhibitors are now an integral part of the management not only of type 2 diabetes but also its cardiovascular and renal complications.

LS6

The place of DPP4 inhibitors in type 2 diabetes therapeutics

Sung Hee Choi
Seoul National University, Korea

Recently, many treatment guidelines for T2D emphasize the importance of SGLT-2 inhibitor and GLP1 analogues in individual patients with high cardio-renal metabolic risks. However, the use of DPP4 inhibitor still have important position for the treatment of diabetes. In this session, among DPP4 inhibitors, will focus on the distinct property of teneligliptin and its clinical trial results including Korean data.

LS7

Efficacy and safety of evogliptin add on therapy to DAPA/MET combinations in poorly controlled patients with type 2 diabetes

Sung Hoon Yu
Hanyang University, Korea

Objective: The study is purposed to investigate the efficacy and safety of evogliptin as an add-on therapy in poorly controlled type 2 diabetes with metformin and dapagliflozin combinations.
Methods: In this phase 3 double-blind, randomized, placebo-controlled, multi-centre trial, we assigned 283 patients with HbA1c 7.0-10.5%, who had already used dapagliflozin 10 mg and metformin (≥1,000mg) (DAPA/MET), in 1:1 ratio to receive once-daily evogliptin 5 mg or placebo for 24 weeks. The primary outcome was change from baseline in glycated haemoglobin (HbA1c) at week 24.
Results: There was a substantial reduction in HbA1c with evoglitpin added to DAPA/MET than placebo (least square [LS] mean difference -0.65 % [95 % confidence interval [CI] -0.79, -0.51]; p<0.0001). Furthermore, the percentage of patients who achieved HbA1c levels <7.0% was higher in evogliptin group than placebo (42.14 % versus 9.93 % in placebo; p<0.0001). Reductions were also observed in fasting plasma glucose (FPG), postprandial plasma glucose (PPG) and mean daily glucose levels with the improvement of HOMA-β (LS mean difference 9.15 [95% CI 4.15, 14.15]; p=0.0004) with evogliptin. Adverse events (AEs) were similar across treatment groups and no major hypoglycaemic events and treatment related discontinuation were reported.
Conclusion: In this 24-week trial, evogliptin adding to metformin and dapagliflozin in patients with poorly controlled type 2 diabetes significantly reduced HbA1c compared to placebo and no significant difference was observed between groups regarding adverse events.

LS8

The combination of DPP-4 inhibitor plus SGLT-2 inhibitor as attractive treatment option: from rationale to clinical aspects

Yun Kyung Cho
University of Ulsan, Korea

Type 2 diabetes (T2D) has a complex pathophysiology composed of multiple underlying defects that lead to impaired glucose homeostasis and various complications. Over the past few decades, an increased understanding of T2D pathophysiology has led to the development of various anti-hyperglycemic agents with various mechanism, and it provides an opportunity to choose the appropriate medication for an individual patient with T2D. The Korea Diabetes Association (KDA) guidelines recommends the combination therapy, if current glycosylated hemoglobin is above the target HbA1c. Of the currently available glucose-lowering therapies, dipeptidyl peptidase-4 inhibitor (DPP-4i) and sodium-glucose cotransporter-2 inhibitor (SGLT-2i) can be a safe and effective treatment choice for patients with T2D considering their complementary mechanism of action. The combination of DPP-4i and SGLT-2i can be a good option in view of not only glucose-lowering efficacy but also tolerability or safety profile (risk of hypoglycemia, weight change). In addition, the beneficial effect of SGLT-2i and neutral effect of DPP-4i on cardiovascular or renal risk/progression proven in large clinical trials will support their combination therapy.
Gemigliptin is a potent, selective and long-acting DPP-4 inhibitor. In this symposium, the result of recently completed a 52-week extension of the SOLUTION study, examining the beneficial effects of gemigliptin as add-on therapy to Metformin/Dapagliflozin, will be reviewed.

OP1-1 Basic & translational diabetes research 1

A mouse model for metabolic stress-induced nonalcoholic fatty liver disease and subsequent hepatocellular carcinoma

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Objective: Nonalcoholic fatty liver disease (NAFLD) is a rapidly growing metabolic disease that presents with a wide range of clinical manifestations from fatty liver to hepatocellular carcinoma (HCC). However, there are limitations in NAFLD research due to lack of appropriate animal models that reflects the full range of the disease with physiological relevance. In this study, we used controllable methods to generate a mouse model of NAFLD and subsequent HCC that closely recapitulates human disease and its physiological relevance.

Methods: To generate NAFLD mouse model, we first induced diabetic condition. Briefly, male C57BL/6J mice were injected with low dose streptozotocin (40 mg/kg) for 5 consecutive days from 7 weeks of age. Then mice were fed standard chow diet (SCD) (STZ-SCD mice) and or high fat diet (HFD) from 8 weeks of age (STZ-HFD mice). Hepatic histology, transcriptomes and metabolic phenotypes were evaluated at multiple time points. Mouse transcriptomic data were also compared to human transcriptomic data with similar hepatic histology.

Results: Control STZ-SCD mice showed mild hepatic inflammation transiently without hepatic steatosis or fibrosis. In contrast, STZ-HFD mice developed hepatic steatosis, steatohepatitis, progressive hepatic fibrosis, and HCC at 14, 20, 32, and 38 weeks of age, respectively. Metabolic phenotypes of STZ-HFD mice also showed similar physiological features of human NAFLD including hyperglycemia, obesity, dyslipidemia, adipocyte hypertrophy and adipose tissue inflammation. A substantial association between STZ-HFD mice and human NAFLD patients with similar liver histology was observed in overall gene expression alterations at transcriptome level, which shared the key signaling pathways in NAFLD progression, including fatty acid degradation and the p53 signaling pathway.

Conclusion: We have developed a novel and easily manageable mouse model of NAFLD and subsequent NAFLD-related HCC. This model mimics physiological, metabolic, histological and transcriptomic alterations that occur in human patients as NAFLD progresses.

OP1-2 Basic & translational diabetes research 1

BRD7 as a player in the alternative insulin signaling pathway

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Objective: The molecular mechanism by which obesity and type 2 diabetes develop is not fully understood. We have shown that bromodomain containing protein 7 (BRD7) levels are significantly reduced in the liver of obese mouse models. The objective of this study is to understand the insulin signaling pathway during obesity, and the role of BRD7 in the suggested alternative insulin signaling pathway.

Methods: We used liver-specific insulin receptor knockout (LIRKO) and liver-specific insulin receptor substrate 1/2 knockout (IRS DKO) mouse models to study the insulin signaling pathway. We challenged them with a high-fat diet, upregulated BRD7 in the liver, and monitored various parameters of glucose metabolism.

Results: Our results show that BRD7 acts to improve glucose homeostasis in obesity, and insulin receptors are required for BRD7's action. We show that BRD7 interacts with the insulin receptor. Of interest, insulin receptor substrate 1/2 (IRS1/2) are dispensable for BRD7's action on glucose metabolism in obesity. Upregulation of hepatic BRD7 significantly reduces the blood glucose levels and restores glucose homeostasis in high-fat diet challenged IRS DKO mice. Furthermore, upregulation of BRD7 suppresses hepatic gluconeogenesis even without IRS1/2 through FoxO1. Notably, upregulation of BRD7 increases hepatic gluconeogenesis without the effects of AKT.

Conclusion: These data support the existence of an alternative insulin signaling pathway that suppresses gluconeogenesis independent of IRS1/2, and provide new insight into a previously unknown insulin signaling pathway in obesity.

OP1-3 Basic & translational diabetes research 1

Diabetes primes neutrophils for neutrophil extracellular trap formation through trained immunity

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Objective: Neutrophils are primed for neutrophil extracellular trap (NET) formation during diabetes and excessive NET formation from primed neutrophils compromises wound healing in patients with diabetes. Here, we demonstrate that trained immunity mediates diabetes induced NET priming in neutrophils.

Methods: Neutrophils were incubated under either normal- or high-glucose conditions and then stimulated with either vehicle, LPS, or PMA. To determine the effects of metabolic pathway inhibitors, neutrophils were treated with the indicated inhibitors. The oxygen consumption rate of neutrophils was measured. Western blot, RNA sequencing analysis, and metabolic flux anlaysis study was carried out to determine metabolic pathway altered by hyperglycemia. Human neutrophil samples were collected from patients with diabetes at Kyungpook National University Hospital.

Results: Under diabetic conditions, neutrophils exhibit robust metabolic reprogramming comprising enhanced glycolysis via the pentose phosphate pathway and fatty acid oxidation, which result in the accumulation of acetyl-coenzyme A (CoA). ATP-citrate lyase (ACLY)-mediated accumulation of acetyl-CoA and histone acetyltransferases (HATs) further induce the acetylation of lysine residues on histone 3 (AcH3K9, AcH3K14, and AcH3K27) and histone 4 (AcH4K8). The pharmacological inhibition of ACLY and HATs completely inhibited high glucose-induced NET priming. The trained immunity of neutrophils was further confirmed in neutrophils isolated from patients with diabetes.

Conclusion: Our findings suggest that trained immunity mediates functional changes in neutrophils in diabetic environments, and targeting neutrophil- trained immunity may be a potential therapeutic target for controlling inflammatory complications of diabetes.

OP2-1 Clinical diabetes and therapeutics 1

Weight change and remission in newly diagnosed type 2 diabetes mellitus: a nationwide cohort study in Korea

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Objective: This study aimed to investigate the general weight change and its correlation with spontaneous remission in newly diagnosed type 2 diabetes mellitus (DM) patients who received standard medical therapy.

Methods: Using claims and health check-up data from the Korean National Health Insurance Service, newly diagnosed type 2 DM patients who were prescribed diabetes drugs two or more times within one year were screened. Remission was defined as cases where the fasting blood glucose level was less than 126 mg/dL at two or more consecutive medical examinations after stopping the medications.

Results: A total of 114,874 newly diagnosed type 2 DM patients was analyzed. Of these, 23,156 (20.2%) lost more than 5% of their body weight during the first 2 years, and 2,429 (2.1%) showed remission. In the patient group who achieved early weight loss of 5% or more, the adjusted odds ratio for reaching diabetic remission was 2.56 (95% confidence interval 2.35-2.79) compared to the group without weight change. The effects of weight loss on remission were significantly greater in subgroups of age younger than 65 years, and BMI greater than 25 (p for interaction < 0.01).

Conclusion: In the patient group who received standard medical therapy without specific interventions, the weight loss achievement rate was low, and spontaneous remission was rare. Losing more than 5% of body weight within the first 2 years of diagnosis may increase the likelihood of diabetes remission. Therefore, we suggest that more attention be paid to weight management in newly diagnosed type 2 DM patients, especially for young and obese individuals.

OP2-3 Clinical diabetes and therapeutics 1

Efficacy and safety of enavogliflozin monotherapy in Korean patients with type 2 diabetes mellitus inadequately controlled with diet and exercise (ENHANCE-A)

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Objective: The aim of this study was to evaluate the efficacy and safety of a novel sodium-glucose cotransporter 2 inhibitor, enavogliflozin, as a monotherapy in Korean patients with type 2 diabetes mellitus (T2DM).

Methods: Participants with inadequately controlled diabetes (HbA1c of 7.0-10.0%) with diet and exercise entered a 2-week, single-blind, placebo run-in period, followed by a 24-week, double-blind period during which participants were randomized to receive enavogliflozin 0.3mg or placebo. The primary efficacy endpoint was changes in HbA1c at week 24 from baseline. Pre-specified secondary endpoints included changes in fasting plasma glucose (FPG), proportion of patients reaching HbA1c <7.0%, and proportion of patients achieving a reduction of >0.5% of HbA1c or HbA1c <7% at week 6, 12, 18 and 24. Adverse events (AEs) were recorded throughout the study.

Results: Overall, 161 patients were included in the full analysis set (enavogliflozin 0.3mg: N=82, placebo: N=79). Patients with enavogliflozin had significantly reduced HbA1c compared to placebo at week 24 (-0.84%, and 0.12%, respectively; P<0.0001). Mean change of FPG from baseline at week 24 were -30.0±20.7 mg/dL and 9.9±39.4 mg/dL in enavogliflozin and placebo, respectively (P<0.0001). The proportion of patients reaching HbA1c <7.0% at week 24 were significantly higher in the enavogliflozin group than in the placebo group (70.7%, and 24.1%, respectively; P<0.0001). More patients had HbA1c reduction >0.5% or HbA1c <7% at week 24 with enavogliflozin 0.3mg versus placebo (82.9%, and 31.6%, respectively; P<0.0001). Overall there was no significant difference in AEs between the two groups (26.5% in enavogliflozin, and 22.6% in placebo; P=0.56). The incidence of hypoglycemia and genital infection were similar across groups.

Conclusion: In this phase 3 clinical trial, once-daily enavogliflozin monotherapy for 24 weeks was an effective, safe and well-tolerated treatment for patients with T2DM.

OP2-4 Clinical diabetes and therapeutics 1

Chronobiology at play: effect of time restricted meal (TRM) intake on anthropometric, biochemical and lipid profile parameters in patients of type 2 diabetes mellitus

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Objective: To study the effect of TRM on anthropometric, biochemical and lipid profile parameters in patients of Type 2 diabetes mellitus

Methods: 400 diabetics enrolled from OPD, Endocrinology, KGMU were randomly divided based on whether they have consented (TRM(time restricted meal),case group) or not (control group).Baseline parameters were recorded and follow up was done at 6,12 and 18 months for anthropometric measurement, height, weight, waist hip ratio, aBSI, neck size, blood sugar (Fasting and post prandial), HbA1C and lipid profile. A single intervention was done that the timing of dinner was at or around 7 in the evening for the TRM group.

Results: In the TRM group mean age was 47.17 in the control group 46.97 TRM group Mean height=1.58 control group Mean=1.59 BMI TRM group mean=27.84 control group mean=28.82 Neck size (in centimetres) TRM group 36.56 mean control group=40.59 Waist size (in centimetres) TRM group=91.70 mean control group=91.85 Hip Size (in centimetres) TRM group=101.32 mean control group=107 HbA1c TRM group=7.89 mean control group=8.23 Total Cholesterol TRM group=163.32 mean control group=183.2 Triglycerides TRM group=106.07 mean control group=152.6 LDL C TRM group= 63.99 mean control group= 93.49 HDL C TRM group= 53.64 mean control group=50.93 VLDL C TRM group=25.98 mean control group=31.08

Conclusion: This is the final result after one and a half year of follow up. A detailed version regarding baseline, 1st follow up, 2nd follow up and 3 rd follow up will be presented at the conference.

OP2-5 Clinical diabetes and therapeutics 1

Glucotoxicity is a critical determinant of insulin secretion over treatment types or disease duration in type 2 diabetes

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Objective: Progressive deterioration of insulin secretion is a characteristic of type 2 diabetes (T2D). This study aimed to identify the major factors affecting insulin secretion among patients with T2D.

Methods: From an observational diabetes cohort, 467 T2D patients with disease duration of 0 to 40 years were included. Insulin secretion was estimated by insulinogenic index (IGI) and homeostasis model assessment of β-cell function (HOMA-B) based on 75g oral glucose tolerance test (OGTT). The relative contributions of age, sex, disease duration, body mass index (BMI), HbA1c at the time of OGTT (HbA1c on time), area under the curve of HbA1c over time (AUC HbA1c), coefficient of variation in HbA1c (CV HbA1c), and types and duration of anti-diabetic drug use to insulin secretion were compared by estimating beta coefficients per 1-standard deviation (β).

Results: The mean age of patients was 59.1 (±11.8) years and the median duration of disease 8 (0-15) years. The annual decline of IGI was 2.7%. In the multivariate regression analysis, female sex (β=0.231, p=0.011) and BMI (β=0.234, p<0.001) were positively associated with IGI while the duration of disease (β=-0.158, p=0.032) and HbA1c at the time of OGTT (β=-0.425, p<0.001) were negatively associated. These associations were similar for HOMA-B. Compared with patients with HbA1c ≥9% at the time of OGTT, IGI was 1.9, 2.7, 3.6, and 5.0-fold higher in those with HbA1c of 8-<9%, 7-<8%, 6-<7%, and <6%, respectively, after adjusting for other factors (p for trend <0.001). In contrast, insulin secretion was not affected by the types and duration of anti-diabetic drugs, AUC HbA1C and CV HbA1c.

Conclusion: Insulin secretion steadily declines over time in T2D patients, however, it is largely affected by the moment's hyperglycemia itself. Specific drug use does not seem to be related to insulin secretion.

OP3-2 Clinical diabetes and therapeutics 2

A randomized, multicenter, open, parallel, phase 4 study to compare the efficacy and safety between high-intensity rosuvastatin and moderate-intensity rosuvastatin/ezetimibe in high atherosclerotic cardiovascular disease risk patients with type 2 diabetes (CREATE study)

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Objective: To investigate the efficacy and safety of moderate intensity rosuvastatin/ezetimibe combination compared to high intensity rosuvastatin in high atherosclerotic cardiovascular disease (ASCVD)risk patients with type 2 diabetes.

Methods: This study was a randomized, multicenter, open, parallel phase 4 study, and enrolled type 2 diabetic subjects with an estimated 10-year ASCVD risk ≥7.5%. The primary endpoint was the LDL-cholesterol (LDL-C) change rate after 24- week rosuvastatin 10mg/ezetimibe 10mg treatment was non-inferior to that of rosuvastatin 20 mg. The achievement proportion of 10-yr ASCVD risk <7.5% or comprehensive lipid target (LDL-C <70 mg/dL, non HDL-C <100 mg/dL, and Apo B <80 mg/dL) without discontinuation, and several metabolic parameters were explored as secondary endpoints.

Results: Total of 106 patients were randomly assigned to both groups equally. In a per-protocol analysis, both groups showed significant reduction in % change of LDL-C from baseline at week 24 (-63.90±6.89 vs. -55.44±6.85, rosuvastatin 10 mg/ezetimibe 10 mg vs. rosuvastatin 20 mg; p=0.0378 respectively), and the combination treatment was superior to high-intensity monotherapy in LDL-C change (%) from baseline (least squares (LS) mean difference -8.47, 95% confidential interval (CI) [-16.44, -0.49]; p=0.0378). Combination treatment showed a higher proportion of achieved comprehensive lipid targets rather than monotherapy (85.4 % vs 62.2 % in monotherapy; p=0.017) at week 24. Moreover, the ezetimibe combination significantly improved HOMA-β whereas decreased in monotherapy group (LS mean difference 17.13; p=0.0185) even without A1c changes.

Conclusion: In high ASCVD risk patients with type 2 diabetes, the combination of moderate-intensity rosuvastatin and ezetimibe was not only non-inferior but also superior to improving dyslipidemia with additional benefits compared to high-intensity rosuvastatin monotherapy.

OP3-3 Clinical diabetes and therapeutics 2

Antidiabetic effect of dasatinib in prediabetic and diabetic patients

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Objective: Tyrosin kinase inhibitor (TKI) treatments are performed in cases of an underlying chronic disease such as leukemia, gastrointestinal stromal tumor, and some other forms of cancer. In recent studies, the antidiabetic effects of imatinib and dasatinib had been reported, which was partly explained by its senolytic property. This study is aimed to investigate the antidiabetic effects of these drugs in Korean patients with chronic myeloblastic leukemia (CML).

Methods: A total of 664 subjects who had been treated with either dasatinib or imatinib for more than 1 year were collected from July 2008 through May 2022 via Clinical Data Warehouse of Seoul National University Hospital. Narrowing the underlying malignant disease to Chronic myeloblastic leukemia (CML), 110 subjects in Dasatinib group and 205 subjects in Imatinib group were identified. In each treatment group, the diabetic parameters including diabetic medications, fasting blood glucose (FBG), and hemoglobin A1c (HbA1c) were retrospectively collected from the initial and 1-year periods of the TKI treatment and compared.

Results: Baseline characteristics of age, gender, FBG, HbA1c, and the glycemic status (one of the following categories: diabetic, prediabetic/impaired glucose tolerance (IGT), or normal glucose tolerance (NGT)) were similar in both groups. After 1 year of TKI treatment, antidiabetic effects were seen in both dasatinib and imatinib groups. However, significant improvements in the glycemic status of previously prediabetic subjects to NGT and previously diabetic subjects to prediabetic/IGT were seen in dasatinib group compared to imatinib. The outcome ratio of the NGT subjects were 58.5% vs 29.2%, and prediabetic/IGT subjects were 36.8% vs 11.4% in dasatinib and imatinib groups, respectively ($p<0.05$).

Conclusion: In treatments with TKI, dasatinib was associated with more beneficial antidiabetic effect compared to imatinib. Under dasatinib treatment, significant improvements were identified in the glycemic status of prediabetic/IGT patients to NGT state and patients with underlying DM to prediabetic/IGT state.

OP3-5 Clinical diabetes and therapeutics 2

Precision nutrition counseling using continuous glucose monitoring in type 2 diabetes patients: a randomized controlled trial

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Objective: Conventional diet education in type 2 diabetes (T2D) has usually been performed with general content, not individualized glucose data-driven content. This study aimed to evaluate the effect of precision nutrition education using continuous glucose monitor (CGM) in glycemic control in patients with T2D.

Methods: In this randomized controlled study, fifty patients with T2D were randomly assigned to the CGM group and control group in a 1:1 ratio. All participants used 6 days of blinded CGM and wrote a food log in the beginning. CGM group received an education based on CGM data and food logs. Every consumed food was ranked according to postprandial glucose response calculated by a 2-hour incremental area under curve of sensor glucose level. The control group received conventional diet education only based on food logs without CGM data. All participants were encouraged to do lifestyle modification based on education for 3 months. The primary outcome was a change in HbA1c at 3 months. The satisfaction questionnaire and microbiome were evaluated as a part of secondary outcomes.

Results: All 50 participants completed the study (baseline HbA1c 7.9±0.5%, diabetes duration 17.4±8.0 years). At three months, although both groups showed HbA1c reduction (CGM group, −0.7±0.2%; control group, −0.4±0.2%), CGM group had better improvement (adjusted difference = −0.34%; P=0.044). According to the questionnaire, the CGM group experienced more novel information than the control group (P=0.048). For microbiome analyses, alpha diversity indices were significantly increased in only CGM groups (Shannon index, P=0.04). In addition, only the CGM group showed significantly differentially abundant genera between baseline and 3 months; decreased abundances of PAC000683_g and Fusimonas, and increased abundances of Morganella and Providencia.

Conclusion: In patients with T2D, individualized diet education based on CGM data was an effective method for glucose control and changing the microbiome environment compared to conventional diet education.

OP4-1 Diabetes complications-clinical & epidemiology 1

Association between trajectory of metabolic syndrome and knee pain over 11 years in middle-aged adults

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Objective: Metabolic syndrome (MetS) is characterised by the clustering of central obesity with metabolic abnormalities. MetS has been suggested as having a role in osteoarthritis (OA) pathogenesis. 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 the Childhood Determinants of Adult Health (CDAH)-1 study (year:2004-6;n=2447;mean age:31.48±2.60) and at 10-13 year follow-up 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. Participants were grouped in four MetS trajectories—'No MetS': no MetS at either life stage; 'Improved MetS': MetS only at young adulthood (CDAH-1); 'Incident MetS': MetS only at mid-adulthood (CDAH-3); and 'Persistent MetS': MetS at both life stages. Knee symptoms were assessed using the WOMAC scale at the CDAH-3. Univariable and multivariable (age, sex, and BMI adjusted) zero-inflated Poisson regression models were used for analysis.

Results: The prevalence of MetS increased from 8% at young adulthood (female:52.06%) to 13% in mid-adulthood (female:53.78%). 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 most 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 follow-up.

Conclusion: In middle-aged adults, there was an independent 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.

OP4-2 Diabetes complications-clinical & epidemiology 1

Association between hypertension and myosteatosis evaluated by muscle quality map from abdominal computed tomography

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Objective: Few studies have examined the relationship between myosteatosis and hypertension, with none for the Asian population. They also showed discordant results, possibly due to using conventional myosteatosis indices that are prone to interference from computed tomography (CT) contrast. Therefore, we investigated the association between myosteatosis and hypertension in Asians using novel CT markers that are less affected by contrast.

Methods: The total abdominal muscle area (TAMA) was determined from abdominal CT scans taken at the L3 level. Based on the mean CT attenuation, TAMA was divided into intramuscular adipose tissue and skeletal muscle area (SMA), which was further segmented into normal attenuation muscle area (NAMA) and low attenuation muscle area (LAMA). The SMA, NAMA, and LAMA divided by body mass index, as well as the NAMA/TAMA index, were chosen for myosteatosis indices. The hypertension risk for each quartile of the NAMA/TAMA index was calculated by logistic regression analysis.

Results: In a total of 18,262 participants, hypertensive subjects were 39.5% and 23.2% in men and women, respectively. People with hypertension showed more unhealthy profiles of myosteatosis compared to normotensive controls. Similarly, a lower NAMA/TAMA index was significantly associated with a greater hypertension risk. The lowest quartile group of the NAMA/TAMA index exhibited a 75% and 91% higher risk of hypertension than the highest quartile in men and women, respectively.

Conclusion: Advanced myosteatosis assessed by abdominal CT was significantly related to a higher risk of hypertension. Improving myosteatosis may be a new approach to prevent cardiovascular disease, including hypertension.

OP4-4 Diabetes complications-clinical & epidemiology 1

Risk factor control and cardiovascular events in patients with type 2 diabetes mellitus

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Objective: Patients with type 2 diabetes mellitus (T2DM) have an increased risk of cardiovascular events, and risk factor interventions are known to reduce cardiovascular disease (CVD). The aim of this study was to evaluate whether there was a difference in CVD events according to risk factor control in high-risk and low-risk diabetic patients using a Common Data Model (CDM).

Methods: We analyzed 6,678 subjects with T2DM and 52,475 subjects without diabetes mellitus older than 40 years old who had visited Ewha Womans University Medical Center from January 2001 to December 2019 using the electronic health record (EHR) data transformed into the CDM. CVD events were defined as the composite outcomes of coronary heart disease, hospitalization for heart failure, and stroke. Baseline high CVD risk was defined as prior CVD or eGFR <45 mL/min/1.73m2.

Results: During the study period, CVD events occurred in 8,600 (16%) subjects without diabetes mellitus and 1,573 (24%) subjects with T2DM with a mean diabetes duration of 6 years. The incidence rate of coronary heart disease was 13% (n=843), hospitalization for heart failure was 5% (n=301), and stroke was 12% (n=810) among diabetic patients. In the low CVD risk group, the hazard ratio for total CVD events was 5.17 (P<0.001), coronary heart disease was 4.05 (P=0.090), hospitalization for heart failure was 5.50 (P=0.235), and stroke was 6.12 (P=0.001) for diabetic patients with uncontrolled four risk factors compared with diabetic patients without suboptimally controlled risk factors. However, the CVD events did not differ according to risk factor control in T2DM patients with high CVD risk.

Conclusion: Cardiovascular risk factor control significantly reduced the CVD events in T2DM patients with low baseline CVD risk. More intensive cardiovascular risk factor interventions would be needed for reduction of cardiovascular events in subjects with T2DM, especially in diabetic patients with low CVD risk.

OP4-5 Diabetes complications-clinical & epidemiology 1

Association between sarcopenic obesity and poor muscle quality assessed by muscle quality map using abdominal computed tomography

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Objective: Sarcopenic obesity is a clinical and functional condition characterized by the coexistence of excess fat mass and sarcopenia. We evaluated whether sarcopenic obesity is closely associated with muscle quality measured by abdominal computed tomography.

Methods: We conducted a cross-sectional study on 13,612 subjects who underwent abdominal computed tomography between 2012 and 2013 during health examinations. The cross-sectional area of the skeletal muscle was measured at the L3 level (total abdominal muscle area) and segmented into normal attenuation muscle area (NAMA), low attenuation muscle area (LAMA), and intramuscular adipose tissue (IMAT). We calculated the NAMA/TAMA index, of which a higher value reflected a higher proportion of good quality muscle (normal attenuation muscle area) and a lower proportion of myosteatosis (low attenuation muscle area and intramuscular adipose tissue). Sarcopenia was defined using body mass index (BMI)-adjusted appendicular skeletal muscle mass and obesity was defined as a BMI of 25 kg/m^2 or higher. We evaluated the association between the NAMA/TAMA index and sarcopenic obesity.

Results: Participants with sarcopenic obesity had lower NAMA/TAMA index than non-sarcopenic non-obese participants (76.7±8.3 vs. 68.1±12.9, p<0.001). When we defined myosteatosis as the highest quartile of NAMA/TAMA index, the prevalence of myosteatosis was significantly higher in participants with sarcopenic obesity (17.9% vs. 54.2%, p<0.001). The odds ratio (95% CI) for having myosteatosis was 5.41 (4.30-6.81) in participants with sarcopenic obesity, compared to non-sarcopenic non-obese reference. After adjusting for age, sex, smoking, drinking, exercise, hypertension, diabetes, LDL-C, and hsCRP, the association between sarcopenic obesity and myosteatosis was still significant [odds ratio (95% CI), 3.70 (2.87-4.76)].

Conclusion: Sarcopenic obesity was significantly associated with myosteatosis, which is representative of poor muscle quality.

OP5-1 Basic & translational diabetes research 2

N-acetylcysteine increases non-thermogenic energy expenditure by increasing lipolysis in white adipose tissue

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Objective: The white adipose tissue (WAT) is the energy reservoir that secretes various hormones and cytokines that regulate metabolism and insulin resistance. N-acetylcysteine (NAC) is a thiol compound, which acts as an antioxidant and an anti-inflammatory agent. Furthermore, there is growing evidence supporting the use of NAC for treating metabolic disturbances, including insulin resistance, glucose intolerance, and dyslipidemia. We aimed to investigate whether NAC exerts its anti-obesity effect through suppression of NLRP3/caspase-1 pathway, inhibition of fibroblast activation protein (FAP), and finally, recovery of defective lipolysis induced by a high-fat diet (HFD).

Methods: To evaluate the effect of NAC on HFD-induced obesity in vivo, eight-week-old C57BL/6J mice and Ucp1 knockout mice were fed with either a normal chow diet (ND) or an HFD. Then, mice were fed HFD with or without NAC (10 mg/mL). To investigate ex vivo lipolysis, epididymal adipose fat pads from mice were isolated and treated with or without norepinephrine.

Results: We showed that NAC prevents HFD- induced obesity and insulin resistance independently of uncoupling protein 1. NAC increased mRNA expression of hormone-sensitive lipase and lipolysis in epididymal white adipose tissue (eWAT), thereby reducing lipid droplet size of adipocytes in mice fed HFD. Our study reveals that HFD-induced reactive oxygen species (ROS) drives the accumulation of adipose tissue macrophages (ATMs) and leads to catecholamine degradation in ATMs, suppressing lipolysis in eWAT, whereas NAC significantly reverses this effect. NAC prevents HFD-induced obesity in mice by deactivating the NLRP3/caspase-1 pathway, reducing catecholamine degradation by MAOA, and restoring catecholamine-induced lipolysis. NAC increased plasma FGF21 levels by decreasing the expression of FAP in eWAT. Administration of FAP inhibitor improved HFD-induced obesity by increasing lipolysis.

Conclusion: This study suggested that NAC prevents obesity and enhances non-thermogenic energy expenditure in white adipose tissue by inhibiting the NLRP3/caspase-1 pathway and being involved in catecholamine-stimulated lipolysis and FGF21 signaling.

OP5-2 Basic & translational diabetes research 2

Higher genetic risk for type 2 diabetes is associated with faster decline of beta cell function: findings from Ansan-Ansung cohort study

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Objective: Polygenic risk scores have been reported to be useful in assessing risk for developing type 2 diabetes (T2D). We aimed to evaluate the clinical utility of polygenic risk scores in anticipating the trajectory of beta cell function in a community-based prospective cohort.

Methods: We analyzed 7298 participants without T2D at baseline from Ansan-Ansung cohort with oral glucose tolerance tests every 2 years for 16 years. Disposition index (DI), derived from insulinogenic index at 60-minute and composite (Matsuda) insulin sensitivity index, was used as surrogate markers for beta cell function. Polygenic risk score (PRS) was calculated using >1.2 million genetic variants from summary statistics of trans-ancestry T2D genome-wide association study using a Bayesian polygenic risk scoring method, and participants were stratified into low (1st quintile), intermediate (2nd to 4th quintile) and high (5th quintile) genetic risk.

Results: During 16 years of follow-up, 184 people (12.5%) of low genetic risk, 941 (21.5%) of intermediate genetic risk, 404 (28.0%) of high genetic risk developed T2D. Participants with high genetic risk, compared to those with low genetic risk, had 35% lower DI at baseline (52.6 [95% CI 49.9, 55.5] vs 80.4 [76.3, 84.8]; p-value <0.001), and 45% lower DI at end of follow-up (37.8 [35.6, 40.1] vs 67.9 [64.0, 72.0]; p-value <0.001). The rate of decline in log2(DI) was 1.96-fold higher in high genetic risk group (-0.068 [-0.055, -0.082] vs -0.035 [-0.048, -0.022], p-value 0.00053). In addition, we found significant interaction between follow-up time and genetic risk for T2D (p-value 0.00047). In predicting people with decline rate of DI in the highest quintile, PRS was useful in addition to traditional T2D risk factors (AUROC 0.549 [0.531, 0.567] vs 0.567 [0.549, 0.585], p-value 0.0054).

Conclusion: Polygenic risk score for T2D is clinically useful in predicting the rate of decline of beta-cell function in people without T2D.

OP5-3 Basic & translational diabetes research 2

The potential beneficial effect of brown adipocyte secreted factors on type 1 diabetes mellitus

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Objective: Type 1 Diabetes Mellitus (T1D) patients suffer hyperglycemia due to the absence of insulin secretion from autoimmune destruction of the pancreatic β-cells and abnormal hypersecretion of glucagon from pancreatic α-cells. While insulin therapy is available to compensate for the lack of insulin secretion, there is no effective therapeutic tool to target the hyperglucagonemia of T1D. Recently, brown adipose tissue (BAT) has been gaining attention for treating metabolic diseases due to its importance in whole-body energy metabolism. The Piston lab showed that subcutaneous transplantation of embryonic BAT into T1D mouse models reverses hyperglycemia and reduces plasma glucagon levels. However, the major player for this beneficial effect and its mechanisms remain unclear. To further elucidate the mechanism behind the recovery of euglycemia from BAT transplants, this project focuses on 1) investigating brown adipocytes secreted factors that suppress the glucagon secretion, 2) investigating the molecular mechanism of BAT-secreted factor-mediated suppression of glucagon secretion, and 3) investigating the mechanism behind the long-term recovery of euglycemia upon administration of BAT-secreted.

Methods: BAT-secreted factors are investigated through reverse-phase Chromatography, anion exchange Chromatography, size-exclusion chromatography, and exosome isolation and profiling. The molecular mechanism of BAT-secreted factor-mediated suppression of glucagon secretion was investigated by imaging Ca2+ and cAMP activity. The long-term effects of euglycemia recovery in these mouse models was investigated using RNA-sequencing and differential gene expression analysis.

Results: BAT-secreted exosomes suppress glucagon secretion in a Ca2+- and cAMP-independent manner. BAT-conditioned buffer treatment to T1D resulted in the recovery of euglycemia and reversal of the T1D-associated decrease in BAT activity.

Conclusion: Crosstalk between BAT and pancreatic islets through exosomes affects the glucagon secretion from pancreatic α-cells during T1D. In addition, BAT-secreted factors promote long-term recovery of euglycemia and improve metabolic activity by increasing BAT activity.

OP5-4 Basic & translational diabetes research 2

Effects of maternal protein restriction diet and growth hormone treatment on glucose metabolism and taste buds homeostasis in mouse offspring

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Objective: Small for gestational age (SGA) offspring has a higher risk of developing metabolic disorders in adulthood. Growth hormone (GH) is one of the counterregulatory hormone against insulin, and GH treatment for SGA children who failed catch-up growth might worsen their risk of diabetes, which has not been studied in clinical trials. Maternal nutrition is important for normal taste development while maternal malnutrition is a risk of SGA. In this study, we aimed to evaluate the effect maternal protein restriction diet and growth hormone treatment on glucose metabolism and taste cell development in mouse offspring.

Methods: Pregnant C57BL6/J mice were fed a normal Chow diet (NCD) or protein-restricted diet (PRD; 9% protein) during pregnancy and lactation periods. SGA pups from PRD-fed dam were divided into GH-treated group (5 mg/kg, from weaning until 8-week-old) or vehicle-treated group. Body weight and nose-to-anus length were serially measured. Glucose homeostasis were evaluated by glucose tolerance test (GTT) in adulthood. Immunohistochemistry was conducted to reveal the differences in the morphology and cell types of taste buds among different groups.

Results: SGA group showed less body weight at birth and reduced body length at 3 weeks compared to NCD-fed controls. Vehicle-treated SGA offspring was shorter than control in adulthood, which was recovered by GH treatment. Glucose tolerance was impaired in SGA group, which was improved by GH treatment in female offspring. The number of taste buds was reduced in SGA group, which was rescued by GH treatment.

Conclusion: Maternal protein restriction led to smaller body size and dysregulated glucose metabolism, which all rescued by GH treatment. These results suggest that GH treatment may not, at least, deteriorate glucose metabolism in SGA offspring. Further studies are needed whether changes in taste buds are mechanically related with metabolic phenotypes.

OP5-5 Basic & translational diabetes research 2

Role of brain G protein-coupled estrogen receptor in growth and glucose metabolism

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Objective: Estrogen affects physical development and metabolism in human. Recent reports have shown that modulation of G protein-coupled receptor 30 (GPR30), a membrane-bound estrogen receptor, can change the body composition and energy metabolism in adulthood. However, it is unknown whether GPR30 in brain regulates metabolism during development. Here we aimed to elucidate the role of brain GPR30 in body size and energy metabolism.

Methods: The brain-specific GPR30 knockout mice (GPR30 KONestin) were generated by crossing GPR30-floxed mice and Nestin-Cre mice. Normal Chow diet (NCD) or high-fat diets (HFD, from 9-week-old age for 20 weeks) were provided ad libitum. Body weight and random blood glucose levels were measured weekly. Nose-to-anus distance was measured in adulthood. Plasma level of insulin-like growth factor (IGF-1) was measured by ELISA. Glucose tolerance test and insulin tolerance test were performed to evaluate glucose homeostasis in HFD-fed mice.

Results: In NCD-fed mice, the body weight was significantly lower in male GPR30 KONestin mice, while NCD-fed female mice and HFD-fed mice had no difference between groups. The body length of female GPR30 KONestin mice was shorter than control mice in both diets, while male mice were shorter only in HFD-fed group. The GPR30 KONestin mice showed markedly lower plasma concentrations of IGF-1 than control mice in HFD-fed group. Random blood glucose levels were not different between groups, but glucose tolerance and insulin sensitivity were improved in male GPR30 KONestin mice.

Conclusion: GPR30 in brain might be a potential regulator of growth and glucose metabolism, whose effects are dependent on nutrition and sex. Further studies are needed to identify how GPR30 in brain controls stature and insulin sensitivity at the molecular level.

OP6-1 Clinical diabetes and therapeutics 3

Endocrine disruption and alteration in clock gene is the result of late night eating and delayed sleep

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Objective: The aim of this study is to investigate the hormonal disruption & genetic expression of circadian clock genes (related to metabolic homeostasis) RevErb alpha and ROR alpha in Type 2 diabetic T2DM patients with Morningness, Eveningness and intermediate chronotype.

Methods: A total of 245 subjects' age 18 to 60 years were recruited in Clinical OPD of General Medicine, KGMU. We have tested FBG & PP level, lipid profile HbA1c, Insulin, Leptin and Cortisol level, & genetic expression by RT-PCR.

Results: When we compared these 3 groups, Significant Different was found in various parameters like FBG (P=0.01) Postprandial (P=0.003) HbA1c (P=0.001) TG (P=0.001), Total Cholesterol (P=0.01) & VLDL (P=0.005). Serum leptin (17.01+11.70) also reduced in eveningness when compared to morningness type, which may increase appetite & reduce energy expenditure leading in turn to the development of obesity & deterioration of metabolism. It also shows the complete inversion of the cortisol level (180.55+51.70). IL-6 (2.97+0.55) & IL1- β (11.97+3.55) also increased in intermediate and eveningness subjects. ROR α expression was reduced in eveningness (p=0.071) and mixed chronotype (p=0.025) when compared with morningness chronotype (p=0.091). Also comparison of REV ERB α expression was reduced in eveningness (p=0.039) & mixed chronotype (0.047) when compared with morningness type or early eaters.

Conclusion: Results were completely different to our expectation. Involved hormones inflammatory markers & Clock gene (REV ERB α & ROR α) mRNA expression is significantly altered in eveningness and mixed chronotype as compared to morningness type in T2DM Patients. RT-PCR determination of this specific clock gene may be helpful for earliar detection of T2DM in patients with altered feeding habit & unbalanced lifestyle.

OP6-2 Clinical diabetes and therapeutics 3

Efficacy of intermittent short-term use of a real-time continuous glucose monitoring system in non-insulin-treated patients with type 2 diabetes: a randomized controlled trial

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Objective: Studies assessing the use of real time-continuous glucose monitoring systems (RT-CGMs) in non-insulin-treated patients with type 2 diabetes (T2D) are rare. This study aimed to evaluate the efficacy of intermittent short-term use of a RT-CGM in non-insulin-treated T2D patients uncontrolled with oral anti-diabetic drugs (OADs).

Methods: In this multicenter randomized prospective study, 61 participants were randomly assigned to treatment group 1 (one session of RT-CGM), treatment group 2 (two sessions of RT-CGM with a three-month interval between sessions), and a control group. All participants used blinded CGMs for up to 6 days with education before randomization, and RT-CGM was additionally applied for 1 week in the intervention groups. The primary outcome was change in HbA1c at 6 months.

Results: Among 61 participants, 48 subjects completed the study (baseline HbA1c 8.2±0.5%). At three months, significant HbA1c reduction was observed in treatment group 1 (adjusted difference=-0.60%, P=0.044) and treatment group 2 (adjusted difference=-0.64%, P=0.014) compared to the control group. However, at six months, only treatment group 2 achieved significant HbA1c reduction (adjusted difference=-0.68%, P=0.018). Especially in the treatment groups, patients performing self-monitoring of blood glucose (SMBG) ≥1.5 times/day showed significant HbA1c improvement at both three months and six months, but those performing SMBG <1.5 times/day showed no significant improvement.

Conclusion: In non-insulin-treated T2D patients uncontrolled with OADs, intermittent short-term use of RT-CGM was an effective method for glucose control, especially in those performing SMBG frequently.

OP6-3 Clinical diabetes and therapeutics 3

Improvement of heart rate variability after metabolic bariatric surgery in Korean subjects with obesity

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Objective: Obesity is a major risk factor for cardiovascular autonomic neuropathy (CAN), one of chronic vascular complications of diabetes. Metabolic bariatric surgery (MBS) improves diabetes through weight loss and hormonal changes. In this study, we investigated the influence of MBS on CAN and heart rate variability (HRV), an early indicator of CAN, in Korean subjects with obesity.

Methods: Patients who underwent MBS from February 2020 to August 2021 were recruited prospectively. CAN was evaluated before and 1 year after surgery by Ewing method (change in blood pressure (BP) and heart rate (HR) according to deep breathing, Valsalva maneuver, postural change, and sustained handgrip) and HRV (standard deviation of NN interval, root mean square of successive RR interval difference, total power, and very low, low, and high frequency (HF)) by AFT-800 (MEDICORE, Gyeonggi-do, Republic of Korea).

Results: Of 30 patients enrolled, 10 (33.3%) were male, and 19 (63.3%) had diabetes. Mean age and body mass index were 40.6±8.2 years and 36.0±5.0 kg/m2, respectively. The mean follow-up duration was 310 days. There was no significant difference in number of patients with abnormal CAN from 20 (66.7%) before surgery to 21 (72.4%) after surgery and parameters of Ewing method also were not significantly different before and after surgery. However, the resting HR was decreased significantly from 80.8±14.0 to 66.6±8.0 bpm after surgery (P<0.001). HF increased significantly from 131.3±196.5 ms2 to 318.7±446.7 ms2 (P=0.024) and LF/HF ratio decreased significantly from 2.1±1.7 to 1.3±1.2 (P=0.025). In a correlation analysis, an increase in HF and a decrease of LF/HF ratio were correlated with the magnitude of body weight reduction.

Conclusion: MBS significantly improved indicators of parasympathetic denervation, an early manifestation of CAN. This improvement of HRV was related with robust reduction of body weight after metabolic bariatric surgery.

OP6-4 Clinical diabetes and therapeutics 3

Effectiveness of education on economic burden of diabetes care expenditure in North Indian Asian adults

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Objective: The present study aimed to investigate the effectiveness of education on economic burden of diabetes care expenditure in North Indian Asian Adults.

Methods: One-to-one diabetes education in the form of personal discussion were given to eligible study participants having type 2 diabetes mellitus (T2DM) for a period of one year with session frequency of 2 hour per week. Data were collected from study participants at different time interval including baseline and thereafter every 3rd month till 1 year. The primary outcomes include the hemoglobin A1c (HbA1c) and direct, indirect cost expenditures. Data collected were analyzed using student's "t" test along with linear mixed model regression for assessing the effectiveness of one-to-one education over time

Results: The age of study participants were found in the range of 43-67 years contributing 46% of male and 54% of female Asian North Indian population. Majority of study participants have lower educational qualification with lower income source. Eligible study participants showed baseline HbA1c as 8.74% followed by substantial reduction from baseline and every follow-up (P<0.001). Significant reduction in direct and indirect cost was also reported from baseline and every follow-up (P<0.001).

Conclusion: Results of the present study demonstrated effectiveness of one-to-one education in glycemic management along with reduction of direct and indirect costs. The intervention also helped in reduction of diabetes associated complications occurrence in Asian North Indian population. Such cost effective intervention can be implemented at large scale at community level in countries with higher burden of diabetes mellitus.

OP6-5 Clinical diabetes and therapeutics 3

Aging-related changes in volumetric body composition measured by artificial intelligence and its association with 10-year incidence of diabetes mellitus

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Objective: We presented aging-related, and sex-stratified reference data of volumetric body composition (BC) measured by computed tomography (CT) in Asians. In addition, we verified the usefulness of BC for the diagnosis of type 2 diabetes mellitus (DM) and the prediction of 10-year incident DM.

Methods: The 15,330 subjects who 1) completed the health screening program from January, 2011 to September, 2012 at Seoul National University Hospital Healthcare System Gangnam Center, and 2) had CT in abdomen-pelvic region were recruited for cross-sectional analyses. Among them, 11,693 subjects with follow-up data by April, 2022 were included for longitudinal analyses. AI-based CT-image analysis software (DEEPCATCH) separates 7 body segments; abdominal skeletal muscle (ASM), abdominal visceral fat (AVF), subcutaneous fat (SF), bone, central nervous system, skin, and internal organs, and quantified each volume.

Results: AVF proportion increased, and SF and ASM proportion decreased linearly with aging. AVF/SF volumetric ratio (ASvR) linearly increased by 0.08 per 10 years except for men with BMI 23 or higher. It increased more rapidly by 0.18 per 10 years in men with BMI of 23 or higher (All, p<0.001). Each group with higher ASvR [>1.2 in men, OR 2.1, (95% CI 1.8-2.4); >0.5 in women, 3.1, (2.4-3.9)] showed a significant correlation with the prevalence of DM. Each group with normal glucose tolerance and higher ASvR [>1.3 in men, HR 1.2, (95% CI 1.1-1.3); >0.5 in women, 1.4, (1.2-1.6)] was more likely to develop prediabetes or DM in 10 years than each group with lower ASvR.

Conclusion: This is the first study to show volumetric reference data of aging-related, and sex-stratified BC using CT. We verified that ASvR is the best indicator that shows aging-related BC changes and deterioration of glucose tolerance.

OP7-1 Diabetes complications-basic & translational

Effect of tocotrienol-rich fraction on retinal vessel diameter and angiogenesis-related markers in rats with streptozotocin-induced diabetic retinopathy

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Objective: Diabetic retinopathy (DR), the commonest ocular complication of diabetes mellitus, is associated with serious sight-threatening problems and vision loss. Angiogenesis or neovascularization is an important pathological feature in DR. In DR, higher expression of hypoxia-induced factor-1 alpha (HIF-1α), a key transcription factor in angiogenesis, is associated with increased expression of vascular endothelial growth factor (VEGF) and insulin-like growth factor-1 (IGF-1). This study investigated the effect of tocotrienol-rich fraction (TRF), which has anti-angiogenic properties, towards the retinal expression of these angiogenic biomarkers in streptozotocin (STZ)-induced diabetic rats.

Methods: Sprague-Dawley rats (200-250g) were grouped into; normal (N), diabetic-vehicle (DV) and diabetic TRF-treated (DT) groups. N received intraperitoneal (IP) injection of citrate buffer, whereas DV and DT were injected with STZ (IP, 55 mg/kg body weight). DT was treated with 100 mg/kg of TRF, whereas DV and N received vehicle. Treatment was given via oral gavage, once daily, for 12 weeks. Fundus images were captured at baseline, week 6 and 12 post STZ-induction for vessels diameter analysis. At the end of the experiment, rats were euthanized and retinas were collected for measurement of HIF-1α, IGF-1 and VEGF protein expression using ELISA.

Results: Larger retinal venous diameter was observed in DV compared to N at week 6 and 12 ($p<0.05$). DT exhibited smaller venous diameter compared to DV ($p<0.05$) at the same time points. The vascular findings correlated with the higher retinal HIF-1α, VEGF and IGF-1 protein expression in DV compared to N (1.34-fold, 3.05-fold, 7.48-fold respectively; $p<0.001$), whereas the same in DT was comparable to N. Lower HIF-1α, VEGF and IGF-1 expression were observed in DT compared to DV (1.05-fold, 1.29-fold, 2.75-fold respectively; $p<0.05$).

Conclusion: Twelve weeks of oral TRF supplementation preserves retinal venous diameter and lowers retinal HIF-1α, IGF-1 and VEGF expression in the STZ-induced diabetic rats.

OP7-2 Diabetes complications-basic & translational

Mitochondrial dynamics and neuroinflammation in progression of hypoglycemic neuronal damage

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Objective: Severe hypoglycemia with brain damage is one of the most dangerous adverse effects of insulin therapy. It has been reported that mitochondrial impairment and inflammatory activation may play crucial role during neuronal damage. Here, we evaluated temporal changes of mitochondrial dynamics and neuroinflammation during brain damage after hypoglycemia.

Methods: Male C57BL/6 (9-weeks-old) mice were fasted overnight and hypoglycemia (below 20 mg/dL) was induced by intraperitoneal (i.p.) injection of Humulin R (20 U/kg) twice at 1-hour intervals. After 3 hours of hypoglycemic period, glucose solution was i.p. injected for rescue. Control mice were i.p. injected saline instead. All groups are sacrificed at 7 days after hypoglycemia. To investigate progression in severe hypoglycemic brain damage, the hypoglycemic period was extended to 5 hours and mice were sacrificed 1, 4, and 7 days after hypoglycemia. The cortex and/or dentate gyrus were stained for signals of damage and inflammation. The molecular changes in the cortex samples were analyzed to observe brain damage, inflammation, and mitochondrial dynamics by immunoblot.

Results: Even when the signal of brain damage [increased 4-hydroxynonenal (4-HNE) and decreased microtubule-associated protein 2 (MAP2)] is not significant in hypoglycemia group (HG), activated microglia [immunoreactivity of Iba-1], IL-1β, and mitochondrial fission [pDrp1(Ser616)/Drp1 ratio] were significantly increased. When serially assessed, damage signals [4-HNE and TUNEL] were gradually increased and became significantly high at day 7 in HG, while neuronal markers [MAP2 and NeuN] were gradually decreased. The number of activated microglia was peaked even in day 1 and maintained until day 7 in HG.

Conclusion: In the brain of our mouse model of severe hypoglycemia, mitochondrial alteration and inflammatory activation were preceded, followed by a progressive neuronal damage. Crosstalk between mitochondria and neuroinflammation and their causality during hypoglycemic neuronal damage progression are needed to be further studied.

OP7-3 Diabetes complications-basic & translational

1H nuclear magnetic resonance (NMR) analysis of urinary exosomal lipids identifies prediabetes signatures: non-invasive diagnostic approach

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Objective: The present study aim to exploit the urinary exosomal lipids for screening of novel biomarker signature sequences for diagnosis of prediabetes.

Methods: First midstream urine samples from healthy and prediabetic patients were collected. Exosomes from the urine sample were isolated followed by isolation of total lipids using biphasic method using chloroform:methanol in the ratio of 2:1. Exosomes size was evaluated by nano tracking analysis (NTA) and exosomal lipids were detected by 1H NMR technique

Results: The urine exosome isolated from healthy and pre-diabetes patients showed an average size range of 293.3 +/- 6.3 nm and 167.4 +/- 4.6 nm respectively with relatively less population in prediabetic subjects compared to healthy. Moreover, 1H NMR spectra of prediabetic urinary exosomal lipids showed a signature peak at 3.882 ppm, while the healthy spectra devoid of such peak.

Conclusion: Exosomal content can be explored further for diagnosis of prediabetes using sensitive NMR technique using novel biomarker signatures.

OP7-4 Diabetes complications-basic & translational

Correlation between inflammatory and mitochondrial biomarkers, renal function and continuous glucose monitoring (CGM) metrics in diabetes patients with chronic kidney disease (CKD)

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Objective: Mitochondrial dysfunction and systemic inflammation contribute to progression of diabetic kidney disease (DKD). We hypothesized increased glucose variability (GV), as compared to chronic hyperglycemia, may induce greater oxidative stress, profound mitochondrial dysfunction and microvascular damage. We investigated the relationship between continuous glucose monitoring (CGM) metrics, inflammatory biomarkers and mitochondrial function in DKD.

Methods: Circulating markers of inflammation and mitochondrial dysfunction, plasma creatinine, urine albumin-creatinine ratio (uACR) and blinded continuous glucose monitoring (CGM) recordings were collected at baseline and the end of a 16-week randomized controlled trial, which included 65 type 2 diabetes patients with CKD G3b-5 (65.4±9.0 years (mean±SD), estimated glomerular filtration rate (eGFR):26.1±9.6 ml/min/1.73 m^2, %HbA1c:7.4±0.8 mmol/L, uACR 87.4(274.6) mg/g). Tumor necrosis factor receptor (TNFR) was measured by standardized enzyme-linked immunosorbent assay (ELISA), while urinary supernatant mitochondrial DNA (mtDNA) level was measured by digital polymerase-chain-reaction. GV was expressed as % coefficient variation, SD of sensor glucose and mean amplitude of glycemic excursion (MAGE).

Results: Plasma TNFR-1 and plasma TNFR-2 were negatively correlated with eGFR (TNFR1: r=-0.72, $p<0.001$, TNFR2: r=-0.66, $p<0.001$) and positively correlated with urine ACR in the whole group (TNFR1: r=0.327, $p<0.001$, TNFR2: r= 0.330, $p<0.001$). Urine mtDNA was positively correlated with uACR (r=0.214, p=0.015). However, there was no significant association between TNFR1, TNFR2, urine mt-DNA and %CV (TNFR1: r=-0.147, p=0.1, TNFR2: r=-0.168, p=0.057, urine mtDNA r=0.13, p=0.15). No significant correlations were observed between kidney biomarkers and glucose SD or MAGE.

Conclusion: TNFR1 and TNFR2 were strongly associated eGFR and urine mt-DNA with uACR, but no associations were observed with indices of GV. Further studies are needed to investigate of the contribution of glycemia towards systemic inflammation in the pathogenesis of DKD.

OP7-5 Diabetes complications-basic & translational

Alleviation of diabetic gastroparesis by vagal modulation and its pertinent non-invasive markers

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Objective: Diabetic gastroparesis (DG) is a serious complication of long-standing diabetes and a manifestation of autonomic neuropathy, which cannot be adequately controlled or monitored by current modalities. In this study, we examined whether vagal stimulation can improve gastric emptying in mouse models of DG. We also aimed to discover exhaled volatile organic compounds (VOCs) as the surrogate marker of diagnosis and monitoring of DG.

Methods: To evaluate the rate of gastric emptying, streptozotocin (STZ)-induced type 1 diabetic mellitus (T1DM) mice were fasted for 6 hours and then orally administered acetaminophen (100 mg/kg). The serial levels of acetaminophen in blood were determined using liquid chromatography with tandem mass spectrometry (LC-MS/MS). Mouse exhalation was collected using a custom exhaled gas-collection device and exhaled VOCs were analyzed using a thermal desorption-gas chromatography-mass spectrometry (TD-GC-MS). To evaluate the efficacy of vagal stimulation, the vagal-specific DREADDs mice (Nav1.8-Cre::hM3Dq) were produced by crossing Nav1.8-Cre mice [expressing Cre in vagal afferents] and Cre-dependent hM3Dq mice [expressing chemogenetic receptor for activation]. Clozapine-N-oxide (CNO, 10 mg/kg, ligand for hM3Dq) were injected for these mice 30 min before administration of acetaminophen.

Results: Eight weeks after induction of diabetes, the plasma levels of acetaminophen were significantly decreased in T1DM mice compared to control mice, implying decreased gastric motility (as a model of DG). In VOCs analysis, 79 VOCs were finally compared between groups after pre-processing. In a two-fold change analysis, 7 VOCs and 25 VOCs were significantly increased and decreased, respectively in DG mice. Plasma levels of acetaminophen were significantly increased by CNO treatment in diabetic Nav1.8-Cre::hM3Dq mice compared to diabetic control group.

Conclusion: Vagal stimulation could improve gastric motility in our DG mouse model. The expiratory VOCs differently detected between groups might be candidates for diagnostic/therapeutic markers of DG.

OP8-1 Diabetes complications-clinical & epidemiology 2

Performance of simple fibrosis scores in non-alcoholic fatty liver disease with and without type 2 diabetes

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Objective: We aimed to evaluate the diagnostic performance of nonalcoholic fatty liver disease (NAFLD) fibrosis score (NFS) and fibrosis-4 score (FIB-4) for screening liver fibrosis in NAFLD according to the presence of diabetes in tertiary care setting.

Methods: This cross-sectional study prospectively enrolled 267 patients with NAFLD assessed by ultrasound or transient elastography (TE), who counseled hepatologists or endocrinologists. NFS, FIB-4, and liver stiffness measurement (LSM) by TE were assessed to evaluate liver fibrosis. The performance of NFS (≥-1.455) and FIB-4 (≥1.3) was evaluated to diagnose advanced fibrosis defined LSM ≥8kPa in Type 2 diabetes (T2D, n=87) and non-T2D (n=180).

Results: The mean age and body mass index were 47.6 years and 28.3 kg/m^2, respectively. Though the NFS and FIB-4 did not differ comparing with or without T2D, LSM was significantly higher in T2D (5.8±2.7 kPa vs. 6.8±3.7 kPa, p=0.026). A total of 23 non-T2D (12.8%) and 15 T2D (17.2%) patients had advanced fibrosis. Almost 10-15% of low NFS and FIB-4 were false-negative in T2D patients, which was higher than that in non T2D (5-8%). Combined screening using NFS and FIB-4 did not reduce false-negative in T2D patients. The diagnostic performance of NFS and FIB-4 was suboptimal in T2D (area under curve [AUC]=0.623 and 0.653, respectively) compared to that in non-T2D (AUC=0.732 and 0.826, respectively).

Conclusion: The diagnostic performance of NFS and FIB-4 in patients with T2D was suboptimal when compared to those without T2D in tertiary care setting.

OP8-2 Diabetes complications-clinical & epidemiology 2

Remnant cholesterol is an independent predictor of type 2 diabetes: a nationwide population-based cohort study

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Objective: Although the atherogenic effect of remnant cholesterol (remnant-C) has been widely recognized, the relationship between remnant-C and glucose metabolism remains unclear. This retrospective longitudinal study investigated the relationship between remnant-C and incident type 2 diabetes (T2D) in a nationwide cohort of Korean adults.

Methods: A total of 8,485,539 Korean adults without diabetes participated in the national health screening in 2009 and were followed up until 2019. The relationship between remnant-C quartiles and incident T2D was examined by Cox regression models. The risk of incident T2D over the continuum of remnant-C was examined with cubic spline analysis.

Results: During the median follow-up period of 9.28 years, 584,649 (6.8%) individuals developed T2D. In multivariable-adjusted analyses, participants in the upper quartile of remnant-C had a higher risk of developing T2D, with hazard ratios of 1.25 (95% CI, 1.24-1.27) in the second quartile and 1.51 (95% CI, 1.50-1.53) in the third quartile, 1.95 (1.93-1.97) in the fourth quartile, compared to the lowest quartile. The increase in the risk of T2D owing to high remnant-C concentration was more profound in individuals with fewer traditional T2D risks such as female sex, and absence of metabolic abnormalities including impaired fasting glucose, hypertension and atherogenic dyslipidemia. Moreover, the magnitude of the increased risk for ncident T2D in individuals with higher remnant-C quartiles was higher in younger than in older participants.

Conclusion: These findings demonstrate that remnant-C changed early in the course of the pathophysiological processes that lead to the development of T2D, even before metabolic abnormalities are established.

OP8-4 Diabetes complications-clinical & epidemiology 2

Diffusion tensor imaging of the tibial nerve can detect peripheral neuropathy in type 2 diabetes

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Objective: Magnetic resonance imaging (MRI) has played little role for the study of peripheral nerve disease. However, recent technological advances in MRI have provided us more information about neural microstructure and higher resolution in peripheral nerves. The aim of this study is to evaluate whether diffusion tensor imaging (DTI) parameters in MRI can detect peripheral neuropathy in type 2 diabetes (T2D).

Methods: In this prospective, single-center study, eight T2D patients (mean age, 62.1±10.8 yr; 5 M/3F) with peripheral neuropathy and seven healthy controls (65.0±3.3 yr, 7F) were included. All T2D patients underwent Michigan Neuropathy Screening Instrument questionnaire and quantitative sensory testing. MRI including DTI and axial T2-weight Dixon sequence was performed for each participant. Region of interest analysis was independently performed by one radiologist on each side of tibial nerve at two levels: lower margin of adductor magnus muscle insertion (level 1), and quadriceps femoris tendon at patellar attachment (level 2). DTI parameters including cross-sectional areas (CSA), fractional anisotropy (FA), as well as diffusivity (mean (MD), axial (AD), and radial (RD)) were calculated.

Results: FA was significantly lower in T2D patients with peripheral neuropathy than controls at both level 1 (396±74 vs. 541±141, P<0.05) and level 2 (422±65 vs. 565±108, P<0.05). AD was significantly lower in T2D patients with peripheral neuropathy than controls at level 2 (2,207±492 vs. 2,884±497, P<0.05). RD was significantly higher in T2D patients with peripheral neuropathy than controls at level 1 (1,156±313 vs. 867±147, P<0.05). No difference in the CSA of the tibial nerve was seen in both levels between two groups.

Conclusion: Our data have shown that DTI parameters detect nerve abnormalities of the tibial nerve in T2D patients, suggesting DTI may be useful as a biomarker in diabetic peripheral neuropathy.

OP8-5 Diabetes complications-clinical & epidemiology 2

A virtual diagnosis of diabetic nephropathy using proteomics in place of kidney biopsy

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Objective: Diabetic kidney disease is generally diagnosed with clinical features and laboratory data such as serum creatinine and albuminuria, but several glomerulonephritis (GN) could be combined with biopsy-confirmed diabetic nephropathy (DN). This study aims to define serum and urine proteome that can virtually diagnose DN instead of kidney biopsy.

Methods: Patients with type 2 diabetes mellitus (T2DM) who underwent kidney biopsy from 2010 to 2020 at Pusan national university hospital were retrospectively reviewed. The most combined GN was IgA nephropathy (IgAN) and membranous glomerulonephritis (MN). Thus, we selected age- and sex-matched patients with pure DN, pure non-DN (IgAN, MN) for proteomic analysis. The control group was donors for living kidney transplantation. Experimental groups were four and each group consisted of 11 patients. Comparative proteome analysis was performed using high resolution mass spectrometry coupled with nanoflow liquid chromatography. Resulting relative protein quantity of each group was extracted using label free manner and statistical analysis was performed to discover group specific protein biomarker candidate.

Results: In serum sample set, total 1,220 proteins were identified, and 30 proteins were clustered to be highly expressed in DN group and decreased in control, IgAN and MN group. Among 30 proteins, serum protein A001 was increased in DN group 8.75 times higher than control group and its expression level ratio in IgAN and MN compared to control group was 0.982 and 1.179, respectively. From urine sample set, 1,579 proteins were identified, and protein expression was divided into 4 clusters via hierarchical cluster analysis. Gene ontology analysis for urine DN specific cluster indicated that urine DN specific increased proteins were involved in complement system.

Conclusion: Serum and urine proteome can be useful to diagnose biopsy-confirmed DN and guide the indication of kidney biopsy with T2DM having kidney damage.

PE001 Basic & translational diabetes research

Arsenic toxicity on metabolism and autophagy in brown adipose tissue

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Objective: Arsenic is an element that occurs naturally in the environment. Humans are likely to be exposed to higher amount of arsenic through arsenic contaminated drinking water and consuming foods including fruits and vegetables, and the arsenic can accumulate in the human body at high concentrations. Previous research has shown that arsenic induces oxidative stress linked to metabolic diseases such as diabetes. In mice, arsenic exposure during embryonic development is linked to an early puberty and adult diabetic pathologies. Recent findings of brown adipocytes, capable of dissipating energy as heat, in adult humans have promised new hope for diabetes treatment and prevention. Therefore, understanding the pathophysiological role of brown adipocytes and uncoupling protein 1 (UCP1) regulation in thermogenesis can provide effective strategies against diabetes.

Methods: Here, we investigated the effects of arsenic on differentiation, mitochondrial respiration, thermogenesis and autophagy in immortalized murine brown adipocytes and mice studies.

Results: We observed that arsenic significantly reduced brown adipocyte differentiation in dose dependent manner. Arsenic suppressed autophagy activity, mitochondrial respiration and biogenesis, leading to attenuated brown adipocytes specific thermogenesis functions including UCP1 in immortalized murine brown adipocytes. In mice studies, we confirmed the heavy arsenic accumulation in brown adipose tissue (BAT) and the suppression of gene expression levels of mitochondria specific markers and autophagy genes including Sestrin2 and ULK1 after the oral administration of arsenic into mice at dose of 10 mg/kg/day for 9 days. Arsenic significantly suppressed the BAT thermogenesis marker UCP1 when exposed to cold temperature for 24 hr at the last day of oral gavage.

Conclusion: These results reveal the underlying mechanism of how arsenic aggravates metabolic diseases such as diabetes by suppressing brown adipocyte differentiation, mitochondria function and thermogenesis, which can be utilized for development of arsenic-specific inhibitor drugs protecting essential physiological functions of BAT in human diabetes patients.

PE002 Basic & translational diabetes research

Overexpression of system xc^- protects renal tubular epithelial cells from 2-Deoxy-D-Ribose-induced oxidative damage

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Objective: Oxidative stress in renal tubular cells is known to be one of the etiologies of diabetic nephropathy. 2-Deoxy-D-ribose (dRib) causes oxidative damage by depleting GSH in cells, including beta cells. System xc^- is a membrane transporter that moves extracellular cystine into cells independent of sodium, and cystine uptake through system xc^- is a rate-limiting step for intracellular GSH synthesis, which is important for protecting cells from oxidative stress. We conducted this study to determine whether dRib causes oxidative damage in renal tubular cells and, specifically, to investigate the mechanism through which dRib increases oxidative stress

Methods: L-[14C]cystine uptake, GSH content, reactive oxygen species (ROS) levels, and cell viability were measured in NRK-52E cells, a renal tubular cell line, and the mRNA and protein expression of xCT, the functional unit of system xc^-, were investigated. The xCT gene was then overexpressed in NRK-52E cells using lentivirus. L-[14C]cystine uptake, GSH, and cell viability were also measured in primary renal tubular epithelial cells isolated from rats.

Results: When NRK-52E cells were stimulated with various concentrations of dRiB, L-[14C]cystine uptake decreased, mRNA and protein expression of xCT increased, and intracellular GSH and ROS levels and cell viability were significantly decreased in a dose-dependent manner. L-[14C] cystine uptake, intracellular GSH and ROS levels, and cell viability reduced by dRib were all significantly recovered by xCT overexpression. In primary renal tubular epithelial cells, dRiB also significantly reduced L-[14C]cystine uptake, GSH content, and cell viability, and these were almost completely recovered by pretreatment with 2-mercaptoethanol, a cystine uptake enhancer.

Conclusion: In renal tubular epithelial cells, dRib depletes GSH by reducing cystine uptake through inhibition of xCT. The resulting oxidative damage can be prevented by overexpressing xCT. Therefore, it is thought that the oxidative damage in renal tubular cells can be prevented through system xc^- regulation.

PE004 Basic & translational diabetes research

Measurment of malondialdehyde (MDA) level and superoxide dismutase (SOD) activity in the pancreatic tissue after the intervention of orange water kefir in the hyperlipidemic rats model

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Objective: Hyperlipidemia can cause pancreatic tissue injury due to high oxidative stress. One of the oxidative stress signs is increased malondialdehyde level (MDA) and a decrease in superoxide dismutase activity (SOD). Previous research has shown that probiotics (water kefir) may improve lipid profile and oxidative stress in the pancreatic tissue. This research aims to know the effect of orange water kefir on MDA level and SOD activity in the pancreatic tissue of the hyperlipidemic rats model.

Methods: This research design is quasi-experimental. Three groups (K+, K-, P) each consist of 10 rats. All intervention was given by the sonde method. All groups were given fed ad libitum until the end of this research. For the first 4 weeks, K+ and P groups were induced by quail egg yolk with the dosage is 5 ml/200-gram body weight (grBW). In the second 4 weeks, a group of P was given orange water kefir with 5 ml/ 200 grBW. orange water kefir was made in accordance with good manufacturing product (GMP) standards for making the probiotic beverage. All rats are terminated by anesthesia and decapitation to take the pancreatic. Then, the pancreatic tissue will be examined for MDA level and SOD activity.

Results: Mean of MDA (mg/dl) levels were 10.17+0.11 (K+), 0.79+0.09 (K-), 2.78+0.12 (P). Mean of SOD activity (%) were 43.21±3,45 (K+), 83,57±2,48 (K-), 73,92±1,65 (P). One-way ANOVA test results showed significant differences in MDA level with a p-value <0.001 and SOD activity with a p-value $p<0.05$. statistical analysis showed there are significant differences in MDA level and SOD activity in pancreatic tissue between all groups after the intervention of orange water kefir ($p<0.001$).

Conclusion: The intervention of orange water kefir has an effect to improve the MDA level and SOD activity in the pancreatic tissue of the hyperlipidemic rats model ($p<0.0001$).

PE005 Basic & translational diabetes research

Identification of total protein and antioxidant activity in rice contaminated with high concentration of pesticides

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Objective: Rice, the second major important crop in the world, demands high production to satisfy its needs. However, dangerous options have been taken by farmers including the usage of high concentrations of pesticides to overcome the pest problem. Several research studies are addressing the side effect of pesticide-contaminated foods which have a solid link to several types of diabetes mostly type 2 diabetes. This becomes a great concern in global public health considering the daily intake of rice in human life for a persistent period (years to a decade), it is very interesting to study the effect of these pesticides on rice and how rice responds to high concentrations of pesticide. Hence, this study was chosen to determine the impact of high concentrations of pesticides on total protein and antioxidant activities in rice.

Methods: In this research, Oryza sativa variety MR263 was chosen and planted using a 3:2:½:½ ratio of soil, sand, organic fertilizer, and peat moss respectively. Then, rice was contaminated with a high concentration of pesticides, four and six times from normal concentration before proceeding to examine the total protein and antioxidant activities using Bradford and CAT assays respectively, through UV-Vis Spectrophotometer.

Results: Our results show sudden changes ($p<0.05$) in total protein and catalase activity (antioxidant) when rice was contaminated with pesticides. These can be seen from samples treated with a six-time concentration of pesticides.

Conclusion: In conclusion, using pesticides with higher concentrations could trigger oxidative stress resulting from the buildup of heavy metals in rice plants which may have adverse health effects on rice consumers. Hence, detailed identification of antioxidant protein in rice plants is required to assist the development of biosensors in identifying foods contaminated with high concentrations of pesticides.

PE008 Basic & translational diabetes research

Hydrogen peroxide promotes cell viability and migration at low dose via vegf- α and tgf- α gene expression

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Objective: Production of oxidant and antioxidant are important in wound healing process. Imbalance of the production might lead to oxidative stress thus causing many complications including deficiency in wound healing activity which usually happened to diabetic patients. Cells such as fibroblast cells, produce superoxide, a strong oxidant which can dismutase into hydrogen peroxide (H2O2) and oxygen (O2). It is known that excessive production of H2O2 might lead to oxidative stress in cell but less has known that low dosage of H2O2 are also needed in wound healing process.

Methods: Therefore, we chose to conduct an experiment on fibroblast cells using low dosage of H2O2 (lower than 50 μM) to observe the ability of the treatment to promote cell viability and migration and to investigate the expression of VEGF-α and TGF-α gene after treated with low dosage of H2O2.

Results: AlamarBlueTM cell viability, scratch assay, and qRT-PCR analysis of VEGF- α and TGF- α gene expression were done and the cell viability was significantly increased after 48 h and 72 h at 12.5μM, 25μM, and 50μM of H2O2 and cells were significantly migrated after treated with 6.25μM of H2O2. VEGF- α gene was highly expressed in qRT-PCR analysis while TGF- α GENE was found to be low.

Conclusion: Nevertheless, the results revealed a positive progress in healing process after treated with low dose of H2O2 where VEGF- α gene was expressed after the treatment. This suggests that low dosage of H2O2 induced certain gene in cell thus helping in promoting cell viability and cell migration.

PE009 Basic & translational diabetes research

The impact of chromolaena odorata methanolic extract and quercetin in wound healing activity and in inducing vegf-α gene expression

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Objective: Diabetes can cause diabetic neuropathy which affect wound healing efficiency on the body. There are a lot of factors that affects wound healing process and one of it is excessive production of free radicals. The production of free radicals however can be controlled with the existence of antioxidants. Quercetin is an antioxidant that can easily be found in plants and also in C. odorata has high therapeutic properties to protect cells against oxidative damage and free radicals, while Chromolaena odorata decoction of fresh leaves has already been used for many years in many tropical countries as a traditional medicine for the treatment of burn wounds, skin infection and also for some other medical uses including antihypertensive, anti-inflammatory and diuretic.

Methods: Therefore, we have conducted a few test to evaluate the cell viability, cell migration and gene expression on C. odorata and quercetin treatment using AlamarBlueTM cell viability, migration assay, and qRT-PCR analysis of VEGF-α gene expression, respectively.

Results: The results have demonstrated that the treatment of on C. odorata and quercetin has significantly increased the cells viability at 24h and 0.415 mg/mL of quercetin has increase the migration of the treated fibroblast cells. VEGF-α gene was significantly expressed in the treatment of quercetin.

Conclusion: Quercetin is regarded as major antioxidants substance which can scavenge free radical very well thus the result has actually proven that quercetin has an important role in promoting wound healing thus enhancing the viability and migration of the cell and also inducing growth factor that helps in cellular activity.

PE012 Basic & translational diabetes research

Study of ALAN (Artificial Light At Night) as a zeitgeber affecting anthropometric and biochemical parameters in patients of metabolic syndrome background

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Objective: Study the effect of blue light/mobile exposure on anthropometric and biochemical parameters in patients of metabolic syndrome.

Methods: We have studied the effect of ALAN on 80 patients of metabolic syndrome using questionnaires like Diurnal type score questionnaire (DTSQ) Torsval and Akerstedt (1980) constructed, questions on sleep habit (bedtime, wake-up time, sleep hours of both weekdays and weekend), questions on mental health (irritation, anger, out of controlling emotion, depression), questions on usage of mobile phones (types of the phones, frequency to use, day of time for usage, usage duration per one time). We have accumulated data on height, weight, waist size, hip size, neck size, waist : hip ratio, body mass index,HbA1c, fasting blood sugar, post prandial blood sugar, uric acid, systolic blood pressure, diastolic blood pressure, lipid profile. In our study, there were 40 cases and 40 controls. Cases were defined as patients of metabolic syndrome using smartphones whereas controls were defined as patients of metabolic syndrome not using smartphones.

Results: Height difference between cases and controls was -2.756±2.938, change in hip size: -1.181±3.211, neck size: -1.906±1.389, waist in centimetres: -4.573±3.948, weight in kgs: -6.640±4.628, DBP: -3.030±4.616, Fasting blood sugar: -83.09±44.46, HbA1c: -1.636±0.7154, HDL- C: -5.091±5.056, Heart rate: -2.640±4.406, LDL C: -20.05±9.764,Post prandial: 16.42±64.03, S.cholesterol: -34.57±15.28, S.Triglycerides :-48.01±24.91, Uric Acid: -0.1228±0.6238, SBP: 7.155±6.981, SGPT: -11.78±5.817, VLDL C: 3.846±7.876. The findings are based on cases using smartphones and controls not using smartphones. There seems to be a significant association of exposure to blue light and worsening of biochemical parameters. Our data shows that barring hip size (in centimetres),post prandial blood sugar, systolic blood pressure, high density lipid, heart rate all other parameters were decreased in controls with respect to cases.

Conclusion: This study is a part of the project No.- 45/3/2020-PHY/BMS funded by ICMR Indian Council of Medical Research.

PE013 Basic & translational diabetes research

Impact of type 2 diabetes-associated PAX4 variant on pancreatic beta cell function

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Objective: Pax4 is a key transcription factor that regulates pancreas development and beta cell differentiation. It has been reported that PAX4 Arg192His (R192H) variant was associated with increased risk of type 2 diabetes (T2D) in Korean. This study aims to unveil the mechanism underlying PAX4 R192H variant-related T2D phenotypes.

Methods: Animal model of human PAX4 R192H variant was generated by knock-in of point mutation in mouse Pax4 gene. Pax4WT/WT (Pax4-WT) and Pax4R192H/R192H (Pax4-R192H) mice were fed either standard chow diet (SCD) or high-fat diet (HFD). Metabolic phenotypes were analyzed by measuring body weight, blood glucose level, glucose tolerance, and glucose-stimulated insulin secretion. Beta cell mass was quantified using insulin-stained pancreas sections. Transcriptomic analysis was performed by using single-cell RNA-sequencing on isolated mouse pancreatic islets.

Results: Metabolic profiles of Pax4-WT and Pax4-R192H mice fed with SCD were similar. However, after 4 weeks of HFD feeding, Pax4-R192H mice showed impaired glucose tolerance and decreased insulin secretion, as well as delayed expansion of beta cell mass in response to metabolic stress. Transcriptomic analysis revealed that HFD-fed Pax4-R192H mice had beta cells with decreased expression of key genes regulating beta cell function and increased expression of stress-related genes compared to HFD-fed Pax4-WT mice, which was not observed in SCD-fed state.

Conclusion: Pax4-R192H mice exhibited diabetic phenotypes and transcriptomic changes indicating impaired beta cell function after HFD. These findings suggest that PAX4 R192H variant disturb beta cell response to metabolic stress.

PE014 Basic & translational diabetes research

Antihyperglycemic role of chromium oxide nanoparticles on hepatic function in fat-fed and streptozotocin-treated rats

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Objective: Diabetes is a metabolic disorder and It is characterized by hyperglycemia resulting from absolute insulin deficiency or insufficient insulin secretion and/or insulin sensitivity. The present study investigated the impact of chromium oxide nanoparticles (Cr2O3NPs) on serum parameters of hepatic function, on oxidative stress markers (malondialdehyde [MDA] and 8-isoprostane), and on expression level of insulin receptor, glucose transporter 2 (GLUT2), glucokinase genes and heat-shock proteins (HSPs) in rats.

Methods: Male Wistar rats (n=64, 10 weeks old) were divided into four groups. Group 1 received a standard diet (12% of calories as fat). Group 2 received a standard diet, plus Cr2O3NPs; received a single daily oral dose of Cr2O3NPs of 100 mg/kg in suspension. Group 3 received a high-fat diet (40% of calories as fat) for 2 weeks, and was then injected with streptozotocin (STZ) on day 14 (STZ, 40 mg/kg intraperitoneally). Group 4 was treated in the same way as group 3 (HFD/STZ), but was supplemented with Cr2O3NPs 100mg /kg/body weight/day. Oxidative stress in the kidneys of diabetic rats was evidenced by an elevation in levels of MDA and 8-isoprostane. Protein concentrations of insulin receptor, GLUT2, glucokinase genes and heat-shock (HSP60 and HSP70) in renal tissue were determined by Western blot analyses.

Results: Cr2O3NPs supplementation lowered kidney concentrations of MDA, 8-isoprostane levels, serum urea-N, and creatinine, and reduced the severity of renal damage in the STZ-treated group (i.e., the diabetes-induced group). The expression of insulin receptor, GLUT-2, glucokinase genes and HSPs was lower in the STZ group that received ZnONPs than in the group that did not. No significant effect of Cr2O3NPs supplementation was detected in regard to the overall measured parameters in the control group.

Conclusion: This study supported the efficacy of Cr2O3NPs in reducing renal risk factors and impairment because of diabetes and act as potent antidiabetic agent.

PE015 Basic & translational diabetes research

Somatic mutations of primary hepatocellular carcinoma in non-alcoholic fatty liver disease mouse model

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Objective: Although the prevalence of hepatocellular carcinoma (HCC) arising in non-alcoholic fatty liver disease (NAFLD) is rapidly increasing, little is known about its cancer genome landscape. Herein, we deciphered the somatic mutational landscape of NAFLD-related HCC by whole-genome sequencing (WGS) in a mouse NAFLD model.

Methods: Seven-week-old male C57BL/6J mice were injected with low-dose streptozotocin (40 mg/kg) for 5 days and fed with high-fat diet (HFD) from 8 weeks of age. Mice were sacrificed after HFD feeding for up to 60 weeks. WGS was performed with 9 tumor tissues and 7 adjacent non-tumor liver tissues harvested from 7 mice of age ranging from 38 to 56 weeks. Somatic mutations were searched in tumors using adjacent non-tumor tissue as the matched-normal.

Results: Tumor prevalence was 70-100%, and it increased with the duration of HFD. Histologically, steatohepatitic variant HCC was found among the tumors. The median numbers of single nucleotide variants (SNVs) and short insertion/deletions were 2,812 (range, 2,077-4,993) and 211 (range, 40-280), respectively. Mutational signature of SNVs showed endogenous, 'clock-like' signature predominantly (median contribution 63.1%) with accompanying signature from alkylating agent-mediated mutations (median contribution 17.2%). Driver mutations were detected in the Wnt/β-catenin pathway (4 HCCs), chromatin modifiers (4 HCCs), and p53 (1 HCC). Interestingly, all three Ctnnb1 mutations showed mutations in serine residues (p.S45F, p.S33P), crucial phosphorylation sites for ubiquitin-mediated degradation as well as well-known mutation hotspots in human HCCs. Among the three Ctnnb1 mutated tumors, two were from a single mouse with same driver mutation (p.S45F), suggesting convergent evolution during NAFLD progression.

Conclusion: The somatic mutations of HCC in mouse NAFLD model resembled that of human HCC regarding mutational burden and driver mutations. Further studies in this mouse model will help decipher the dynamic changes in the genomic landscape during the clonal evolution of hepatocytes from NAFLD to HCC.

PE016 Basic & translational diabetes research

Natural COA water inhibits mitochondrial ROS-mediated apoptosis through Plk3 downregulation under STZ diabetic stress in pancreatic β-cell lines

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Diabetes from pancreatic β cell death and insulin resistance is a serious metabolic disease in the world. Although the overproduction of mitochondrial reactive oxygen species (ROS) plays an important role in the pathogenesis of diabetes, its specific molecular mechanism remains unclear. Here, we show that the natural Charisma of Aqua (COA) water plays a role in Streptozotocin (STZ) diabetic stress-induced cell death inhibition. STZ induces mitochondrial ROS by increasing Polo-like kinase 3 (Plk3), a major mitotic regulator, in both Beta TC-6 and Beta TC-tet mouse islet cells and leads to apoptosis. Overexpression of Plk3 regulates an increase in mitochondrial ROS as well as cell death, also these events were inhibited by Plk3 gene knockdown in STZ diabetic stimulated-Beta TC-6 cells. Interestingly, we found that natural COA water blocks mitochondrial ROS generation through the reduction of Plk3 and prevents apoptosis in STZ-treated beta cells. Furthermore, using the 3D organoid (ex vivo) system, we confirmed that the insulin secretion of the supernatant medium under STZ treated pancreatic β-cells is protected by the natural COA water. These findings demonstrate that the natural water COA has a beneficial role in maintaining β cell function through the inhibition of mitochondrial ROS-mediated cell death, and it might be introduced as a potential insulin stabilizer.

PE017 Basic & translational diabetes research

Causal role of iron in excess on increased risks of type 2 diabetes, metabolic syndrome, and associated components among Taiwan Han Chinese and UK Whites

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Objective: Epidemiological studies have implicated that elevated iron levels are associated with higher risks of cardiometabolic outcomes, including type 2 diabetes (T2D) and metabolic syndrome (MetS). Genetic susceptibility and environmental factors were reported to cause a number of cardiometabolic outcomes. However, there has been scarcity of data on the susceptibility genes of iron status, especially among non-European populations. It is also not completely clear whether variants of iron homeostasis genes causally influence the development of MetS. Our study elucidates the causal effects of iron in excess in precipitating the risk of T2D, MetS, and its associated key components.

Methods: We first conducted genome-wide association studies of blood hemoglobin (Hb) concentration among the Taiwan Han Chinese (HC) and Europeans of White ancestry. Ethnic-specific genetic risk scores from Hb-associated SNPs (Hb-GRS) were then constructed as instrumental variables for iron status. We next titrated the associations between Hb deciles and T2D, MetS, as well as its individual components through observational studies. In our Mendelian Randomization analyses, we performed multivariate logistic regressions that investigated the causal associations between Hb-GRS and T2D, MetS, and other outcomes.

Results: We found evidence to support the causal associations between increasing Hb-GRS and risks of T2D, MetS, and its components in both the Taiwanese HC and European White groups. This corroborates the results of our observational studies, wherein an association between stronger risks and increasing Hb deciles was observed with all metabolic components except T2D. Interestingly, both the highest Hb decile groups and contrarily the lowest ones were associated with higher odds of T2D in both ethnicities.

Conclusion: Our findings suggest the causal role of elevated iron levels in the pathophysiology of T2D, MetS, and other metabolic dysfunctions. Such will contribute to the improvement of public health in the near future.

PE018 Basic & translational diabetes research

Impact of coconut oil versus palm oil on obesity related outcomes: a sequential feeding clinical trial

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Objective: Overweight and obesity are the major public health consequences because these increase the risk of various co-morbidities including diabetic mellitus. Excess fat intake, such as from saturated fat sources has been linked to an increase in overweight and obesity, particularly in developing nations. As palm oil and coconut oil are the major saturated fat sources on a regular basis among South Asian and South-East Asian nations, it is useful to compare the effect of coconut oil and palm oil on anthropometric parameters in healthy adults.

Methods: The study was carried out as a sequential feeding clinical trial with 40 healthy adults dividing into two feeding periods of 8 weeks each. Participants were provided palm oil for the first feeding period followed by coconut oil with a 16-week washout period in between to incoporate into their daily meals (breakfast, lunch, dinner, and snacks). The dosage of required oil was calculated based on the participant's usual calorie intake derived from 24 hour dietary recall. The outcomes measured were the difference in body weight, body mass index (BMI), waist circumference (WC), hip circumference (HC), and waist-to-hip ratio (WHR) which were measured at the bigining and end of the each intervention period. Dietary intake and physical activity levels were assessed as potential confounding variables.

Results: At the initial point of palm oil feeding and the initial measure of coconut oil feeding, no significant differences in all the anthropometric parameters were observed. No changes were observed with respect to the body weight, BMI, and other anthropometric measures (WC, HC, and WHR) after both oil treatment periods. No significant difference was observed for anthropometric parameters between the two oil treatments.

Conclusion: This study revealed that coconut oil in comparison to palm oil did not change anthropometric-related cardiovascular risk factors such as body weight, BMI, WC, HC, and WHR.

PE019 Basic & translational diabetes research

Effects of coconut oil versus palm oil on blood glucose and lipid parameters in healthy adults

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Objective: A high content of saturated fatty acids (SFAs) in the diet is associated with insulin resistance, development of type 2 diabetes and cardiovascular diseases. We aimed to compare changes in blood lipid profile and fasting plasma glucose after consumption of coconut and palm oils in healthy adults.

Methods: A sequential feeding clinical trial with two feeding periods of 8 weeks each was conducted among 40 healthy adults. Participants were provided palm oil in the first feeding period followed by coconut oil with a 16-week washout period in between to incorporate their daily meals. The quantity oil was calculated based on the participant's usual calorie intake. The outcomes measured were the difference in serum low-density lipoprotein cholesterol (LDL-C), total and high-density lipoprotein cholesterol (TC and HDL-C), TC/HDL-C ratio, triglycerides (TG), very low-density lipoprotein cholesterol (VLDL-C), and fasting plasma glucose (FPG) at the beginning and end of the each treatment periods.

Results: FPG was significantly increased by coconut oil from 3.3% (p=0.014), while FPG was significantly different (p=0.017) between the two treatment phases. LDL-C was significantly decreased by palm oil from 13.04% (p<0.001) while coconut oil increased it from 5.59% ((p= 0.044), causing significantly different between the two treatment oils (p<0.001). Similarly, TC was significantly decreased by palm oil from 9.9% (p<0.001) while coconut oil increased it from 4% ((p= 0.044). TC/HDL-C ratio was significantly decreased by palm oil from 9.4% (p<0.001) while no significant difference from coconut oil. However, HDL-C (p=0.919), VLDL-C (p=0.059), TG (p=0.059) did not show any statistically significant difference.

Conclusion: Consumption of palm oil decreased serum TC, LDL, TC:HDL-C, and FPG in healthy adults in comparison to coconut oil. No significant difference was observed in direct serum LDL-C, HDL-C, TG, VLDL-C between oils, although individual effect from palm oil significantly improved TG and VLDL-C levels.

PE020 Basic & translational diabetes research

Time restricted feeding as a behavioural intervention can prevent obesity in wistar rats

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Objective: Obesity is the risk factor of diabetes, cancer, cardiovascular disease (CVD) and non-alcoholic fatty liver disease. Time restricted feeding is a type of intermittent fasting that is being used to lose weight and for treating metabolic disorders. Hence, the aim of this study was to see the effect of TRF intervention on diet induced obese rats and their association with circadian gene expression of Per1 and Bmal1.

Methods: A total of 15 Wistar rats were included in the study and divided into two groups. Control group and High Fat diet (HFD) group which consisted of six rats and nine rats respectively. HFD group was fed fatty diet (ad lib) for two months to develop obesity. Lipid profile, blood glucose level, insulin and melatonin levels were studied in blood samples taken from the two groups and body weight was measured monthly. These HFD rats were shifted to TRF for three months, after which they were again put back on ad lib (24 hr feeding). At the end of the experiment, these rats were sacrificed.

Results: The body weight and blood glucose level of HFD group was significantly increased as compared to control rats respectively. The level of insulin, melatonin (p=0.006) and HDL were reduced in rats fed with HFD whereas total cholesterol, TG and LDL were increased. TRF intervention reduced body weight, blood glucose level, TG, LDL, Per1 expression and elevated the level of insulin, melatonin, total cholesterol, HDL and Bmal1 expression. TRF in HFD induced obesity showed its legacy effect when put on ad lib.

Conclusion: Thus, this study revealed that TRF is a behavioural intervention that can prevent and treat obesity by improving the metabolic parameters in obese Wistar rats.

PE021 Basic & translational diabetes research

DN200434 has anti-atherosclerotic effects via inhibition of VSMCs proliferation and mitochondrial oxidative phosphorylation

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Objective: Excessive proliferation and migration of vascular smooth muscle cells (VSMCs), which contributes to the development of occlusive vascular diseases, requires elevated mitochondrial oxidative phosphorylation to meet the increased requirements for energy and anabolic precursors. Therefore, therapeutic strategies based on blockade of mitochondrial oxidative phosphorylation are considered promising for treatment of occlusive vascular diseases. Here, we investigated whether DN200434, an orally available estrogen receptor-related gamma inverse agonist, inhibits proliferation and migration of VSMCs and neointima formation by suppressing mitochondrial oxidative phosphorylation.

Methods: VSMCs were isolated from the thoracic aortas of 4-week-old Sprague-Dawley rats. Oxidative phosphorylation and the cell cycle were analyzed in fetal bovine serum (FBS)- or platelet-derived growth factor (PDGF)-stimulated VSMCs using a Seahorse XF-24 analyzer and flow cytometry, respectively. A model of neointimal hyperplasia was generated by ligating the left common carotid artery in male C57BL/6J mice.

Results: DN200434 inhibited mitochondrial respiration and mammalian target of rapamycin complex 1 activity and consequently suppressed FBS- or PDGF-stimulated proliferation and migration of VSMCs and cell cycle progression. Furthermore, DN200434 reduced carotid artery ligation-induced neointima formation in mice.

Conclusion: Our data suggest that DN200434 is a therapeutic option to prevent the progression of atherosclerosis.

PE022 Basic & translational diabetes research

Mechanisms of the protective effect of philanthotoxin against NMDA-induced retinal oxidative and nitrosative stress

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Objective: This study investigated the role of p53-mediated Bcl-2/Bax/caspase-3 apoptosis pathway in the mechanism of protective effect of Philanthotoxin-343 (PhTX-343) against N-methyl-D-aspartate (NMDA)-induced retinal oxidative and nitrosative stress, one of the most common finding in diabetic retinas.

Methods: Sprague-Dawley rats were divided into 3 groups; Groups 1 and 2 were intravitreally injected with phosphate buffer saline (PBS) and NMDA (160 nM), respectively. Group 3 was pre-treated with PhTX (160 nM) 24-hour prior to NMDA injection. Seven days post-treatment, retinal oxidative stress was measured by quantifying the levels of reduced glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT). To estimate retinal nitrosative stress, inducible nitric oxide synthase (iNOS) expression was determined using immunohistochemistry (IHC) and ELISA. Retinal protein expression of nuclear factor kappa B (NF-κB), p53 and caspase-3 were determined using ELISA and IHC.

Results: PhTX-343 significantly increased the retinal GSH, SOD and CAT levels compared to Group 2 by 7.26-, 1.44- and 2.89-fold respectively. Retinal iNOS expression in PhTX-treated group was suppressed compared to NMDA-treated group as detected by IHC. ELISA showed a 3.92-fold lower iNOS expression in PhTX-343 compared to NMDA-treated group. PhTX-treated group also showed lower NF-κB and p53 levels by 1.56 and 1.44-fold, respectively, compared to NMDA-treated group. Retinal caspase-3 expression was significantly lower by 1.41-fold after PhTX-343 treatment compared to NMDA treatment alone. Similar observations were made for NF-κB, p53 and caspase-3 using IHC.

Conclusion: In conclusion, PhTX-343 pre-treatment in rats protects against NMDA-induced retinal oxidative and nitrosative stress. The mechanisms associated with these effects of phTX-343 seem to involve reduced expression of NF-κB and p53. PhTX also suppressed caspase-3 expression, hence it is likely to protect against NMDA-induced retinal cell apoptosis.

PE023 Basic & translational diabetes research

Vitamin D3 supplementation ameliorated the reduction of muscle strength via elevation of apelin expression in muscle

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Objective: Age-related frailty and reduced physical activity contribute to a degenerative loss of muscle mass, function, and strength, referred to as sarcopenia. Indeed, aging is associated with elevations in a number of circulating inflammatory proteins. Vitamin D deficiency has been involved in the pathogenesis of diabetes, metabolic syndrome, muscle atrophy, and bone less, and is common in elderly due to age-related changes in lifestyle and physical exercise. There are many studies have been made that vitamin D plays a beneficial role in inflammatory response and muscle health. However, the molecular mechanisms of vitamin D have not fully elucidated. In this study, we tried to demonstrate whether vitamin D3 could overcome the muscle atrophy due to aging.

Methods: We fed young (10 months) or aged (22 months) mice with chow diet or vitamin D supplemented diet (20,000 IU/kg) for 4 months, and then measured changes in body weight and skeletal muscle strength by grip strength and rotarod test.

Results: We found that the reduction of the grip strength and muscle mass due to aging was recovered by vitamin D3 supplementation. Also, the increase of factors involved in muscle atrophy, such as FOXO3A and atrogin, was decreased by vitamin D3 supplementation. Interestingly, there was a significant increase in levels of apelin and its receptor (APLNR) by vitamin D3-supplemented diet. Furthermore, markers of skeletal muscle senescence, as p21, p53 and p16, were elevated in muscle of aged mice compared to the young mice, but vitamin D3 supplementation ameliorated muscle senescence. Notably, levels of the angiogenic factors, CD31 and VEGFa, were significantly increased in the muscle of aged mice fed with the vitamin D3-supplemented diet.

Conclusion: Our present data suggests that vitamin D ameliorates aging-induced muscle loss and function, suggesting that a potential role of vitamin D as an intervention target to prevent aging-induced metabolic diseases

PE024 Basic & translational diabetes research

Abnormal tau phosphorylation in the diabetic nephropathy of NOX5 pod+ mice

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Objective: Tau, major microtubule associated protein (MAP), regulates the assembly and maintenance of the structural stability of microtubules. Abnormal phosphorylation of tau is well known as a major cause of Alzheimer's disease by inducing neuronal cell death. The renal mesangial cells are known to have contractile properties and regulate the filtration pressure of glomerulus. In damaged mesangial cells, cytoskeletal rearrangement occurs and disrupts actin cytoskeleton leads to renal dysfunction. To understand of the role of tau phosphorylation in diabetic nephropathy, we investigated the relationship between renal injury and tau phosphorylation in this study.

Methods: We evaluated the tau phosphorylation in the diabetic nephropathy of NOX5 pod+ transgenic mouse. Insulin resistance and kidney damages were induced with high-fat diet (60% kcal fat). To evaluate the phosphorylation of tau according to the kidney damage, HFD was supplied for 3, 6, and 12 weeks. And cellular cytoskeletal structure changes and phosphorylated tau expressions were observed in mesangial cells.

Results: The expression of pTauSer202, Thr205, one of the phosphorylated residues of tau, showed the most significantly increased at the 6 week of high- fat diet, and after 12 weeks, α-SMA was increased while the phosphorylation of tau was rather decreased. TGF-β induced fibrosis or thapsigargin induced ER stress increased tau phosphorylation however, the inhibition of tau phosphorylation or ER stress improved cellular damage in mesangial cells.

Conclusion: This finding suggests that tau phosphorylation is involved in the development of diabetic nephropathy, and it may be a therapeutic target in diabetic nephropathy.

PE025 Basic & translational diabetes research

Effect of ethanolic extract of moringa root (moringa oleifera, lam.) on histopathology of inflammatory liver tissue of white rat (rattus norvegicus) hyperlipidemia and type 2 diabetes mellitus model

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Objective: This study aims to determine the effect of Moringa root extract on the liver histopathology of white rats with gyperlipidemia and type 2 diabetes mellitus model.

Methods: The study is an experimental laboratory with the method of pre and posttest control group design and posttest only with group design. Rats were divided into 5 groups, namely K1 negative control; K2 positive control; K3 made hyperlipidemia, type 2 diabetes mellitus and Moringa root extract dose of 150 mg/kgBW; K4 made hyperlipidemia, type 2 diabetes mellitus, and Moringa root extract dose 250 mg/kgBW; and K5 made hyperlipidemia, type 2 diabetes mellitus, and root extract Moringa 350 mg/kgBW. Induction of hyperlipidemia was by giving duck egg yolk 1 ml/10mgBw. Type 2 diabetes mellitus was obtained by induction of STZ-Na. Analysis of liver inflammation after administration of Moringa root ethanolic extract using the Kruskal-Wallis test followed by the Mann-Whitney test.

Results: The results of the Kruskal-Wallis test showed a p value <0.005, which means that the data on liver inflammation in all groups had a significant difference.

Conclusion: Moringa root extract doses of 150 mg/kgBW, 250 mg/kgBW, and 350 mg/kgBW can improve liver function by decreasing the number of foci of liver inflammation in white rats of hyperlipidemia and type 2 diabetes mellitus model, and significantly at a dose of 350 mg/KgBW.

PE026 Basic & translational diabetes research

Effect of ethanolic extract of moringa root (moringaoleifera, lam.) on IL-1β protein expression in liver tissue of white rat (rattusnorvegicus) hyperlipidemia and type 2 diabetes mellitus model

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Objective: This study aims to determine the effect of ethanolic extract of Moringa root on the expression of IL-β in the liver tissue of hyperlipidemia and T2DM rats.

Methods: This study is an experimental laboratory type with a post-test only group design, at the Food and Nutrition Laboratory of Gadjah Mada University and the Anatomical Pathology Laboratory, Sebelas Maret University. Rats were divided into 5 groups, namely K1 negative control; K2 positive control; K3 made hyperlipidemia, T2DM, and Moringa root extract dose of 150 mg/kgBW; K4 made hyperlipidemia, T2DM and Moringa root extract dose 250 mg/kgBW; and K5 made hyperlipidemia, T2DM and root extract Moringa 350 mg/kgBW. Induction of hyperglycemia in rats was done by giving duck egg yolk 1 ml/10mgBW, beef fat 1ml/100mgBW. T2DM was achieved by the STZ-Na induction process. IL-1β expression data were tested with Saphiro-Wilk. If the data is normally distributed, it will be continued with one-way ANOVA and post hoc with HSD test. If the data is not normally distributed, the Kruskal Wallis test and post hoc test with Man-Whitney will be used.

Results: The results of the Kruskal-Wallis test gave a value of p=0.001 ($p<0.05$), indicating a significant difference in IL-1β protein expression between the five groups.

Conclusion: Administration of the ethanolic extract of Moringa root (Moringa oleifera, Lam) at a dose of 250 mg/kgBW and a dose of 350 mg/kgBW significantly reduced IL-1β protein expression in the liver tissue of white rats (Rattus norvegicus) hyperlipidemia and T2DM models.

PE027 Basic & translational diabetes research

Polystyrene microplastics mixtures affects lipid and glucose metabolism

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Objective: 1) To analyze the effect of polystyrene microplastic mixtures (PM) on fat and glucose metabolism in 3T3-L1 adipocytes and high-fat diet-induced zebrafish larvae. 2) To investigate the correlation between PM exposure and type 2 diabetes (T2DM) or insulin resistance (IR).

Methods: PM was prepared by mixing microplastic and nanoplastic at ratio of 1:1 and treated to 3T3-L1 cells and high-fat diet-induced obese zebrafish larvae. MTT assay, Oil Red O staining, 2NBDG assay, and western blot and qPCR analysis were performed in the absence or the presence of PM and insulin.

Results: In vitro: PM exposure significantly increased cell viability, promoted adipocyte differentiation, and enhanced protein expressions of adipogenesis (peroxisome proliferator-activated receptor γ, PPARγ) or lipogenesis (sterol regulatory element binding protein-1c, SREBP-1c; fatty acid synthase, FAS). After differentiation into 3T3-L1 adipocytes, PM exposure significantly decreased glucose uptake. In addition, PM exposure effectively activated the phosphorylation of insulin receptor substrate-1 (IRS-1) at serine 307 residues and inhibited the expression of phosphoinositide 3-kinase (PI3K), protein kinase B (AKT), and glucose transporter 4 (GLUT4) proteins. However, it was restored to normal by insulin administration. In vivo: When PM was administered to high-fat diet (HFD)-induced obese zebrafish larvae, body weight and glucose concentration were significantly increased compared to the HFD group. In addition, mRNA expressions of preproinsulin (Insa), AKT, and GLUT2 related to glucose homeostasis were significantly decreased in the PM-treated group. Finally, mRNA expression of PPARγ, fatty acid synthase (FASN), and fatty-acid-binding proteins (FABP), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) related to fat metabolism and inflammation was significantly increased by PM administration in HFD-induced obese zebrafish larvae.

Conclusion: PM may induce metabolic diseases such as T2DM closely associated with lipid and glucose metabolism in 3T3-L1 adipocytes and HFD-induced obese zebrafish larvae.

PE028 Basic & translational diabetes research

CycloZ improves hyperglycemia and lipid metabolism by modulating lysine acetylation in KK-Ay mice

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Objective: To elucidate the mode of action of CycloZ, a mixture of zinc and cyclo-His-Pro (CHP), in improving diabetes and lipid metabolism.

Methods: KK-Ay mice, a type 2 diabetes (T2D) model, were administered CycloZ starting from 6- or 12-week-old age for 20 weeks, as a preventive intervention or for 12 weeks, as a therapy, respectively. Improvement of glycemic control was evaluated by oral glucose tolerance test (OGTT) and glycated hemoglobin (HbA1c) levels. Liver and white adipose tissue (WAT) were used for histological evaluation, gene expression analysis, and protein expression analysis.

Results: In both the prophylactic and the therapeutic studies, CycloZ administration showed improvement of glycemic control in KK-Ay mice. The lysine acetylation of peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC1α), liver kinase B1 (LKB1), and p65 was decreased in liver and WAT by CycloZ. In addition, CycloZ was efficacious for improving mitochondrial function, lipid oxidation, and inflammation in liver and WAT. It increased the level of β-Nicotinamide adenine dinucleotide (NAD+), which is related to the activity of non-histone deacetylases, such as Sirt1.

Conclusion: Our findings suggest that the beneficial effects of CycloZ on diabetes and obesity occurred through the increased NAD+ synthesis, which modulates the activity of the Sirt1 deacetylase in the liver and WAT. As the mode of action of an NAD+ booster or a Sirt1 deacetylase activator is different from that of traditional T2D drugs, CycloZ should be considered as a novel class drug.

PE029 Basic & translational diabetes research

Antidiabetic effect of thaliporphine against streptozotocin induced diabetes: alteration of gut microbiota

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Objective: Diabetes mellitus (DM) and its related complications such as neurotoxicity and cardiotoxicity is the serious health problem. During the DM and its complications altered the gut microbiota due to expansion of disease. Thaliporphine a alkaloids commonly exhibited the preventive effect against the inflammation and oxidative stress. In this experimental study, we try to explore the neuroprotective and cardioprotective effect of Thaliporphine against streptozotocin (STZ) induced renal and cardiac disease via alteration of gut microbiota.

Methods: Single intraperitoneal injection of STZ (60 mg/kg) was used for induction the diabetes. The rats were divided into different groups and received the various doses of Thaliporphine and rosiglitazone (1 mg/kg). blood glucose level, body weight, food intake, water intake and urine out put were estimated. Cardiac, renal, hepatic, antioxidant, apoptosis, inflammatory and inflammatory cytokines were estimated. Fecal sample was used for the determination of gut microbiota.

Results: Thaliporphine treatment significantly ($P<0.001$) suppressed the glucose level, water intake, food intake, urine output and enhanced the body weight. Thaliporphine treatment significantly ($P<0.001$) suppressed the cardiac parameters such as LDH, CK-MB, CK, cTnI and cTnt; renal parameters include total bilirubin, albumin, creatinine, uric acid, urea. Thaliporphine treatment significantly ($P<0.001$) suppressed the oxidative stress via increased the level of SOD, GPx, CAT, GSH and suppressed the level of MDA. Thaliporphine treatment significantly ($P<0.001$) suppressed the inflammatory cytokines such as TNF-α, IL-1β, IL-6, IL-8; inflammatory mediators include COX-2, TGF-β, PGE2, NF-κB in the renal and cardiac tissue. Thaliporphine treatment considerably altered the Bifldobacteriales, Bacteroidates, Burkholderiaies, Clostridiales, Coriobacteriales, Campylobacterioles, Enterobacteriales, Desulfovibrionales, Lactibacllales, Eryslpelotrichales, Verrucomicrobiales and Selenomonadales bacteria in the faces of STZ induced diabetic rats.

Conclusion: Thaliporphine exhibited the renal and cardioprotective effect against STZ induced DM rats via reduction of oxidative stress, inflammatory reaction and gut microbiota.

PE031 Basic & translational diabetes research

Emerging changes in IL-6 level in gestational diabetes mellitus

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Objective: Gestational diabetes mellitus (GDM) is a state of leptin resistant which develops a vicious cycle of hyperinsulinemia and hyperleptinemia leading to aggravation of an inflammatory situation. The objective of this study was to measure the level of serum leptin, insulin and IL-6 among GDM, Non-GDM and healthy non-pregnant women and to find out the correlation among the study group.

Methods: This cross-sectional study was performed on 100 GDM, 100 non-GDM and 50 non-pregnant women. DIPSI (Diabetes in Pregnancy Study Group India) criteria were used for screening GDM among pregnant women. GDM and non-GDM pregnant women were further categorized into three groups according to the trimester of pregnancy. The level of serum leptin, insulin and IL-6 were analyzed in all the enrolled women.

Results: Serum IL-6 level was higher among GDM women as compared to Non-GDM and non-pregnant women though the difference was statistically significant and serum leptin and insulin were also higher in GDM, but it was not statistically significant. When GDM and Non-GDM women were categorized in three trimesters serum leptin was found to be significantly elevated in 3rd trimester ($p< 0.002$) and IL-6 in 1st trimester ($p< 0.017$) in GDM women. No correlation was observed between leptin, Insulin and IL-6 in GDM women.

Conclusion: Absence of any significant association of leptin with IL-6 signifies that leptin may not be associated with inflammation in gestational diabetes. However IL-6 may serve as an early marker for screening glucose intolerance during pregnancy.

PE032 Basic & translational diabetes research

Exercise and vitamin D3 supplementation could improve brain-skeletal muscle interaction via elevation of apelin and apelin receptor expression in aged mice

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Objective: The peptide, apelin (AP), exerts a unique effect through the AP/apelin receptor (APJ) system. The role of AP/ APJ system in brain-peripheral organ axis upon aging is lacking. Here, we investigated APJ expression in the brain and compared its role in muscle function between young (14 weeks) and old (20 weeks) mice.

Methods: Male C57BL/6J mice divided into six groups; control, exercise (treadmill, 13m/min for 20 min /day/twice per a week for 8 weeks followed by three times per a week for 11 weeks), and vitamin D3 (20000 IU/kg b.w. vs. control group 1000 IU/kg b.w.) in young and old mice, respectively. The brain sections were processed chromogenic immunohistochemistry to visualize APJ. The skeletal muscle functions and AP levels were evaluated.

Results: We found old mice to have higher expression levels of APJ in the locus coeruleus (LC) and trigeminal nucleus (TN) of hindbrain, those in young mice. LC and TN connect to the spinal nucleus for the regulation of muscle tone. In contrast to the high APJ expression levels in these nuclei, low levels of muscle AP in the skeletal tissue with reduced muscle mass and function were observed. Interestingly, exercise and vitamin D3 improves not only muscle strength and the sustenance of high AP levels in skeletal muscles, but also the APJ expression levels in the LC and TN of the hindbrain. We assume that the increased APJ expression in LC and TN in old mice is to compensate for the reduced skeletal muscle mass and function due to low AP levels.

Conclusion: Taken together, although the function of the AP/APJ system from the brain to the skeletal muscle slows down upon aging, it recovers through exercise and vitamin D supplementation. Therefore, the brain-peripheral AP/APJ system is a possible target for clinical improvement of skeletal muscle function.

PE033 Basic & translational diabetes research

Exploration the mechanism of TNF-α-induced insulin resistance in 3T3-L1 adipocytes by integration of metabolomics and protein expression data

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Objective: Insulin resistance is a major contributor to the development of type 2 diabetes mellitus (T2DM). Tumor necrosis factor-alpha (TNF-α) is one of the most important pro-inflammatory cytokines that significantly involved in the development of insulin resistance. However, the molecular mechanism of the effects of TNF-α on insulin resistance is still unclear. This study aims to investigate the metabolic responses of 3T3-L1 adipocyte cells in TNF-α-induced insulin resistance via metabolomics and protein expression approaches.

Methods: The 3T3-L1 adipocyte cells were stimulated to insulin resistance with 1.0 ng/mL TNF-α. 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 TNF-α in 3T3-L1 adipocytes, and metabolomics pathway analysis (MetPA) was used to analyse and visualise the metabolic pathways involved. Protein expression related to the insulin signaling pathway was determined using Western blotting.

Results: Metabolomic analysis on TNF-α induced insulin resistance 3T3-L1 adipocyte cells revealed ten potential biomarkers and six major metabolic pathways related to amino acid, lipid, cofactors and vitamins, and nucleotide metabolism. Spermidine, betaine aldehyde, 5,6-dihydroxyindole, (Z)-5-oxohex-2-enediote, creatine, 7-dehydrodesmosterol, spermine, docosohexaenoic acid, phosphatidylethanolamine, and prostaglandin E2 were identified as potential biomarkers related to the mechanism of action of TNF- in 3T3-L1 cells. The major metabolic pathways for TNF-α in 3T3-L1 cells are sphingolipid metabolism, glycine, serine, and threonine metabolism, beta-alanine metabolism, lysine degradation, retinol metabolism, and purine metabolism. The expression of GLUT4, PI3K, AKT, and IRβ proteins in the insulin signaling pathway were decreased after TNF-α exposure.

Conclusion: This study showed that there were distinct changes in biological metabolites of TNF-α in 3T3-L1 cells and six differential metabolic pathways might be of key importance in mediating the mechanism of action of TNF-α in 3T3-L1. This may occur due to its effect on decreasing several insulin signalling protein expression.

PE034 Basic & translational diabetes research

Hippo/Mst1 is essential for adipose tissue aging and lipid metabolism

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Objective: The metazoan lifespan is determined by a complex signaling network that regulates energy metabolism and stress responses. Key signaling hubs in this network include insulin/IGF-1, AMPK, mTOR, and sirtuins. The Hippo/Mammalian Ste20-like Kinase1 (MST1) pathway has been reported to maintain lifespan in Caenorhabditis elegans, but its role has not been studied in higher metazoans. Thus, we aimed to study the function of lipid metabolism in adipose tissues in aging-associated diabetes.

Methods: We utilized Drosophila melanogaster, Mouse primary adipocytes and C. elegans models to investigate the roles of lipid metabolism in longevity regulation and adipocyte differentiation.

Results: In the present study, we report that overexpression of Hpo, the MST1 homolog in Drosophila melanogaster, decreased lifespan with concomitant changes in lipid metabolism and aging-associated gene expression, while RNAi Hpo depletion increased lifespan. These effects were mediated primarily by Hpo-induced transcriptional activation of the RNA-binding protein maternal expression at 31B (Me31b)/RCK, resulting in stabilization of mRNA-encoding a lipolytic hormone, AKH. In mouse adipocytes, Hpo/Mst1 mediated adipocyte differentiation, phosphorylation of RNA-binding proteins such as Rck, Decapping MRNA 2 (Dcp2), Enhancer Of MRNA Decapping 3 (Edc3), and Nucleolin (NCL), and Glucagon mRNA stability by interacting with Rck. Decreased lifespan in Hpo-overexpressing Drosophila lines required expression of Me31b, but not DCP2, which was potentially mediated by recovering expression of lipid metabolic genes and formation of lipid droplets.

Conclusion: Taken together, our findings suggest that Hpo/Mst1 plays a conserved role in determining longevity by regulating adipogenesis and fatty acid metabolism, implicating potential significance in aging-associated diabetes.

PE035 Basic & translational diabetes research

Assessment of pattern of dyslipidemia in normal, prediabetic and diabetic patient

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Objective: To assess the pattern of dyslipidemia in normal, prediabetic and diabetic patients.

Methods: A cross sectional study carried out in Patan Hospital, Lalitpur, Nepal

Results: A total of 130 subjects were enrolled in the study. Out of 130 subjects, 17 (40%) were diagnosed as pre-diabetic patient whereas 57 were diagonised as type 2 diabetes mellitus (DM). Among pre diabetic patient, 64.5% (n=11) has high triglyceride (TG) level followed by hypercholesterolemia (TC) (5.8%, n=1) and 5.8% (n=1) and 70.5 % (n=12) has higher LDL and lower HDL respectively. In case of diabetic one, it is found that 47.3% (n=27) has higher TG followed by hypercholesterolemia (3.7%) and 82.4% (n=47) has lower HDL. The frequency of dyslipidemia was found higher in male of age group 35-45 years as compared to female. The triglyceride level (204±123.8) was found to be significantly higher in pre-diabetic group as compared to diabetic (162±83.5) ($p < 0.035$). Unlike lipid markers, HbA1c was found to be significantly increased in Diabetic group (8.4 + 1.5, $p = 0.001$). TG and TC was found to be positively correlated with blood sugar level (r=0.65, 0.11 respectively) whereas HDL and LDL level was found to be negatively correlated (r =0.76, 0.09 respectively).

Conclusion: Hence, the study revealed that pre diabetic group are also at the risk of developing dyslipidemia and cardiovascular disorder and the younger people are also at risk group. So in addition to diabetic, attention should be given to carry out combined lipid profile to pre- diabetic group too in order to minimize the risk and not only for older age group, lipid profile should be carried out once a year for adult of above 30 years if feasible.

PE037 Basic & translational diabetes research

Antihepatotoxicity potential of α-linolenicacid in high fat-diet/ alloxan-induced diabetes in female rats

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Objective: α-Linolenic acid (ALA) is widely employed for gastrointestinal complaints such as dyspepsia, flatulence, diarrhea, and vomiting. Studies report fish oil based lipid emulsions contain high amounts of omega-3 polyunsaturated fatty acids. Hence, we assessed changes produced by the administration of ALA on biomarkers related to hepatic and antioxidant systems in high fat-diet diabetic rats.

Methods: The study was carried out on 64 diabetic female albino rats; a high-fat diet (HFD) and a single dose of alloxan (25 mg/kg) were utilized for experimental model induction. Diabetic rats were received ALA (100 and 200 mg/kg) intragastrically by gavage per day for 30 days.

Results: Administration of ALA caused a remarkable recovery of kidney weight, kidney function, and aldosterone level, particularly. Proapoptotic, antiapoptotic and inflammatory markers were significantly improved and showing a great retain to their normal levels specifically in ALA (200mg/kg)-treated groups. Also, a marked improvement in the antioxidants defense system was noted.

Conclusion: These findings indicate that ALA can be considered as a potential candidate for in vivo and clinical studies against various metabolic disease.

PE038 Basic & translational diabetes research

Ethanol-exposed hypothalamic neuronal cells undergo changes in expression of genes regulating energy metabolism

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Objective: Excessive alcohol consumption elevates the risk of metabolic diseases, including alcoholic fatty liver, dyslipidemia, and hypertension. The central nervous system regulates energy metabolism. However, the effect of alcohol on the central regulation of metabolic homeostasis, particularly in the hypothalamus, which is primarily responsible for metabolic regulation, remains unknown. Here, we show the direct effects of alcohol on the expression of metabolic genes in the hypothalamic neurons.

Methods: The neuronal hypothalamic cell line mHyoE-N46 was treated with alcohol (100 mM EtOH) or alcohol-free media and incubated for 24 h. The expression levels of genes involved in regulating metabolism in the hypothalamus were measured using real-time polymer chain reaction.

Results: We observed that the EtOH treatment did not change the expression levels of genes involved in anabolic metabolism, including agouti related neuropeptide, neuropeptide Y, and cannabinoid receptor 1, orexin receptor 1 and 2; and glucose metabolism, including glucose transporter 1, 2, and 3, insulin receptor, insulin-like growth factor I receptor, and insulin receptor substrate 2. Interestingly, we observed a significant increase in expression levels of genes participating in negative energy balance, including brain-derived neurotrophic factor (42%), glucokinase (68%), and 5-hydroxytryptamine receptor 1B (75%). Moreover, the expression of melanocortin receptor 4 (240%) showed the maximum increase.

Conclusion: Ethanol-exposed hypothalamic cells demonstrated changes in the expression levels of genes modulating energy metabolism. Further investigation of the intracellular energy homeostasis by ethanol in the hypothalamus is warranted for a deeper understanding of the underlying mechanism.

PE039 Basic & translational diabetes research

Natural product seaweed c.lentillifera as new potential for diabetes treatment

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Objective: Diabetic was one of chronic diseases that occur in our world. According to World Health Organization (WHO), 1.6 million were deaths that cause by diabetes in 2016, due to this, a lot of drug was created to fight diabetes but unfortunately these drugs have their side effect. So instead of using these drugs, we could use natural product to fight diabetes due to less side effect. Our objective is to screening out bioactive peptide from protein of seaweed C.lentillifera that potentially can be used as plenary study for diabetes treatment.

Methods: Ribulose-1 5-bisphosphate carboxylase/oxygenase large subunit, Glyceraldehyde-3-phosphate dehydrogenase-chloroplastic, and Heat shock protein 70 was identified and screened their potential bioactive peptide by using BIOPEP* analysis tool (http://www.uwm.edu.pl/biochemia).

Results: Result in BIOPEP analysis tool has shown motifs that represent both of Angiotensin-converting enzyme (ACE) inhibitor and dipeptide peptidase IV (DPP- IV) inhibitor activity in Ribulose-1 5-bisphosphate carboxylase/oxygenase large subunit was high 110 motif and 161 motif, Glyceraldehyde-3-phosphate dehydrogenase-chloroplastic was 84 motif and 112 motif, and for Heat shock protein 70 was 52 motif and 99 motif respectively. Function of ACE inhibitor was to protect people from diabetic nephropathy, while DPP- IV inhibitor function was to blocking action of DPP- IV in body. In the other hand, we could say that ACE inhibitor and dipeptide peptidase IV inhibitor was shows great potential due to higher amount of motif that present compared to the other bioactivities in three identified sequences that we screened.

Conclusion: Thus, our results suggest that C.lentillifera could be used as potential anti-diabetic agents that come from natural product instead of artificial drug due to high amount of motif in ACE inhibitor and dipeptide peptidase IV inhibitor. Besides that, C.lentillifera also contains soluble fibers that help control blood sugar level in diabetic patient.

PE040 Basic & translational diabetes research

Progressive change in abdominal perivascular adipose tissue with respect to increasing metabolic risk

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Objective: Early detection of metabolic derangement can enable the development of effective preventive strategies. Changes in the perivascular adipose tissue (PVAT) are associated with the risk of metabolic syndrome (MetS). We hypothesized that computed tomography (CT) can detect changes in the quantity and quality of PVAT with increasing cardiometabolic risk.

Methods: This study analyzed the data of 505 participants (males, 72.7%) who underwent general health checkups, including abdominal and pelvic CT. We measured the volume and fat attenuation index (FAI) of the abdominal periaortic and renal sinus adipose tissues. FAI was defined as the average Hounsfield units of the measured fat volume. Participants were categorized into three groups according to the number of MetS components on the basis of the modified ATP III criteria (0, 1-2, and ≥3).

Results: Moving stepwise from the no MetS component group to the 1-2-component group to the MetS group, all PVAT volumes increased and the FAI of all PVATs decreased consistently. An increase in PVAT volumes was independently associated with metabolic derangement in the MetS group, whereas the FAI of all PVATs decreased only in the early stage of metabolic impairment after adjusting for the corresponding fat volumes.

Conclusion: The volume and FAI of intra-abdominal PVAT changed in individuals with even subtle increments in cardiometabolic risk. Image-based assessment of intra-abdominal PVAT may be a potential biomarker of cardiometabolic risk.

PE041 Basic & translational diabetes research

Pancreas protection effect of an oral insulin sensitizer in in vitro and in vivo models of type 2 diabetes

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Objective: Pancreas damage is a critical complication of type 2 diabetes (T2D) that occurs as beta cells are overworked to produce insulin. Insulin sensitizer alleviates insulin resistance and sensitizes cells to the available insulin, therefore reducing stress on beta cells for its protection. HGR4113 is a small molecule insulin sensitizer that is currently at IND stage for a ph1 first-in-human study. Here, we characterize the effects of HGR4113 on T2D and pancreas in preclinical models of T2D.

Methods: In vitro effects of HGR4113 were assessed in C2C12 myotube and 3T3-L1 adipocyte where glucose uptake with or without insulin was measured, and in INS-1 pancreatic cell under high palmitate/glucose condition where cell viability, ER stress, and insulin production were measured. In vivo effects of HGR4113 were assessed in C57BL/6J mice under long term high fat diet treated for 12 weeks, and in C57BLKS/6J-db/db mice treated for 8 weeks; blood glucose, insulin, OGTT, HbA1c, water consumption, and body weight were measured weekly, and terminal pancreas were H&E stained. Pioglitazone was used as positive control.

Results: Treatment of HGR4113 in myocyte induced significant insulin-dependent glucose uptake at a level greater than pioglitazone; no such effect was observed in adipocyte. Treatment of HGR4113 in pancreatic cell under high palmitate and glucose condition significantly enhanced insulin production and cell viability while reducing ER stress at a level similar to pioglitazone. Oral administration of HGR4113 significantly, dose-dependently, and continually reduced fasting blood glucose, insulin, HbA1c, water intake, and body weight while improving glucose tolerance in the rodent models of T2D. Notably, HGR4113-treated groups had visibly clear and well-maintained pancreatic islet in the terminal pancreas section compared to non-treated groups.

Conclusion: HGR4113 as a muscle-specific insulin sensitizer improved T2D-related parameters in rodent models while protecting pancreas from damage in both in vivo and in vitro settings.

PE042 Basic & translational diabetes research

The NQO1 mediated increased AMPK activity ameliorates diet-induced obesity and improves metabolic phenotypes

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Objective: The energy imbalance caused by surplus nutrient intake and lack of physical activity induces diet- induced obesity and associated complications in modern society. Here, we developed a novel activator of NAD(P)H: Quinone Oxidoreductase 1 (NQO1) which is a key enzyme for conversion of NADH to NAD, KL1333, which is expected to treat obesity and associated complications. Accumulating data have suggested that cellular levels of NAD+ are critical to maintain energy homeostasis. To elucidate the effects of KL1333 on obesity and metabolic disorders, we took advantage of diet induced obesity model (DIO).

Methods: We used AML12 hepatocyte for in vitro and C57BL/6J mice (8-week-old) with high fat diet (HFD-60% fat) for DIO model in vivo. We examined indicators of insulin resistance through pharmacological activation of NQO1 (KL1333) and studied its mechanism.

Results: We found treatment of KL1333 exhibited improved metabolic phenotypes such as reduced fat mass, and inflammation in white adipose tissue (WAT). KL1333 treatment alleviates hepatic steatosis, inflammatory response and insulin resistance. These results indicated that KL1333 regulated various metabolic pathways, including fatty acid oxidation, lipid synthesis and lipolysis by modulating cellular energy status. We also found KL1333 treatment elevates the endogenous ratio of NAD+/NADH, leading to activation of AMPK and elevated mRNA levels of hepatic oxidation genes (PPAR-α, Sirt1, PGC1-α, and CPT1-α) while mRNA levels of hepatic lipogenic genes (PPAR-γ, SREBP1-c) and fatty acid uptake (CD36) genes are suppressed. These results indicate that altered cellular NAD+/NADH ratio by KL1333 ameliorates diet-induced obesity, insulin resistance by activating the NAD+ dependent energy sensing signaling pathway.

Conclusion: In conclusion, KL1333, a novel activator of NQO1 represents a promising therapeutic drug as an anti- obesity drug to prevent obesity and related metabolic disorders.

PE043 Basic & translational diabetes research

Effects of thyroxin administration on lipid peroxidation and antioxidant status after sleeve gastrectomy in rats

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Objective: Thyroid dysfunctions bring about pathological changes in different organs of the body. Findings obtained from in vivo and in vitro studies point out that thyroid hormones have a strong impact on oxidative stress. Sleeve gastrectomy has been used for the surgical treatment of morbid obesity. The aim of the present study was to determine the effects of triiodothyronine administration on oxidative stress parameters in male rats.

Methods: Sixty -four male Wistar albino rats were divided into control (n:12), and experimental (n:12) groups and underwent sleeve gastrectomy. Experimental group rats received a single dose of triiodothyronine (400 mg/100 g) in the operation day. Rats were sacrificed on postoperative day 7. Serum thyroid hormones were analysed. The supernatants were used to measure total oxidant status, total antioxidant status, nitric oxide and malondialdehyde levels. All tissue parameters were analysed by spectrophotometric methods. Oxidative stress index values were calculated.

Results: Thyroid stimulating hormone levels in both the control and triiodothyronine group did not significantly change on the 7th postoperative day. Free triiodothyronine levels were significantly higher in triiodothyronine group rats than in control group rats (triiodothyroninevs control. Although total oxidant status levels did not altered by thyroid hormone treatment, total antioxidant status levels significantly decreased. Oxidative stress index values were not statistically different in tissues. Tissue nitric oxide levels were also similar in both groups. Malondialdehyde levels increased in triiodothyronine given rats compared with the control group.

Conclusion: This study showed that total oxidant status levels and oxidative stress index values were similar in both groups. However, triiodothyronine supplementation induced lipid peroxidation by increasing tissue malondialdehyde levels that might deplete tissue antioxidant level.

PE044 Basic & translational diabetes research

The relationship between the start of puberty and diabetes mellitus related risk factors in the Korean adolescents

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Objective: An abnormal start of puberty has been associated with body mass index (BMI) and higher risk of obesity, resulting in enhanced risk of diabetes mellitus (DM). However, understanding of relationships between puberty and DM is still limited and only few studies have been conducted in the Korean adolescents. Here, we studied on the relationship between the start of puberty and DM related risk factors in Korean adolescents.

Methods: This study included 683 adolescents aged 7 to 18 years from the Korean Children-Adolescents Study (KoCAS) conducted by the Korea National Institute of Health. The KoCAS conducted an annual follow-up survey from 2005 to 2016 in Seoul and Gyeonggi-do of Republic of Korea. 'Before puberty' and 'after puberty' were defined as Tanner stage 1 and stages 2-5, respectively. The relationship was analyzed between puberty and DM related risk factors such as BMI, body fat, anthropometric traits, and biochemical variables including glycemic traits and lipids.

Results: After puberty in girls, BMI and body fat mass were significantly higher than those of before puberty. Fat-free mass was significantly higher after puberty when compared to fat-free mass before puberty. Among biochemical traits, there was no significant difference between 'before puberty' and 'after puberty' for insulin, glucose, triglycerides, and total cholesterol.

Conclusion: This study demonstrated that the changes in BMI, body fat mass, and fat-free mass were affected by the status of puberty. However, the results should be validated in an independent cohort due to limited number of samples in this study. Taken together, this study provided valuable insight for a better understanding of relationship between puberty and DM in the Korean adolescents.

PE045 Basic & translational diabetes research

"Hurry up! ready-to-eat food save our time" - a qualitative study of ultra-processed food consumption among adults in Jakarta

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Objective: The factors of choosing ultra-processed food (UPF) should be explored to design the best nutrition intervention for improving diet quality and depressing the risk of metabolic diseases.

Methods: Focused group discussions (FGD) were performed in four administrative cities in Jakarta Province during December 2021. Each group of the FGD consisted of 8-10 adults aged ≥20 years and lasted between 50-60 minutes, covering three topics regarding dietary patterns, the type of food commonly consumed, including the reason for consuming UPF during the last month. The FGD session was conducted by a trained moderator and assisted by two enumerators. The data were transcribed verbatim and analyzed using an inductive thematic approach.

Results: As of 24 adults were dominated by females (87.5%). Four initial themes determined UPF consumption, namely (1)family preferences, (2)practical reason, (3)taste, and (4)nutrient content. The UPF commonly consumed was instant noodles, canned sardines, biscuits, white bread, sugar-sweetened beverages (SSB), sausages, instant coffee drinks, and packaged milk. The frequency of consuming UPF was not often, "I choose instant or ready-to-eat foods when I or my family was in a hurry and have no time to cook fresh food." (Mrs. R, 45 years, a housewife). Some adults were already aware of UPF's negative effects, yet the good taste kept them consuming the food, "I know that instant food is bad for health. However, I thought that if we did not consume the food frequently, it would still be safe." (Mrs. Y, 40 years, a local cadre).

Conclusion: Preferences, practicality, taste, and nutrient content were factors that triggered UPF consumption. Instead of avoiding the bad effects of UPF on health, some adults still attach importance to preferences and sensory appeal. Beyond nutrition education and campaign, creating a healthier food environment is also important to support habitual changes for better diet quality.

PE046 Basic & translational diabetes research

Cyr61 is involved in palmitate-induced insulin resistance and inflammation in HepG2 cells

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Objective: Cysteine-rich protein 61 (Cyr61, also known as Cellular Communication Network Factor 1, CCN1) is involved in a variety of diseases, such as carcinoma, inflammation, and fibrosis. It was recently reported that Cyr61 was associated with nonalcoholic fatty liver disease. Here, we evaluated the effects of Cyr61 on hepatic inflammation and insulin resistance in HepG2 cells and examined the molecular mechanisms involved.

Methods: We treated HepG2 cells with palmitic acid (PA) and then evaluated insulin signaling pathway and inflammatory markers using immunoblotting. After treatment with PA, the pro-inflammatory cytokines, including IL-6, TNF-α, and IL-1β, and Cyr61 were assessed by real-time polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA) in HepG2 cells. To investigate the effects of Cyr61 on insulin resistance and inflammation, we used Cyr61 small interfering (si) RNA and anti-Cyr61 neutralizing antibodies. The Cyr61 siRNA were transiently transfected into HepG2 cells using Lipofectamine 2000.

Results: Compared to the control, PA reduced IR phosphorylation, IRS-1 (Tyr612) phosphorylation, AKT phosphorylation, and GSK-3α/β phosphorylation after insulin stimulation. PA stimulated NF-κB and JNK activation in a dose-dependent manner. PA significantly increased the expression and secretion of Cyr61 and pro-inflammatory cytokines. Interestingly, neutralization of Cyr61 reduced NF-κB and JNK signaling, which was increased by PA, and recovered insulin signaling. In addition, Cyr61-si RNA treatment reduced the mRNA expression of PA-induced IL-6, TNF-α and IL-1β, and decreased NF-κB and JNK signaling.

Conclusion: Inhibition of Cyr61 recovered insulin signaling and reduced inflammation in HepG2 cells. Cyr61 may play a role in PA-induced insulin resistance and inflammation in HepG2 cells.

PE047 Basic & translational diabetes research

Oxidative stress, lipid profile, glycemic status and hepatic enzymes among Nepalese obese & non-obese adults

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Objective: Obesity is a condition of excessive body fat accumulation concomitant with oxidative stress directed to morbidity such as hyperglycemia, dyslipidemia and liver disease. We investigated the relationship between total peroxide (measure of oxidative stress), lipid profile, glycemic state & hepatic enzymes in obese and non-obese Nepalese adults.

Methods: Total peroxide by spectrophotometer technique, total cholesterol (TC) and triglyceride (TG) by enzymatic colorimetric, lipoprotein density-cholesterol (LDL & HDL) by direct homogeneous enzymatic colorimetric, hepatic enzyme aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) by IFCC method and γ-glutamyl-transferase (GGT) by enzymatic rate method using fully automated "Snibe Bioassay 240 plus- China" clinical chemistry analyzer. Glycated hemoglobin by nephelometry with "MISPA-i3". Each of the measurements was compared between, consenting age-matched (40.75±0.82 yrs.) non-obese, (n=105) and obese, (n=105) subjects without diabetes, hepatitis and not under pain killer & ani-epileptic medication. The data are expressed as mean±SE.

Results: Obese Vs. non-obese: Total peroxide (18.33±0.74 vs. 13.65±0.28, µmol H2-O2/liter, p<0.001), TC (185.70±5.81 vs. 143.58±2.54, mg/dl, p<0.001), TG (196.12±8.96 vs. 139.43±5.89, mg/dl, p<0.001), LDL-C (114.67±6.76 vs. 79.85±2.80, mg/dl, p<0.001), HDL-C (40.72±0.66 vs. 45.68±1.29, mg/dl, p<0.01), FBS (86±2.13 vs. 78.34±0.81, mg/dl, p<0.01), HbA1C (7.04±2.03 vs. 5.8±1.07, p< 0.001), (ALT (62.40±4.63 vs. 40.77±5.20, U/L, p<0.001), γ-GT (52.75±6.36 vs. 38.85±4.32 U/L, p<0.001), ALP (100.30±3.93 vs. 94.47±2.90, U/L, p<0.01) and AST (34.20±1.93 vs. 33.67±1.20, U/L, p=0.07). Positive correlation was found between ALT with total peroxide level (r= 0.740, p<0.01) as well as γ-GT with total peroxide level (r=0.46, p<0.05)

Conclusion: Obesity is associated with high level of oxidative stress directed to hyperglycemia and dyslipidemia leading to fatty liver disease visualized through the significant increase in the level of hepatic enzymes. Hence, obesity associated oxidative stress, hyperglycemia, lipid deviation & hepatic changes should be monitored routinely to prevent worsening of metabolic disorders even in least developed country.

PE048 Basic & translational diabetes research

Profiling of changes in gene expression associated with epigenetic changes in peripheral blood cells under hyperinsulinemic euglycemic clamp condition

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Objective: Effects of supraphysiologic insulin action are very diverse, and further studies are required. And, epigenetic regulation of acute hyperinsulinemia on gene expression has not been studied a lot. In the present study, we evaluated DNA methylation and related changes of mRNA expression level in peripheral blood cells before and after hyperinsulinemic euglycemic clamp (HEC) condition in healthy adults. Through this, we investigated whether specific gene methylation induced by acute hyperinsulinemia cause a change in gene expression.

Methods: Two stage HEC (insulin infusion rate: 10 and 80 mU/m^2/min) studies were performed in 5 non-diabetic subjects. Buffy coat sample was taken in each subject before and after the clamp study and RNA-seq and Methyl-seq were performed using blood cells before (0 min) and after hyperinsulinemia (200 mins). Differentially expressed genes (DEGs) were identified in RNA-seq data. Among DEGs that were identified, genes with a significant change in methylation of specific regions such as, promoter and gene body were selected based on Methyl-seq data.

Results: Among 697 DEGs, 112 genes with a methylation change after HEC were identified and classified as "methyl-DEGs". And, in an analysis using MSigDB, among the 697 DEGs, 43 genes were involved in four major pathways (i.e., inflammation, insulin signaling, oxidative stress, and carbohydrate metabolism): we classified these genes as "phenotypic-DEGs". A network was constructed between the methyl-DEGs and phenotypic-DEGs. As a result, we found a subnetwork formed by many genes including seven common DEGs (ESR1, PRKAR1B, PER1, B3GALNT1, GAST, CEL, FGF4). Both DNA methylation and gene expression levels of the seven genes were altered by the insulin clamp.

Conclusion: Via combined analyses of RNA-seq and Methyl-seq data of human peripheral blood cells, we showed that a significant epigenetic regulation of seven genes could occur in these cells after HEC, which may be important in the pathophysiology of hyperinsulinemia.

PE049 Basic & translational diabetes research

The change of HGF/c-Met signaling pathway in gestational diabetes (GDM)

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Objective: The purpose of our study was to explore changes in serum levels and placenta expression of HGF and c-Met, and to determine how HGF/c-Met signaling contributes to the pathophysiology of GDM.

Methods: A total of 37 pregnant women with normal glucose tolerance (NGT) and 30 pregnant women with GDM were studied. Plasma samples were taken just before delivery, and placenta tissue was taken immediately after cesarean delivery. Serum levels of HGF, c-Met, insulin, and glucose were measured by enzyme-linked immunosorbent assay (ELISA). The mRNA expression of HGF and c-MET was measured in the placenta. In addition, we explored the relationship and GDM using a high fat diet (HFD) mouse model. Mating was done at the 6th week of HFD, and at which point the gestational day (GD) is set to 0 day. The glucose tolerance test (GTT) was performed at GD 10, and measured the levels of HGF and c-MET at GD 16.

Results: Serum c-Met levels were significantly higher in the GDM group (1248.36±36 vs. 1631.94±43 ng/mL, p <0.01). There was no difference in serum HGF levels between the GDM group and the control group (613.48±36 vs. 527.14±25 pg/mL, p=0.166). There were more patients with increased expression of HGF and c-MET mRNA in the placenta. Maternal serum levels of c-MET in HFD mice were higher than in non-pregnant HFD mice and pregnant chow diet mice. Expression of c-MET in islets was increased in pregnant HFD mice.

Conclusion: We observed the differences in serum levels and expression of HGF and c-Met between GDM and control pregnant women in human and mice model. Our results suggest that HGF/c-MET signaling may be altered in GDM pregnancy, which have a role in β-cell function and insulin resistance in GDM.

PE050 Basic & translational diabetes research

Mig-6 modulates adipogenesis and thermogenesis in brown adipose tissue

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Objective: Stimulating the metabolic function of BAT, due to special ability to dissipate energy as heat, represent potential therapeutic strategies for increasing energy expenditure and reducing obesity. Mitogen-inducible gene 6 (Mig-6), a tumor suppressor gene, is a negative regulator of the EGFR signal. Recently, Mig-6 has an important role in the regulation of cholesterol homeostasis and lipid metabolism in the liver. In previous study, we demonstrated the association between EGFR signaling and NAFLD. However, the roles of Mig-6 in BAT remain poorly understood.

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 (UCP1Cre;ROSA LSL) and knock-out (UCP1Cre;loxP/loxP) models using a genetic strategy. BKI and BKO mice were measure GTT, ITT, biochemical parameters and energy expenditure. Western blot and Q-PCR were performed to analyze related genes.

Results: Here, we showed that 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 by anti-UCP1 IHC in Mig-6 KI BAT. Of note, Mig-6 augmented the expression of thermogenesis relative genes (UCP1, Pgclα, Cieda, PPARα, Elovl3), consistent with the increased UCP1 in the BAT of mice. In addition, the absence of Mig-6 reduced the thermogenesis relative genes.

Conclusion: In conclusion, our findings demonstrate that Mig-6 is as potential factor improving obesity by regulating adipogenesis and thermogenesis in the BAT.

PE051 Basic & translational diabetes research

The ameliorative effects of exogenous L-glutathione on testicular cell apoptosis in STZ-induced diabetic C57BL/6 mice

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Objective: This study assesses the ameliorative effect of L-glutathione (GSH) towards apoptosis in testis of STZ-induced C57BL/6 diabetes mice.

Methods: Adult male C57BL/6NTac mice were divided into four groups; NC, NG, DC, and DG (n=6). The diabetic mice (DC and DG) were injected with streptozotocin (STZ) at 50 mg/kg/bw in 0.1 ml of Na-Citrate buffer whilst control mice were injected with equivalent doses of Na-Citrate buffer. Testes were collected for evaluation after 42 days of treatment. The testicular morphology and apoptotic activity using Johnsen score analysis and TUNEL fluorescence assay were studied. The antioxidant activity such as TAOC, SOD, CAT, and reduced GSH were identified. In addition, transcriptional changes of apoptosis related gene (Bax and Bcl-2) and its related protein expression were also examined. Data were analysed using one-way ANOVA.

Results: The apoptotic index using TUNEL assay was seen to reduce in the diabetic mice as seen in DG group compared to DC group, though the Johnsen score between all groups is not significantly altered. The TAOC and reduced GSH concentration were found higher in DG group compared to DC group while CAT decreased, and SOD unchanged. In addition, Bax was down regulated while Bcl-2 was upregulated in DG compared to DC. While for protein, BAX was down regulated, and BCL-2 was unchanged in DG compared to DC.

Conclusion: The testicular tissue of STZ-induced diabetic C57BL/6 mice experiences apoptosis due to endogenous GSH shortage, which is thought to generate excessive OS. The results of this study supported the hypothesis that diabetes induces apoptosis in the seminiferous tubule by likely activating the caspase-apoptosis related pathway. On the other hand, it is diminished by the activity of exogenous GSH.

PE052 Basic & translational diabetes research

Association of T cell senescence with liver diseases ranging from steatosis to liver cirrhosis in humans

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Objective: Perturbation of immune homeostasis initiates and promotes persistent liver injury and inflammation, resulting in liver pathology. However, comprehensive observation of relationship between the senescence and exhaustion of T cells and spectrum of liver diseases ranging from simple steatosis to liver cirrhosis remains to be elucidated.

Methods: We investigated the immunophenotype of T cells in peripheral blood mononuclear cells from 59 patients with type 2 diabetes (T2D) who were also evaluated for nonalcoholic fatty liver diseases using MRI-PDFF and MR elastography. To further study liver T cell exhaustion and senescence in patients with nonalcoholic steatohepatitis or cirrhosis patients, single-cell RNA sequencing data, which were deposited in Pubmed, were also analyzed with R software v4.0.2.

Results: Patients with higher level of HOMA-IR showed significantly higher population of the CD28−CD57+ senescent T cells among CD4+ and CD8+ T cells compared to the patients with lower level of HOMA-IR. TNF-α production in memory CD8+ T cells were also significantly increased in the patients with lower level of HOMA-IR. Moreover, there was a significant relationship between liver fat deposition measured by MRI-PDFF and senescent CD8+ T cells in patients with T2D. Liver fibrosis status assessed by MR elastography was also associated with the frequencies of senescent CD4+ T cells and HOMA-IR in patients with T2D. In the single cell transcriptome data analysis, we found significantly higher expressions of genes-related to T cell senescence and exhaustion were observed in CD4+ and CD8+ T cells of the nonalcoholic steatohepatitis or cirrhosis patients, implying association of T cell dysfunction with liver disease progression in humans.

Conclusion: T cell senescence is associated with insulin resistance, which involves in the hepatic steatosis and fibrosis in patients with T2D. Single cell transcriptome data also demonstrate that T cell senescence and exhaustion may contribute to the progression of fatty liver disease in humans.

PE053 Basic & translational diabetes research

Predominantly sociodemographic risk factors that attributed to the overnutrition among healthy adults population in urban, suburban, and rural areas

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Objective: As overweight and obesity (overnutrition) surged in Indonesia over the last decade, many studies have identified determinants and risk factors of the problems. Various sociodemographic profiles could be the underlying cause of overnutrition. We aim to examine the predominantly sociodemographic factors that contributed to overnutrition

Methods: Cross-sectional study was conducted from 2016 to 2018 and involved 415 healthy adults 19 to 64 years of age in urban, suburban, and rural Yogyakarta Province, Indonesia. The urban represented the most populated urban area and the rural represented lowland, mountainous, and coastal areas. The pregnant or breastfed woman was excluded. Data collection included sociodemographic and body mass index (BMI, kg/m^2). The BMI was determined as underweight if <18.5 kg/m^2, normal BMI 18.5-24.9 kg/m^2, and overweight or obesity ≥25.0 kg/m^2.

Results: The prevalence of overnutrition was 40.8%. Compared to normal BMI, gender, occupation, smoking history, and dwelling area increased the risk of overnutrition, in which female was more likely 2.7 times higher risk of being overnutrition (p<0.001, PR 95%IC 1.8-4.2) than male, unemployed/housewife/student was 2.4 times higher risk of overnutrition than their counterparts (p<0.001, 95%IC 1.5-4.1), smokers were 2.8 times higher risk of overnutrition than non-smokers (p<0.001, PR 95%IC 1.7-4.5), and urban adults were 2.2 times higher risk of overnutrition than non-urban (p<0.001, PR 95%IC 1.4-3.3). Compared to normal BMI, older adults increased 4 times higher risk of being underweight than their other counterparts (p=0.021, PR 95%IC 1.2-6.4)

Conclusion: Being female, unemployed/housewife/student, smokers, and living in urban were increased the risk of overnutrition, while older adults increased the risk of being underweight than their other counterparts. The importance of designing different interventions which were suitable for the different sociodemographic backgrounds is important to tackle overnutrition.

PE055 Basic & translational diabetes research

Biological effect of engeletin on osteoarthritis: medicinal importance and therapeutic benefit through scientific data analysis

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Objective: Engeletin is a naturally occurring flavonoidal class phytochemical that is widely distributed in vegetables and fruits in the nature. Engeletin has been proven for their health beneficial properties in the medicine. Osteoarthritis is a progressive disease characterized by pain and impaired joint functions in the human being.

Methods: In order to know the biological potential of engeletin on osteoarthritis, here in the present work numerous scientific data has been searched and analyzed. Biological effect of engeletin on osteoarthritis has been investigated through scientific data analysis of various research works. Other pharmacological activities of engeletin has been also correlated with the present work through Scientific data analysis.

Results: Scientific data analysis of different scientific research work revealed the medicinal properties of engeletin. Biological effect of engeletin on osteoarthritis has been investigated through scientific data analysis of various scientific research works and revealed that engeletin alleviated TNF-α-induced inhibition of extracellular matrix components in the scientific research work. Further, engeletin also scavenged intracellular ROS signified their biological application on osteoarthritis.

Conclusion: Scientific data analysis revealed the biological effect of engeletin on osteoarthritis.

PE056 Basic & translational diabetes research

N-Methyl-D-aspartate receptors induce M1 polarization of macrophages: feasibility of targeted imaging in macrophage-mediated inflammation

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Objective: N-methyl-d-aspartate receptors (NMDARs) are considered to be involved in several physiological and pathophysiological processes in addition to the progression of neurological disorders. However, how NMDARs are involved in the glycolytic phenotype of M1 macrophage polarization and the possibility of using them as a bio-imaging probe for macrophage-mediated inflammation remain unclear.

Methods: We analyzed cellular responses to NMDAR antagonism and small interfering RNAs using mouse bone marrow-derived macrophages (BMDMs) treated with lipopolysaccharide (LPS). An NMDAR targeting imaging probe, N-TIP, was produced via introduction of NMDAR antibody and the near-infrared (NIR) fluorescent dye FSD FluorTM 647. N-TIP binding efficiency was tested in intact and LPS-stimulated BMDMs. N-TIP was intravenously administered to mice with carrageenan (CG)- and LPS-induced paw edema, and in vivo NIR fluorescence imaging was conducted. The anti-inflammatory effects of dexamethasone were evaluated using the N-TIP-mediated macrophage imaging technique.

Results: NMDARs were overexpressed in LPS-treated macrophages, subsequently inducing M1 macrophage polarization. Mechanistically, NMDAR-mediated Ca2+ accumulation resulted in LPS-stimulated glycolysis via upregulation of PI3K/AKT/mTORC1 signaling. In vivo NIR fluorescence imaging with N-TIP showed LPS- and CG-induced inflamed lesions at 5 h post-inflammation, and the inflamed lesions could be detected until 24 h. Further, our N-TIP-mediated macrophage imaging technique helped successfully visualize the anti-inflammatory effects of dexamethasone in mice with inflammation.

Conclusion: This study demonstrates that NMDAR-mediated glycolysis plays a critical role in M1 macrophage-related inflammation. Moreover, our results suggest that NMDARs are a feasible bio-imaging marker for M1 macrophages and that our NMDAR-mediated imaging technique may be useful in research on macrophage-related inflammation.

PE058 Basic & translational diabetes research

Biological potential of artemetin in the medicine for their hypotensive effect against cardiac complication

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Objective: Artemetin is an important phytochemical of C. verbenacea which is having significant anti-inflammatory activity in the different experimental models in rats. Further in order to explore the structure-activity relationships, synthesis of C- and O-prenylated derivatives of artemetin have been also prepared in the scientific research work using artemetin as a starting material.

Methods: Biological importance of artemetin in the medicine for their hypotensive effect has been investigated through scientific data analysis of numerous scientific research works. Pharmacological activity data were investigated through scientific data analysis of research work.

Results: Scientific data analysis revealed the biological importance of artemetin in the medicine for their hypotensive effect against cardiac complications. In the scientific research work, artemetin from Achillea millefolium reduced the mean arterial pressure and reduced the hypertensive response to angiotensin I. It also reduced plasma and vascular angiotensin converting enzyme activity in the scientific research work data collected from various databases.

Conclusion: Scientific data analysis revealed the biological potential of artemetin in the medicine for their hypotensive effect.

PE059 Basic & translational diabetes research

The effects of Tocotrienol Rich Fraction (TRF) and vitamin c supplementation on antioxidant enzymes activities and body mass index in down syndrome individuals

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Objective: The Cu-Zn superoxide dismutase (SOD) gene is present on chromosome 21, thus, individuals with Down syndrome (DS) may be under oxidative stress. Our previous study found that DS is associated with higher BMI and elevated antioxidant enzyme activities. A link between oxidative stress and obesity has been described frequently in the literature. Antioxidant supplementations are thought to decrease oxidative stress levels. The objective of this study was to determine the effects of TRF and vitamin C supplementation on antioxidant enzymes and body mass index (BMI) in DS individuals.

Methods: Sixty individuals (aged 2 to 29 years old) with DS were recruited and randomly assigned to receive either supplementation (n=30) with TRF (150 mg) and vitamin C (250 mg) or placebo (n=30). Measurement of height and weight was conducted and BMI was calculated. Blood samples were obtained from each subject at 0, 3rd and 6th months for the measurement of the antioxidant enzyme [superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx)].

Results: Changes in the activities of antioxidant enzymes with TRF and vitamin C were not observed when comparing the baseline to 3 and 6 months for SOD, CAT and GPx activities ($p>0.005$). There were also no significant changes in BMI after the intervention ($p>0.005$). The height of subjects ranged from 0.83 m to 1.59 m and the weight ranged from 9.97 kg to 82.9 kg. The mean BMI of DS subjects ranged from 12.8 kg/m^2 to 42.45 kg/m^2. Eighteen DS subjects (30%) were overweight or obese with BMI values above the recommended level (more than 25 kg/m^2).

Conclusion: In summary, there was no significant difference in the levels of antioxidant enzymes after the intervention. With respect to the higher BMI level in 30% of the subjects, further study should be conducted in order to understand the mechanism/s that contributed to this condition.

PE060 Basic & translational diabetes research

PDK4 mediates energy stress-induced imbalance in mitochondrial dynamics and bioenergetics

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Objective: We investigated the role of pyruvate dehydrogenase kinase 4 (PDK4), a critical regulator of mitochondrial metabolic flexibility in the structural remodeling of mitochondria and cellular bioenergetics

Methods: SILAC analysis is performed to identify potential PDK4 phosphorylated substrates, followed by immunofluorescence and western blot techniques. Genetic ablation models of PDK4 and fission/fusion mediators are used to validate the effects on cellular bioenergetics and mitochondrial dynamics.

Results: We found that PDK4 is genetically required for cells to undergo rapid mitochondrial fragmentation when challenged with ETC toxins. Phosphoproteomic screen for PDK4 substrates revealed cytoplasmic GTPase, Septin 2 (SEPT2), as the key effector molecule that acts as a receptor for DRP1 in the outer mitochondrial membrane to promote mitochondrial fission.

Conclusion: The PDK4-SEPT2-DRP1 axis as a regulator of mitochondrial function at the interface between cellular bioenergetics and mitochondrial dynamics.

PE061 Basic & translational diabetes research

Lobeglitazone stimulates production of specific resolvins and regulates hepatic fat accumulation and NLRP3 inflammasome activation via FFAR4/GPR120 signaling pathway

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Objective: Thiazolidinediones, acting as peroxisome proliferator-activated receptor gamma (PPARγ) ligands, has been reported to reduce hepatic steatosis in human and animals. However, the underlying mechanism remains largely unknown. The purpose of this study was to investigate changes in oxylipins (oxygenated fatty acid derivatives) and underlying mechanism by treatment with lobeglitazone (LOBE), a PPARγ ligand in an animal model of obesity and type 2 diabetes.

Methods: Male obese and diabetic OLETF rats were orally administered either vehicle (CONTROL) or LOBE (1 mg/kg) fed on high fat/ high carbohydrate diet for 15 weeks. Blood and liver tissue were harvested after overnight fasting at the end of study. Biochemical and histological assessment were performed in plasma and liver. Oxylipins in plasma and liver were analyzed via metabolomic analyses. For in vitro study, oxylipins were treated on HepG2 human hepatoma cell line and THP-1 human monocyte cell line were treated with oxylipins and siRNA targeting the FFAR4/GPR120.

Results: OLETF rats that received LOBE showed decreased in hepatic fat accumulation in liver and improvement of lipid profiles in liver and plasma including total cholesterol, triglyceride and free fatty acid compared to CONTROL rats. LOBE treatment significantly altered levels of oxylipins including resolvins, specialized pro-resolving mediators derived from essential fatty acids, in the plasma and liver. Among the oxylipins we identified, resolvins showed improvement in hepatic fat accumulation and inflammation mediated by FFAR4/GPR120 signaling in HepG2 and THP-1 cells.

Conclusion: Our results demonstrate that LOBE can regulate oxylipin metabolism including resolvins in a rat model of obesity and type 2 diabetes, which could contribute to the improvement of hepatic steatosis and inflammation.

PE064 Basic & translational diabetes research

The effectiveness of a digital story intervention on healthy eating and physical activity of young people in Sri Lanka

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Objective: Unhealthy eating and physical inactivity are two major risk factors for obesity and chronic diseases including diabetes. Effective interventions to improve health-related practices are required to target young people for long-lasting impact. This study evaluated the effectiveness of a digital story to improve the healthy eating and physical activity of young people in Sri Lanka.

Methods: A Digital Story consisting of four episodes (4-5 minutes each) was developed and evaluated for the intervention. The intervention targeted knowledge, intention, attitudes, subjective norms (SN), perceived behavioural control (PBC), and behaviour related to healthy eating and physical activity. A non-randomized control trial was conducted among Grade 9 and 10 students in two schools in Colombo. The Intervention Group (IG) watched the story (one episode a day) within 2 weeks. The Control Group (CG) received no intervention. Baseline and post-intervention data were collected using a pre-validated questionnaire assessing a range of behaviours, beliefs, and attitudes. All baseline data were collected face-to-face. Post-intervention data from the IG were collected face-to-face in week 2. CG was not reachable in parallel due to Covid-19, so data were collected online between weeks 3-5. Linear Mixed Models were used to compare outcomes over time across groups.

Results: The sample (N=267; IG=143, CG=124) consisted of 191 males and 76 females, aged 14-15 yr. A significant Group*Time interaction was observed in all outcomes related to healthy eating [knowledge ($p=0.014$), intention ($p<0.001$), attitudes ($p<0.001$), SN ($p=0.002$), PBC ($p<0.001$), behaviour ($p<0.001$)]; and physical activity [knowledge ($p=0.005$), intention ($p<0.001$), attitudes ($p=0.003$), SN ($p=0.018$), PBC ($p<0.001$), behaviour ($p<0.001$)].

Conclusion: The intervention improved outcomes related to healthy eating and physical activity. A limitation of this study was the use of a different mode and duration in collecting post-intervention data from CG. Further studies are recommended to confirm the results and to evaluate the long-term effect of the intervention.

PE065 Basic & translational diabetes research

Ectopic olfactory receptor reduces fat preference by secreting cholecystokinin

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Objective: Previous studies demonstrated that activation of ectopic olfactory receptor X (OlfrX) by odorant A reduces fat accumulation and shifts fuel preference to fats. We further investigated whether administration of odorant A and activation of OlfrX alter fat preference.

Methods: Two-food choice studies: Wild-type or OlfrX knockout (KO) mice were divided into three groups: control, odorant A (a ligand of OlfrX), and odorant A+proglumide (cholecystokinin (CCK) antagonist) groups. High fat diet (HFD) or normal diet (ND) were provided in a separate container in a mouse cage. Food intake of HFD and ND in each mouse cage was measured daily. ELISA: Plasma (in vivo) and duodenal (ex vivo) CCK levels were measured by ELISA assay.

Results: Odorant A reduced HFD intake in wildtype mice but not in OlfrX KO mice. Reduced fat preference is CCK dependent. Control mice consumed 88.5% of daily calories from HFD intake, but oral administration of odorant A significantly reduced HFD consumption thus 44.9% of daily calories were consumed from HFD. Injection of proglumide abrogated odorant A effect thus mice consumed 90.01% of daily calories from HFD in odorant A+proglumide group. The effect of odorant A on HFD intake disappeared in OlfrX KO mice. Odorant A increased plasma and duodenal CCK concentrations but not in OlfrX KO mouse. In wildtype mice, the levels of CCK was increased by odorant A administration (1.5 to 2.9 pM for in vivo; 95.0 to 332.4 pg/mg protein for ex vivo). Odorant A had no effect on CCK levels of OlfrX KO mice.

Conclusion: OlfrX, sensing odorant A, reduces fat preference in wildtype but not in OlfrX KO mice. Odorant A induces CCK secretion in vivo and ex vivo. Results demonstrate that reduced HFD by odorant A is OlfrX dependent and is correlated with CCK levels.

PE066 Basic & translational diabetes research

Endocrine disrupting chemical perfluorooctane sulfonate continual exposure impairs glucose-stimulated insulin secretion by inhibiting cAMP pathway

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Objective: Altered metabolism has been implicated in the pathogenesis of beta-cell failure in type 2 diabetes. Of them, many clinical studies have confirmed a positive correlation between plasma and tissue levels of several Endocrine Disrupting Chemical species (e.g. PFOS) play a major role in inflammatory and stress responses that induce type 2 diabetes. Here we investigated the chronic effect of PFOS and its impact for the beta-cell function (GSIS) and toxicity.

Methods: We subjected pancreatic INS-1 cells and human pancreatic 1.1b4 beta cells to PFOS with different doses for 48 hours. Insulin secretion was measured by non-radioactive Millipore ELISA Kit. Cyclic AMP was measured by Bio Vision's cAMP Assay Kit.

Results: Exposure of INS-1 cells or human pancreatic 1.1b4 beta cells with PFOS-stimulated the expression of active RAC1-GTP compared with control cells. PFOS treatment elevated NADPH oxidase activity in a RAC1-GTP dependent manner which correlated with a loss of mitochondrial membrane potential $\Delta\psi$ followed by mitochondrial release of cytochrome c into the cytosol leads to caspase-3 activation. Further, NADPH oxidase activity mediates the degradation of cAMP levels and potentiated the PFOS-induced INS-1 and human pancreatic 1.1b4 beta cell apoptosis. Pharmacological inhibition of RAC1-GTP using NSC23766 blocked PFOS-induced RAC1-GTP activation with a reduction of NADPH oxidase activity. This effect was associated with inhibition of mitochondrial dysfunction with an accumulation of cAMP and reduction of cell apoptosis. Moreover, accumulation of cAMP enhanced glucose stimulated insulin secretion (GSIS).

Conclusion: Perfluorooctane sulfonate triggers the RAC1-GTP mediated upregulation of NADPH oxidase activity. This is associated with downregulation of cAMP pathway and a rise in mitochondrial dysfunction with cell apoptosis. Thus, inhibition of RAC1-GTP signaling may promote beta cell survival under PFOS-induced beta cell toxicity. Collectively, our results unveil a novel role of PFOS leading to the pathogenesis of pancreatic beta-cell dysfunction and failure.

PE067 Basic & translational diabetes research

Lack of protective benefit with a necrosis inhibitor against the development of type 1 diabetes

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Objective: During the process of autoimmune destruction of beta-cells in type 1 diabetes, HMGB1 and other danger signal molecules are passively released from necrotic beta cells. We investigated if a clinical grade necrosis inhibitor (NI) can be a novel strategy to delay the development of type 1 diabetes.

Methods: Each 10 units/mL of IL-1β, IFN-γ were treated to islets isolated from male C57BL/6 mice with or without the presence of NI (5 μM). Islet viability was confirmed by AO/PI staining. The amount of IL-1β, IFN-γ, and IL-6 was analyzed using ELISA. Diabetes was induced by multiple low-dose streptozotocin (MLD-STZ; 30, 40, 50 mg/kg) for 5 days. Glucose levels at the time of termination in NI group (Day 6-8, Day 1-10: oral 30 mg/kg, Day 1-10: i.p. 15 mg/kg, n=7) was compared with control group (STZ alone, n=5).

Results: In both NI co-treatment and pre-treatment conditions, NI did not reduce the decrease in viability caused by cytokines, and inflammatory cytokines increased. In MLD-STZ model, NI did not show any inhibitory effect at the diverse STZ concentration; STZ alone: 30 mg/kg (157.75±15.28 mg/dL), 40 mg/kg (336.5±29.5 mg/dL), 50 mg/kg (409.50±117.95 mg/dL), STZ + NI: 30 mg/kg (205.20±15.31 mg/dL), 40 mg/kg (246.00±61.25 mg/dL), 50 mg/kg (346.00±102.21 mg/dL). When the NI was pretreated before STZ treatment, higher blood glucose levels were also observed in the NI group; STZ 50 mg/kg alone (257.75±52.76 mg/dL), STZ + NI oral (282.42±86.47 mg/dL), STZ + NI i.p. (289.14±102.38 mg/dL).

Conclusion: NI did not have a protective effect against beta-cell destruction induced by proinflammatory cytokines in vitro. In the MLD-STZ-induced diabetes model, there was no effect on the development and progression of diabetes through treatment of NI before and/or after the MLD-STZ treatment.

PE068 Basic & translational diabetes research

Eating and lifestyle habits of healthcare workforces

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Objective: This study aimed to identify the eating and lifestyle habits of healthcare workforces.

Methods: A cross-sectional study was conducted among healthcare workforces in the First Central Hospital of Mongolia. We used self-report questionnaires to study 244 workers. Eating and lifestyle habits were assessed with ten food frequency questionnaires (maximum, 10 points) Dietary Variety Score (DVS), and six lifestyle factors (maximum, 6 points) Cumulative Lifestyle Index (CLI). Workers were grouped into medical staff n=165 (doctors, nurses) and non-medical staff n=79 (management, safety, and others) based on the ISCO-2008 revision. We performed binary logistic regression analysis between DVS, CLI (higher in 3 points: 0, lower in 3 points: 1), and obesity risk.

Results: Mean scores of DVS and CLI were 2.95±1.5 and 3.76±1.3. DVS and CLI were categorized into the highest, middle, lowest (6.6%, 53.7%, 39.8%) and lifestyle are right, needs to be improved, needs to be changed (33.6%, 46.7%, 19.7%). DVS and CLI mean scores were significantly lower ($p<0.05$) in medical staff with obese: medical staff (non- obese 3.20±1.69 and 4.04±1.1, obese 2.95±1.65 and 3.49±1.4) and non-medical staff (non-obese 2.61±1.3 and 3.70±1.5, obese 2.77±1.4 and 3.89±1.1) groups respectively. In this study, 36.1% and 13.9% of all participants had overweight and obese. 17.6% of participants who work for medical staff and 6.3% of non-medical staff were obese ($p<0.041$). After adjusting for potential confounders (age, gender, education), regression analysis shows that lower dietary scores and lifestyle index were associated with a higher risk of medical staff with obese: the OR (95% CI) was 3.03 (1.14; 8.07) and 0.40 (0.17; 0.95) for medical staff with obese when comparing with non-medical staff.

Conclusion: These results suggest improving eating and lifestyle habits among healthcare workforces. A lower DVS and CLI were associated with a higher risk of obesity in medical staff workers in healthcare workforces.

PE069 Basic & translational diabetes research

Hypolipidemic impacts of phytosterols on gut microbiota alteration in sugar rich diet induced diabetic female rats

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Objective: Hypolipidemic foods have attracted attention for its considerable health benefits, in particular, for the prevention of obesity and type 2 diabetes. Phytosterols (called plant sterol and stanol esters) are found in plant cell membranes. Phytosterols are similar in structure to cholesterol in the human body and block cholesterol from being absorbed. Sugar rich diet induces inflammation and insulin resistance mainly through gut microbiota alteration. This study was aimed to investigate the beneficial effects of phytosterols administration on gut microflora mediated signaling pathways. inflammation indexes to prevent the diet induced diabetic rats.

Methods: Sixty-four female wistar rats were divided into non-diabetic group with a normal diet (CD), diabetic group with high sucrose diet (HSD) and treatment group with HSD and phytosterols (25,50 and 100 mg/kg). During 4 weeks of experimental study, we assessed nutrient intake, food-related behavior, fecal microbiota composition, microbial fermentation, and gastrointestinal symptoms.

Results: After 4 weeks of the study, significant alterations in two major gut dominant microbial phyla i.e firmicutes and bacteroides and four dominant microbial species i.e. Lactobacilli, Bifidobacteria, Escherichia and Clostridia were observed in HSD group compared to CD. This microbial dysbiosis in dominant phyla was significantly prevented in phytosterols administrated HSD group. Phytosterols (100 mg/kg) administration had also reduced the HSD induced activation of Toll like receptors and Nod like receptors signaling pathways compared to HSD control group to reduce the inflammation.

Conclusion: These suggest that phytosterols can prevent the progression of type 2 diabetes through gut microbiota alteration, reducing endotoxin and microbes mediated inflammation.

PE070 Basic & translational diabetes research

Biological potential and therapeutic effectiveness of berbamine in the medicine for their anti-hypercholesterolemic effect

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Objective: Phytochemicals are pure, active plant chemicals found to be present in the flower, leaf, seed, stem, root, vegetables, herbs, and fruits. Phytochemicals have been utilized as a source of Nutraceuticals by human beings for a long time to treat disease in medicine. A large number of useful drugs for the treatment of diabetes and related disorders were mainly derived from plants and their byproducts. Diabetes is the disorders of carbohydrate and protein metabolism. Berbamine is an active phytochemical of Berberis amurensis.

Methods: Biological importance of berbamine in the medicine for their effectiveness against diabetes and its related secondary complications has been investigated in the present work through scientific data analysis. Numerous scientific research works have been analyzed in the present work through scientific data analysis of different research works. Scientific data were collected and analyzed in the present work to know the anti-hypercholesterolemic effect of berbamine in the medicine in high fat diet and streptozotocin induced diabetic rats.

Results: Scientific data analysis of different research work revealed the biological importance and therapeutic potential of berbamine in the medicine. Scientific data analysis revealed that berbamine improved insulin secretion and showed significant effects on different enzymes of carbohydrate and lipid metabolism in the scientific work. However, other scientific research work also supported the anti-hypercholesterolemic effect of berbamine as its have significant effect on carbohydrate metabolic enzymes.

Conclusion: Scientific data analysis revealed the anti-hypercholesterolemic effect of berbamine in the medicine.

PE071 Basic & translational diabetes research

Microbiota composition in people with diabetes

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Objective: Studies continue to suggest that it is important to maintain gut microbiota as a treatment in order to improve diabetes control and prevention. The composition of normal gut microbiota depends on lifestyle, diet and obesity. Aim of study was to evaluate gut microbiota in people with diabetes.

Methods: This case-control study was conducted as part of the Asian Microbiome Project IV. The ratio was 1:1 in case (n=76, people with diabetes) and control (n=76, people without diabetes). Gut microbiota was determined in the feces. Food consumption of 6 food groups was studied using a 24-hour diet diary.

Results: A total of 152 people were surveyed, with an average age of 50.7±7.7 and 54.6% (n=89) were men. Rural participants accounted for 55.2% (n=90). Total diversity of gut microbiota was 128.5±1.5 and 125.9±1.8 in people with and without diabetes respectively. However, the difference was not significant ($p>0.05$). Although it was not significant but the diversity number of gut microbiota in obese people was decreased. Furthermore, people with diabetes had a lower level of Firmicutiswhile the level of Bacteroidetes was higher when compared to people without diabetes ($p<0.05$). In addition, the amount of Firmicutes tends to decrease and the amount of Bacteroidetes and Fusobacteria tends to increase when BMI increases ($p<0.05$). However, there was no significant association between ratio of Firmicutes/Bacteroidetes and food groups. Regression analysis showed that the effect of BMI on the increase in the ratio of Firmicutes/Bacteroidetes was independent of age, sex, civil status (urban or rural), and diet characteristcs ($p<0.05$).

Conclusion: In people with diabetes, the gut microbiota is altered as decreases and increases in Firmicutis and Bacteroidetes respectively. The alteration of gut microbiota is associated with obesity showing that the ratio of Firmicutis and Bacteroidetes decreases by 0.270 when increases of 1 kg/m^2 BMI in people with diabetes.

PE073 Basic & translational diabetes research

The comparison of the gut microbiota of mongolian people with that of five asian countries

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Objective: Prevalence of obesity and T2DM is increasing annually due to urbanization, lack of physical activity and increasing use of high carbohydrate diet. Both conditions are serious problems in Mongolia and in the world. Previously it was demonstrated there is association between gut microbiota and conditions including T2DM and obesity. To describe how gut microbiota of Mongolian subjects and its association with obesity and T2DM.

Methods: Subjects aged between 24-90 were involved in this study. Stool samples were collected from healthy (n=114), Obese (n=49), Non-obese/T2DM (47) and Obese/T2DM (n=40) subjects. DNA was extracted from the stool samples and analyzed for 16sRNAV3-V4 regions. Based on sequencing gut microbiota cluster was determined in each group. And food consumption of the study subjects were collected through questionnaire. Subjects were from 6 countries including Mongolia, Japan, China, Thailand, Korea and Indonesia included AMP-4 project.

Results: Different food has its unique microbiota affect to human gut. Whole grains, refined carbohydrate, dairy products and animal fat will cause bacteriode, lactobacillus, Cantenibacterium and Prevotella respectively. Most Mongolian healthy subjects belong to Prevotella cluster and it is likely due to high consumption of whole grains while T2DM group has Prevotella and Bacteroides cluster. There were a number of microbial groups in each group and Lactobacillus and Cantenibacterium were found in obese and obese/T2DM groups.

Conclusion: It can be concluded that a number of different microbiota in each group results from different food consumptions and gut microbiota is affected by westernization of food consumption. And it may lead to metabolic diseases.

PE074 Basic & translational diabetes research

Red blood cell parameters and their correlation with glycated hemoglobin among diabetes mellitus patients: a hospital-based data analysis in Mongolia

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Objective: To study the association between red blood cells (RBCs) parameters and glycated hemoglobin (HbA1c) in patients with type 2 diabetes (T2D).

Methods: This cross-sectional study was conducted including 269 T2D patients who attended an outpatient clinic at Mongolia-Japan Hospital from August 2021 to January 2022. Data were analyzed using SPSS version 27 software based on the results of patients' CBC and HbA1c. A glycated hemoglobin test was used to evaluate the glycemic control among T2D patients into categories of below or above 7% as considered good and poor control respectively. A one-sided statistical significance was set at p-value <0.05.

Results: A total of 269 patients were found eligible for the study, with a mean age of 58±10.8 years, and out of those 119 patients, males were 152 (56.9%) and females were 117 (43.1%). The mean body mass index (BMI) was 30.3±6.9 kg/m2 and the mean duration of diabetes was 8±5.7 years. The average fasting blood glucose was 10.4±4.78 mmol/l, and the average HbA1c was 8.41±2.32%. HbA1c>7% or good glycemic control of type 2 diabetic patients were 31.2% (n=84) and HbA1c<7% or poor glycemic control of type 2 diabetic patients were 67.7% (n=182). The study found that red blood cell distribution width has a significant correlation (RDW, r=0.147 p=0.024) with HbA1c. Furthermore, mean RDW was significantly different in HbA1c below or above 7% groups: mean RDW was 11.8±1.1 in HbA1c<7% group while it was 10.8±1.5 in HbA1c>7 group (p=0.035). In addition, the estimated mean of RDW was 13.8±1.1 and 10.0±0.7 in HbA1c<7 and HbA1c>7 groups separately when adjusted for duration of diabetes and diabetic complications (p=0.041).

Conclusion: Red blood cell parameters need to be further investigated concerning diabetic complications in patients with T2D in Mongolia.

PE075 Basic & translational diabetes research

Lipid profile in patients with type 2 diabetes: a hospital-based data analysis in Mongolia

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Objective: To evaluate the serum lipid profile in patients with type 2 diabetes mellitus (T2DM), compared with reference values.

Methods: In this cross-sectional study, we used the data of 158 T2DM patients who attended an outpatient clinic at Mongolia-Japan Hospital from August 2021 to January 2022. Data of lipid profiles included LDL, HDL, TG, and total cholesterol. According to the clinical guidelines on type 2 Diabetes mellitus in Mongolia 2021, recommended values for lipid profiles are as follow: LDL<2.5 mmol/l, HDL>1.0 mmol/l, TG<1.5 mmol/l, and total cholesterol<4.5 mmol/l.

Results: One hundred fifty-eight T2DM patients (49.4% of males with a mean age of 57.1±9.4 years) were included in the study. The mean BMI was 30.4±5.7кг/м2 and the mean of HbA1c was 8.9±2.5%. The duration of diabetes was 8.2±3.2%. The means of lipid profiles were 3.21±0.91 mmol/l, 3.5±10.04 mmol/l, 1.39±0.97 mmol/l, and 3.21±0.91 mmol/l for total cholesterol, triglyceride, HDL, and LDL respectively. The prevalence of patients who did not meet the recommendation was 72.3%, 62%, 79.5%, and 20.2% for total cholesterol, triglyceride, HDL, and LDL respectively. There was no statistically significant difference in mean HbA1C between patients with and without dyslipidemia but a high statistically significant difference in BMI was observed. Mean BMI was 31.7±6.2 kg/m2 with dyslipidemia patients and 28.3±4.3 kg/m2 without dyslipidemia patients (p=0.021).

Conclusion: Dyslipidemia was common in patients with T2DM and the majority of those people were obese. This suggests improving the prevention of cardiovascular complications in patients with T2DM in Mongolia.

PE076 Basic & translational diabetes research

Correlation plasma resistin level with body mass index in yogyakarta Indonesia

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Objective: Resistin is adipokine secreted by white adipocytes tissue and has been proposed as a link between obesity, diabetes mellitus and cardiovascular diseases. Resistin level has been associated with obesity in some report. We aimed to investigate the possible association of plasma resistin level with body mass index.

Methods: The design of this research was a cross-sectional study with 122 total subjects in Yogyakarta, Indonesia. Plasma was used to measure the resistin level. Resistin level was measured using ELISA (RayBiotech).

Results: Mean plasma resistin level in obese subjects was 374 pg/mL and in the non-obese subjects was 363 pg/mL. Plasma resistin levels in the obese subject were associated with body mass index but not correlated in non-obese subjects. Correlation resistin level with body mass index in this study showed resistin levels inversely related to BMI.

Conclusion: Resistin level has a negative correlation with BMI in Yogyakarta Indonesia.

PE077 Basic & translational diabetes research

Identifying the role of Zinc to protect functional β cell

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Objective: Type 2 diabetes is characterized by the loss of functional beta cell mass and mature beta cell identity. However, the mechanism by which beta cells keep their functional mass and identity is not well understood.

Methods: Here, we used an inducible knockout of the PRMT1 gene specifically in beta cells to create a novel mouse model of beta cell dematuration and dedifferentiation (PRMT1 BiKO). We treated the zinc-based drug (Cycloz) and induced metabolic stress with HFD.

Results: HFD-fed PRMT1 BiKO control groups developed diabetic phenotypes and lost the mature beta cell marker. However, treatment groups had relatively healthy metabolic phenotypes and high levels of expression of mature beta cell identity related transcriptional factors including MAFA, UCN3, SLC2A2. Treatment groups had higher levels of insulin, insulin biosynthesis related genes, and zinc homeostasis related genes, according to single cell transcriptomic analysis. Treatment groups also had lower levels of beta cell mass, plasma pro-insulin, and ROS.

Conclusion: This result demonstrated that Cycloz treatment aids PRMT1 BiKO mice in maintaining glucose homeostasis by protecting mature beta cell identity during HFD. And decreasing levels of proinsulin and beta cell mass of treatment group indicate that their beta cell functionally improved than control group. The mechanisms of Cycloz is linked to a decrease insulin demand, ROS level, and regulate zinc homeostasis in beta cells. These findings reveal a direct relationship between zinc and beta cell function. And it can provide a new insight into the how beta cell keeps their functional mass and identity.

PE078 Basic & translational diabetes research

Deletion of G protein-coupled estrogen receptor in POMC or AgRP neurons alters energy metabolism

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Objective: Estrogen plays pivotal role in regulating energy metabolism. Recent rodent studies showed that G protein-coupled estrogen receptor (GPER) can modulate energy homeostasis, but how GPER in brain can regulate peripheral metabolism is not clear. As arcuate nucleus (ARC) is the main control center of energy balance, we aimed to determine role of GPER in POMC and AgRP neurons in ARC on energy homeostasis.

Methods: AgRP-GPERKO or POMC-GPERKO mice were generated by intercrossing AgRP-Cre or POMC-Cre mice with GPER-floxed mice, respectively. High-fat diet (HFD) was provided from 8 weeks of age. Body weight was measured weekly. Glucose homeostasis was evaluated by glucose tolerance test and insulin tolerance test, and energy expenditure by indirect calorimetry. Body composition was measured by micro-CT, and 2 weeks later, tissue samples were collected.

Results: Female AgRP-GPERKO mice showed higher body weight than control mice after HFD challenge with increased gonadal white adipose tissue, while male AgRP-GPERKO mice had more lean mass. Glucose clearance and insulin sensitivity of AgRP-GPERKO mice is comparable to control. However, female AgRP-GPERKO mice showed less energy expenditure, VO2 and VCO2 without alteration in locomotor activity. Similarly, female POMC-GPERKO mice showed higher body weight after HFD challenge with a trend to increased subcutaneous white adipose tissue. Glucose clearance and insulin sensitivity of POMC-GPERKO mice is comparable to control. However, female POMC-GPERKO mice showed significantly less energy expenditure, VO2 and VCO2 without alteration in locomotor activity.

Conclusion: Considering the phenocopy of AgRP-GPERKO and POMC-GPERKO mice, GPER in ARC neurons might be critical for energy expenditure in female mice. Further studies are needed to investigate how GPER signaling in AgRP or POMC neuron controls these peripheral energy metabolism.

PE079 Clinical diabetes and therapeutics

Beta cell based regenerative therapy for treatment of diabetes mellitus: a metabolic disorder

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Objective: Diabetes mellitus (DM) is the most common metabolic disorder that occurs due to the loss or impaired function of insulin-secreting pancreatic beta cells of two types - type 1 (T1D) and type 2 (T2D). To cure the DM, replacement of the destroyed pancreatic beta cells of islet of Langerhans of pancreases is the utmost widely practised treatment.

Methods: For this, isolating neuronal stem cells and cultivating them as a source of renewable beta cells is a significant breakthrough in medicine. The functions, growth, and gene expression of insulin-producing pancreatic beta cells and neurons are similar in many ways.

Results: A diabetic patient's neural stem cells (obtained from the hippocampus and olfactory bulb) can be used as a replacement source of beta cells for a regenerative therapy to treat diabetes. The same protocol that was used to create functional neurons from progenitor cells can be used to create beta cells.

Conclusion: Recent research suggests that replacing lost pancreatic beta cells with autologous transplantation of insulin-producing neural progenitor cells may be a perfect therapeutic strategy for diabetes, allowing for a safe and normal restoration of function, as well as a reduction in potential risks and a long-term cure.

PE080 Clinical diabetes and therapeutics

Drug-drug interactions between hypoglycemic and non-hypoglycemic medication in diabetic patients with comorbidities in a tertiary care center: a descriptive cross-sectional study

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Objective: The objective of this study was to find out the prevalence of drug-drug interactions in diabetic patients.

Methods: It was a descriptive cross-sectional study that was conducted among previously diagnosed diabetic patients visiting the outpatient department of medicine at a tertiary care hospital between March 2021 and August 2021. Ethical approval was taken from the institutional review committee (Ref no: 030-076/077). Data was collected from diabetic patients presenting to the outpatient department of medicine using a preformed self-constructed questionnaire. Convenient sampling was done. Statistical Package for Social Sciences version 16 and Microsoft Excel was used for data analysis. Point estimate at 95% confidence interval was calculated along with frequency and proportion for binary data.

Results: The prevalence of drug-drug interaction between hypoglycemic and non-hypoglycemic medication was seen in 56 (44.1%) (35.5-52.7 at 95% Confidence Interval) of the patients out of which at least one drug-drug interaction was seen in 48 (37.8%) of the patients.

Conclusion: Our study showed the prevalence of drug-drug interactions in diabetic patients to be higher than in other studies done in similar settings. Based on the severity, we observed two types of drug-drug interactions; close monitoring and minor drug-drug interaction.

PE081 Clinical diabetes and therapeutics

The serum concentration of soluble CD81 during oral glucose tolerance test: a novel marker of pancreatic insulin-secretory function?

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Objective: Recent research has suggested CD81 marks dedifferentiated β-cells in metabolically stressed environments. However, clinically nothing is known about changes in soluble CD81 (sCD81) in the serum of diabetes or normal people. Therefore, through a 75g oral glucose tolerance test (OGTT), we measured sCD81 in the serum in patients diagnosed with diabetes and those with normal glucose tolerance.

Methods: We studied 101 patients who underwent an OGTT to diagnose diabetes. The test results were divided into a group diagnosed with diabetes (DM group) and a group with normal glucose tolerance (NGT group). We measured serum levels of sCD81 at 0 and 120 min during OGTT. Then we compared the change in the serum concentration of sCD81 between the two groups.

Results: First, there was a decrease in serum sCD81 from 0.65±0.66 ng/mL at baseline to to 0.57±0.52 ng/mL, at 120 min of OGTT in entire patients (P=0.014). In addition, serum sCD81 levels at baseline were statistically significantly higher in the DM group compared to the NGT group, and levels at 120 min of OGTT were also significantly higher in the DM group. Furthermore, we found that there was no change of serum sCD81 during OGTT in the NGT group, but a significant decrease in the DM group (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: Through this study, we found that serum concentration of sCD81 was elevated in patients diagnosed with type 2 diabetes, and a significant decrease was observed during OGTT. Changes to the glucose level during OGTT confirmed its potential as a novel marker to reflect the stress state of pancreatic β-cells and functional conditions such as insulin secretion.

PE083 Clinical diabetes and therapeutics

Association between body fat index and gestational diabetes mellitus

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Objective: To compare risk of developing GDM between pregnant women with body fat index (BFI) >0.5 and ≤0.5

Methods: In each pregnant woman, abdominal subcutaneous and visceral adipose tissue (SAT and VAT) thickness were measured by ultrasonography before 14 weeks of gestation and BFI was calculated (VAT x SAT / height). Study group were 160 women with BFI >0.5 and comparison group were 80 women with BFI ≤0.5. All women received GDM screening during first antenatal visit and at 24-28 weeks of gestation. Rate of GDM were compared between the 2 groups. Correlation between BFI and BMI and their diagnostic ability for GDM were evaluated. Logistic regression analysis was performed to determine independent associated factors for GDM.

Results: Women with BFI >0.5 were significantly older (p=0.033), had higher BMI (p<0.001) and more likely to be overweight or obese (p<0.001). BFI correlated well with BMI (correlation coefficient 0.736, p<0.001). GDM were significantly more common in women with BFI >0.5 (24.4% vs. 11.3%, p=0.017). The diagnostic ability of GDM between BFI and BMI were comparable (areas under ROC curves of 0.641 and 0.646, respectively). Significant independent risk factors for GDM were BFI >0.5 and BMI ≥25 kg/m2 (adjusted OR 3.8, 95%CI 1.5-9.2), age ≥30 years (adjusted OR 2.8, 95%CI 1.2-6.4), and family history of DM (adjusted OR 4.0, 95%CI 1.9-8.3).

Conclusion: Women with BFI >0.5 were significantly increased the risk of developing GDM. Diagnostic ability of BFI and BMI for GDM were comparable. Independent associated factors for GDM were BFI >0.5 and BMI ≥25 kg/m^2, age ≥30 years, and family history of DM.

PE084 Clinical diabetes and therapeutics

The associations of perceived hypoglycemia, diabetes self-care behaviors, sleep quality and quality of life in persons with type 2 diabetes

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Objective: Experiencing hypoglycemia leads to negative perception and psychological distress (e.g., fear, anxiety) on diabetes and its management behaviors. Since hypoglycemia often occurs at home and rarely reports to health care providers, the patients' experiences affecting diabetes self-management behaviors and quality of life remain unanswered. This study examined how perceived hypoglycemia affects diabetes self-care behaviors, sleep quality, and quality of life in persons with type 2 diabetes.

Methods: A cross-sectional, correlational design was used. Participants aged 20 years or older (N=177, men= 113 [63.8%]) were recruited from a diabetes clinic affiliated with a university hospital. Socio-demographic variables (sex, age), self-reported questionnaires (Diabetes Control Problem Scale, Summary of Diabetes Self-Care Activities Questionnaire, Pittsburgh Sleep Quality Index, SF-12) and clinical outcomes (HbA1C, fasting glucose) were used to compare those with/without perceived hypoglycemia. All statistical analyses were performed using SPSS for Windows (version 26.0). The level of significance was set at α=.05 (two-tailed)

Results: About one-third (n=67, 37.9%; mean age [yr] =59.06±12.06) reported hypoglycemia in the past 3 months. Compared to those without perceived hypoglycemia (mean age: 62.05±12.80), patients with hypoglycemia more frequently monitored blood glucose (3.94 vs. 2.79, p=.007) and feet (4.36 vs. 3.31, p=.026) while other self-care behaviors (e.g., diet, physical activity, smoking) were insignificantly different between two groups. Overall, sleep quality were same in two groups, but hypoglycemic group reported more cold feelings (0.48 vs. 0.17, p=.008) and bad dreams (.57 vs. 31, p=.048) during the sleep and reported poorer quality of life (4.01 vs. 3.61, p=.001). However, there were no significant differences on HbA1C (7.38 2% vs. 7.378, p=.987) and fasting glucose (165.37 vs.156.69, p=.414) between two groups.

Conclusion: Health care providers pay more attentions to patients' subjective experiences in addition to clinical outcomes in order to provide precision health in diabetes care and support.

PE085 Clinical diabetes and therapeutics

Glycaemic variability of oral semaglutide vs empagliflozin: a post-hoc analysis of PIONEER 2

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Objective: Oral semaglutide is effective at reducing HbA1c vs a range of comparators, but its effect on glycaemic variability needs to be understood. Therefore, we have assessed the change in glycaemic variability and its possible relationship with HbA1c in PIONEER 2 trial comparing with the sodium-glucose co-transporter-2 (SGLT2) inhibitor empagliflozin in patients with type 2 diabetes (T2D).

Methods: The seven-point self-measured blood glucose profile (7-point SMBG) was assessed at baseline and at weeks 26 and 52 in the PIONEER 2 trial. The standard deviation (SD) of the measurements in the 7-point SMBG profile was used as a measure of glycaemic variability. A post-hoc mediation analysis was performed to explore the indirect effect of HbA1c concentration on the direct relationship between treatment and glycaemic variability (the SD of the 7-point SMBG).

Results: The SD of the 7-point SMBG at baseline for the once-daily oral semaglutide 14 mg (N=411) and empagliflozin 25 mg (N=410) treatment arms was 2.06 and 2.05 mmol/l, respectively. The change from baseline in the SD of the 7-point SMBG in the oral semaglutide and empagliflozin arms was -0.67 and -0.44 mmol/l, respectively, at week 26, and -0.69 and -0.49 mmol/l, respectively, at week 52. The treatment differences (95% CI) for the SD of the 7-point SMBG for oral semaglutide vs empagliflozin at weeks 26 and 52 were -0.23 (-0.33, -0.12; p<0.0001) and -0.20 (-0.31, -0.09; p=0.0003) mmol/l, respectively. The mediation analysis showed that the indirect effect of HbA1c accounted for -0.06 (-0.10, -0.02; p=0.0029) and -0.03 (-0.06, 0.00; p=0.08) mmol/l of the treatment difference for the SD of the 7-point SMBG at weeks 26 and 52, respectively.

Conclusion: Oral semaglutide significantly reduces glycaemic variability, as assessed by the SD of the 7-point SMBG, compared with empagliflozin, and most of this effect was not explained by an indirect effect of HbA1c.

PE086 Clinical diabetes and therapeutics

Effect of semaglutide versus placebo on cardiovascular outcomes by baseline HbA1c: SUSTAIN 6 and PIONEER 6 post hoc analysis

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Objective: Cardiovascular (CV) outcome trials have demonstrated CV benefits with once-weekly semaglutide vs placebo (SUSTAIN 6), and non-inferiority for reduction in major adverse CV events (MACE) with oral semaglutide vs placebo (PIONEER 6) in people with type 2 diabetes (T2D) at high CV risk. This post hoc analysis of SUSTAIN 6 and PIONEER 6 evaluated treatment effect of semaglutide vs placebo on MACE by baseline HbA1c.

Methods: Using pooled data from SUSTAIN 6 and PIONEER 6, MACE (a composite of death from CV causes, nonfatal myocardial infarction [MI] and nonfatal stroke) with semaglutide vs placebo was evaluated across baseline HbA1c. A quadratic spline function of baseline HbA1c by treatment was used to analyse treatment effect on time to first MACE across a continuum of baseline HbA1c values. MACE and its components were also compared between baseline HbA1c subgroups (<8; ≥8%; cut-off selected as close to the median).

Results: HRs for risk of MACE favoured semaglutide vs placebo across a continuum of baseline HbA1c values (>6.5-<12.6%). When assessing individual MACE components by baseline HbA1c subgroups, interaction p-values were all >0.05, indicating no statistically significant difference in treatment effect on any CV outcome between baseline HbA1c subgroups (consistent between adjusted and unadjusted analyses). HRs for all CV outcomes were consistently <1.0 with semaglutide vs placebo. HRs in the adjusted analysis [95% CI] for MACE, death from CV causes, nonfatal MI and nonfatal stroke were 0.80 [0.57;1.11], 0.87 [0.49;1.56], 0.98 [0.60;1.59] and 0.52 [0.26;1.05], respectively, with baseline HbA1c <8%, and 0.72 [0.56;0.93], 0.70 [0.46;1.07], 0.83 [0.57;1.20] and 0.74 [0.44;1.22], respectively, with baseline HbA1c ≥8%.

Conclusion: The effect of semaglutide vs placebo on MACE and its components was consistent across baseline HbA1c in the SUSTAIN 6 and PIONEER 6 pooled T2D population. These data indicate that the beneficial CV effect of semaglutide is consistent regardless of HbA1c values.

PE087 Clinical diabetes and therapeutics

Study to evaluate the efficacy and safety of enavogliflozin in patients with T2DM who have inadequate glycemic control on metformin and DPP4 inhibitor (ENHANCE-D)

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Objective: Enavogliflozin was a newly developed SGLT2 inhibitor in Korea, and this phase 3 clinical trial aimed to evaluate the efficacy and safety of enavogliflozin versus dapagliflozin add-on therapy in adults with type 2 diabetes and inadequately controlled with metformin and gemigliptin

Methods: This study was conducted in 28 sites in Korea as a randomized, double-blind, active-controlled manner in patients with type 2 diabetes that were inadequately controlled with metformin and gemigliptin. After a 2-weeks placebo run-in period, patients were randomized (1:1) to receive once-daily enavogliflozin 0.3 mg or dapagliflozin 10 mg as add-on therapy to metformin and gemigliptin for 24 weeks. The primary endpoint was the change of glycated heamoglobin A1c(HbA1c) level from the baseline. The secondary endpoints included proportion of patients reaching HbA1c <7% and proportion of patients achieving HbA1c <7% or a reduction of >1% in HbA1c.

Results: A total of 242 patients were included in the Per-Protocol Set (enavogliflozin 0.3 mg: n=119, dapagliflozin 10 mg: n=123). At week 24, a least square mean HbA1c reduction was -0.92% in the enavogliflozin group and -0.86% in the dapagliflozin group with no significant difference between the two groups (least squares (LS) mean difference -0.06, 95% confidence interval (CI) [-0.19, 0.06]). There was no significant difference between two groups for the proportion of patients reaching HbA1c <7% and the proportions of patients achieving HbA1c <7% or a reduction of >1% in HbA1c. Further, there was no significant difference in two groups for overall adverse event (AE)s (22.59% and 23.53%, in enavogliflozin and dapagliflozin respectively). Enavogliflozin was associated with slightly lower incidences of special interest AEs

Conclusion: Enavogliflozin demonstrated its non-inferiority compared to dapagliflozin as a combination therapy with metformin and gemigliptin in HbA1c change. In addition enavogliflozin showed a noticeable blood glucose lowering effect and favorable safety profile.

PE088 Clinical diabetes and therapeutics

Plasma AKR1B10 is the biomarker that shows the best performance in the diagnosis of NASH and hepatic fibrosis in combination with currently available diagnostic markers

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Objective: No single biomarker can predict the progression of NAFLD across a broad range of spectrum. We found that aldo-keto reductase family 1 member B10 (AKR1B10) reflected the progression of nonalcoholic fatty liver disease (NAFLD) very well. Thus, we evaluated the performance of currently available blood and imaging biomarkers for the diagnosis NASH and advanced hepatic fibrosis (F3-4) in NAFLD in combination with plasma AKR1B10.

Methods: In our combined prospective cohort study on NAFLD, there were 24 healthy control subjects who had normal liver function on blood test and no evidence of steatosis and 92 patients with biopsy-proven NAFLD (47 patients with NAFL and 45 patients with NAFLD activity score 4 or more). In addition to plasma AKR1B10, other biomarkers tested in the present study were as follows: 1) as blood biomarkers, AST, ALT, enhanced liver fibrosis score and its individual components (TIMP1, PIIINP, and hyaluronic acid), the M30 fragment of cytokeratin 18 (CK-18)], complement C3 and C4, and other clinical laboratory parameters; and 2) as imaging markers, magnetic resonance-based imaging markers,

Results: In the diagnosis of NASH, a biomarker combination with the best performance was AKR1B10, CK-18, AST, and ALT at an AUROC value of 0.935 with their diagnostic cutoff values of 1303.8 pg/ml, 120.2 U/L, 24 U/L, and 32 U/L, respectively. In a multiple regression analysis, only plasma AKR1B10 remained an independent predictor of NASH. For the diagnosis of advanced fibrosis, a combination of plasma AKR1B10 with MRE-LSM showed an excellent performance with AUROC and diagnostic threshold values of 0.981 When we combined blood markers only, AKR1B10 performed best in combination with CK-18 for the diagnosis of NASH (AUROC=0.913) and with AST for the diagnosis of advanced fibrosis (AUROC=0.900).

Conclusion: Plasma AKR1B10 in combination with other currently available biomarkers showed an excellent performance for the diagnosis of both NASH and hepatic fibrosis.

PE089 Clinical diabetes and therapeutics

Efficacy of vildagliptin for the treatment of nonalcoholic fatty liver disease with newly diagnosed type 2 diabetic Mongolian patients

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Objective: In Mongolia, liver disease, cancer (8 times the global average) are the leading cause of death. Non-alcoholic fatty liver disease (NAFLD) is closely associated with type 2 diebetes mellitus (T2DM), cardiovascular disease, and cirrhosis, hepatocellular carcinoma. Overweight, obesity and insulin resistance (IR) have been strongly linked with NAFLD. Insulin resistance is accompanied by increased insulin levels that in the presence of increased lipolysis or increased fat intake, promote hepatic triglyceride synthesis. Dipeptidyl peptidase-4 inhibitors (DPP4-I) is useful for the treatment of T2DM. Several studies have evaluated the efficacy of DPP4-I administration in the treatment of NAFLD with T2DM patients. The present study aimed to evaluate the efficacy vildagliptin in NAFLD with newly diagnosed type 2 diabetes mellitus (NDT2DM)

Methods: 28 NDT2DM patients were enrolled in the study January 2022 and until April 2022. Serum levels of fasting plasma glucose (FPG), insulin, liver transaminases (alanine trans transaminase-ALT, aspartate transaminase-AST) and Homeostatic Model Assessment (HOMA)-IR, HOMA-β indexes were calculated. Nafld was diagnosed increased echogenicity by ultrasonography. After baseline assessment all patients took vildagliptin (50mg/day) for 3 months. We collected venous blood samples the study beginning and the end of the study. Statictical analysis was made using SPSS19.

Results: After the treatment significantly decreases of the fasting plasma glucose, insulin levels, HOMA-IR index, and increased HOMA-β. ALT fell from 46IU/L to 42IU/L after the treament. There were no significant changes of Body mass index (BMI kg/m2).

Conclusion: Our study showed in an improved insulin sensitivity, beta cell function, and reduced ALT in small. May suggesting that DPP4-Inhibitors could reduce early liver steatosis and may provide therapeutic efficacy slowing the progression of NAFLD.

PE092 Clinical diabetes and therapeutics

Total daily dose of Cambodian diabetic patients using insulin pumps during hospitalization

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Objective: The aim of this study is to estimate the total daily dose of insulin and satisfaction of patients with diabetes using insulin pump General Medicine "A" Department of Calmette hospital.

Methods: We conveniently selected 39 diabetic patients based on the selecting criteria. They were interviewed in Khmer language, face-to-face using structure-questionnaire and inpatient insulin pump protocol. The statistical data are analyzed by STATA version 14.2.

Results: The average age of patients was 60 (±14.70) years. Type 2 diabetes represented a large portion of the participants. The mean duration of diabetes was 84.76 (±98.68) months. The mean HbA1C was 12.77% (±3.60%). 84.62% of patients used oral hypoglycemic agents since diagnosis. Approximately 90% of patients were subjected to routine exercise. More than half of the patients diagnosed with sepsis. The mean total daily dosage of insulin was 41.31 (±16.41) IU. While the average basal insulin level represented about 48% of total daily dose. Precisely, the total daily intake of insulin in the CSII as a proportion of body weight was 0.69 (±0.34) IU per kilogram per day. The majority of patients were satisfied with CSII management during their hospital stayed. They never experienced hypoglycemia and no signs of infection at the injection site.

Conclusion: We observed that the total daily dose of insulin in our series is moderately higher due to intercurrent illnesses. Most of the patients were satisfied with this new technically innovations.

PE093 Clinical diabetes and therapeutics

Efficacy and safety of enavogliflozin in patients with T2DM who have inadequate glycemic control with metformin (ENHANCE-M)

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Objective: SGLT2 inhibitors have benefits of cardiovascular and renal diseases in addition to type 2 diabetes mellitus. We firstly reported the results of comparative clinical study for metformin combination treatment with enavogliflozin, a newly developed SGLT2 inhibitor in Korea, compared to metformin with dapagliflozin.

Methods: This study was conducted in 24 sites in Korea as a randomized, double-blind, active-controlled manner in a total of 274 patients with type 2 diabetes. 200 who met the criteria were enrolled, 101 were randomly assigned 1:1 to administer enavogliflozin 0.3mg once-daily, and 99 to administer dapagliflozin 10mg once-daily. The primary end point was the change from baseline in HbA1c level after 24 weeks. The secondary end points were changes from baseline in FPG and proportion of subjects achieving HbA1c target of <7% at week 6, 12, 18, 24.

Results: At week 24, a least square mean HbA1c reduction was 0.80% in the enavogliflozin group and 0.75% in the dapagliflozin group with no significant difference between the two groups (LS mean difference -0.04, 95% CI [-0.21, 0.12]). In addition, the proportion of patients achieving HbA1c target of 7% at week 24 was 61.1% in the enavogliflozin group and 62.2% in the dapagliflozin group, where there was no statistically significant difference (odds ratio 0.97, p=0.94). Adverse drug reactions reported were more significantly frequent in dapagliflozin groups than enavogliflozin groups (7%, 1%, respectively; p=0.0341). Enavogliflozin was associated with slightly lower incidences of special interest AEs including hypoglycemia, genital infection, UTI and pollakiuria than those of dapagliflozin (one [1%] vs three [3%]).

Conclusion: This study showed enavogliflozin 0.3 mg was non-inferior in HbA1c change at week 24 to dapagliflozin 10 mg. Enavogliflozin 0.3 mg improved glycemic control, weight, and insulin resistance with HOMA-IR, and not only was well tolerated but showed better safety profile than dapagliflozin in patients with type 2 diabetes receiving metformin.

PE094 Clinical diabetes and therapeutics

Clinical determinants and implication of glycemic variability from continuous glucose monitoring in insulin treated patients with type 2 diabetes

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Objective: We evaluated the clinical determinants of glycemic variability (GV) by considering various lifestyle habits and compared the performance of GV metrics to identify patients with adequate glycemic control and hypoglycemia.

Methods: We recruited 97 patients with type 2 diabetes mellitus from the Korea University Ansan Hospital. Participants wore Dexcom G6 and Fitbit for ten days. Dietary intake was identified using a diary and photographs. The standard deviation (SD), coefficient of variation (CV), mean of the interquartile range, and mean of daily differences in glucose values were calculated. Multivariate-adjusted regression models were conducted with age, sex, body mass index, estimated glomerular filtration rate (eGFR), hemoglobin A1c (HbA1c), duration of diabetes, 2-hour postprandial C-peptide-to-glucose ratios (PCGR2), daily calorie, daytime step counts, and sleep duration as covariates. The performance of GV indices was evaluated by comparing the area under the curve (AUC) of the receiver operating characteristic for adequate glycemic control, defined as co-achievement of the target of continuous glucose monitoring, and with time below range (TBR) 70 mg/dL <4%.

Results: The mean age was 53.9±11.8 years, and about 70% of the participants used both basal and prandial insulin. All GV indices showed the inverse association with eGFR and PCGR2 and a positive association with HbA1c except CV. Logistic regression analysis revealed low HbA1c, and high PCGR2, and women were associated with the concurrent achievement of the CGM-derived glucose target range. Analysis of the ROC curves showed that the best AUC for co-achievement of the target and TBR 70 mg/dL <4% were found in SD (AUC=0.93) and CV (AUC=0.892), respectively.

Conclusion: We confirmed that renal function and residual insulin secretion, in addition to chronic hyperglycemia, are related to GV and the achievement of the recommended targets. SD and CV were the most useful for identifying individuals with adequate glycemic control and hypoglycemia.

PE095 Clinical diabetes and therapeutics

Development of a glucose level prediction model in insulin treated patients with type 2 diabetes

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Objective: As a component of the artificial pancreas, continuous glucose monitoring (CGM) has recently gained attention. However, previous studies have focused on type 1 diabetes. This study aims to develop an algorithm for predicting future glucose levels in patients with type 2 diabetes(T2DM) with insulin treatment.

Methods: We used data of 97 insulin-treated Koreans with T2DM. The dataset consisted of CGM data from Dexcom G6, calorie consumption and sleep information from Fitbit, nutritional data using a diary and photo, and anti-diabetic medication for 10 days. We developed algorithms for predicting glucose levels 30 min later using five machine-learning models: Huber regressor, ridge regression, ElasticNet, least absolute shrinkage and selection operator regression, and nonlinear multilayer perceptron model. We tested the performance of models according to three compositions of dataset: 1) dataset 1: CGM data only; 2) dataset 2: diet, calorie consumption, and CGM data; and 3) dataset 3: adds information about anti-diabetic medication to the dataset 2. Additionally, we tested whether the accuracy of models was enhanced after clustering by the duration of diabetes or HbA1c. With 5-fold cross-subject validation, we adopted root mean squared error (RMSE) to estimate the prediction capacity.

Results: All models were able to predict the glucose levels with an overall 20 mg/dL of RMSE. The error grid results indicated that more than 90% of the predicted values were in region A. The RMSEs of datasets 2 or 3 were lowered compared with those of dataset 1 using CGM data only. The Ridge model tended to show a low mean RMSE for almost all datasets. However, there were no statistically significant differences between the datasets and clustering models.

Conclusion: We developed machine-learning algorithms for patients with T2DM to predict the glucose value at 30 min from the time point with 20 mg/dL of the gap between measured and predicted glucose values.

PE096 Clinical diabetes and therapeutics

Therapeutic potential of phytochemical drug in treatment of type-2 diabetes

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Objective: Diabetes mellitus is a global metabolic disorder characterized by the inefficiency of the pancreas to produce enough insulin and the glucose level increases. Currently, there are a lot of drugs in addition to insulin for the treatment of T2DM but cause adverse side effects as thiazolidinediones are oral hyperglycemic drugs targeting the PPAR-gamma receptor which boosts insulin sensitivity. Serious complications emerge from the controversial belief that prescription drugs (drugs) (individually or in combination) during the treatment of type 2 diabetes may increase or decrease the risk of cancer or affect the prognosis of cancer. We also explore possible therapeutic targets and illustrate the utility of fucoidan and its derivatives as diabetes treatment option.

Methods: We assessed 25 randomly selected reviews in more detail. As a result, we have compiled in vitro and in vivo research done in the last ten years. We anticipate that this review and several others will serve as a theoretical foundation for comprehending fucoidan and serve as an inspiration for future product development.

Results: Fucoidan is one brown seaweed polysaccharide. Fucoidan has bioactive potential because seaweed biodiversity is diverse and largely unexplored. The study (based on the systematic analysis of various papers) indicated that fucoidan with high concentration has maximum efficacy, and fucoidan with low concentration has minimum efficacy as an anti-diabetic agent. It also shows the inhibition of dipeptidyl peptidase IV by fucoidan. This enzyme is responsible for increasing the production of insulin, preventing hyperglycemia and degradation of incretin hormones. Also, it has been observed that fucoidan increases the stool frequency and enhances the sensitivity of taste which is a common problem suffered by most type 2 diabetic patients

Conclusion: In comparison to the synthetic chemotherapeutic medications now used as antidiabetic treatments, fucoidan as a marine bioproduct is thought to be less toxic and has fewer adverse effects.

PE097 Clinical diabetes and therapeutics

Cardiovascular outcomes with fenofibrate vs. omega-3 fatty acids in people with metabolic syndrome: a propensity matched cohort study

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Objective: Comparative effectiveness of triglyceride-lowering therapy, fenofibrate or omega-3 fatty acids, for reduction of residual cardiovascular risk is not determined.

Methods: From a national population-based cohort in Korea, 78,330 people with metabolic syndrome (≥30 years) receiving statin therapy were matched 1:1 by propensity score into the statin plus fenofibrate group and statin plus omega-3 fatty acids group. The primary outcome was the occurrence of composite cardiovascular events including incident ischemic heart disease (IHD), ischemic stroke (IS), and death from cardiovascular causes.

Results: Cumulative incidence for composite cardiovascular events at 6 years was 14.9% in the fenofibrate group and 19.0% in the omega-3 fatty acids group. Fenofibrate therapy significantly reduced the risk of composite cardiovascular events (HR, 0.79; 95% CI, 0.74-0.83; p<0.001) compared to omega-3 fatty acids. Individuals with preexisting cardiovascular disease showed marked benefits of fenofibrate treatment (HR, 0.73; 95% CI, 0.69 to 0.79; p<0.001). The rate of incident IHD (HR, 0.72; 95% CI, 0.67-0.77; p<0.001), IS (HR, 0.90; 95% CI, 0.81-1.00; p=0.057), and hospitalization for heart failure (HR, 0.90; 95% CI, 0.82-0.97; p=0.001) was lower in fenofibrate therapy group than omega-3 fatty acids group. The lower risk of composite cardiovascular events with fenofibrate therapy was prominent in patients aged <65 years or with preserved kidney function.

Conclusion: In this propensity-weighted cohort study, the addition of fenofibrate was associated with a significantly lower risk of major cardiovascular events than omega-3 fatty acids in people with metabolic syndrome on statin therapy.

PE098 Clinical diabetes and therapeutics

Correlation of derived time in range (dTIR) and time in range (TIR) in people with type 2 diabetes (T2D) treated with IDegLira (IDL), degludec, or liraglutide: a post hoc analysis of the DUAL I trial

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Objective: TIR measured by continuous glucose monitoring (CGM), provides a more comprehensive picture of glycemic control than A1c alone. Derived TIR (dTIR), a calculated estimate of TIR, is useful when CGM data are unavailable. This post hoc analysis of DUAL I investigated the correlation between dTIR and TIR in patients with CGM data.

Methods: In DUAL I, people with T2D uncontrolled on oral antidiabetic drugs (n=1663) were randomized 2:1:1 to IDL, degludec or liraglutide, for up to 52 weeks. CGM data were collected using IPro1 and IPro2 (Medtronic). dTIR was calculated from 9-point self-measured blood glucose (SMBG) profiles (minimum 6 points). The Pearson correlation coefficient was used to assess correlation between dTIR and TIR at baseline, and at weeks 26 and 52. Also assessed were the correlation between change in dTIR and change in TIR, from baseline to end of trial (EOT), and the proportion of patients achieving a ≥5% increase in TIR or dTIR at weeks 26 and 52.

Results: 260 patients had CGM data. Using dTIR calculated from patients with ≥6-point SMBG profiles, a strong correlation was seen between dTIR and TIR at baseline (n=2 observations; correlation 0.8838), with a moderate correlation also seen at week 26 (n=165; correlation 0.5512) and week 52 (n=152; correlation 0.5184). Change in dTIR and change in TIR, from baseline to EOT, were also correlated (n=137; correlation 0.7686). Similar results were seen using dTIR calculated using ≥7- or ≥8-point SMBG profiles. A numerically greater proportion of patients achieved a ≥5% increase in dTIR vs. TIR at weeks 26 and 52 (78% vs. 54% and 62% vs. 50%, respectively), perhaps due to missed nocturnal hypoglycemia, and limited data points, measured by SMBG.

Conclusion: These data support the use of dTIR as a surrogate endpoint when CGM data are unavailable, to provide additional information on glycemic control.

PE099 Clinical diabetes and therapeutics

Association of selected laboratory markers with a length of hospital stay in COVID-19 Filipino patients with diabetes mellitus: a single-center study

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Objective: The presence of co-morbidities such as diabetes mellitus (DM) can aggravate the symptoms of coronavirus disease-19 (COVID-19) infection. With the lack of literature on the association of routine markers with the length of hospital stay among COVID-19 Filipino patients with diabetes mellitus, this study was developed.

Methods: A single-center retrospective data collection was performed in a tertiary facility in Pampanga, Philippines. Electronic clinical data from January to December 2021 were retrieved using a data abstraction form and statistically analyzed.

Results: Data on 174 clinical records (grouped to DM, DM with co-morbidity, No DM) were retrieved. Correlation of days of hospital stay showed significant positive correlations with neutrophil-to-lymphocyte ratio, basophil count, creatinine, ALT, and potassium. On the other hand, a significant negative correlation was observed with RBC count, hemoglobin, and hematocrit (H & H). One-way analysis of variance for the difference of the markers across the three groups yielded significant findings for RBC count, H & H, and creatinine.

Conclusion: Overall, our results show that some routine markers may indicate the length of stay of COVID-19 Filipino patients with DM. Given the limitations of this retrospective research, further studies may be done to investigate the utility of the said markers as predictors of COVID-19 disease severity in the target population.

PE100 Clinical diabetes and therapeutics

Deletion mutation in the glutathione s-transferase gene (GSTM1 and GSTT1) and their association with gestational diabetes development: a meta-analysis

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Objective: The etiology of gestational diabetes mellitus (GDM) has not yet been fully explained. Several studies suggested an association between two deletion mutations (GSTM1 and GSTT1) of the GST, a gene that encodes for the enzyme glutathione s-transferase, and GDM susceptibility. However, limited studies are available, which prompted us to perform a meta-analysis to increase the power of existing studies.

Methods: Relevant studies were searched in PubMed, Google Scholar, ScienceDirect, and Cochrane Library and were selected according to the inclusion criteria set. Data were extracted and analyzed using Review Manager 5.4.1. Pooled odds ratios and 95% confidence intervals were computed to measure the association of the deletion polymorphism with the onset of GDM.

Results: A total of five studies involving 1633 participants (782 GDM and 851 non-GDM) were included in the meta-analysis. Overall analysis showed that pregnant women with the GSTM1 deletion mutation in the GST gene are more susceptible to GDM. In contrast, no significant association was observed for the GSTT1 deletion mutation.

Conclusion: Results of this meta-analysis suggest that pregnant women with the GSTM1 deletion mutation are more likely to develop GDM. However, further studies are needed to confirm our claims and to determine its applicability to the Filipino population.

PE101 Clinical diabetes and therapeutics

Effects of a low-calorie meal replacement on body composition and metabolic parameters in shift workers with obesity: a randomized controlled trial

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Objective: Shift work has been identified as a risk factor for several chronic health conditions including obesity. This study aimed to evaluate the impact of a low-calorie meal replacement (MR) as a dinner substitute on body composition and metabolic parameters in shift workers with obesity.

Methods: A parallel, randomized controlled trial for 8 weeks was conducted among shift workers with obesity. The intervention group (IG) (n=25) was provided with a low-calorie MR shake (~ 200 kcal) for dinner, and the control group (CG) (n=25) continued their routine diet. Anthropometric measurements were taken at 0, 4, and 8 weeks. Body composition, biochemical, dietary, and physical activity data were assessed at the first and last visits. Percentage changes in the body composition measurements pre- and post-intervention were reported. Analyses were done per protocol (PP) and by intention to treat (ITT).

Results: PP analyses included 20 and 18 participants in CG and IG respectively. Significant reductions in anthropometric and body composition variables, including body weight (-2.93±1.34%), BMI (-2.83±1.27%), waist circumference (WC) (-4.70±3.69%), Waist-Hip ratio (WHR) (-3.07±3.73%) and body fat (BF) (-0.92±1.6%), were observed among the IG. There was a significant improvement in HDL and reduction in VLDL cholesterol from baseline only in the IG. Additionally, the IG's total energy, carbohydrate, and fat intake significantly decreased from baseline (P<0.05). ITT analysis (n=50) revealed a significant group-by-time interaction for body weight, BMI, WC, WHR, and carbohydrate intake, showing the efficacy of the MR over time.

Conclusion: The low-calorie MR shake contributed to weight loss and significant improvement in body composition and biochemical parameters in shift workers with obesity. It is a feasible and successful weight loss strategy for the workplace.

PE102 Clinical diabetes and therapeutics

Cardiovascular outcomes of lixisenatide vs. dulaglutide: a retrospective study in patients with type 2 diabetes

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Objective: We compared cardiovascular outcomes between lixisenatide and dulaglutide with basal insulin using the Korean Health Insurance claims database.

Methods: We followed 85,646 patients who had GLP-1RA administered between 2010 and 2020. After statistical matching (age, sex, start year, DM duration (less or more than 3 years), HTN status, insulin status (less than one year before GLP-1 RA start), 4,994 patients of lixisenatide and 14,982 patients of dulaglutide were included for the subjects of the study.

Results: A total of 124 acute myocardial infarction (AMI) cases were occurred (2.5%) in the lixisenatide group and 355 (2.4%) AMI cases were occurred in the dulaglutide group, while the non-fatal MI (AMI to death was more than 30 days of the onset, or not dead) was 120 (2.4%) cases in lixisenatide and 336 (2.2%) cases in dulaglutide group. Cardiac death (AMI to death within 30 days) was 4 (0.1%) cases in lixisenatide group and 19 (0.1%) cases in dulaglutide group, and the difference between the two groups was not significant (P=0.479). Stroke had 217(4.3%) cases in lixisenatide group and 612(4.1%) cases in dulaglutide group, and death was 129 (2.6%) cases in lixisenatide and 379 (2.5%) cases in dulaglutide, but this also showed no significant difference between the two groups. There was no significant difference between two groups in AMI (HR, 1.06; 95% CI, 0.86-1.30; P=0.574), non-fatal MI (HR, 1.08; 95% CI, 0.88-1.33, P=0.459), and cardiac death (HR, 0.67; 95% CI, 0.23-1.96; P=0.460). In Stroke, there was no significant difference between the two groups (HR, 1.06; 95% CI, 0.91-1.24, P=0.433).

Conclusion: We observed similar cardiovascular outcomes among patients treated with lixisenatide vs. dulaglutide in real world practice.

PE103 Clinical diabetes and therapeutics

Shift work increased the risk for diabetes in the hospital setting

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Objective: Shift work is considered necessary to ensure continuity of care in hospitals and residential facilities. Shift employment frequently results in metabolic disturbances that promote the onset and progression of chronic diseases like diabetes. In this study, we compared the glycemic parameters and prevalence of dysglycemia between shit-workers and non-shift workers in a hospital setting.

Methods: A cross-sectional study was carried out among a sample of health workers aged ≥18 years at Nawaloka Hospital, Colombo. A sample of both shift and non-shift workers was recruited by stratified random sampling. The data were collected through questionnaires and collecting blood samples. Fasting blood sugar (FBS) and HbA1c tests were used to diagnose diabetes (FSG ≥126 mg/dL or HbA1c ≥6.5%) and dysglycemia (FSG ≥100 mg/dL or HbA1c >5.7%) in accordance with American Diabetes Association (ADA) criteria. The independent t-test and Chi-square test were used.

Results: This study consisted of 36 (M:17; F:19) non-shift workers and 40 (M:19; F:21) shift workers. Mean ages for the non-shift and shift work groups were 36.9±10.9 and 39.1±12.0 years, respectively (P=0.85). In non-shift and shift workers groups, the mean FBS and HbA1c levels were (FBS, 94.03 mg/dL±21.59 vs 109.75 mg/dL±41.84; P=0.001) and (HbA1c, 5.48%±0.88 vs 6.28%±1.79; P<0.001). Dysglycemia was prevalent in 16.7 % (6/36) of non-shift workers and 45.0% (18/40) of shift workers (P=0.008). In comparison to the non-shift workers, the prevalence of diabetes was significantly associated with shift workers (8.3% (3/36) vs 27.5% (11/40); P=0.031) (OR 4.17; 95% CI, 1.06-16.43).

Conclusion: Shift workers were associated with a high risk of developing increased blood glucose parameters compared to day workers in this hospital setting. Since our sample size was limited, large-scale future studies are recommended for stronger evidence.

PE104 Clinical diabetes and therapeutics

Adherence to antidiabetic medications among Sudanese patients with type 1 and type 2 diabetes mellitus and factors associated with it in zenam diabetic center, 2021

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Objective: Adherence to antidiabetic medications is crucial for optimum glycemic control and decreasing complications. Despite that, medication nonadherence is extremely common in diabetic patients. The aim of this study is to assess medication non- adherence and its associated factors among diabetic patients in Zenam diabetic center in Khartoum, Sudan in the year 2021- 2022.

Methods: This is a descriptive cross-sectional hospital- based study involved 230 participants. Data were collected using interviewed structured questionnaire by systematic random sampling and analyzed using statistical package for social sciences (SPSS) version 25. Chi-square analysis was conducted, and multivariable logistic regression analysis was used. A P value of less than 0.05 was used to declare statistical significance.

Results: Among 230 participants, 117 (50.9%) were female diabetes patient. The mean age (±SD) of the study participant was 53.67 (±14.55) years. Based on the MMAS-8 scale, non-adherence to diabetes medication was 156 (67.8%). In multivariables analysis only female sex was associated with adherence (O. R= 3.79, CI: 1.636-8.779). Patients attributed their nonadherence to forgetfulness (61.5%) and medications side effect (37.5%).

Conclusion: Level of adherence to anti diabetic medications was low and unsatisfactory as only 32% showed high level of adherence. Female sex was the only predictor for adherence level in this study. Effective interventions should be implemented to improve medication adherence including involvement of patient in the treatment plan and appropriate patient education about the disease and medications by health care providers. Also public awareness programs, self monitoring of blood sugars, regular follow-up visits to health care facility and ensuring the drug compliance by inquiring and educating the patient and a responsible family member to improve the glycaemic control and reduce the diabetes related complications.

PE106 Clinical diabetes and therapeutics

Modulation of antimony mediated therapy for an optimal insulin secretion during visceral leishmaniasis infection

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Objective: Visceral Leishmaniasis is a macrophage associated disorder for the treatment of which antimony based drug like Sodium Antimony Gluconate has been the first choice in the recent past. About 5 percent of the patients may develop insulin dependent diabetes mellitus. It appears to have a direct action on pancreatic beta cells, resulting in initial insulin release followed by impaired insulin secretion. Within this context we looked into alternate therapies of treatment along with SAG on triggering the CD2 epitope.

Methods: We have evaluated the effect of combining CD2 with conventional antimonial (sb) therapy in protection in BALB/c mice infected with either drug sensitive or resistant strain of Leishmania donovani with 3 million parasites via-intra-cardiac route. Mice were treated with anti CD2 adjunct SAG sub-cutaneously twice a week for 4 weeks. Assessment for measurement of weight, spleen size, anti-Leishmania antibody titer, T cell and anti-leishmanial macrophage function was carried out day 0, 10, 22 and 34 post treatments. Insulin levels were also determined on the same intervals.

Results: The combination therapy was shown boosting significant proportion of T cells to express CD25 compared to SAG monotherapy. Although, the level of IFN-γ was not statistically different between combination vs monotherapy (p=0.298) but CD2 treatment even alone significantly influenced IFN- γ production than either SAG treatment (p=0.045) or with CD2 adjunct SAG treatment (p=0.005) in Ld-S strain as well as in Ld-R strain. The influence of CD2 adjunct treatment was also documented in anti-leishmanial functions in macrophages. Interestingly insulin levels were observed to be optimal on supplementing SAG along with CD2

Conclusion: SAG along with CD2 could be used as a potential therapy to overcome incidences of Diabetes mellitus during Visceral Leishmaniasis

PE107 Clinical diabetes and therapeutics

Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as inflammatory markers in type II diabetic patients

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Objective: Neutrophil-Lymphocyte ratio (NLR) and Platelet-Lymphocyte ratio (PLR) recently has become useful biomarkers in number of chronic inflammatory diseases. In this study, we evaluated NLR, PLR as inflammatory markers in type II diabetic patients and correlate them with C-reactive protein (CRP) and HBA1c.

Methods: A Hospital based cross-sectional study was conducted from September 2021 to April 2022 at Star Hospital, Lalitpur, Nepal. This study includes total 200 diabetic patients and 200 age matched healthy subjects. 5 ml of blood sample was collected, blood count, CRP level and HBA1c were analyzed at hematology and biochemistry lab.

Results: NLR and PLR were significantly higher in diabetic patients than healthy subjects (1.75±0.51 vs 1.36±0.26 and 106.06±33.96 vs 79.94±17.33; p value=0.001). There were also positive correlation between NLR, PLR CRP levels and HBA1c.

Conclusion: NLR and PLR could become potential marker of inflammation for type II diabetic patients.

PE108 Clinical diabetes and therapeutics

A retrospective multi-center non-interventional study investigating the effectiveness and safety of insulin degludec / insulin aspart (IDegAsp) in a real-world adult population with type 2 diabetes in South Korea

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Objective: To investigate the effectiveness of glycemic control and safety issues in a real-world population of adult type 2 diabetes (T2DM) patients in South Korea, whose treatment was switched on insulin degludec/insulin aspart (IDegAsp) in routine clinical practice.

Methods: This was a non-interventional, retrospective, chart review study of T2DM patients who were treated with any basal insulin or premix insulin (± OAD) for at least 26 weeks prior to switching to IDegAsp and treated for at least 26 weeks on IDegAsp (±OAD). Data was collected for the 26 weeks pre-switching period and 26 weeks post-switching period to IDegAsp. The analyses included the changes in glycosylated hemoglobin (HbA1C), fasting plasma glucose (FPG), proportion of patients with HbA1c <7.0%, weight, hypoglycaemia, insulin dose.

Results: Among 200 subjects initially enrolled, 196 subjects with mean age of 65.95±11.23 years and mean duration of T2DM of 18.99±9.15 years were included for the final analysis. The mean change in both HbA1c and FPG during the 26 weeks were significantly different between the pre-switching and the post-switching period (0.28 vs. -0.51%, p<0.001; 5.21 vs. -23.10 mg/dL, p=0.005). The proportion of patients to reach the HbA1c goal of <7.0% was significantly higher at week 26 than week 0 (11.26% vs 5.10%, p=0.012). No significant differences in changes in weight, hypoglycemia incidence, and insulin dose were found between the pre-switching and the post-switching period.

Conclusion: In a real-world setting, IDegAsp effectively improved HbA1c and fasting plasma glucose levels and did not increase hypoglycaemia incidence in patients with uncontrolled T2DM previously treated with basal or premix insulin.

PE109 Clinical diabetes and therapeutics

Subgroups of adult-onset diabetes by cluster analysis and comparison between young-onset versus late-onset type 2 diabetes mellitus

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Objective: Type 2 diabetes (T2D) presents significant heterogeneity in clinical presentation. We aimed to classify adult-onset diabetes in Koreans according to cluster analysis following recent data driven novel classification of T2D, and to compare the distribution of subgroups between young-onset diabetes (YOD) and late-onset (LOD) in T2D.

Methods: This data-driven cluster analysis included 2,126 study participants who were diagnosed with T2D within two years with six parameters including glutamate decarboxylase antibodies, age of onset, body mass index, glycated hemoglobin A1c, and homoeostatic model assessment 2 estimates of β-cell function and insulin resistance.

Results: Patients were clustered into 4 subgroups: 25.6% were in the severe insulin-deficient diabetes (SIDD, cluster 1) subgroup. 5.7% were in the severe insulin-resistance diabetes (SIRD, cluster 2) subgroup, 26.8% were in the mild obesity-related diabetes (MOD, cluster 3) subgroup and 41.9% were in the mild age-related diabetes (MARD, cluster 4) subgroup. The proportion of the SIDD subgroup was the highest in the YOD patient group with 46.4%. In contrast, only 22.7% of LOD subjects were classified as SIDD. The concomitant risk of retinopathy and chronic kidney disease was significantly different between clusters (all p <0.05). The prevalence of retinopathy was highest in SIDD group, and the prevalence of chronic kidney disease was highest in SIRD group.

Conclusion: The data driven novel classification of T2D was applicable to Korean patients with adult-onset diabetes. The proportion of patients with SIDD subgroup was relatively high in YOD patient group.

PE110 Clinical diabetes and therapeutics

Fasting plasma glucose-to-estimated average glucose ratio as an indicator of glycemic variability in patients with type 2 diabetes on basal insulin

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Objective: Decreasing glycemic variability is an important aspect in management of diabetes. However, indicators for glycemic variability are not standardized and glycemic variability is difficult to estimate in usual clinical setting. In this study, we analyzed clinical implications of fasting plasma glucose-to-estimated average glucose (FPG/eAG) ratio as an indicator of glycemic variability in patients under basal insulin therapy.

Methods: Patients with type 2 diabetes on basal insulin and oral agents were recruited, who were presumed to have marked prandial hyperglycemia, given persistent FPG lower than predicted by the concurrent HbA1c. After receiving informed consents, clinical information was collected, eAG was calculated using HbA1c, and the patients were divided by FPG/eAG ratio. Blinded CGM was applied for 1 week and glycemic variability was evaluated.

Results: Fifty five patients were enrolled (men 40%, mean age 64 years, HbA1c 8.3%). There were no significant differences in sex, age, BMI, HbA1c, and insulin doses between the 2 groups. In the low FPG/eAG group (median [IQR] 0.46 [0.41-0.50]) compared to the high group (0.62 [0.58-0.67]), coefficient of variation and time below rage were significantly higher (mean±SD 38.3±7.2 vs. 33.2±6.0%; 3.1±4.5 vs. 0.9±1.8%, all P<0.05). Mean glucose, time in range, and time above range were comparable between the groups. Hypoglycemia was more frequent in the low FPG/eAG group, and most of them occurred around 6 AM. Fasting glucagon levels were not different while glucose-stimulated C-peptide was significantly lower in the low FPG/eAG group, suggesting contribution of insulin deficiency to the findings.

Conclusion: Lower FPG/eAG ratio could reflect higher glycemic variability, leading to more hypoglycemia at dawn. This study would contribute to tailored insulin therapy. Funding NRF grant (2019R1A2C1007397 and 2022R1A2C2004570) by the Ministry of Science and ICT, Korea

PE111 Clinical diabetes and therapeutics

A profound renoprotective effect of SGLT2 Inhibitor in subjects with type 2 diabetes with ketonuria

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Objective: Euglycemic ketoacidosis and ketonuria have been reported in subjects with Type 2 Diabetes (T2DM) when treated with sodium-glucose cotransporter 2 (SGLT2) inhibitors. Landmark studies showed strong renoprotective effects of SGLT2i, and the potential of additional renoprotection by moderately enhancing ketogenesis has been further discovered in cellular and animal experiments. This study is aimed to investigate whether there is a potential role of ketonuria, an indicator of ketogenesis, in the renoprotective effects of SGLT2i.

Methods: Subjects with T2DM who had been treated with SGLT2i for more than 6 months were collected from January 2014 to January 2022 via Clinical Data Warehouse (CDW) of Seoul National University Bundang Hospital. A total of 199 subjects were analyzed with consecutive urinalysis conducted for a 6-month follow-up. Subjects were classified into two groups: ketonuria (-) and ketonuria (+). Biochemical parameters in each group were retrospectively collected from the initial, 3-month, and 6-month periods of SGLT2i treatment.

Results: After matching age, gender, duration of T2DM, hemoglobin A1c (HbA1c), and estimated glomerular filtration rate (eGFR), 57 subjects were identified in each group. Levels of body weight, body mass index, fasting plasma glucose, and HbA1c were significantly reduced in both groups with similar degree. The eGFR were significantly improved only in the ketonuria (+) group: mean difference of -1.18±14.1 in the ketonuria (-) group vs 8.31±24.0 mL/min/1.73m^2 in the ketonuria (+) group (p<0.05). In the linear regression analysis, more improvement in eGFR at 6-month was correlated with female gender, and negatively correlated with baseline body weight, diastolic blood pressure, and eGFR in the ketonuria (+) group.

Conclusion: The presence of ketonuria was associated with profound renoprotective effects under SGLT2i treatment. Under SGLT2i treatment, patients of female gender with a lower initial eGFR and lesser degree of obesity were associated with more improved renal function.

PE112 Clinical diabetes and therapeutics

Combination of moderate-intensity statin and ezetimibe versus high-intensity statin monotherapy on primary prevention of cardiovascular disease and all-cause death: a propensity-matched nationwide cohort study

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Objective: This study aims to compare the preventive effect of moderate-intensity statin with ezetimibe combination therapy and high-intensity statin monotherapy on cardiovascular disease (CVD) and all-cause death in a real-world setting.

Methods: The Korean National Health Insurance Service datasets were used for this nationwide cohort study. Both statin and ezetimibe have been prescribed for 90 and more days. Using 1:1 propensity score matching procedure, 34,744 patients were assigned to combination therapy group and another 34,744 patients to the high-intensity statin monotherapy group. Primary outcome was a composite of myocardial infarction (MI), stroke, and all-cause death, and secondary outcome was an individual event. The date of the initial check-up was considered to be the baseline. The study population was followed from baseline until the date of events, or the last health check-ups, whichever came first.

Results: The incidence rate per 1,000 person-years of composite event was 7.3 for combination group and 11.1 for statin monotherapy group. Compared to high-intensity statin monotherapy group, the hazard ratio (HR) was 0.84 (95% confidence interval [CI] 0.77-0.92; P<0.001) for composite outcomes, 0.81 (0.71-0.94; P <0.001) for MI, 0.78 (0.65-0.93; P<0.01) for stroke, and 0.89 (0.78-1.02; P=0.090) for all-cause death in moderate-intensity statin with ezetimibe combination therapy group. Although baseline low-density lipoprotein cholesterol (LDL-C) level was significantly higher in combination group, the achieved LDL-C level was significantly lower in combination group than that of statin monotherapy group (93.6±46.5 vs. 100.7±48.0 mg/dL, P<0.001).

Conclusion: Moderate-intensity statin with ezetimibe combination therapy was superior to high-intensity statin monotherapy for prevention of CVD and all-cause death in population without previous CVD.

PE113 Clinical diabetes and therapeutics

Effect of probiotics supplementation on gut microbiota of type-2 diabetes mellitus: a meta-analysis of randomised controlled trials

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Objective: Dysbiosis, an imbalance in gut microbial community, contributes to the pathogenesis and metabolic disturbance 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. Random effects models were used to calculate efficacy as pooled mean difference (MD) across probiotic species, single vs. multiple species, dosages, and length of treatment. Changes in microbial diversity were expressed as MD with 95% confidence interval (CI) 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 (1.79, 95% CI -1.80, 5.38, p=0.33) and lower Bacteroidetes (−3.69. 95% CI -8.06, 0.68, p=0.10). At the genus level, significantly higher proportions of Bifidobacterium (3.46. 95% CI 2.73, 4.18, 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, was associated with positive microbiome effects on T2DM. More randomized placebo-controlled trials with large sample sizes are warranted to corroborate our conclusions.

PE114 Clinical diabetes and therapeutics

Comparison of SGLT2 inhibitors versus DPP-4 inhibitors as combination with metformin in patients with acute myocardial infarction and concomitant diabetes mellitus

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Objective: This study was designed to evaluate cardiovascular outcomes by comparing SGLT-2 inhibitors versus DPP-4 inhibitors as combination with metformin in type 2 diabetic patients with acute myocardial infarction (AMI).

Methods: Among 15,628 consecutive patients from the Korea Acute Myocardial Infarction Registry-V (KAMIR-V) registry, we identified 779 subjects with type 2 diabetes who were receiving combination of metformin plus DPP-4 inhibitor and metformin plus SGLT2 inhibitor. The primary endpoint was 1 year of major adverse cardiac and cerebrovascular events (MACCEs), composite of all-cause mortality, non-fatal myocardial infarction, any revascularization, cerebrovascular accident, and stent thrombosis, and all other clinical outcomes were analyzed. To correct selection bias and adjust for confounders, two propensity score weighting methods including propensity score matching (PSM) and inverse probability of treatment weighting (IPTW) were performed.

Results: After PSM and IPTW, SGLT2 inhibitor did not result in a lower rate of MACCEs compared with DPP-IV as combination with metformin (PSM; hazard ratio [HR], 0.84; 95% confidence interval [CI], 0.36 to 1.94, P=0.684, IPTW; HR, 0.6; 95% CI, P=0.237). After IPTW, SGLT2 inhibitor resulted in a lower rate of anyvascularization than DPP-4 inhibitor (HR, 0.40; 95% CI, 0.17 to 0.94, P=0.036), but there was no between-group difference in myocardial infarction, cerebrovascular accident. After IPTW, left ventricle systolic function was significantly improved in patients treated with SGLT2 inhibitors compared with DPP4 inhibitors.

Conclusion: Our findings demonstrated that SGLT2 inhibitor did not result in a higher or lower rate of MACCEs compared with DPP4 inhibitor as combination with metformin in patients with AMI and concomitant diabetes mellitus, but did result in improved myocardial systolic function.

PE115 Clinical diabetes and therapeutics

Association of smokeless tobacco with an increased risk of type 2 diabetes

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Objective: Managing diabetes is challenging, and tobacco use can make it even more so. Nicotine increases blood sugar levels and makes them harder to handle. **Objective:** The objective of this study was to examine the impact of smokeless tobacco use on blood sugar levels of diabetic tobacco users.

Methods: In this study we recruited the subjects from outpatient department (OPD) of KGMU. Total 80 subjects (40 diabetic non- tobacco users + 40 diabetic tobacco users) were enrolled in the study and their fasting blood sugar (FBS), post prandial glucose (PPG) and HbA1c levels were assessed.

Results: Study participants were aged between 48±10 years. FBS was 163.11±62.7mg/dL, PPG was 246.8±96.4 mg/dL and HbA1c was 7.96±1.6% in diabetic subjects while FBS was 175.9±76.2 mg/dL, PPG was 261.1±104.3 mg/dL and HbA1c was 8.6±2.5% in diabetic tobacco users.

Conclusion: Smokeless tobacco use can even degrade existing status of diabetes in diabetic tobacco users. Thus, tobacco cessation should be promoted as an essential public health practice for diabetes management.

PE116 Clinical diabetes and therapeutics

Long-term effects of COVID-19 social distancing on glycemic control in patients with type 2 diabetes

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Objective: Lifestyle modifications are one of the important strategies for managing type 2 diabetes well. We investigated the impact of prolonged social distancing due to the COVID-19 pandemic on glycemic control in patients with type 2 diabetes.

Methods: This retrospective multicenter cohort study included patients with type 2 diabetes who regularly visited the medical centers in Gyeonggi province from April 1, 2019 to June 30, 2021. Demographic, anthropometric, prescription medications, and laboratory data were reviewed retrospectively from medical records. Participants responded to questionnaires that included changes in dietary habits, physical and social activity, alcohol consumption, smoking, workload, sleep duration, medication adherence, and emotional health. We compared whether these variables affect hemoglobin A1c (HbA1c) levels each year, and analyzed their correlation coefficients through Pearson and Spearman correlation analyses.

Results: Total 393 patients (mean age, 58.5±9.2 years; male sex 61.6%) were enrolled, and their food intake significantly increased but their physical and social activities decreased (all p<0.05). Patients with higher BMI (≥25.0kg/m2) had transient increases in HbA1c levels but eventually recovered (pre-pandemic vs. early vs. prolonged, 7.3±1.2 vs. 7.4±1.3 vs. 7.3±1.1, p=0.038 and 0.042, respectively). Patients with high HbA1c (≥7.0%) had increased HbA1c levels (7.8±1.3 vs. 7.8±1.2 vs. 7.9±0.9, each p=0.037 and 0.038), while those with low HbA1c (<7.0%) had decreased (6.7±0.9 vs. 6.6±0.6 vs. 6.4±0.3, all p<0.001) during the pandemic. Among medications, insulin was associated with a decrease of HbA1c levels (pre-pandemic vs. prolonged, 8.4±1.5 vs. 8.0±1.2, p=0.003), especially significant in patients injected with low-dose of insulin (<0.5units/kg, 8.4±1.6 vs. 7.8±1.3, p=0.014).

Conclusion: Sedentary lifestyle, such as increased food intakes and decreased physical activities, and emotional stress were associated with increases of HbA1c levels, but there was no significant difference. HbA1c and fasting plasma glucose levels, and insulin use were correlated with change of HbA1c levels (partial correlation coefficient r=0.429, 0.437 and 0.222, all p<0.001).

PE118 Clinical diabetes and therapeutics

Evolution of synergistic effect of herbo probiotic on clinical and metabolic responses in subject with metabolic syndrome

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Objective: Due to rapid economic development and improved quality of life, our lifestyle and diet have changed substantially, leading to the rapid occurrence of metabolic illnesses including MetS, Type II Diabetes, etc. MetS is a cluster of risk factors that ultimately leads to CVD. Since ancient times, herbal remedies have been utilised to cure a variety of illnesses. Probiotics have clearly reported encouraging results in a number of metabolic disease. This study's objective was to evaluate the efficacy of herbal probiotic therapy in the treatment of MetS.

Methods: A randomized placebo control trial was conducted on 50 volunteers aged 30-65 years of either gender who attended the weekend Diabetic Clinic, Health Centre, Jiwaji University, India. For three months, 25 participants in each group were given a placebo or a probiotic capsule along with herbal medicine, and their therapeutic potential was examined by monitoring several biochemical markers such as hematological parameter, fasting blood glucose, C-peptide, lipid, liver and kidney profile, and anthropometric data. SPSS 20 software was used to analyse the data using paired t-tests and student t-tests.

Results: Probiotic therapy for three months resulted in significant reductions in blood glucose and HbA1c. In the probiotic and placebo groups, Probiotic treatment enhanced C-peptide levels (P<0.01). Total cholesterol and triglyceride levels were significantly lowered in both groups (P=0.01). Subjects in both groups improved significantly in all metabolic abnormalities, and there was a significant difference between the groups (probiotic vs. placebo) observed for the majority of the biochemical and physiological parameters.

Conclusion: Probiotic supplementation has been demonstrated to have a synergistic impact when combined with herbal therapy. All MetS values improved significantly with probiotic supplementation.

PE121 Clinical diabetes and therapeutics

Effect of lifestyle interventions on the risk of incident diabetes in people with isolated impaired fasting glucose: a meta-analysis of individual participant data from randomized controlled trials

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Objective: We performed a systematic review and an individual participant data meta-analysis to examine the efficacy of guideline-based lifestyle interventions in reducing diabetes incidence in people with isolated impaired fasting glucose (IFG), a form of prediabetes.

Methods: We searched PubMed, MEDLINE, Embase, and Scopus databases until 01 August 2022 for lifestyle-based randomized controlled trials that included people with isolated IFG (fasting plasma glucose 100-125 mg/dl and 2-hour plasma glucose <140 mg/dl). Lifestyle interventions in these trials were focused on achieving 5-7% weight loss, increasing moderately intense physical activity to ≥150 min/week, reducing total calorie intake per day by ~500 calories, and/or improving the quality of dietary fat (e.g., <30% of daily calorie intake from fat). We estimated the hazard ratio (HR) for incident diabetes using random-effects models, and heterogeneity was assessed using I2 statistic. We used the Grading of Recommendations, Assessment, Development and Evaluation system to rate the quality of evidence. The study is registered with the International Prospective Register of Systematic Reviews (CRD42020197356).

Results: We included the data of 1132 participants from all three eligible trials (two from India and one from Japan). Of which, incident diabetes was observed in 12.9% (n=71) of participants in the intervention groups and in 12.5% (n=73) of participants in the control groups during a mean follow-up of 2.5 years. The pooled HR for incident diabetes was 1.01 (95% CI 0.67-1.52; I2=0%) compared with the control groups. The quality of evidence was high.

Conclusion: Lifestyle interventions recommended by the guidelines were not effective in reducing diabetes incidence in people with isolated IFG. Isolated IFG is the most common form of prediabetes in Asians and Caucasians, and they incur a high risk of developing cardiovascular disease and of premature mortality. Therefore, there is an urgent need to identify effective interventions for this high-risk group.

PE122 Clinical diabetes and therapeutics

A multicenter, randomized, open-label Study to compare the effects of gemigliptin add-on or dose escalation of metformin on glycemic control and safety in patients with inadequately controlled type 2 diabetes mellitus on metformin and SGLT-2 inhibitors (SO GOOD study)

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Objective: The present study aimed to compare the efficacy and safety between gemigliptin add-on versus dose escalation of metformin in patients with T2DM who were inadequately controlled with metformin and SGLT2 inhibitors.

Methods: This was a multicenter, randomized, open-label, active-controlled, parallel-group, comparative study. Subjects with T2DM uncontrolled on metformin and SGLT2 inhibitors were randomized to receive gemigliptin 50 mg add-on (GEM group) or dose escalation of metformin 500mg (MET group) for 24 weeks. The primary endpoint was the change from baseline in glycosylated hemoglobin (HbA1c) at week 24.

Results: A total 67 patients were included in the analysis (GEM:MET=33:34). At weeks 12 and 24, the GEM group showed significantly greater reduction in HbA1c level compared to the MET group (GEM:MET=-0.64%±0.34% vs. -0.36%±0.50%, p=0.009 at week 12; -0.61%±0.35% vs. -0.33%±0.70%, p=0.045 at week 24). The proportion of patients who achieved a target HbA1c level of <6.5% and <7% at week 12 and 24 were greater in the GEM group than in the MET group. An index of β-cell function was significantly improved in the GEM group. There were no differences in safety profiles between the two groups.

Conclusion: Addition of gemigliptin improved glycemic control and HbA1c goal attainment, compared to the dose escalation of metformin in patients with T2DM who are inadequately controlled with metformin and SGLT2 inhibitors.

PE123 Clinical diabetes and therapeutics

MAFLD and NAFLD in the prediction of incident diabetes

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Objective: The definition of metabolic dysfunction-associated fatty liver disease (MAFLD) includes individuals with excessive alcohol consumption or viral hepatitis, which are known risk factors for diabetes and have been excluded from the nonalcoholic fatty liver disease (NAFLD) diagnostic criteria. We aimed to investigate whether the MAFLD criteria is a more appropriate definition as a predictor of incident diabetes than the NAFLD criteria.

Methods: This was a 5.0-year (interquartile range, 2.4-8.2) retrospective longitudinal cohort study of 21,178 adults who underwent at least two serial health checkup examinations. Presence of hepatic steatosis was determined by abdominal ultrasonography at the first health examination. Cox proportional hazard analyses were used to compare the risk of incident diabetes among non-fatty liver disease (FLD) without metabolic dysregulation (MD), non-FLD with MD, MAFLD-only, NAFLD-only, or both-FLD groups.

Results: Incident diabetes cases occurred in 1,296 participants (6.1%). When non-FLD without MD group was set as a reference, the risk of incident diabetes increased in the order of NAFLD-only (adjusted hazard ratio [aHR] 2.67, 95% confidence interval [CI], 1.58-4.51), non-FLD with MD (aHR 3.74, 95% CI 2.94-4.77), both FLD (aHR 6.14, 95% CI 4.93-7.63), and MAFLD-only (aHR 8.83, 95% CI 6.50-11.99) groups, respectively. Presence of excessive alcohol consumption and/or viral hepatitis, hepatic steatosis determined by ultrasonography, and metabolic syndrome synergistically increased the risk of incident diabetes.

Conclusion: The MAFLD definition including individuals with FLD accompanied by excessive alcohol consumption or viral hepatitis would be more appropriate to predict the development of diabetes than the NAFLD definition.

PE125 Clinical diabetes and therapeutics

Glucose tolerance test in probands of patients suffering from chronic mental illness

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Objective: There is evidence that diabetes has an increased prevalence in the relatives of people with chronic mental illness like schizophrenia, and that deficit and nondeficit schizophrenia differ with regard to family history of Diabetes Mallitus. This is an attempt to study the variability of GTT between the deficit and non deficit subjects. We also intend to study whether there are variations in GTT in the first-degree relatives of probands with deficit versus non deficit schizophrenia

Methods: This was a cross sectional study, carried out on a sample of 30 drug free patients each with deficit & non-deficit Schizophrenia, the first degree relatives of deficit schizophrenia and normal controls. The samples were drawn out of Purposive sampling method. Normal controls were taken from the community in vicinity of hospital. Tools used were General Health Questionaire-12, The Schedule for the deficit Schizophrenia, Positive & negative Symptom scale for Schizophrenia. Data regarding the metabolic profile (GTT results, fasting glucose levels, pulse pressure, BMI score) were recorded.

Results: Our study found a significant impairment in the blood glucose levels on oral glucose tolerance test in patients with deficit schizophrenia as compared to their first degree siblings ($p<0.05$), non deficit schizophrenia probands ($p<0.001$) and normal controls ($p<0.001$). Dysglycemia was found in 40% of the subjects in the deficit cohort with 10% of deficit subjects being diagnosed as type II diabetes mellitus. A distinct gradation was observed in the dysglycemia patterns with highest abnormalities in the deficit probands, followed by their first degree siblings, non deficit probands and least in the normal control probands.

Conclusion: The patients of deficit Schizophrenia have greater risk of developing Diabetes Mallitus II and they need to be regularly investigated for it.

PE126 Clinical diabetes and therapeutics

Aldose reductase inhibitory potential of hybanthus enneaspermus: biological importance in the medicine for the treatment of diabetes related secondary complication

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Objective: Hybanthus enneaspermus have numerous pharmacological activities and have been used in the traditional medicine for the treatment of urinary calculi. Aldose reductase inhibitory (ARI) potential of pure phytoconstituents has been evaluated in the present investigation to know their therapeutic value of herbal medicine against diabetes and related secondary complications.

Methods: Hot extraction techniques have been used for the extraction of Hybanthus enneaspermus using ethyl alcohol as solvent. Further this crude extract has been fractionated into various phytoconstituents rich fractions using solvent of varying polarities. Phytochemical analysis has been performed to know the chemical composition of ethanol extract. Aldose reductase inhibitory potential of pure phytoconstituents has been investigated in vitro using rat lens. Adult Wistar albino rats weighting between 150-200 g have been taken in the present investigation. All the standard parameters such as 12 h light and 12 h dark cycle, 25-30 OC and 35-60% relative humidity were maintained during the study. Experimental protocol has been approved by the Institutional Animal Ethics Committee.

Results: Phytochemical analysis signified the presence of various types of phytoconstituents in the ethanol extract of Hybanthus enneaspermus. Column chromatography separation of ethanol extract revealed the separation of pure phytochemical. TLC analysis confirmed the presence of numerous secondary phytochemical in the ethanolic extract. Aldose reductase inhibitory potential of crude extract in rat lens signified the biological importance of Hybanthus enneaspermus against diabetes and related secondary complication.

Conclusion: Present investigation revealed the biological importance of Hybanthus enneaspermus extract against aldose reductase enzymes which signified their role in the treatment of diabetes and related secondary complications.

PE127 Clinical diabetes and therapeutics

Type 2 diabetes patients with cyclic vomiting syndrome after rapid blood glucose correction: two case reports

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Introduction: Cyclic vomiting syndrome (CVS) is a rare disorder characterized by recurrent episodes of sudden severe nausea and vomiting and then end abruptly. There are several hypotheses related to migraine headaches, stress responses caused by hypothalamic-pituitary-adrenal axis, or mutation in mitochondria. We describe a case of CVS in two patients with a short disease duration of type 2 diabetes (T2DM). Case 1. A 41-year-old female was admitted with severe nausea and vomiting. She diagnosed with T2DM with retinopathy 6 months ago. A little nausea always persisted, but when the constipation got worse, the uncontrolled vomiting started and improved suddenly within a few days. Her HbA1c was 5.8% and no specific finding in laboratory test. Ondansetron and lorazepam were improved symptoms. Case 2. A 47-year-old female was admitted with severe nausea and vomiting. She diagnosed with T2DM with peripheral neuropathy 5 months ago. The symptoms suddenly began usually after overworking and improved within a week. Her HbA1c was 6.0% and no specific finding in laboratory test. Gastric emptying study showed delayed gastric empting state. The prokinetic, metoclopramide, duloxetine and nortriptyline were improved symptoms. Vital sign was stable in both patients. Upper gastrointestinal endoscopy, abdominopelvic CT and brain image test revealed no specific findings in both patients.

Conclusions: In above cases, HbA1c at the first diagnosis of diabetes was 13% and 15%, respectively, and decreased to less than 6.5% between 3 and 6 months after diagnosis. Moreover, they have in common that there are trigger factors and already had established diabetic microvascular complications. It is well known that glucose variability exacerbates microvascular complications. In conclusion, it is necessary to investigate the possibility that rapid correction from severe hyperglycemia to normoglycemia radically changed the patient's peripheral nerve biochemical environment, making them more vulnerable to the stressful environment and, as a result, promoted complications.

PE128 Clinical diabetes and therapeutics

Chronotherapeutic effect of time restricted feeding on metabolic disorder: a challenging lifestyle modification

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Objective: Time-restricted feeding (TRF) regulates the circadian rhythm of food intake that protects against metabolic disorders. The aim of our study is effect of time restricted feeding on circadian rhythm regulating gene in diet induces obese rats model.

Methods: Total 21 Wistar rats were included i.e. control, TRF and High Fat diet (HFD) group. HFD group was fed with fatty diet at ad lib for two months and shifted to TRF (12 hours feeding i.e 8:00pm - 8:00am) for three months, after which they were again put back on ad lib. TRF group fed chow diet during 8:00pm to 8:00am for three months and then these rats shifted to ad lib for three months. Control group fed chow diet at ad lib. Body weight was calculated and blood samples were collected to measure blood glucose, insulin, lipid profile and gene expression.

Results: The body weight of HFD group were significantly increased and TRF with chow diet were significantly decreased as compared to control rats ($p=0.0263$) and ($p=0.0054$) respectively. The level of HDL was reduced in rats fed with HFD whereas total cholesterol, TG and LDL were increased. TRF intervention with HFD diet reduced body weight, blood glucose level, TG and LDL and elevated the level of insulin, total cholesterol and HDL. Per1 and Bmal1 gene were up regulated in HFD group and after TRF intervention had reduced mRNA expression. TRF intervention with HFD and chow diet showed its legacy effect when put on ad lib.

Conclusion: TRF intervention is easily adaptable lifestyle modification and non-pharmacological strategy can reduces the risk factor of obesity and its associated metabolic disorders.

PE129 Clinical diabetes and therapeutics

Alleviation of metabolic abnormalities induced by streptozotocin in wistar rats by tinospora cordifolia nanoparticles- a preliminary study

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Objective: Diabetes mellitus is a metabolic disorder, which disrupts glucose, lipid, and protein metabolisms due to defective insulin secretion or activity. The disease is in desperate need of multidisciplinary treatments that are both effective and affordable. Herbal medicines have been used in the treatment of Diabetes mellitus and various other problems for a long time in folk system of medicine. Nowdays herbal nano formulation have major interest due to bioavailability, The present study was performed to see the effect of Tinospora cordifolia nanoparticles on metabolic abnormalities in streptozotocin induced Wistar rats.

Methods: Nanoparticles with an average size of 50nm were made from the stem extract of Tinospora cordifolia, characterized by biophysical techniques such as FTIR, DSR, XRD, Particle size analysis etc. and their role in alleviation of metabolic abnormalities induced by Streptozotocin in Wistar rats was studied. Therapeutic potential of nanoparticles of T. cordifolia was studied in comparison to ethanolic extract and Glybenclamide. The biochemical parameters assessed before and at 21 days of therapy included fasting blood glucose, lipid profile, kidney and liver function tests besides histological examination of pancreatic tissue.

Results: Following 21 days of administration to diabetic animals, the rate of blood glucose reduction was 57% with nanoparticle formulation compared to its ethanolic extract(45%). A promiment reduction in cholesterol and triglyceride levels were recorded. The rate of reduction of Creatinine, urea, uric acid was superior with nanoparticle formulation. A significant improvement in both enzymatic and non-enzymatic parameters were recorded with Nano-formulation compared to that of ethanolic extract. Histological examination of kidney, liver and pancreatic tissues revealed near normalization of cellular structure.

Conclusion: The present study nanoparticles of T. cordifolia supplementation exhibited a significant positive impact on all metabolic parameters. Nanoparticles of T. cordifolia appeared superior to ethanolic extract.

PE130 Clinical diabetes and therapeutics

Anti-diabetic and pancreo-protective activity of Indian herbal medicine tinospora cordifolia (willd.) and honey in streptozotocin induced diabetic rats

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Objective: From centuries Tinospora cordifolia (Willd.) (Guduchi) and honey are used as a drug of choice for Type II diabetes mellitus in traditional Indian system of medicine. It's different formulations are widely used for many disorders. Here it was planned to evaluate its anti-diabetic activity.

Methods: Aqueous extract of Tinospora cordifolia was prepared by traditional procedure of Ayurveda and assessed for its anti-diabetic activity. Diabetes was induced in normal Wistar strain albino rats by injecting streptozotocin in dose 40 mg/kg body weight (IAEC-06/09-11/02). Powdered aqueous extract of Tinospora cordifolia Linn in dose of 42.34 mg/kg was mixed with honey and administered orally to rats for 20 days respectively. Glibenclamide, in the dose 0.45mg/kg was administered to standard drug control group. The effects of treatment on bodyweights and blood glucose level were quantified on day 1,5,10,15, and 21 of experiment. On 21st day animals were sacrificed and gross histopathological changes in liver, kidney and pancreas were illustrated. By adopting standard methods, blood sugar levels, glycated hemoglobin, serum cholesterol, serum triglycerides, serum HDL, serum glutamic-pyruvic transaminase, serum glutamic oxaloacetic transaminase, serum creatinine, blood urea and serum protein levels were estimated.

Results: Significant decrease in glycated hemoglobin (pÃ0.01) and blood sugar level (pÃ0.01) were observed in treated animals comparing with diabetic rats. Serum glutamic-pyruvic transaminase (pÃ0.01) significantly reduced in test drug treated rats. In histopathological studies test drug showed moderate hepato-protective and reno-protective action. Pancreo-protective action was observed in test drug treated and standard control drug treated animals.

Conclusion: Present study shows that aqueous extract of Tinospora cordifolia (Willd.) with honey significantly reduces blood sugar levels and shows anti-diabetic effect. Hepto-protective, reno-protective and pancreo-protective actions of Tinospora cordifolia (Willd.) were revealed in this study. Tinospora cordifolia (Willd.) showed significant attenuation of increased levels of glycated hemoglobin which indicates its potential against diabetes and related complications.

PE131 Clinical diabetes and therapeutics

Clinical stages of T2DM

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Objective: The aim of this study was to analyze the results of OGTT to determined clinical stage of T2DM.

Methods: Clinic based cross-sectional study was included 332 participants with high risk of T2DM. 75gr OGTT, laboratory tests and physical examination were determined. By the OGTT results participants divided by 5 groups: Normal OGTT, IFG, IGT, IFG+IGT and Diabetes. Laboratory tests: Fasting glucose, HbA1C, Insulin, C-peptide, lipid profiles were measured and we calculated HOMA-IR, HOMA-B, HOMA-S indices.

Results: Among them 238(71.7%) women were analyzed. The mean age of the participants was 42.4±13.7 years old. Mean results of anthropometric measurement: body weight 82.2±16.7 kg; BMI 30.1±5.4 kg/m2; BF 40.1±8.6%; BM 26.1±7.2% and VF 9.9±3.6%. Mean results of laboratory tests: FBG 6.1±1.4 mmol/l; 2 hours blood glucose 9.3±3.4 mmol/l; HbA1C 5.8±1.04%; insulin 24.6±19.1 mkU/ml, C-peptide 4.3±3.2 mkU/ml, HOMA-IR 3.2±2.0, HOMA-B 140.9±60.0%, HOMA-S 48.3±35.5%, total cholesterol 4.8±0.8 mmol/l, triglyceride 2.0±0.9mmol/l, HDL 1.2±0.3 mmol/l, LDL 2.5±0.8 mmol/l were determined. Results of OGTT: There were 43 (12.9%) normal, insulin resistance 21 (6.3%), IFG 60 (18.1%), IGT (14.2%), IFG and IGT both 106 (31.9%), T2DM 54 (16.3%).

Conclusion: The results of OGTT shown 19.6% of diabetes high risk people have a normal glucose tolerance, Prediabetes and T2DM were diagnosed 80.4%. The onset of insulin resistance may be an early sign in diabetes. Therefore, addition to OGTT for screening of T2DM, it is important detection for insulin resistance.

PE133 Diabetes care & education

Expenditure pattern related to diabetic risk factors in Indonesia: a national report based study

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Objective: It is still debatable whether socio-economic factors affect the incidence of diabetes in Indonesia. We aimed to find the correlation between one of the economic factors (expenditure) with diabetes mellitus (DM) risk factors in Indonesia.

Methods: A correlational study with cross-sectional approach was conducted. Independent variable was expenditure and dependent variables were prevalence of consumption of sweet beverages, fatty foods, instant foods, lack of physical activity and central obesity prevalence. Samples were Indonesians aged at least 10-years old from 33 provinces. We obtained expenditure data from Human Development Index 2018 Report. Diabetes risk factors data were obtained from 2018 Indonesia Basic Health Research. Analysis was done by bivariate correlation tests.

Results: Expenditure was significantly related to the fatty foods and sweet beverages consumptions prevalence with r=0.422 (p=0.014) and r=0,37 (p=0.034) respectively. The 33 analyzed provinces was broken down into provinces with high and low category expenditure by median as cutoff point. From high expenditure groups, we found correlation between DM and fatty foods consumption prevalence r=0.634 (p=0.006), while from low expenditure groups, there was a correlation between DM and instant food consumption prevalence r=-0.544 (p=0.29).

Conclusion: This study explains the previous finding regarding the insignificant correlation between socioeconomic factor and diabetes in Indonesia. After splitting the provinces based on expenditure level, fatty food consumption was correlated with DM prevalence in high expenditure groups while no risk factors was found to be associated with DM in low expenditure groups. This shows a tendency towards diabetes based on food consumption in high expenditure groups, indicating that diabetes awareness is quite low among the high-spending population. This raises concern for the Indonesian government to promote awareness evenly to all degree of population in the country, especially in high expenditure groups. Further research is needed to discover the true relationship between socioeconomic factors in respect to diabetes.

PE134 Diabetes care & education

Pregnancy and diabetes disease history: correlated?

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Objective: Pregnancy, gestational diabetes and induced hypertension are frequently observed in practice among the pregnant women, but their relationships are not well realized. The article aims to develop the relationship of pregnancy on diabetes, hypertension and some other related parameters.

Methods: Statistical joint generalized linear method is used to derive the relationship.

Results: It is derived herein that diabetic women (P=0.0053) become pregnant earlier than normal women. Mean pregnancy is positively linked to glucose level (P=0.0013) and age (P<0.0001), while it is negatively linked to their joint interaction effect Glucose*Age (P=0.0003). It is partially positively linked to body mass index (BMI) (P=0.1129) and free of triceps skinfold thickness (TST) (P=0.2747), while it is negatively linked to their joint interaction effect TST*BMI (P=0.0039), and it is also positively linked to TST*Age (P<0.0001). In addition, mean pregnancy is negatively linked to insulin level (P=0.0170) and diabetes pedigree function (DPF) (P=0.0890). Variance of pregnancy is positively linked to glucose level (P=0.1061) and diastolic blood pressure (DBP) (P=0.0657), while it is negatively linked to their joint effect Glucose*DBP (P=0.0125). Variance of pregnancy is negatively linked to TST (P<0.0001) and positively linked to DPF (P=0.0309), while it is negatively linked to the interaction effect TST*DPF (P=0.0985), and positively linked to DBP*TST (P= 0.0006). In addition, variance of pregnancy is negatively linked to insulin level (P=0.0871), while it is partially positively linked to the interaction effect Insulin*DBP (P=0.1652), but free of BMI (P=0.7468).

Conclusions: It is concluded that mean pregnancy is well related to the diabetic functions such as glucose & insulin levels, diabetes history, DPF, BMI, while pregnancy's variance is well related to the diabetic functions and hypertension parameter DBP. Diabetes women become pregnant more earlier than normal women.

Key Words: Body mass index, Diastolic blood pressure, Gestational diabetes, Pregnancy

PE135 Diabetes care & education

Classification and heterogeneity of diabetes mellitus in Korea

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Objective: The individual has a wide spectrum of clinical manifestations in type 2 diabetes mellitus (T2DM). There is a lack of previous researches studying subgroups of T2DM in Korea. The purpose of this study was to define characteristics of Korean with T2DM according to subgroup.

Methods: 520 T2DM patients from Korea national diabetes program were divided into three subgroups based on BMI (≥ 25 kg/m2) as mild obesity-related diabetes group (MOD), insulinogenic index (IGI, < 0.4) as severe insulin-deficient diabetes group (SIDD) and HOMA-IR (≥ 2.7) as severe insulin-resistant diabetes group (SIRD). The subgroups were analyzed body composition and blood analysis data using SPSS program (version 27.0).

Results: In Korea, the MOD group (60.0%) was more common than the SIDD (51.9%) and SIRD group (36.7%). The results of comparing the distribution by subgroup with other countries are as follows. Germany 68.4% and Japan 52.5% in MOD group, and China 51.2% and Japan 34.4% in SIDD group were ranked. In the SIRD group, Germany 25.6%, and Japan 13.0% were ranked. Japan and Germany showed similar results to Korea. The alanine aminotransferase (ALT) level was higher in the MOD group, and the weight-related indexes and ALT level were lower in the SIDD group than other groups. The body fat percent, IGI and ALT level were higher in the SIRD group. The weight-related indexes were lower in the SIDD & SIRD group, and the insulin, HOMA-IR and ALT level were higher in the MOD & SIRD group than other groups.

Conclusion: These results indicated that the ratio of the MOD group was highest among the diabetes subgroups in Korea. An interest in obesity-related diabetes needs to increase, and treatment should also vary according to the clinical manifestations. Therefore, more research is needed in diabetes subclassification of Korea.

PE136 Diabetes care & education

A correlation between high-risk food consumption and diabetes mellitus prevalence in Indonesia: a 10 years national health report

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Objective: High-risk food consumption contributes to diabetes mellitus (DM). We aimed to find a correlation between the high-risk food consumption prevalence and DM prevalence in Indonesia.

Methods: This is a correlation study with cross-sectional approach. Independent variable is prevalence of consumption of sweet beverages, fatty foods, and instant foods with dependent variable is DM prevalence. Samples were Indonesians aged at least 10-years old from 33 provinces. All data were obtained from 2013 and 2018 Indonesia Basic Health Research. Correlations between variables were assessed by bivariate correlation and linear regression test.

Results: The results of regression analysis, it was found that in 2007-2013, instant food consumption prevalence had a correlation with DM prevalence r=0.508 (p=0.006). In 2013-2018, the results of correlation analysis, it was found that instant food and fatty foods consumption prevalence had a correlation with DM prevalence with r=-0.476 (p=0.005) and r=0.587 (p=0.000) respectively. However, in regression analysis it was found that instant food consumption prevalence isn't correlated with DM prevalence and fatty foods consumption prevalence is correlated with DM prevalence r=0.432 (p=0.016). Sweet beverages consumptions isn't correlated with DM prevalence in the last 10 years.

Conclusion: From 2007-2013 eating habit that have an impact on DM prevalence are from instant food, then in the last 5 years turned into fatty foods. Instead of sweet beverages, Consumption of fatty and/or instant foods has a tendency to DM incidence in Indonesia. This supports the established theory that fatty and instant foods contribute to metabolic syndrome leading to insulin insensitivity affecting DM. Moreover, this finding shows a shifting trend in people's eating habits, contributing to the development of the Indonesian food and beverage industry. Therefore, the government needs to pay attention to the current diet of Indonesian people to prevent chronic diseases. For Indonesian society, awareness needs to be improved in their daily diet.

PE137 Diabetes care & education

Impact of dietary mediation using low-carbohydrate diet to manage newly diagnosed type 2 diabetes mellitus patients in a tertiary care hospital

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Objective: The purpose of this study is to observe the effect of dietary intervention using low-carbohydrate diet to manage newly diagnosed type 2 diabetes mellitus

Methods: Fifty-four newly diagnosed type 2 diabetes mellitus without any treatment were selected for solely low-carbohydrate diet intervention (<130g carbohydrate) in the endocrinology unit of Tribhuvan University Teaching Hospital, Kathmandu from March to August 2019. Antidiabetic medications were not used. Individualized diet plans and repeated counseling were given and followed for 3 months. Blood glucose (fasting and postprandial), glycated hemoglobin A1c, weight, and waist circumference were compared at entry and 3 months. Statistical analysis was done using SPSS version 21.

Results: The mean±SD age was 44.77±10.32 years. The mean body weight decreased by 4.52±1.79 kg (p<0.001), mean waist circumference decreased by 7.85±0.72 cm (p<0.001), mean fasting blood glucose decreased from 10.44±3.52 mmol/L to 6.18±1.02 mmol/L (p<0.001), mean postprandial blood glucose decreased from 16.76±8.26 mmol/L to 8.26±1.66 mmol/L (p<0.001) and mean glycated hemoglobin A1c decreased by 2.38±1.49 % (p<0.001) after 3 months of low-carbohydrate diet intervention.

Conclusion: The use of a low-carbohydrate diet may effectively produce glycemic control and decrease glycated hemoglobin A1c without medication in newly diagnosed type 2 diabetes mellitus. Additionally, this diet may also help to lower weight and waist circumference in newly diagnosed type 2 diabetes mellitus.

PE138 Diabetes care & education

Age-specific diabetes education needs for persons with type 2 diabetes at younger age

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Objective: More young adults are vulnerable to Type 2 diabetes (T2D) and poorer diabetes self-management behaviors have been observed in persons with T2D at younger age. This study examined the differences on diabetes self-management behaviors, spiritual health, the quality of life, and glycemic control by age group to identify a need of age-specific diabetes education.

Methods: A cross-sectional, correlational design was used. Persons with T2D aged 20 years or older (N=178, men=114 [64.0%], mean age= 60.92±12.76; age range: 22-88 years) were recruited from a university hospital. Based on age, participants were divided by four groups (Group A (n=27) <50 years old; Group B (n=47) those in 50's; Group C (n=54) those in 60's; Group D (n=48) ≥70 years old). Diabetes self-care behaviors (Summary of Diabetes Self-Care Activities Questionnaire), spiritual health (FACIT-Sp-12) and quality of life (SF-12) were assessed with self-reported questionnaires. Glycemic control was assessed by HbA1C. All statistics analyses were performed using SPSS for Windows (version 26.0). The level of significance was set at α=.05 (two-tailed)

Results: With regard to dietary regimen, Group A, the youngest group, consumed more red meat or full-fat dairy products and poorly adhered healthy eating plan, followed by Groups B, C, D (p=.043). Group A less participated in at least 30 minutes of physical activity in the past 7 days and reported the lowest spiritual health and highest emotional distress scores. Negative expectations on the consequences of illness was reported in this group although their current physical function was the best among the groups. HbA1C (7.53%) was the highest in Group A, followed by Groups C, B, and D while statistically insignificant.

Conclusion: Interventions to support healthy coping and facilitate lifestyle modification with practical goals should be developed for people with T2D at younger age in order to enhance their empowerment.

PE139 Diabetes care & education

Wearable technology and Geo-fencing device are a boon for hypertension patients with type 2 diabetes

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Objective: It is important to monitor daily life routine activities data by a wearable devices that can obtain real-time hypertension data, help technologists understand medical aspects, and clinicians to understand technological processes them and provides assistance based on pre-determined specifications in hypertension patients. To study role of wearable (MI Band 6) and Geo-Fencing technology on nephrology data in relation to hypertension in type 2 diabetic patients in Jaipur city, India.

Methods: Total of 62 hypertension patients with type 2 diabetes were taken as subject with an equal ratio of male and female and age group between 50 to 70 years. Wearable monitoring devices like MI band-6 and Geo-Fencing device were put on the wrist of patients for 30 days and a questionnaire was filled out by each patient. In all subjects, blood pressure, blood glucose was measured on daily basis with monitoring of step count, calorie burnt, motion time, sleep monitoring, calorie consumption, monitoring heart rate to know daily routines and recording them for health purpose. Wearable bands, automatically provides a cueing sound with sensing alert when patients move out of the geo-fenced area and which stays until the subject resumes walking in virtual boundary.

Results: Present results shown that both wearable device reading showed there was a normal heart rate, more calorie burnt with better control of sugar control and average good sleep count in more physically workout, include walking in hypertension patients with type 2 diabetes compared to less physically workout patients, identified by professional physiotherapists. Both device reading showed that after changing lifestyle routine among less physically active patients, their memory loss and wandering events normalize with less requirement of drug dose.

Conclusion: By using, these wearable devices ensured their health awareness with more concerned towards exercising and demonstrate the benefit of such a context-aware system and motivate further studies.

PE140 Diabetes care & education

Diabetes knowledge in a Mongolian mothers survey by web based

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Objective: Knowledge seems more responsive to performance-based, self-care to perception-based, and glycemic control to both measures, with a preference for performance-based tools. The purpose of this study was to measure the no level of diabetes knowledge in a representative group of Mongolian mothers.

Methods: Total of 102 antenatal mothers were included in the study, who filled in a close-ended questionnaire. The questionnaire comprised of 13 questions (6 on knowledge about GDM and its risk factors, 4 about GDM screening and treatment and 3 about the consequences of GDM). The data was analyzed and results were entered using simple means and percentage. All questions were given categorical responses (yes and no) and were applied with an item score of '1', '0' respectively for positive knowledge. All participants who answered 'Yes' were given score of '1' and those who answered 'No' were given a score of '0'. The average score of mothers on knowledge of GDM and its risk factors, screening and treatment and consequences of GDM was calculated. The study is conducted by cross-sectional analytical study methods, including random sampling questionnaires and vascular blood glucose tests. Absolute values, percentages and absolute frequency and median distribution were described according to the normality data.

Results: In results Mean age was 26.7±4.9 years. 51.5% of mothers were primigravida and 0.5% of mothers had history of GDM either in present or previous pregnancy. The total knowledge score about gestational diabetes was 4.8. The score for knowledge on GDM and its risk factors was 3.18. The knowledge score for awareness on screening and treatment was 1.5 and a consequence of GDM was 0.9.

Conclusion: The amount of participants knowledge about diabetes-related issues was low in this representative Mongolian mothers.

PE142 Diabetes care & education

Nutritional management diabetes knowledge among health science undergraduate students

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Objective: To assess the level of nutritional management diabetes knowledge among health sciences students and to explore the association between knowledge and demographic profile.

Methods: In this cross-sectional study, The Nutritional Management Diabetes Knowledge Test (NMDKT) questionnaire that evaluates the knowledge of diabetes nutritional management was distributed via an online platform to the participants. A sample of 307 students for the Faculty of Health Sciences was recruited to take part in this study. A knowledge score of more than 16 over 31 was classified as good. The data were analysed by using SPSS version 20 software for Windows. Descriptive analysis was deployed to determine the score of knowledge. In addition, Pearson's Chi-square test was used to identify the association of knowledge scores with demographic data.

Results: A total of 307 students from seven different health science-related undergraduate programs, namely Nursing, Medical Laboratory Technology, Medical Imaging, Environmental Health and Safety, Physiotherapy, Occupational Therapy, and Optometry, participated in this study. The results demonstrated that Health Sciences students have poor knowledge of diabetes nutritional management as the mean score was 15.43±3.02. Students from the Nursing Program get the highest, while those from Environmental Health and Safety Program earn the lowest with the mean score of 16.42±2.80 and 14.37±3.04, respectively. Further investigation found that year of study and having a family history of diabetes were associated with the knowledge score.

Conclusion: This paper concluded that students' knowledge is poor. Therefore, it is crucial to revise the existing syllabus or curricula of the diabetes education program by improvising the topic lacking to increase awareness and knowledge of health sciences students whom one day will become health professionals.

PE143 Diabetes care & education

Assessment of diabetics community awareness in Al debag area at Wad-Madani, Gezira state, Sudan 2022

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Objective: Al-Debaga is located at Wad-Medani (Gezira state capital) with population of 4600.Its composed of 120 family and most of them have problems such as lack of awareness regarding diabetes riskfactors and complications. The aim of this study is To assess diabetics community awareness regarding type 2 diabetes and its morbidity.

Methods: A population based retrospective study have been done in a period of 5 months, we selected 200 diabetic patients out of 4600 of the general population representing 23% of the community(100 male and 100 female) between age of 35 - 54 years old, we have conducted face to face interviews, during the interview we asked about the duration of the diabetes, general knowledge about the disease, risk factors, complications, management and lifestyle modifications.

Results: Based on our conducted interviews and answers given by the patients The study have shown that 45% of the patients have uncontrolled blood glucose level, 50% of them don't differentiate between type 1 and type 2 diabetes, 20% of them don't know about the DM risk factors, 30 % have regular follow up with a doctor in the area.

Conclusion: In conclusion, half of the diabetics community at Al-Debaga area have lack of diabetes care and control, and also half of them have a lack in the knowledge and a bad attitude regarding diabetes, this is a bad indicator for their health and major cause of increasing morbidity. The diabetes care and self management programmes are highly recommended, by dedicated medical professionals and social workers who are required to provide better care and management of diabetes at the area.

PE144 Diabetes care & education

The impact of COVID 19 pandemic and economic status on diabetes care in Sudan

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Objective: The whole world is facing the current COVID-19 pandemic, the most serious Health crisis in modern times. This pandemic affects all people but it's serious in the case of Diabetes. Although Sudan has a well-established healthcare system, yet it has so many Drawbacks mainly due to economic and managerial reasons. The aim of this study is to give an insight over the diabetes care in Sudan, Assess The patient's access to medications, and assess the situation from both economic status and Patients prospective.

Methods: This is meta analysis as reviewing article using secondary data from many accredited electronic databases: Ministry of health and WHO Sudan reports and direct observation from hospitals and public pharmacies.

Results: The economic situation of Sudan and COVID 19 crisis led to a negative impact on Nutrition; Since the implementation of the complete curfew in Sudan, the closure of Markets, lack of vegetables, fruits, and the lack of basic foods, led to poor nutritional states in diabetics. It also affected Daily exercises which are one of the most important parts of Treatment, as curfew reduced the daily exercise; result in the failure to regulate blood sugar Levels. And it also affected the patient follow up due to decrease in medical staff in hospitals and closure of most follow up clinics by 62%. It also affected the Availability of the Medications Treatment was deficient in all hospitals and pharmacies by 65%, which led to The monopoly of the remaining medicines and sold at a double price.

Conclusion: Due to the Covid-19 crisis and the bad economic status of the country, Lack of healthy food, poor follow up and unavailability of medications; Diabetic Patients face a higher chances of experiencing serious complications especially when Infected with the virus.

PE145 Diabetes care & education

Effects of the insulin adherence program for patients with type 2 diabetes

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Objective: This study was conducted to evaluate the effects of the insulin adherence program(INSTAGRAM) for patients with type 2 diabetes mellitus.

Methods: This study examined a total of 63 type 2 diabetic patients for whom the initiation of insulin therapy is being considered or for patients within 6 months of undergoing insulin therapy. INSTAGRAM is a stage-matched intervention consisting of strategies for motivating patients to initiate and maintain insulin therapy using the Transtheoretical model on the stages of change, process of change, and self-efficacy. Participants were randomly assigned to either the INSTAGRAM group(experimental group, n=32) or the standard diabetes education group(control group, n=31). The INSTAGRAM group received 6 sessions(face-to-face education was conducted for the first and last sessions and telephone coaching was conducted for the second to fifth sessions) for 8 weeks. The outcomes measured were psychological insulin resistance, self-efficacy, stages of change for insulin adherence, and glycosylated hemoglobin(HbA1c).

Results: Psychological insulin resistance($p<.001$), self-efficacy($p=.001$), stages of change for insulin adherence($p=.008$) and HbA1c($p=.048$) of participants in INSTAGRAM significantly improved compared to those of the control group.

Conclusion: INSTAGRAM is effective in overcoming psychological insulin resistance and improving self-efficacy, insulin adherence, and HbA1C. Therefore, the insulin adherence program of INSTAGRAM can be recommended as a nursing intervention for type 2 diabetic patients who delay the initiation of insulin therapy.

PE146 Diabetes care & education

Nutritional status is associated with postoperative outcomes among patients with diabetes undergoing cardiac surgery: a preliminary finding

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Objective: As the prevalence of diabetes increases, the number of cardiac surgeries due to diabetic complications has sharply increased. Recent systematic review and meta-analysis has been reported that diabetes was significantly associated with postoperative outcomes. This study aimed to examine factors associated with postoperative outcomes among Korean patients undergoing cardiac surgery.

Methods: This study is a retrospective survey design using medical records. Data were collected from 758 patients who underwent elective cardiac surgery at the University-affiliated Hospital, Korea. Disease severity was measured using the European System for Cardiac Operative Risk Evaluation. Postoperative complications included clinical outcomes and length of hospitalization. Other factors included demographic and disease-related characteristics, comorbidity score, physical activity level, and nutritional status.

Results: The mean age was 62.8 years and 70.2% was men. The overall incidences of postoperative outcomes such as pleural effusion, pneumonia, pressure sore, atelectasis, and wound infection were 25.1%, 16.4%, 10.9%, 10.2%, and 2.9%, respectively. The more than average length of hospitalization days and length of intensive care unit stay days were 26.8% and 16.5%, respectively. Over 41% of patients undergone cardiac surgery had diabetes. Of postoperative outcomes, there were significantly differences in pressure sore and wound infection according to presence of diabetes ($p<.05$). In the overall population, higher malnutrition rate of postoperative nutrition status is associated with the incidence of pressure sore (OR=5.75, 95% CI=3.28, 10.10). In the subgroup analysis by presence of diabetes, only higher alcoholic intake in the group with diabetes was associated with the incidence of pressure sore (OR=2.27, 95% CI=1.00, 5.17).

Conclusion: Nutritional status should be assessed before cardiac surgery prehabilitation and may help improve postoperative outcomes. Optimal nutritional support and diabetes management should be considered in developing future cardiac rehabilitation strategies.

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PE147 Diabetes care & education

Evaluation of nutrition education interventions for type II diabetic patients

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Objective: This study evaluated the efficacy of an evidence-based nutrition education in persons with type 2 diabetes in order to identify a direction for future full-fledged community-based nutrition education to help adequate dietary modification in this population.

Methods: Patients aged between 20 and 70 years (N=30, men= 4 [13.3%], A1C>7.5%) were recruited from a diabetes clinic affiliated with a university hospital. Nutrition education consisted of orientation (writing a dietary journal), basic nutrition education (principles of diabetic diet, weight management, glycemic index), and advanced nutrition education (managing additional sugar and salt consumption after taste test). To determine the intervention efficacy, the following variables except socio-demographics were assessed twice (before and after intervention) : socio-demographic variables, dietary items from the Summary of Diabetes Self-Care Activities Questionnaire, nutritional knowledge, dietary attitude, dietary behavior, body measurement index (BMI), blood pressure, and HbA1C. All statistics analyses were performed using SPSS for Windows (version 26.0). The level of significance was set at α=.05 (two-tailed).

Results: The mean number of days to follow dietary regimen (△1.1±2.2/wk., p=0.04) and glucose monitoring (△1.9±2.5/wk., p<0.001) significantly increased, and the frequency of hypoglycemia symptoms were significantly decreased (p<0.05) after nutrition education. However, the mean score for nutritional knowledge (△0.5±2.9, p=0.50) and dietary attitude (△0.1±0.38, p=0.38) were not increased after education while dietary behavior scores increased in 10 out of 12 items, and four of the items showed significant positive changes (p<0.05). While there were no significant changes on BMI and blood pressure, HbA1C significantly decreased (△-0.7±1.3, p=0.04) after the education.

Conclusion: After the nutrition education, persons with T2D showed positive changes in dietary modification leading to glucose control. Since prevalence of type 2 diabetes is increasing in Korea, implementation of an evidence based nutrition program to those with T2D residing in a community would be important to managing diabetes and making healthier community.

PE148 Diabetes care & education

Capability of fasting plasma glucose to detect gestational diabetes

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Objective: To determine the capability of fasting plasma glucose (FPG) as a sole predictor for gestational diabetes mellitus (GDM) between 24-28 gestational weeks (GW) in a high-risk population.

Methods: This was an observational prospective study performed in the Endocrinology Department, Dr. José E. González University Hospital in Monterrey, Mexico. We included all pregnant women between 24-28 GW in who a 75-gram oral glucose tolerance (OGT) test was indicated from January 2017 to May2019. Only 325 out of 1280 pregnant women taking the testwere between 24-28 GW, and 127 women under 18 years, with pregestational diabetes, twin pregnancies or incomplete OGT test were excluded.

Results: Overall, median age was 24 (20-28) years and 41/198 subjects (24.5%) developed GDM. As expected, higher mean body weight (76.8±17.6 vs 67.4±13.3 kg, P<0.001), BMI (30.4±6.5 vs 27.4±4.9 kg/m2, P=0.002), diastolic blood pressure (69.6±6.9 vs 64.9±7.4 mmHg, P<0.001) and FPG (94.2±11.8 vs 78.9±8.0 mg/dL, P<0.001) were observed in patients with GDM, compared to healthy subjects, respectively. Of the 41 patients with GDM, 68% had an altered FPG. After a ROC analysis, we determined that a FPG cut-offs of 81 mg/dLand 91 mg/dL had a sensibility of 88.4% and 72.5%, andnegative predictive value of 93.8% and 91.6% for GDM, respectively. No differences in maternal-fetal outcomes were observed.

Conclusion: According to our data, 66% (125/198) pregnant women between 24-28 GW could have avoided a 75-gram OGT by only considering a FPG under 81 mg/dL and above 91 mg/dL. Therefore, in a high-risk population such as ours, more than 50% of oral glucose tolerance tests could be avoided, while being prioritized in patients between these FPG cut-offs, representing a reduction in health care costs in our health care system.

PE149 Diabetes care & education

Women with diabetes and depression: a psychosocial challenge

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Objective: To evaluate the levels of depression faced by diabetic women.

Methods: This pilot study was conducted on 40 diabetic women's between the age group of 30-65 years who were selected by random sampling method. The data were collected with the help of a patient health questionnaire (PHQ-9) which is a standard questionnaire to assess the level of depression.

Results: Result showed that 56 % diabetic women's PHQ-9 scores ranges between 5-9 that shows mild depression while 18 % PHQ-9 scores around 10-14 that represent moderate depression and 9% were found moderately severe depressed with PHQ-9 score between 14-19.

Conclusion: Most of the diabetic women's were affected by mild depression. It is essential for health care providers to use appropriate coping mechanism such as building psychological contact with the patient, including family and friends as part of social support and empower patient and also needs to increasing awareness, regular monitoring and consulting the doctor with complete process of managing diabetes. This study needs to be conducted on a large sample size and it will be helpful to get better results.

PE150 Diabetes care & education

National model of diabetes and diabetic retinopathy care in Mongolia

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Objective: To create Mongolian model of integrated, high quality and affordable care for DM and its complications.

Methods: Mongolian diabetes association together with Ministry of health and Orbis international is implementing National model of diabetes and diabetic retinopathy care in Mongolia project funded by World Diabetes Foundation. The project implemented from November 9, 2020, to November 09, 2023.

Results: Five fully equipped diabetes centers established in Ulaanbaatar-3, in Darkhan-Uul province-1 and Khovd province-1. WHO package of essential NCD interventions (PEN) and HEARTS-D protocol adapted into Mongolian health system settings. The essential tools and equipment supplied from Orbis international. Forty-five health professionals including endocrinologists, diabetes educators, ophthalmologists, nutritionists, and physical therapists have trained.

Conclusion: Building capacity is essential for diabetes treatment service strengthening. This WDF project is the best practice of international partnership and cooperation.

PE151 Diabetes care & education

Development of augmented reality-based food model to demonstrate the estimation of food portion in adherence with 3J diet recommendation for diabetes mellitus patients in Indonesia

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Objective: Prevalence of Diabetes Mellitus in Indonesia increased from 1.5% to 2.0% within 5 years period. Diabetes mellitus patients were advocated to implement 3 J principal namely "Jumlah" (Food Portion); "Jenis" (Food Variety); and "Jam" (Eating schedule) during nutrition counseling. The Pandemic disruption made nutrition counseling shift from the conventional method to tele-counseling method, which needs some adjustment in communication delivery and supporting media. As a result, we developed a novel food model using augmented reality technology to demonstrate food portion estimation.

Methods: The application development involved ideation, composing 3D assets, building the augmented reality application, and beta testing. Ideation was carried out to consider the need for nutrition counseling media and food variety that are widely consumed to be displayed as food model, Food model 3D assets preparation was carried out by taking photos and measuring actual food ingredients in one portion to be the material 3D assets design.

Results: The mobile application was developed for the Android operating system. The number of 3D assets for the food model consists of 7 groups, namely staple food ingredients, animal protein, vegetable protein, vegetables, fruit, milk, and fat sources in one serving. The application is used by scanning the marker in the form of a barcode then a food model will appear in the form of a 3-dimensional augmented reality image. The data displayed is the name of the food, size dimensions, weight for each 1 serving, and nutritional content for 1 serving. Beta testing of the application is carried out by health nutrition students by comparing the results of the size and appearance displayed in the form of 3-dimensional augmented reality images and dimensions of real food ingredients.

Conclusion: Augmented reality-based food model could be used in tele-counseling and improvement to add more variety 3D-assets of food model is needed in the future.

PE152 Diabetes care & education

The association between relative handgrip strength and type 2 diabetes among Korean midlife women

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Objective: Midlife women are at a risk of developing diabetes owing to a decrease in female hormones due to menopause. Determination of handgrip strength (HGS) is a basic method for evaluating muscle strength, which also decreases with age. This study aimed to investigate the association between HGS and type 2 diabetes in Korean midlife women.

Methods: We selected 4,261 midlife women aged 40-65 years (52.01±7.2 years) from the participants of the Korea National Health and Nutrition Examination Survey (KNHANES; 2017-2019). HGS was measured using a digital grip meter, and the prevalence of diabetes was calculated by dividing HGS into four quantiles. The data were analyzed by Independent t-test, Chi-square, one-way ANOVA, and Logistic regression analysis using the SPSS 28.0 software.

Results: The prevalence of type 2 diabetes in the study participants was 7.5% (n=318). Age, family income, education, alcohol consumption, body mass index, menopausal status, performing aerobic exercise, restriction in activity, performing strengthening exercise, presence of chronic diseases, and HbA1c were significantly associated with relative HGS. Participants in the normal, pre-diabetic, and diabetic groups had low absolute HGS (p=.026; F=3.64) and relative HGS (p<.001; F=90.12), respectively. Logistic regression analysis revealed that the odds ratios (OR) (95% confidence intervals) for diabetes were 0.59 (0.43-0.81), 0.68 (0.48-0.97), and 0.63 (0.40-0.98), based on the first quantile of HGS, which is the lowest relative HGS while controlling for confounding variables.

Conclusion: This study revealed the significant association between type 2 diabetes and relative HGS among midlife women. Interventions for increasing HGS is recommended to improve diabetes control for midlife women in Korea.

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PE153 Diabetes care & education

The mediating effect of depression in relationship between stress and suicide ideation in patients with diabetes

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Objective: The purpose of this study was to examine the mediating effect of depression on the relationship between stress and suicide ideation.

Methods: A total of 173 patients in diabetes group education at K University Hospital by completing the following questionnaires: Stress, Depression, Suicide Ideation. Frequency analysis, descriptive statistics, mean comparison, correlation analysis, and mediating effect analysis were performed with questionnaires data.

Results: As a result of the study, 53.8% of patients who experienced moderate or more stress, 57.9% of patients who experienced mild or more depression (20.9% of moderate or more), and 10.4% of patients had suicidal ideation. All variables showed a positive correlation. Depression in diabetic patients was found to significantly mediate the effect of stress on suicidal ideation even when education level, marital status, occupation, health insurance, smoking cessation, drinking, exercise, and subjective health were controlled.

Conclusion: Stress management and depression screening is important for preventing suicide and improving mental health in diabetic patients. So Psychosocial interventions such as Stress management and depression screening need to be included in diabetes education counseling.

PE154 Diabetes care & education

Utilization of diabetes care services during covid 19-pandemic in pokhara metropolitan, Nepal: a cross sectional study from the perspectives of diabetes mellitus patients

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Objective: Diabetes Mellitus is a metabolic disorder requiring continuous medical care. People with diabetes suffer disproportionately from acute Corona Virus Disease-19 (COVID-19) with serious complications. Lockdown strategies compromised routine diabetic care services. American Diabetes Association (ADA) has recommended to visit the diabetes centers more than two times in a year for those with deranged glycemic level as the effective utilization of diabetes health service. We aim to explore the factors affecting diabetes care services utilization during COVID 19 pandemic in resource constrain nation.

Methods: Consented 160 adult diabetes patients aged >18 years with at least one year history of diabetes mellitus and at least second time of visiting one of the large tertiary hospital and diabetes dedicated clinic with highest patients flow. Semi structured questionnaire was adopted for self-reported utilization of diabetes care services dated October 2020 to October 2021. Utilization of diabetes health service during COVID pandemics as >2 visits/year based on. Univariate and bivariate analyses done to determine the factors associated with diabetes care utilization.

Results: Only 42% got COVID positive and 46% of diabetic patients utilize the diabetes health service as recommended by ADA (>2 visits/year). Only 20% of them utilized the service through video call and telephone. Duration of disease, cancellation of appointment, occupation, residency, mode of transport, treatment place, travel expense, satisfaction with health-workers were significantly associated with utilization (P<0.001). Formal sector occupation, urban & semi-urban residency, specialized health service prioritizer and duration of diabetes with less than 4 years were more likely to utilize diabetic care services during pandemics. (OR: 6,3,13 & 2 with P<0.05)

Conclusion: Diabetes health service utilization during pandemic was compromised. But the rays of hope still exist through virtual technology. We suggest future integration of digital tools during and beyond the unforeseen pandemic to prevent further deterioration of metabolic disorders.

PE155 Diabetes care & education

A systematic review of taxonomy and intervention strategies to improve medication adherence using emerge approach: a preliminary finding

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Objective: Common problems include unclear or inconsistent definition and taxonomy for medication adherence (MA). This systematic review aimed to evaluate the intervention strategies of RCT using new guidelines to improve the quality of MA research reporting.

Methods: This systematic review included twenty studies of nurse-led interventions on MA for adults taking medication for diabetes or metabolic syndrome. The ESPACOMP Medication Adherence Reporting Guidelines (EMERGE) includes outlining the minimum reporting criteria for MA research: three phases of MA (initiation, implementation, and persistence); precise operational definition; MA measurement; and the analysis results relevant to each phase. CMA 3.0 was used to calculate the pooled effect sizes with 95% CIs.

Results: Most studies included the implementation or persistence phase of MA, while only one included all phases of MA. Five studies did not report which phases of MA were examined, as recommended by the EMERGE. While eight studies provided a precise operational definition, the other ten only provided an operational definition as a measurement scale. Two studies did not report a precise operational definition of MA. All studies used multiple strategies with a mode of three intervention strategies out of 15 categories, ranging from 2 to 8. 'Provision of device/material' and 'education/discussion' were the most frequently used strategy (n=14), followed by 'use of guideline/protocol/script', 'problem-solving', training/ monitoring', and 'behavioural incentives/reinforcement. A quarter of studies provided interventions to healthcare providers, families, and patients.

Conclusion: While two and more intervention strategies were used to improve MA, the lack of a standard taxonomy made it difficult to systematically classify the strategies in this study. Thus, future research for MA should include the minimum reporting criteria relevant to each phase of MA using EMERGE.

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PE156 Diabetes care & education

Treatment cost of type 1 diabetic patients in Mongolia

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Objective: Type 1 diabetes is the most common autoimmune disorder in childhood and adolescence. Treatment of type 1 diabetes consists of life long insulin depedency which multiple injections per day. Blood glucose monitoring is essential in the safe management of diabetes to help prevent acute and chronic complications. Over a million children and adolescents have type 1 diabetes. In IDF Diabetes Atlas 8th Edition 2017 reports, Mongolia has 183 children and adolescence with type 1 diabetes and newly diagnosed each year 24 children and adolescents. Aim of this study was to estimate economic burden for Type 1 diabetic patients around a year in Mongolia.

Methods: We analysed only insulin injection related consumption costs by prices of short and long-acting insulins, insulin pen and pump, blood glucose (SMBG, CGMS), keton and HbA1c monitoring by 200 patients per year in statewide. Estimation of economic burden for Type 1 diabetic patients in Mongolia based on real market price and by levels of care structure such as recommended, limited and comprehensive care.

Results: Recommended level of care: demanded 641.664 USD per year/200 patients. Thereof 36% from state budget and 64% from patients pocket today. Comprehensive level of care: demanded 1.696.512 USD per year/200 patients. Thereof 7% from state budget and 93% from patients pocket. Limited level of care: demanded 251.136 USD per year/200 patients. Thereof 55% from state budget and 45% from patients pocket.

Conclusion: Estimated economic burden is very high by recommended level of care for Type 1 diabetic patients in Mongolia. It mean parents which Type 1 diabetes children and adolescence need to pay 2059 USD per year from pocket and it is 42% of family income. In Mongolia, it is neccessary to decrease economic burden of family which Type 1 diabetic patients by increasing state budget and improving health insurance system.

PE157 Diabetes care & education

Behavioral study of bakery users in diabetes

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Objective: Health and food sectors in Mongolia are in the development stage comparatively with the world, diabetes is increasing dramatically as estimated by the survey of International Diabetic Association. For instance the registered diabetic patients are increased from 97300 in 2017 to 119000 in 2021. Exercises and proper nutrition are crucial for diabetic patients in sugar as well, then these people needs to take attention in food. However, many studies are done in nutrition, no research has not been done particularly on behavior of persons who consume sugar free cakes and cookies.

Methods: The survey respondents were 200 inpatients of Endomed endocrine-diabetes hospital by the individual interview method; and 138 participants from Facebook group for diabetic patients by online questionnaire. When we explain importance of sugar free cakes and cookies, they became motivated and involved actively in the survey. Cronbach' alpha score of the survey was 0.871 and considered the survey data is reliable.

Results: Totally 279 survey participants out of 368 or 75.8 percent answered that they are in trouble when use products with sugar. But 176 participants out of 368 or 47.8 percent do not substitude sugar when they are in trouble using sugar. In total 37.2 percent of participants seek sugar free cakes and cookies, 25.5 percent seek sometimes and 37.2 percent do not seek it. This shows that sugar free cakes and cookies are not readily available. It is evident by the answer that such products are seldom found by 54.9 percent of participants and not available by 45.1 percent of participants. Then no participant answered that it is available.

Conclusion: Special bakery is in need to diabetic patients in order to improve their quality of life and maintain treatment results

PE158 Diabetes care & education

Effect of Zouitina Prestige Extra Virgin Olive Oil (EVOO) enriched in bioactive compounds on anthropometric indices and appetite among individuals at risk for diabetes

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Objective: Diabetes is one of the global burden disease and responsible for 6.7 million deaths and it can be prevented by adequate strategies in dietary intake. Consumption of EVOO in daily diet have reported benefits on human health associated with enhanced anti-oxidant, insulin sensitivity, and anti-cholesterol functions, which are considered integral to prevent and manage T2DM.The best and highest quality of EVOO must be able to pass a organoleptic evaluation by a panel recognized by the International Olive Council (IOC), rich in essential fatty acids and polyphenols. This study aims to analysis organoleptic, fatty acids profiles, polyphenols and assess the effects on supplementation consumption of EVOO on anthropometrical parameters and food intake frequencies among Zouitina Prestige EVOO consumers.

Methods: Organoleptic test, fatty acids profiling and polyphenols were analysed according to standard methods recognized by IOC. Randomize online questionnaire surveying was distribute for historical and anthropometric data (weight, BMI, mid upper arm circumference (MUAC), waist circumference, hip circumference and shoulder width) to determine of normal, pre diabetic and diabetic consumers. Furthermore, recall method for the food intake of participants before and after consumption EVOO also recorded. Based on this, food intake frequencies and nutritive value of diets of subjects was calculated.

Results: High quality of Zouitina Prestige EVOO with low acidity (0.09%), organoleptic test of median defect 0, have high MUFA such as oleic acid (72.98%) and PUFA (6.93%) and total polyphenols 215 mg/kg caffeic acid. Demographic data pattern showed consumers mostly age range 30 and above, majority previously had consumes olive oil. No significance different in BMI, however slightly showed reduction in certain anthropometrical parameters.

Conclusion: This study contributes to understanding on anthropometric status of the participants and how consumption of EVOO in their diet contribute to their food intake frequencies in preventing and managing diabetic dietary and at same time controlling diabetic disease.

PE159 Diabetes complications-basic & translational

Association of blood pressure with epigenetic modification of candidate gene in patients with type 2 diabetes

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Objective: The coexistence of diabetes and hypertension worsen clinical outcomes with respect to both microvascular and macrovascular disease. The coexistence of T2DM and hypertension confers a dramatically increased risk of vascular complications and death by 2-4 folds, compared with the normotensive and nondiabetic adults. **Objective:** The aim of study is to evaluate systolic and diastolic pressure in patients with T2DM with special reference to DNA methylation status of promoter region in CpG island of TGFβ-1 gene and its association with circulatory TGFβ-1.

Methods: A total of 98 subjects including 59 T2DM and 39 healthy controls were recruited in study. Individuals with more than 5 years history of diabetes were recruited in T2DM group. Circulatory TGFβ-1 levels were measured by ELISA and DNA methylation study was performed using methylation specific PCR.

Results: Diabetic family history, tobacco chewing habit and glycosylated hemoglobin were also found significantly associated with T2DM. Mean of systolic and diastolic pressure were found significantly increased in diabetic group as compared to control (130.35±23.69 mmHg vs 115.08±8.01mmHg, $p < 0.0001$ and 77.37±11.84 mmHg vs 70.74±9.95 mmHg, 0.006 respectively). Circulatory levels of TGFβ-1 were significantly higher in T2DM (p=0.006). ROC analysis of TGFβ- 1 showed 81.0% sensitivity, 71.8% specificity at cut off value 244.75 ng/ml and area under curve was 84.3%. Systolic pressure and diastolic pressure were significantly increased in unmethylated individuals (p=0.038, p=0.035). A total of 20 DM patients had hypomethylation in CpG island which was significantly (p=<0.001).

Conclusion: Therefore, methylation status of TGFβ-1 gene promoter can be better predictor for hypertension in T2DM.

PE161 Diabetes complications-basic & translational

The change of pancreatic innervation in relation to the progression of diabetic peripheral neuropathy

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Objective: To investigate the relationship between subcutaneous sensory nerve degeneration and pancreatic autonomic nerve changes in diabetes.

Methods: Animals were divided into 3 groups according to the severity of diabetes, and each group included rats with normal, mild diabetes, and severe diabetes. Peripheral nerves obtained from the skin and pancreas were compared quantitatively at 8, 12, and 16 weeks after diabetes induction.

Results: The intraepidermal nerve fiber density (IENFD) was more decreased according to the severity of hyperglycemia degree and longer duration of diabetes (14.1±1.72, 13.2±1.82, and 12.2±1.50, at 8 weeks, 13.9±1.57, 12.8±1.98, and 11.4±1.07, at 12 weeks, 12.9±1.54, 10.8±1.88, and 7.4±0.57. at 16 weeks, normal, mild DM, and severe DM, respectively, $p<0.05$). Neuronal quantity assessed by PGP 9.5 stained area in the islets of pancreas also declined as diabetes progressed and hyperglycemia was severe (301,910.8±14,554, 266,800.1±12,554, and 147,750.3±11,011, at 8 weeks, 305,620.5±16,565, 254,850.5±12,504, and 135,605.8±12,405, at 12 weeks, 285,780.2±15,405, 215,450.2±16,052, and 105,650.9±14,052, (μm^2), at 16 weeks, normal, mild DM, and severe DM, respectively, $p<0.05$). In the association between IENFD and pancreatic innervation, each group showed a similar trend of reductive relation at 8, 12, and 16 weeks.

Conclusion: Our study showed a close relationship between cutaneous sensory neuropathy and a quantitative decrease in pancreatic nerves in diabetes. Therefore, a more intensive evaluation of autonomic neuropathy in diverse enteric organs including the pancreas needs to be performed when sensory neuropathy is detected in diabetes.

PE162 Diabetes complications-basic & translational

Involvement of calcium regulated proteins in the antiapoptotic effect of philanthotoxin-343 against NMDA-induced retinal ganglion cell apoptosis in sprague dawley rats

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Objective: Irreversible vision loss due to retinal ganglion cell (RGC) apoptosis caused by N-methyl-D-aspartate receptor (NMDAR) mediated excitotoxicity is a common pathological feature in several retinal and optic nerve diseases including diabetic retinopathy. Excessive Ca2+ influx after NMDAR stimulation modulates Ca2+-regulated proteins such as calpain-1, cabin-1 and calcineurin, leading to increased expression of pro-apoptotic proteins BAX and Caspase-3, while reducing anti-apoptotic protein BCL. In the present study, we investigated the mechanisms of neuroprotective effect of philanthotoxin (PhTX)-343 against NMDA-induced excitotoxic injury in rat retinas.

Methods: Sprague-Dawley rats were divided into; Group I (negative control) was intravitreally injected with phosphate buffer saline, Group II with NMDA and Group III with PhTX-343 24 h prior to NMDA. Seven days post-treatment, retinal tissues were harvested and subjected to H&E staining, ELISA (Calpain-1, Cabin-1, Calcineurin, BAX, Caspase-3, BCL), immunohistochemistry (Caspase-3, Brn3A, a marker specific to surviving RGCs) and PCR (calpain, cabin-1, calcineurin).

Results: In comparison with negative control, the NMDA-treated group displayed extensive loss of retinal cell nuclei and thinning of the ganglion cell layer (GCL), greater calpain, calcineurin, BAX, caspase-3, lower cabin-1, BCL, and markedly lower Brn3A expression. Treatment with PhTX-343 resulted in significantly higher number of retinal nuclei within the GCL compared to the NMDA group. Strikingly lower calpain and calcineurin, and greater cabin-1 expression was seen in PhTX-343 treated retinas as opposed to the NMDA group. In PhTX-343 group, retinas showed lower BAX and caspase 3 expression, while BCL-2 expression was greater in contrast to the NMDA group. PhTX-343 treatment was associated with greater RGC survival as the Brn3A expression was significantly greater in comparison to the NMDA group. All parameters measured for PhTX-343 group were statistically comparable with the negative control.

Conclusion: In conclusion, PhTX-343 protected against NMDA-induced RGC apoptosis by modulating the expression of calpain-1, cabin-1, and calcineurin.

PE163 Diabetes complications-basic & translational

Depression associated factors among diabetic patients in Bihar

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Objective: Diabetes mellitus and depression are two major public health problems which can coexist and influence each other. Identification of the predictive and associated factors with depression among diabetics can facilitate the task of clinicians. Evaluate the socio-demographic and clinical factors associated with depression among patients having diabetes mellitus (DM).

Methods: A cross sectional study was conducted among 200 diabetic patients followed in the Endocrinology Department at Muzaffarpur District Hospital. Patients with a psychiatric history were excluded at the outset. Depression was diagnosed according to DSM-V criteria and the severity determined via the Hamilton score scale.

Results: Our patients were aged between 25 and 85 years old, 58% of the participants in the study were women. The mean duration of the diabetic disease was of 10 years (from 1 to 50 years). Type 2 diabetes was found among 87% of patients. According to DSM-V diagnosis criteria, we found that 12% of our patients suffered from Major Depressive disorder (MDD). Among this group having MDD, 64% were female,.We also found that the majority of patients with MDD (80%), had at least one chronic disease in addition to diabetes and that a good proportion of them (75%) was treated with insulin.

Conclusion: Our study showed that diabetic patients suffering from MDD are mostly women but since proportion of women was most important in our study, these results should be evaluated.

PE164 Diabetes complications-basic & translational

Therapeutic role of yogic asana on type 2 diabetes mellitus subjects by measuring glycosylated haemoglobin and evaluating therapeutic modulation

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Objective: The present study was conducted to examine effect of yoga practices onclinical parameters.glycosylated hemoglobin, blood glucose levelin subjects with type 2 diabetes mellitus (T2DM).

Methods: Patients with type 2 diabetes mellitus were randomized in the two groups. Group-A add-on yoga and Group-B without yoga. They were assessed by measurementHbA1C and clinical parameters of Diabetic before and after giving the intervention. The assessments of means were compared and Significance of Chance calculated.

Results: We found Group A there was significant decrease in FBG levels from basal 190.08 +/- 18.54 in mg/dl to 141.5 +/- 16.3 in mg/dl after yoga regimen. The PBG levels decreased from 276.54 +/- 20.62 in mg/dl to 201.75 +/- 21.24 in mg/dl, HbA1C showed a decrease from 9.03 +/- 0.29% to 7.83 +/- 0.53% after yoga regimen. The pulse rate, systolic and diastolic BP decreased significantly from 86.45 +/- 2.0 to 77.65 +/- 2.5 pulse/min from 142.0 +/- 3.9 to 126.0 +/- 3.2 mm of Hg and 86.7 +/- 2.5 mm of Hg to 75.5 +/- 2.1 mm of Hg after yoga regimen respectively.

Conclusion: These findings suggest that better glycaemic control was seen in Type 2 DM. The exact mechanism as to how these postures and controlled breathing interact with somato-neuro-endocrine mechanism affecting metabolic and autonomic functions remains to be worked out that we can conclude that yoga is beneficial as an alternative therapy when combined with the conventional therapy

PE165 Diabetes complications-basic & translational

Advanced Glycation End (AGE) in diabetes and myogenic program: a prospective study of curcumin and gingerol in maintaining the balance between health and the diseased state

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Objective: Explicate the effect of MG induced AGEs in the muscle development program and diabetes, and its possible amelioration on supplementation of natural compounds.

Methods: Methylglyoxal (MG) treated C2C12 cells were accessed for production of AGEs. Different concentrations of MG were accessed for their effect on ROS production, and as such on cellular differentiation. Effect of RAGEkd on cellular differentiation was analyzed by Real time PCR and Western blotting. Natural compounds were screened for effects on proliferation and differentiation of C2C12 cells. Studies pertaining to regulation of MSTN interaction to ACVRIIB were performed using protein-ligand and protein-protein interaction approaches for determining involvement of curcumin and gingerol in the myogenic program.

Results: MG increased production of reactive oxygen species (ROS) and reduced myotube formation. Additionally, RAGE (receptor for advanced glycation end product) expression was found up-regulated and MYOD and myogenin (MYOG) expressions were concomitantly down-regulated in MG-treated cells. RAGE knock-down (RAGEkd) reduced the expressions of MYOD and MYOG and myotube formation. Treating RAGEkd C2C12 cells with curcumin or gingerol diminished the effect of RAGE knockdown on myotube formation, and increased in the expressions of MYOD and MYOG. In silico studies of interactions between curcumin or gingerol and myostatin (MSTN; an inhibitor of myogenesis) and their observed affinities for activin receptor type IIB (ACVRIIB) suggested curcumin and gingerol reduce the interaction between MSTN and ACVRIIB.

Conclusion: The findings of this study suggest enhanced AGE production and subsequent RAGE-AGE interaction obstruct the muscle development program, and curcumin and gingerol attenuate the effect of AGEs on muscle satellite cells (MSCs).

PE166 Diabetes complications-basic & translational

Therapeutic benefit of prunin in the medicine for the treatment of diabetes related complications: pharmacological activities with molecular mechanism

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Objective: In the modern medicine, herbal medicine have important place in the Asian countries. Herbal medicines have numerous pharmacological activities due to the presence of different phytoconstituents in the medicinal plants. Herbal medicine is mainly derived from different natural sources such as roots, seeds, bark, leaf, flowers and whole plants. Prunin was found to be present in the Prunus davidiana. Prunin is an important flavonoidal class secondary metabolite.

Methods: Biological importance of Prunin in the medicine for the treatment of diabetes and related secondary complication has been investigated through scientific data analysis of different research work. Here in the present work, numerous scientific data were analyzed in order to know the therapeutic importance of prunin in the medicine for the treatment of diabetes and related secondary complications. Other pharmacological data were also collected and analyzed in order to support the preset work.

Results: Scientific data were analyzed in the present work and revealed the biological significance of prunin in the medicine for the treatment of diabetes and related secondary complications. Here in the present work, through different experimental works scientific data analysis, it was concluded that prunin can treat diabetes and associated hyperglycemia and hyperlipidemia condition in the diabetic rats. Scientific data analysis also signified the α-glucosidase inhibitory potential of prunin in the medicine, which could be beneficial for the treatment of diabetes and associated complications. However, it also stimulated the glucose uptake in insulin-resistant hepatocytes in some other scientific research work. Further, detailed pharmacological study also signified its effectiveness against insulin resistance.

Conclusion: Scientific data analysis signified the therapeutic effectiveness of prunin for the treatment of diabetes and associated secondary complications in the medicine.

PE167 Diabetes complications-basic & translational

Transcriptomic profiling of human placenta in gestational diabetes mellitus

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Objective: Gestational diabetes mellitus (GDM) is associated with an increased risk of adverse pregnancy outcomes. Increasing evidence shows that placentation defects may play important roles in GDM. However, our understanding of the human placenta remains limited. This study is to investigate the role and contribution of placenta in the GDM.

Methods: Twelve GDM patients and Ten normal pregnant participant were recruited from Chungnam National University Hospital. All of the GDM patients were diagnosed according to the guideline of Korean Diabetes Association. Transcriptomics analysis were performed on the placental tissues from GDM patients and normal pregnant participants. Differentially expressed canonical pathways were analyzed between GDM group and control group based on RNA seq.

Results: Differentially expressed genes (DEGs) were identified using the DESeq with P value<0.05 for significantly differential expression. CNN1, ACTG2, ANGPT1, TNMD, GPC6, ACTA2, VCAM1 were significantly upregulated in GDM patients compared to in controls. GO enrichment and KEGG pathway enrichment analysis of DEGs revealed the upregulation of calcium dependent cell to cell adhesion signaling, cilium organization signaling, non-motile cilium assembly signaling, and vascular smooth muscle contraction signaling in placentas from GDM patients compared to in controls.

Conclusion: The results of the current study demonstrated transcriptomic profiling of human placenta and the contributions of altered diverse signaling in GDM placenta.

PE168 Diabetes complications-basic & translational

Therapeutic potential of kakkalide in the medicine for the treatment of diabetes and related secondary complications of human being

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Objective: Plants have been used as an alternative medicine for the treatment of human health complications including diabetes and associated secondary complications. Several medicinal plants and their derived secondary products have been used as a medicine and food because of their rich source of natural active phytochemicals. Plant derived products have been used in medicine for the treatment of numerous human health complications since very ancient times. Kakkalide is the isoflavone class phytochemical found to be present in the Pueraria lobata.

Methods: Therapeutic potential of kakkalide for the treatment of diabetes and related secondary complications have been investigated in the present work through scientific data analysis in order to know their therapeutic effectiveness in the medicine. Here in the present work, antidiabetic, Hypolipidemic and aldose reductase potential of kakkalide have been investigated through scientific data analysis of various research works. Biological potential of kakkalide in the medicine for the treatment of Human metabolic disorders have been investigated through scientific data analysis. However molecular mechanism of kakkalide for their anti-diabetic potential has been also investigated through scientific data analysis.

Results: Scientific data analysis revealed the biological importance of kakkalide in the medicine because of their significant antihyperlipidemic, and antioxidant activity. Scientific data analysis of different scientific research work revealed their biological potential on insulin resistance and ameliorated insulin-resistant endothelial dysfunction. Further scientific data analysis also signified the biological potential of kakkalide in the medicine for their inhibitory potential on rat lens aldose reductase which could be beneficial for the treatment of diabetes and associated secondary complications including glaucoma. However in some other scientific research work kakkalide have significant effect on total cholesterol and triglyceride level in the hyperlipidemic mice.

Conclusion: Scientific data analysis of different research work revealed the therapeutic potential of kakkalide in the medicine for the treatment of diabetes and related secondary complications.

PE169 Diabetes complications-basic & translational

GA/HbA1C ratio as a reliable follow up marker in different CKD stages with T2DM

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Objective: The present study aimed to evaluate the reliability of using GA/HbA1c ratio in different stages of chronic kidney disease associated with type 2 diabetes mellitus.

Methods: Glycated albumin (GA) and glycosylated hemoglobin (HbA1c) levels were measured in patients of chronic kidney disease of stages I, II, III and IV based on estimated glomerular filtration rate (mL/min), according to KDOQI guidelines with Type 2 Diabetes Mellitus along with healthy persons as control. GA levels were measured using ELISA method while HbA1c was estimated through chromatography. Using values of GA/HbA1c ratio was obtained and p values

Results: The results showed that GA/HbA1c ratio within patients of CKD stage I, II, III and IV with T2DM were considered to be significant (p

Conclusion: The ratio of GA/HbA1c can be used as a RELIABLE follow up marker especially in different stages of CKD with T2DM where HbA1c alone can't be used due to its false credibility.

PE171 Diabetes complications-basic & translational

Relationships between cardio-ankle vascular index and diabetic retinopathy in Mongolian patients with type 2 diabetes mellitus

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Objective: The aim of this study was to clarify the clinical significance of CAVI for diabetic retinopathy in Mongolian patients with type 2 diabetes mellitus.

Methods: This cross-sectional study enrolled 199 patients with type 2 diabetes mellitus. (153 males and 46 females). DR was diagnosed using the International Clinical Disease Severity Scale of American Academy of Ophthalmology. The VaSera VS-1000N was used to measure CAVI. Associations between CAVI and various clinical parameters were examined. Patients were divided into three groups according to the CAVI: low (CAVI<8, n=89), moderate (8≤CAVI≤9, n=57), and high (CAVI>9, n=53). The clinical characteristics of the groups were compared using an ANOVA and a chi-square test.

Results: The mean age of patients was 53.9±9.7 years and the mean CAVI value was 8.22±1.29. Variables significantly correlated with CAVI were waist circumference (Pearson r=-0.244, p=0.01), BMI (Pearson r=-0.274, p<0.001), Systolic blood pressure (Pearson r=0.187, p=0.008), IMT (Pearson r=0.252 p<0.001), hemoglobin (Pearson r=-0.178 p=0.012), creatinine (r=0.198 p=0.005). The CAVI were significant correlation with age (B=0.075, r2=0.321, 95% CI 0.06 and 0.09, p<0.001) (Pearson r=-0.567, p<0.001). Mean IMT (0.92±0.23 mm vs. 1.02±0.21 mm vs. 1.07±0.28 mm, in the low, moderate, and high groups, respectively) increased with increasing CAVI P=0.001. In the whole population DR was diagnosed in 35 (17.6%) patients. Thirty three patients (16.58%) had a NPDR, 2 patients (1%) had a PDR. CAVI value was clearly higher in patients with DR (8.85±1.22) than in those without DR (8.08±1.26) (P=0.001). The prevalence of PDR (11.2% vs. 12.3% vs. 34% in the low, moderate, and high groups, respectively) increased in proportion to the CAVI score p=0.001.

Conclusion: We showed a significant relationship between CAVI and diabetic retinopathy in patients with type 2 diabetes mellitus. CAVI was positively correlated with IMT.

PE174 Diabetes complications-clinical & epidemiology

Type 2 diabetes and dyslipidemia among Filipino adults

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Objective: This study reviewed the results of the Philippine National Nutrition Survey with the purpose of describing the association between lipid abnormalities and type 2 diabetes mellitus among Filipino adults.

Methods: Multi-stage stratified random sampling was employed and 19,642 participants were enumerated. Blood samples were drawn to determine fasting blood sugar (FBS), cholesterol, HDL and LDL, and triglycerides levels.

Results: The study showed that the prevalence of Type 2 DM in the sample population was 5.8% (N=1137), while the pre-diabetic level was 13.88% (N=2726). The prevalence of dyslipidemia was 47.29% (N=9289) in the sample population. It was found out that the odds of having Type 2 DM was 2.4 times higher among patients with hypertension (95%CI: 2.22, 2.59, p<0.001), while the odds of having Type 2 DM was 1.6 times higher among patients diagnosed with dyslipidemia (95%CI: 1.52, 1.75, p<0.001). Furthermore, type 2 DM is 1.6 times more prevalent in males than females.

Conclusion: Dyslipidemia is significantly associated with Type 2 Diabetes among the sample population. Health protocols can be adjusted to include screening for FBS among patients diagnosed with lipid abnormalities.

PE175 Diabetes complications-clinical & epidemiology

Association of serum gamma-glutamyl transferase with myosteatosis assessed by muscle quality mapping using abdominal computed tomography

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Objective: Although computed tomography (CT) is currently the most common method for evaluating myosteatosis, a new laboratory marker is required to enhance accessibility and eschew the contrast agent interference on CT. This study aimed to investigate whether serum gamma-glutamyl transferase (GGT) levels are associated with myosteatosis indices measured by CT.

Methods: The total abdominal muscle area (TAMA) of 13,452 subjects was measured at the L3 level with abdominal CT. TAMA was segmented into intramuscular adipose tissue and skeletal muscle area (SMA), which was then further classified into normal attenuation muscle area (NAMA) and low attenuation muscle area (LAMA). The following variables were adopted as indicators of myosteatosis: SMA/body mass index (BMI), NAMA/BMI, LAMA/BMI, and NAMA/TAMA. Logistic regression analysis was used to examine the odds ratio (OR) of each GGT quartile for the highest quartile of myosteatosis indices in each sex.

Results: The mean age and serum GGT levels were 53.7 years and 32.8 IU/L (standard deviation [SD], 37.6), respectively, in men, and 53.2 years and 18.4 IU/L (SD, 19.8) in women. In both sexes, the ORs of all myosteatosis indices differed significantly between GGT quartiles. Compared with the lowest quartile group, the probability of high SMA/BMI, NAMA/BMI, and NAMA/TAMA was lower in the highest quartile group by 31%, 38%, and 53% in men and 27%, 34%, and 41% in women, respectively. The risks of high LAMA/BMI in the highest GGT quartile subgroups were 43% and 17% higher than in the first quartile groups for men and women, respectively.

Conclusion: Higher GGT levels were significantly associated with advanced myosteatosis defined by reliable CT indices. This result opens the possibility for using GGT as a cost- effective indicator of myosteatosis. Further prospective research on changes to GGT levels with myosteatosis alleviation will validate GGT as a monitoring marker.

PE176 Diabetes complications-clinical & epidemiology

Light at night and rotating night shift: risk for insulin resistance, type 2 diabetes and other metabolic diseases

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Objective: Compromised quality and quantity of sleep, Exposure of Light at night and Rotating night shift may be a novel risk factor for insulin resistance other metabolic diseases due to interference with diet and circadian metabolic rhythm. Long-term elevated cortisol leads to the high blood sugar level and decreased insulin associated with high cholesterol and triglyceride levels due to disturb circadian metabolic rhythm. The aim of the present study was to investigate the effect of Light at night and Rotating night shift in Night shift nursing professionals.

Methods: In the present case-control study, we recruited 30 night shift nursing professionals, aged 20-40 years, performed frequently rotating day and night shift duties, were randomly selected from the Trauma Center (Tertiary care Hospital) King George Medical University. 30 age sex matched controls were also recruited in this study. Insulin level were measured by ELISA Kit. Insulin Resistance were calulated by HOMA INDEX.

Results: Data were analysed by unpaired t-test. BMI was higher in cases (23.69+1.96) as compared to controls (21.66+4.04) ($p<0.005$). Insignificant difference ($p>0.05$) found in fasting blood sugar between night workers (78.38 +9.40) and controls (75.14+14.77). Fasting insulin level was significantly increased ($p<0.05$) in night workers (4.05+2.45) than controls (2.75+2.53). Insulin resistance was slightly increased among night workers (0.80+0.50) than controls (0.53+0.51) which was statistically significant ($p<0.05$). Triglycerides was significantly increased in night workers (137.99+51.57) as compared to controls (105.00+67.40) ($p<0.05$). Total cholesterol was slightly higher (210.06 + 44.91) in night workers ($p<0.05$). HDL-cholesterol was lower in night workers (40.78 + 10.92) than controls (44.86 + 11.33) but it could not reached at significant level ($p>0.05$).

Conclusion: Light at night and Night shift work is associated with increased risk of insulin resistance and lipid disturbances (i.e. low HDL-cholesterol and high triglyceride levels) making them more prone for metabolic syndrome and Type 2 diabetes in future.

PE177 Diabetes complications-clinical & epidemiology

Morphometric and histopathological changes in placenta affected by gestational diabetes

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Objective: • To find out correlation of the gestational diabetes with demographic profile • To find out correlation of maternal gestational diabetes with fetal outcome • Determine the morphological and histopathological changes of placenta in gestational diabetes and compare with normotensive group

Methods: This study was an OPD based study, done in the department of Obstetrics & Gynaecology, Mahila Chikitshalaya, SMS Medical college & Hospitals, Jaipur. 100 cases of gestational diabetes were included and compared with same age group of controls Biochemical investigations, clinical examination, obstetric history and other relavent data of selected women were collected along with consent form Placenta of selected women were collected and examined for shape, diameter, thickness, weight, number of cotyledons and insertion of umbilical cord etc. For histological examination, sections of placenta were taken and H& E Staining was done. New born were examined for weight and height in labor room. Fetoplacental ratio were calculated

Results: Different maternal disorder cause different morphological and microscopic changes of placenta and accordingly it affects the development of the fetus Mother with gestational diabetes showed increased weight, thickness, area and cotyledon count of the placenta and new borns were significantly more in weight and hight. These mothers were belonged to upper to upper middle class families All the histological findings such as fibrinoid necrosis, syncytial knots, calcification, hyalinization, cytotrophoblastic cellular proliferation, exfoliated trophoblast, stromal fibrosis and thickening of medial coat cell in fetal blood vessels were more pronounced in gestational diabetic cases as compared to normotensive group

Conclusion: Morphometric alterations be studied and analyzed in order to tackle the complications which arise in placental development due to maternal metabolic diseases The results of this study will further help in better management and prevention of consequences of adverse effect of gestational diabetes

PE178 Diabetes complications-clinical & epidemiology

Bidirectional association between diabetic peripheral neuropathy and vitamin B12 deficiency: two longitudinal 9-year follow-up studies using a national sample cohort

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Objective: In this study, we investigated the association among metformin, vit B12 deficiency, and diabetic peripheral neuropathy (DPN) occurrence in diabetic patients.

Methods: This is retrospective, propensity-matched cohort study using the National Health Insurance Service database- National Sample Cohort (NHIS-NSC), which includes 1,000,000 patients of total 50 million people in South Korea. Study 1 analyzed the difference in the incidence of vit B12 deficiency according to the presence or absence of DPN. Study 2 analyzed the difference in the risk of DPN occurrence according to vit B12 deficiency. We also compared the results in relation with the metformin use. Each cohort subject selection period was from 2002 to 2004, and outcome occurrence was evaluated during the follow-up period until 2013.

Results: In study 1, the incidence per 10000 Person Year (PY) for DPN was 179.7 on vit B12 deficiency, and 76.6 on non-vit B12 deficiency group. The adjusted HR was also significant. (1.32 (95% CI; 1.21-1.44)). The prescription of metformin made the effect of vit B12 on DPN clearer and more significant. (HR: 5.76 (95% CI; 5.28-6.29). In study 2, the incidence per 10000 Person Year (PY) for vit B12 deficiency was 250.6 on DPN, and 129.4 on non-DPN group. The adjusted HR of DPN for vit B12 deficiency was 2.44(95% CI; 2.24-2.66). The metformin prescription affected the result of DPN for vit B12 deficiency; HR 0.68(95% CI; 0.62-0.74).

Conclusion: DPN occurrence was increased in vit B12 deficient diabetic patients, and conversely vit B12 deficiency was also increased in DPN patients. However, metformin showed opposite effects in each of the two cohorts. Therefore, further studies should be continued to clarify the causal relationship among DPN occurrence, vit B12 deficiency, and metformin use.

PE179 Diabetes complications-clinical & epidemiology

Validation of the operational definition of type 2 diabetes mellitus based on Korean national health insurance claim data

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Objective: To evaluate the accuracy and validity of the operational definition of type 2 diabetes mellitus (T2DM) based on Korean National Health Insurance (KNHIS) claim data.

Methods: Among the subjects included in Korean National Health and Nutritional Survey (KHANES) from 2008 to 2017, we matched those in the KNHIS health check-up database. The accuracy, sensitivity/specificity, and agreement of T2DM definition by KNHIS criteria were compared with the KNHANES criteria. Definition of T2DM by KNHIS was set as any presence of fasting hyperglycemia, ICD-10 corresponding to T2DM with or without accompanying prescription of any anti-diabetic drugs. Definition of T2DM by KNHANES was defined as having fasting hyperglycemia, high HbA1c, or a previous diagnosis of T2DM or taking medications. The incidence of myocardial infarction (MI) and ischemic stroke was defined according to the first claim data accompanying hospitalization with a wash-out period (from 2007 to the first index date).

Results: Among the study population (N=13,006), the prevalence of T2DM based on either KNHIS or KNANES criteria was 17.9% (n=2,323). When the condition of anti-diabetic drug use was excluded in KNHIS criteria, the overall prevalence increased to 22.9% (n=2,981), but the accuracy (0.93 [95% CI, 0.93-0.94 vs. 0.89 [95% CI, 0.89-0.90]) and agreement (kappa, 0.73 [95% CI, 0.72-0.75] vs. 0.63 [95% CI, 0.61-0.64]) between the T2DM definition by the KNHIS criteria and the KNHANES criteria decreased. Comparing the incidence risk of MI and ischemic stroke according to each definition of T2DM based on KNHIS and KNHANES criteria (four subgroups), KNHIS+/KNHANES- (hazard risk [HR], 2.7; 95% CI, 1.3-5.4) or KNHIS+/KNHANES+ group (HR, 2.1; 95% CI, 1.3-3.3) had significantly higher risk for MI or stroke than KNHIS-/KNHANES- group (reference).

Conclusion: The operational definition of T2DM based on population-based KNHIS claim data could be a valid tool to define the actual patients with T2DM in the Korean population.

PE180 Diabetes complications-clinical & epidemiology

Prediabetes and type 2 diabetes mellitus increases the risk of hepatic fibrosis in individuals with nonalcoholic fatty liver disease in the cardiovascular and metabolic diseases Etiology Research Center (CMERC) cohort

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Objective: Studies have shown that individuals with type 2 diabetes mellitus (T2DM) are at a high risk for steatohepatitis with advanced liver fibrosis but data on the relationship between prediabetes and liver fibrosis are lacking. We aimed to investigate the risk of steatohepatitis with advanced liver fibrosis in those with normal glucose, prediabetes, or T2DM.

Methods: In this cross-sectional study, a total of 6,261 community-dwelling adults were included from the Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) Cohort. Nonalcoholic fatty liver disease (NAFLD) was defined by hepatic steatosis index. Degree of liver fibrosis was assessed by NAFLD fibrosis score (NFS) and Fibrosis-4 (FIB-4). Significant liver fibrosis was defined as FIB-4 ≥2.67 and NFS >0.675.

Results: The prevalence of NAFLD increased according to glycemic status; 721 (16.2%) patients had NAFLD in normal glucose group, 369 (32.0%) in the prediabetes group, and 307 (47.1%) in T2DM group. Proportions of advanced liver fibrosis in normal glucose, prediabetes, and diabetes groups were 1.0%, 15.3%, and 22.7%, respectively (p<0.001). In subgroups stratified according to body mass index and homeostasis model assessment of insulin resistance, a significant association between glycemic status and significant liver fibrosis by NFS was consistently present. Multivariate logistic regression analysis demonstrated that those with prediabetes and T2DM had higher risk of advanced liver fibrosis by NFS after adjusting for other confounders including BMI and HOMA-IR (odds ratio [OR] 17.96, 95% confidence interval [CI] 9.81-32.9 and OR 16.46, 95% CI 8.27-32.79 in prediabetes and T2DM groups respectively).

Conclusion: In this population-based cohort study, both prediabetes and T2DM modestly impacted steatosis. Moreover, both prediabetes and T2DM added a significant risk of fibrosis to individuals with NAFLD, suggesting that screening is imperative in adults with DM as well as prediabetes.

PE181 Diabetes complications-clinical & epidemiology

Association between triglyceride-glucose index and incident colorectal cancer: a nationwide population-based cohort study in Korea

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Objective: The triglyceride glucose (TyG) index, a product of triglyceride and fasting glucose, is a reliable marker for insulin resistance. This study aimed to investigate the association between TyG index and incident colorectal cancer (CRC) risk in adult Koreans.

Methods: This study included 315,207 subjects from the Korean National Health Insurance Service- National Health Screening Cohort. The TyG index was calculated using the following formula: ln (fasting triglyceride [mg/dL] × fasting plasma glucose [mg/dL]/2). Subjects were categorized based on their TyG index quartiles and followed up from 2009 to 2015 for incident CRC. The association of TyG index on incident CRC was investigated using Log-rank test and Cox proportional hazard models, adjusting for sex, age, body mass index, smoking status, alcohol consumption, and physical activities.

Results: Uring the follow-up, 6,346 cases of incidence CRC were documented. The incidence of CRC increased in higher TyG index quartiles (2.0%, 2.0%, 2.2%, and 2.4% in Q1 to Q4). Log-rank test showed that the probabilities of incidence CRC increased for higher TyG index quartiles (log rank p<0.001). The multivariate- adjusted hazard ratios [HRs; 95% confidence interval (CI)] for CRC incidence was significantly increased in the 4th quartile group compared to the 1st quartile group [1.078 (1.005-1.157] in Q4]. In subgroup analyses, the association of TyG index with CRC incidence was definite in men, obese patients and smokers.

Conclusion: High TyG index was significantly associated with CRC. Therefore, physicians may consider screening for CRC in patient with high TyG index.

PE182 Diabetes complications-clinical & epidemiology

Impact of pancreatitis on mortality in patients with diabetes: a population-based cohort study including 2.7 million adults in Korea

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Objective: Acute and chronic pancreatitis are also well-known contributors to the development of diabetes mellitus (DM). However, there has been no epidemiologic investigation into the clinical implication of pancreatitis on the prognosis in patients with DM. To find out, we conducted a population-based cohort study to evaluate the mortality and the cause of death in the DM according to the incidence of pancreatitis.

Methods: A total of 2,746,988 patients with diabetes aged ≥20 years who underwent the National Health Insurance System (NHIS) health examination between 2009 and 2018 were included. Study participants were categorized into 4 groups according to the incidence of acute pancreatitis (AP) and/or chronic pancreatitis (CP). AP was defined as K85 and CP as K860, K861, K868, K903 disease code from the tenth edition of the International Classification of Diseases. The mortality were analyzed from 2009 to 2018.

Results: Among the diabetic patients included in the study, 2,586,324 (99.2%) participants did not develop AP nor CP, 2761 (0.1%) developed AP, 15,343 (0.6%) developed CP and 2063 (0.1%) were diagnosed with both AP and CP. During the follow-up, 255,846 mortality cases were documented. The multivariate-adjusted hazard ratios [HRs; 95% confidence interval (CI)] for mortality were significantly increased in both of the AP group [1.853 (1.716-2.001)] and the CP group [1.573 (1.520-1.629)]. Co- occurrence of AP and CP increased mortality even more, with HRs of 2.425 (95% CI 2.232-2.635). AP and/or CP have consistently been observed as risk factors for higher cancer-related mortality, cardiovascular mortality and death from respiratory causes.

Conclusion: Based on a Korean nationwide cohort study, DM patients with pancreatitis art at higher risk for mortality, and cause- specific death from cardiovascular disease, cancer and respiratory diseases. Therefore, more attention is needed for preventing pancreatitis development in DM patients.

PE183 Diabetes complications-clinical & epidemiology

Prevalence and risk factors of new onset diabetes after living donor liver transplantation (NODAT): a single center experience in Vietnam

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Objective: New-onset diabetes after transplantation (NODAT) is one of the major metabolic complication after liver transplantation. NODAT has been recognized as a complication that may contribute to cardiovascular mortality and graft failure. The present study aimed to estimate the prevalence and investigate the risk factors of NODAT.

Methods: In a cross-sectinal study, 140 non-diabetic adult patients who underwent living donor liver transplantation in Organ Transplantation Center, 108 Military Centre Hospital between October 2017 and July 2022 were evaluated for developing diabetes.

Results: The prevalence of NODAT was 15.5%. The mean age was 52,6± 6,1. Risk factors included recipent age >50 years, body mass index >25 kg/m^2, post-transplant intensive care unit stay >15 days, hepatitis C virus, cytomegalovirus infection, corticosteroid and tacrolimus dose at discharge.

Conclusion: Nonmodifiable risk factors for development of NODAT are age, family history of diabtetes. Modifiable risk factors are obesity, hepatitis C virus, cytomegalovirus infection and immunosuppressive drugs.

PE184 Diabetes complications-clinical & epidemiology

A theoretical framework of ultra-processed foods: commercial determinants of health and the impact on non-communicable diseases and the environment

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Objective: Global industrial systems transform food systems and supplies, resulting in the escalation of ultra-processed foods (UPF) supply and consumption worldwide. The UPF produces some adverse effects on health and the environment. We aim to explain the determinant factors affecting UPF and the impact of UPF on human health and the environment.

Methods: Qualitative document review between 2017-2022 was conducted by the author and team, as registered nutritionists. Sources for scientific articles related to the development of principles, frameworks, and the hierarchy of causality relating to UPF, and its determinants and impacts were searched and reviewed. The articles included systematic reviews and meta-analyses, randomized-controlled trials (RCT), cohorts, and cross-sectional study design.

Results: Two levelled determinants of UPF consumption were manifested in human health and the environment, including [1] basic causes: (a) food system (environmental, socioeconomic, and political drivers), (b) modern food supply chains (production, storage-distribution, processing-packaging, and markets) and [2] underlying causes: (a) food security and quality in community level (accessibility, availability, affordability, food quality and safety), (b) food security and quality in household/individual level (accessibility, availability, food quality, and safety), (c) food literacy, (d) food choice motives. The UPF consumption, parallel with poor diet quality, and less physical activity were then manifested in overnutrition, diet-related diseases, quality of life, and carbon and water footprint.

Conclusion: The determinants of UPF consumption involved fundamental and broad systems such as food systems, food supply chain, food security, and individual aspects such as food literacy and food choice motives. All those things manifested in the shaping of the less healthy food environment, contribute to diet-related diseases and account for the increase in carbon and water footprint. A multidisciplinary approach and collaboration should be initiated to regulate the market, create a healthier food environment, and improve social and behavioral change community to suppress the impacts of UPF consumption.

PE185 Diabetes complications-clinical & epidemiology

A novel anthropometric parameter, weight-adjusted waist index represents sarcopenic obesity in newly diagnosed type 2 diabetes mellitus

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Objective: As metabolic significance of sarcopenic obesity (SO) is revealed, exploring appropriate index to detect SO is important, especially for type 2 diabetes mellitus (T2DM) who have more serious metabolic dysfunction if they accompany SO.

Methods: We used the data of 515 participants from the Korea Guro Diabetes Program (KGDP) cohort to compare the waist-hip ratio (WHR), waist-height ratio (WHtR), and weight-adjusted waist index (WWI) for predicting SO in newly diagnosed T2DM patients. SO is defined as a dual-energy X-ray absorptiometry-measured low muscle mass plus a low muscle strength and/or reduced physical performance as assessed by handgrip strength and gait speed. The WHR, WHtR, and WWI are calculated by dividing the waist circumference (WC) by the hip circumference, height, and √ weight, respectively.

Results: The WHR and WHtR were positively correlated with the amount of fat and muscle mass represented by trunk fat amount (TFA) and appendicular skeletal muscle mass (ASM), whereas the WWI showed an association in the opposite direction: a positive correlation with the TFA (r=0.501, p<0.001) and a negative correlation with the ASM (r=-0.272, p<0.001). When the third tertile of WWI was compared with the first tertile, the odds ratio (OR) for SO was 5.72 (95% confidence interval: 2.06-15.88, p<0.001), the most prominent ORs value among the three indices. Furthermore, the WWI exhibited a significant positive correlation with albuminuria, the mean brachial ankle pulse wave velocity, and low-density lipoprotein cholesterol and triglyceride levels in patients with an age ≥65.

Conclusion: WWI is the preferable anthropometric index for predicting SO in newly diagnosed T2DM participants. A correlation between WWI and cardiometabolic risk factors was evident in elderly patients.

PE186 Diabetes complications-clinical & epidemiology

Using a type 2 diabetes polygenic risk score in predicting metabolic changes in a prediabetic population

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Objective: T2D and its precursor, prediabetes, affect 6.28% and 7.3% of the world's population, respectively. Prediabetes is an intermediate state of hyperglycemia with glycemic parameters above normal but below the diabetes threshold. Clear links between cardiovascular disease, metabolic syndrome, and prediabetes have emerged in recent years. Nevertheless, the pathophysiological defects seen in prediabetes can be managed by lifestyle modifications. The main objective of this research was to create and compare a type 2 diabetes polygenic risk score (PRS) versus changes over time (△) in metabolic parameters related to prediabetes and metabolic complications.

Methods: The genetics of 446 prediabetic patients from the Polish Registry of Diabetes cohort was investigated. Seventeen metabolic parameters were measured (BMI, fat-free mass, fat mass, mass, visceral fat, subcutaneous fat, VAT-SAT ratio, IPAQ, Hba1c, Chol, Tg, Hdl, Ldl, Fasting Glucose, Glucose after 2 hours, Fasting Insulin, Insulin after 2 hours), and compared at baseline and after five years using statistical analysis. Subsequently, genetic polymorphisms present in patients were determined to build a T2D PRS (68 SNPs). Finally, the association between the PRS and the △ of the metabolic traits were assessed.

Results: After a multiple linear regression with adjustment for age, sex, and BMI at a nominal significance of (P<0.05) and adjustment for multiple testing, the T2D PRS was found to be associated with △ fat mass (FM) (p=0.025, β=0.0049 kg).

Conclusion: Our findings suggest that prediabetic individuals with a higher risk for T2D experience increased △ Fat Mass. The associations found in this research could be a powerful tool for identifying individuals with an increased risk of complications at diagnosis.

PE187 Diabetes complications-clinical & epidemiology

Assessing the association of high sensitivity C-reactive protein and nutritional status toward the risk of prediabetes among healthy adults

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Objective: The elevation of serum high sensitivity C-reactive protein (hs-CRP), manifesting in the progression of metabolic diseases, such as prediabetes. We aim to investigate whether nutritional hs-CRP and status are associated with prediabetes.

Methods: A cross-sectional study was conducted from July to September 2021 in urban and rural areas. The urban represented the most populated area and the rural was the mountainous area. A total of 109 healthy adults aged 19 to 64 years were recruited. Pregnant or breastfeeding women were excluded. The data about socio-demographic, body mass index (BMI), fasting blood glucose (FBG), and hs-CRP were collected. A BMI of <18.5 kg/m^2 was classified as underweight, 18.5-24.9 kg/m^2 as normal, and ≥25.00 kg/m^2 as overweight. The FBG 100-125 mg/dl was classified as prediabetes. The hs-CRP of >3.0 mg/L was classified as a high level (at risk).

Results: The subjects were dominated by females and were living in urban (≥50%). As 51.4% were obese, 13.8% were prediabetes, and 32.1% were high hs-CRP. There was an association between BMI and hs-CRP, in which overweight and obese adults were more likely to have a higher level of hs-CRP than normal adults (PR adjusted=3.04, p<0.001, CI95% 2.0-5.2). However, there was no association between BMI and prediabetes as well as between hs-CRP and prediabetes, even after being adjusted by gender, age, and dwelling area. In the prediabetes group, compared to normal FBG, there were no significant differences in the mean BMI (25.3 vs. 25.2 kg/m^2) and hs-CRP (3.0 vs. 2.6 mg/L).

Conclusion: Overweight and obese adults were 3 times higher to have a high level of hs-CRP than normal BMI. However, the BMI and hs-CRP were not the risk factors for prediabetes. Regardless of nutrition status and hs-CRP, prediabetes should be controlled through the refinement of lifestyle, including a healthy diet and being physically active.

PE188 Diabetes complications-clinical & epidemiology

Association between neighborhood food environment and nutritional outcomes of school children in low socio-economic community in Sri Lanka: a GIS based assessment

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Objective: School neighborhood food environment has a greater impact on nutrition status of school children. School build food environment influence the dietary choices of school children, hence triggers the risk of getting Non-Communicable Disease such as diabetes and cardio vascular disease at early stage of life. This study investigated the association between food environment and nutritional outcomes of government school students in a low socio-economic setting, Sri Lanka

Methods: This cross-sectional study surveyed the anthropometric values, dietary behaviour of district representative sample of school children (n=603), and characteristics of neighborhood food environment of selected schools (n=30). Chi-square and spearman correlation tests were performed using SPSS version 23.0 to estimate the associations between food environment and BMI of students, while ArcGIS 10.4.1 was used to analyze GIS data of the study.

Results: Majority of students (35.5%) were 15 years old and approximately 51% were females. Mean BMI of study participants was 18.14 (3.28). More than 90% of shops within close proximity sold unhealthy foods. Consumption of confectionaries was 72.3% of students whereas healthy foods choices was ranged from 5% to 12%.A positive correlation between average BMI and distance to the shops from the school was observed (p<0.05). Risk of being overweight found to be doubled (OR=2.47, 95% CI: 1.52- 3.89) among students studied in schools where shop density was high in closer proximity. Further, students who consumed food from nearest shops were 1.5 times likely to become overweigh (OR=15, 95% 1.01-2.61). Also distance to the nearest shops was inversely associated with the BMI school children.

Conclusion: In conclusion, shops density and the proximity of the school neighborhood environment were positively associated with BMI of students. Hence, this study affirms the importance of introducing new policies to ensure the nutrition quality of neighborhood food environment in low income communities, Sri Lanka.

PE189 Diabetes complications-clinical & epidemiology

Risk for developing recurrent stroke among ischemic stroke with known diabetes: do sex differences?

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Objective: Diabetes is a strong risk factor for stroke. Diabetes is also associated with an increased risk of stroke recurrence. Studied in general population found that stroke is more prevalent in men than in women, but little is known if diabetes stroke men and women had differences risk for recurrent stroke. We examined whether sex differences in risk for developing stroke recurrence in diabetes.

Methods: The medical records of 3,135 acute ischemic strokes admitted to a tertiary care, teaching and referral hospital in southern Thailand within the five years registry were reviewed. There were 753 known diabetes (24.02%), which consisted of 380 women (50.5%) and 373 men (49.5%). The Essen Stroke Risk Score (ESRS) was used to assess risk for recurrence stroke. Score of 3 or above indicated a high-risk level. The Mann-Whitney test was used to compared ESR score. Chi-square, and odds ratio (95%CI) were employed to compare risk levels.

Results: Women had less score on total ESRS (p=0.000). Women had higher score on age (p=0.000), but less score on smoking (p=0.000) indexes, compared with men. Scores on hypertension, myocardial infarction, others cardiovascular disease, peripheral artery disease, and stroke indexes were not differences. More men than did women had high risk level for recurrence stroke (OR 1.65, 95%CI 1.36-1.99). Women were more numbers of older adults (OR 1.44, 95%CI 1.25-1.57), but less smokers (OR 0.13, 95%CI 0.09-0.19), compared with men.

Conclusion: We provided clinical evidences and gained the knowledge that women and men had differences risk for developing recurrence stroke. Although women had lower risk, but in fact, they were older and less smoker. Secondary stroke prevention in women should be considered age-related risk, and in men should be focused on stop smoking.

PE190 Diabetes complications-clinical & epidemiology

Predictive value of the framingham steatosis risk for cardiovascular risk beyond the traditional risk factors: a nationwide population-based cohort study

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Objective: Nonalcoholic fatty liver disease (NAFLD) is common and is associated with incident cardiovascular (CV) disease and mortality. Framingham steatosis index (FSI) is recently proposed as a diagnostic marker of NAFLD, which is calculated from age, body mass index, triglyceride, aspartate aminotransferase, alanine aminotransferase, diabetes history and hypertension status. We aimed to evaluate the predictive ability of FSI for CV risk and mortality using a large-scale population dataset from the Korean National Health Insurance Service-National Health Screening Cohort (NHIS-HEALS).

Methods: Among 514,866 individuals in the NHIS-HEALS, we excluded patients who died or had a history of admission due to a CV event and heavy drinkers. Finally, the study cohort included 283,427 participants. We performed univariate and multivariate Cox proportional hazards regression analyses to determine the association between FSI and major adverse cardiovascular events (MACEs), CV events, CV mortality, and all-cause mortality.

Results: During follow-up, we documented 9674, 8798 and 1602 cases of MACEs, CV events, and CV mortality, respectively. The incidence of MACEs was 0.46%, 0.76%, 0.94%, and 1.26% in 1st to 4th quartiles of FSI, respectively. The multivariate-adjusted hazard ratios [HRs; 95% confidence interval (CI)] for MACEs gradually and significantly increased with the FSI quartiles (1.547 [1.444-1.657] in Q2, 1.974 [1.847-2.110] in Q3, and 2.331 [2.187-2.485] in Q4), following an adjustment for the conventional CV risk factors, including smoking, drinking, physical activities, low-density lipoprotein cholesterol, estimated glomerular filtration rate. Participants with higher FSI quartiles had significantly increased CV event risk and CV mortality. All-cause mortality was also increased in high quartile FSI groups compared to the 1st FSI group (HRs [95% CI]; 1.067 [1.002-1.136] in Q2, 1.183 [1.112-1.258] in Q3, and 1.143 [1.077-1.214] in Q4).

Conclusion: Our study suggests that the FSI, which is a surrogate marker of NAFLD, has prognostic value for detecting individuals at higher risk for cardiovascular events and mortality.

PE191 Diabetes complications-clinical & epidemiology

Income fluctuation and risk of incident type 2 diabetes: a nationwide population-based cohort study

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Objective: Evidence on the association between income fluctuation and risk of type 2 diabetes (T2D) is scarce. We aimed to investigate whether sustained low or high income and income changes are associated with T2D incidence.

Methods: Utilizing the Korean Health Insurance Service database, we studied 6,578,031 adults aged 30-64 years without history of T2D or high fasting glucose(≥126mg/dL) who were enrolled in 2009. Twenty quantiles of monthly health insurance premiums determined income levels. Medical Aid beneficiaries were regarded as those with very low income. Income quartiles were annually analyzed from 2005 to 2009 (lowest quartile corresponded to low income and highest quartile to high income). Cox proportional hazards models were used to assess the association of low- or high-income status and income changes with T2D incidence, adjusting for sociodemographic, lifestyle, and metabolic risk factors.

Results: During a median follow-up of 9.3 years, 483,332 (7.3%) participants developed incident T2D. Participants who repeatedly experienced low income for 5 years showed higher risk of T2D (hazard ratio[HR], 1.10; 95% confidence interval[CI], 1.08-1.11) compared to those who never experienced low income. Interestingly, those who were repeatedly in very low-income status had a 61% higher risk of T2D, compared to those who never experienced very low income (95% CI, 1.30-1.99). In contrast, participants who were repeatedly in high income showed lower risk of T2D, compared to those who never experienced high income (HR, 0.92; 95% CI, 0.91-0.93). When income quartile status was compared between 2005 and 2009, participants who experienced income rises had decreased risk of T2D, while those who experienced income drops had increased risk of T2D in each income quartile group in 2005.

Conclusion: Korean adults who experienced sustained low-income status or declines in income were associated with increased risk of T2D, while those who had sustained high-income status or income rise had decreased risk of T2D.

PE192 Diabetes complications-clinical & epidemiology

Knowledge and practice regarding diabetic retinopathy among Sudanese final and semifinal medical students, university of khartoum faculty of medicine 2022

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Objective: To determine the knowledge of Sudanese medical students about the basics and different aspects of management for patients with diabetic retinopathy and to identify the relationship between the knowledge of those students to their sociodemographics and their Source of information about Diabetic Retinopathy

Methods: This cross-sectional descriptive study was conducted at a College of Medicine University of Khartoum in Sudan in November 2022 and comprised 166 fifth and sixth-year medical students of both sexes. Participants were required to complete a previously validated soft copy questionnaire with additional questions. Data was entered, encoded and analyzed using SPSS software, version 23.

Results: The mean age of participants was [23.96±1.151] years ranging between (21-28). The number of female students was 114 and male students was 52. The mean overall Knowledge score (±SD) for all the respondents was 18.5±4.0 (Maximum, 27), Representing 63.8%. Calculated from basic Knowledge score with a mean of 6.4±1.8 (Maximum, 11), representing 58.2% and practice Knowledge score with a mean of 12.1±2.9 (Maximum, 17), representing 71.2%.The study revealed a significant association between the Journals and continued medical education as source of information about Diabetic Retinopathy and the overall Knowledge score with a p value of 0.026.

Conclusion: The vast majority of students showed good comperhension regarding practice aspects, while showing a moderate level of basic knowledge of diabetic retinopathy. The study revealed a significant association between the knowledge of medical students about diabetic retinopathy and their chosen source of acquisition of said knowledge, As students exposed to journals and continued medical education outside the curriculum showed better levels of knowledge. There is no significant association between the knowledge of medical students and their sociodemographic informations. Medical schools should pay more attention to the students' knowledge about DR - As they are future primary care physicians - because it is a leading cause of blindness in diabetic patients and although it's preventable by early and proper referral.

PE193 Diabetes complications-clinical & epidemiology

Subtypes of type 2 diabetes and their association with outcomes in Korean adults - a community-based prospective cohort study

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Objective: To date, diabetes has been mainly classified into type 1 diabetes and type 2 diabetes. However, clinical manifestation of type 2 diabetes is heterogenous and thus, there has been an attempt to divide type 2 diabetes into subgroups. Although the pathophysiologic mechanism of type 2 diabetes in Asians differs from that of Caucasians, little is known about the subtypes of type 2 diabetes and their association with clinical outcomes in Korean adults.

Methods: We performed data-driven cluster analysis (k-means and hierarchical clustering) in patients with newly diagnosed drug-naive type 2 diabetes (n=759) from the Korean Genome and Epidemiologic Study (KoGES). Clusters were based on five variables (age at diagnosis, BMI, HbA1c, and homoeostasis model assessment 2 β-cell function and insulin resistance), and initiation of glucose-lowering therapy, incident chronic kidney disease (CKD), and incident cardiovascular disease (CVD) were prospectively determined during 14 years of follow-up periods.

Results: We identified four clusters of patients with type 2 diabetes according to k-means clustering: cluster 1 (22.3% (n=169); severe insulin-resistant diabetes, SIRD), cluster 2 (32.8% (n=249); mild age-related diabetes, MARD), cluster 3 (32.7% (n=248); mild obesity-related diabetes, MOD) and cluster 4 (12.3% (n=93); severe insulin-deficient diabetes, SIDD). After adjusting for other risk factors, individuals in cluster 4 had the highest risk for initiation of glucose-lowering therapy than individuals in other three clusters. In particular, individuals in clusters 2 and 4 had significantly higher risk of incident CKD and CVD than individuals in clusters 1 and 3.

Conclusion: We could categorize the patients with type 2 diabetes into four subgroups having different glycemic deterioration and risk of diabetes complications. Thus, physicians should not view patients with type 2 diabetes uniformly; instead, tailored medicine for these patients might be helpful for better glycemic control and prevention of different chronic complications.

PE194 Diabetes complications-clinical & epidemiology

Blood glucose patterns in patients with end stage diabetic nephropathy on hemodialysis: a systematic review and meta-analysis

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Objective: Blood glucose levels might be impaired on hemodialysis especially in patients with diabetic nephropathy, due to renal gluconeogenesis impairment, increased insulin clearance and degradation. We aimed to summarize studies on blood glucose patterns for better management of glycemic control in diabetic nephropathy with hemodialysis.

Methods: Studies were searched from Pubmed, Medrixv and Google Scholar based on PRISMA and PICO criteria. Searching strategy by using keywords: (Diabetic nephropathy) AND (hemodialysis) AND (blood glucose level OR glycemic status OR hypoglycemia). Inclusion criteria were studies involving end-stage diabetic nephropathy (ESDN) patients and/or non-diabetic end-stage renal (ESRD) patients on hemodialysis. We pooled the mean blood glucose (MBG), mean amplitude of glycemic excursion (MAGE) and hypoglycemic events on pre-, on- and post-hemodialysis. All selected studies were assessed for quality with the STROBE checklist.

Results: Seven studies met the inclusion criteria. MBG on-hemodialysis was shown to be lower than post-hemodialysis in the ESDN group compared to the ESRD group. Hypoglycemic events in ESDN patients also occurred more often on-hemodialysis than off-hemodialysis (pre- and post-hemodialysis). However, pre-hemodialysis and post-hemodialysis comparison of MBG showed no difference in both groups. There was also no difference in MAGE between on-hemodialysis and post-hemodialysis, this might be due to a differing result in one study showing higher MAGE on post-hemodialysis than on-hemodialysis in the ESDN group. Nonetheless, most of the reviewed studies showed higher overall MAGE on-hemodialysis compared to post-hemodialysis, and even higher MAGE in the ESDN than ESRD group.

Conclusion: Significant hypoglycemia risk in ESDN patients due to hemodialysis is a concern requiring special attention. Hemodialysis-related hypoglycemia could render less optimal management and potentially lead to poor prognosis. Although glycemic fluctuation as represented by MAGE showed insignificant, this hemodialysis-related complication in diabetic nephropathy still can't be denied. More studies are needed to focus on glycemic fluctuation in this case to provide optimal glycemic control.

PE195 Diabetes complications-clinical & epidemiology

HbA1c as a predictor of diabetic foot ulcer incidence and wound healing events in diabetic patients: a systematic review and meta-analysis

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Objective: Diabetic foot ulcers (DFU) are a major disability complication of diabetes mellitus (DM) potentially resulting in a poor prognosis. The objective was to assess the level of HbA1c as a predictor of diabetic peripheral neuropathy (DPN) or DFU incidence and wound healing rate.

Methods: A comprehensive search was conducted on Pubmed, ScienceDirect and Google Scholar based on PRISMA and PICO criteria. Search strategy using keywords: (diabetic foot ulcer OR diabetic peripheral neuropathy) AND (wound healing) AND (HbA1c). Inclusion criteria were studies involving diabetic patients with or without diabetic foot ulcers. The data analyzed were the mean or baseline HbA1c to predict the risk of diabetic foot ulcers and wound healing. The STROBE checklist was used to assess the quality of all selected articles.

Results: Ten studies matched the inclusion criteria. The mean or baseline HbA1c in the DFU group appeared to be higher than in the non-DFU group. In terms of wound healing, there was insignificant difference in the mean or baseline HbA1c between the resolved and unresolved groups.

Conclusion: The HbA1c level can be used as a predictor of the incidence of DFU or DPN in diabetic patients. However, the HbA1c level cannot be used as a reference to estimate the occurrence of wound healing in the incidence of DFU. This might be due to HbA1c not being the independent variable in respect to wound healing process, but rather involving a whole lot more complicated mechanisms of potential infection, hypoglycemic stress, various pharmacology intervention and diabetes duration.

PE196 Diabetes complications-clinical & epidemiology

Microvascular complications and its predictors among type 2 diabetes mellitus patients at Dessie town hospitals, Ethiopia

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Objective: To determine the prevalence of microvascular problems and their determinants among type 2 diabetes patients.

Methods: A cross-sectional study was undertaken in Dessie town hospitals from February to March 2020. To enroll study participants, we employed simple random sampling and a pre-tested interviewer-administered questionnaire. For analysis, data was imported into Epi-Data 3.1 and exported to SPSS - 23. At p0.25, binary logistic regression was used to select potential factors for adjustment. Variables having a p-value of less than 0.05 were judged statistically significant after running multivariable regression.

Results: The study included 335 type 2 diabetes patients, with males accounting for 54.6% of the total. One hundred and twenty-seven people with diabetes mellitus [37.9% (95% CI: 32.5 percent -43.3 percent)] had at least one microvascular problem. Retinopathy accounted for 24.8 percent, nephropathy 16.1 percent, and neuropathy 8.1 percent of the total. There were statistically significant associations between age 60-87 years (AOR=2.76, 95% CI: 1.02-7.46), diabetes duration >5 years (AOR=4.09, 95% CI: 2.40-6.96), and diabetes and co-morbid hypertension (AOR=3.52, 95% CI: 2.09-5.95).

Conclusion: Diabetic microvascular problems are common in this study. Participants' age, the duration of their diabetes, and co-morbid hypertension were all independent predictors. Early detection and care of microvascular complications should be emphasized by health providers, as should early screening and health education, abrupt medication for elderly individuals with long-term diabetes, and hypertension.

PE197 Diabetes complications-clinical & epidemiology

Type 2 diabetes mellitus in the next 10 years in Vietnam: the CENVIDI study

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Methods: We conduct a cross-sectional study on Vietnamese people ≥ 25 years old, randomly selected by geographical and socio-economic regions. The required sample size is calculated based on the estimated sensitivity and our sample size was 2258 participants. All participants were thoroughly medical examined, taking blood lipid profile and fasting plasma glucose tests, blood pressure, anthropometric indexes, 12-lead electrocardiogram, and interviewed by the Vietnamese version WHO STEPS toolkit. All patients were calculated their risk of developing type 2 diabetes mellitus by ModAsian FINDRISC.

Results: The ratio of developing type 2 diabetes mellitus among the population is 4.21%. There were 2.52% of people at high to very high risk of developing type 2 diabetes mellitus in the next 10 years. Body mass index, waist circumference, family history of diabetes mellitus, and history of taken antihypertensive medication regularly are the most associated factors of the ModAsian FINDRISC.

Conclusion: Screening for type 2 diabetes mellitus and lifestyle intervention focusing on reducing weight, waist circumference, and blood pressure control is needed for better prevention in the Vietnamese population.

PE198 Diabetes complications-clinical & epidemiology

Prevalence of overweight and obesity among adolescents in urban and rural region of Lucknow, Uttar Pradesh, India

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Objective: Overweight and obesity in Adolescent is a serious public health issue worldwide. It increases the risk of hypertension, cardiovascular disease, insulin resistance diabetes, and other conditions in adulthood. According to the World Health Organization, nearly 340 million children and adolescents aged 5 to 19 were overweight or obese in 2016. Obesity and overweight are on the rise in low and middle-income countries. In India, the prevalence of overweight and obesity has risen to 3-24.7% and 1.5-14%, respectively. As a result, the study examined the prevalence of overweight and obesity among teenage populations in Lucknow, UP, India.

Methods: A descriptive cross-sectional study on overweight and obesity was conducted among 480 adolescents (12-18 years) in Chinhat area of Lucknow. The weight and height of the adolescents were measured using standard techniques, and BMI-for-age clinical growth chart from Centers for Disease Control and Prevention was used to categorize like healthy weight (5th to <85th percentile), overweight (85th to <95th percentile) and obesity (≥95th percentile). Data were analyzed using SPSS (version 20).

Results: Among subjects, 72.7, 17.8 and 9.5% were healthy, overweight and obesity respectively. High prevalence of overweight and obesity was found in adolescent boys (22.6%, 11.1%). Obesity incidence of urban-rural adolescents was 12% and 5.7% correspondingly and urban area OR 2.2 (95% CI: 1.1, 4.5). Most of the adolescents were not doing exercise (80.2%, 78.3%), but, they were eating junk food >3 times/week and watching TV >2 hours/day (20.6%, 11.2%) OR 2.1 (95% CI: 0.9, 4.7).

Conclusion: This study revealed that adolescent boys in urban areas are having an increased prevalence of overweight and obesity due to a high conception of Jung food and lack of exercise. Thus, the study underlines the importance of healthy lifestyle to adolescents in order to protect them from serious complications associated with overweight and obesity.

PE199 Diabetes complications-clinical & epidemiology

Underweight and diabetes have a synergistic detrimental effect on the risk of dementia: a population-based cohort study

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Objective: Few studies have evaluated the association between being underweight and the development of dementia in the general population. We investigated the incidence of all-cause dementia, Alzheimer's dementia (AD), and vascular dementia (VD) according to underweight categories in a large population cohort.

Methods: We included 4,238,822 individuals who underwent a health examination conducted as part of the Korean National Health Insurance Service between January 2009 and December 2009 and followed them up until 31 December 2016. Based on the body mass index (BMI), the study population was categorized the participants into normal (18.5-25.0 kg/m^2), mild underweight (17.5-18.5 kg/m^2), moderate underweight (16.5-17.5 kg/m^2), and severe underweight (<16.5 kg/m^2) groups. Cox proportional hazards analyses were performed to calculate the hazard ratios (HRs) for dementia according to the severity of being underweight in reference to the normal weight with adjustment for conventional risk factors. We further calculated the HRs of being underweight with chronic diseases, including diabetes, hypertension and dyslipidemia.

Results: In total, 113,222 cases of dementia occurred during the follow-up period. The risk of all-cause dementia and AD increased proportionally with the severity of being underweight in the multivariate model. The respective HRs (95% CIs) for mild, moderate, and severe underweight were 1.161 (1.116-1.207), 1.238 (1.172-1.307), and 1.283(1.200-1.372) for all-cause dementia. When we examined the effect of comorbidities, being underweight with diabetes most significantly increased the risk of dementia, demonstrating a synergistic detrimental effect [HR (95% CI), 1.212 (1.176-1.250) in underweight only, 1.392 (1.369-1.416) by diabetes only, and 1.786 (1.632-1.955) by coexistence of underweight and diabetes].

Conclusion: Based on a Korean nationwide cohort study, being underweight significantly increased the risk of dementia, and the risk was proportional to the severity of underweight. Furthermore, underweight patients with diabetes are particularly at increased risk of developing dementia.

PE200 Diabetes complications-clinical & epidemiology

Sex differences in the risk of cardiovascular disease events stratified by diabetes status

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Objective: We aimed to investigate the sex differences in the risk of cardiovascular disease (CVD) events stratified by diabetes status.

Methods: This is a prospective cohort study using UK Biobank. We analyzed the sex differences in the risk of CVD. We also performed the analysis for the interaction of five major lifestyles for cardiovascular health and sex differences with the risk of CVD. Cox proportional hazards analyses estimated multiple-adjusted sex-specific hazard ratios.

Results: A total of 458,394 UK Biobank participants with full data available (mean age 57.0 years, BMI 27.4 kg/m2, 54.4% women) were included in the analysis, of which 21,532 (4.7%) had diabetes. Risk of CVD events was higher in men than in women with normoglycemia (hazard ratio 1.91, 95% confidence interval 1.87-1.96). However, the higher risk of CVD events in men was attenuated in the group with diabetes (P for interaction <0.001). Smoking, irregular physical activity, obesity, poor eating habits, and poor sleep habits were associated with a higher risk of CVD events in both sexes. The smoking had additive effect modification for the association between sex and CVD risk (P for interaction <0.001). Non-smoking women and premenopausal women with favorable sleep habits had a lower risk of CVD events compared with their male counterparts.

Conclusion: Sex differences in the risk of CVD events were mitigated in subjects with diabetes. Non-smoking and favorable sleep habits had significant interactions between sex difference and the risk of CVD. This study suggests the importance of sex differences in the effect of diabetes on CVD events, and suggests the necessity of gender-specific lifestyle intervention.

PE201 Diabetes complications-clinical & epidemiology

Normal weight central obesity, physical activity and major adverse cardiovascular events in Korean patients with type 2 diabetes

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Objective: Obesity is a well-known cardiovascular (CV) risk in patients with type 2 diabetes (T2D). However, implication of normal-weight central obesity on the risk for major adverse cardiac events (MACE) in patients with diabetes is less explored.

Methods: We included 771,191 patients with T2D and normal BMI, who underwent a health examination conducted as part of the Korean National Health Insurance Service between 2009 and 2012. WC was categorized into six levels in 5 cm increments, with level 3 (85-90cm in men/80-85cm in women) as the reference group. The primary outcome was incident MACEs, including myocardial infarction (MI), stroke, and CV mortality. The hazard ratios (HRs) with 95% confidence intervals (95% CI) were calculated with adjustments for clinical/demographic characteristics.

Results: In total, 38,092 cases of MACEs occurred during the follow-up period. The risk of MACE was gradually increased as WC increased in T2D patients, even though their BMI were all normal; the HR (95% CI) for MACE were 1.031 (0.996-1.066), 1.199 (1.129-1.274), and 1.379 (1.212-1.570) in WC level 4, 5, and 6, after adjustment for conventional CV risk factors. In centrally obese patients (WC 5th quintile), increased WC over time significantly increased MACE risk [HR (95% CI) for MACE, 1.091 (1.011-1.176) in WC≥5% increase group compared to the stable WC group]. However, WC gain significantly increased MACE risk [HR (95% CI); 1.397 (1.267-1.540)] only in physically inactive patients, while WC gain in physically active patients did not [HR (95% CI); 0.894 (0.729-1.095)].

Conclusion: In T2D patients, normal weight central obesity was a significant CV risk factor. WC increase over time increased MACE risk even more, however, the detrimental effect of WC increase was not observed in physically active patients. Thus, clinicians should emphasize the importance of physical activity for T2D patients with abdominal obesity.

PE202 Diabetes complications-clinical & epidemiology

Cardio-ankle vascular index is associated with diabetic nephropathy in patients with type 2 diabetes mellitus

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Objective: This study aimed to investigate the relationship between cardio-ankle vascular index (CAVI) and diabetic nephropathy (DN) in Mongolian patients with type 2 Diabetes Mellitus (T2DM).

Methods: This cross-sectional study enrolled 199 patients with type 2 diabetes mellitus. (153 males and 46 females; mean age, 53.9±9.7 years (mean±standard deviation)). The VaSera VS-1500N was used to measure CAVI. Associations between CAVI and various clinical parameters were examined. Patients were divided into three groups according to the CAVI: low (CAVI<8, n=89), moderate (8≤CAVI≤9, n=57), and high (CAVI>9, n=53). The clinical characteristics of the groups were compared using an ANOVA and a chi-square test.

Results: The mean age of patients was 53.9±9.7 years and the mean CAVI value was 8.22±1.29. Variables significantly difference CAVI were waist circumference (103.82±12.86, 100.32±10.99, 98.7±12.12 cm p=0.039), BMI (31.62±5.16, 29.22±4.31, 29.71±4.12 kg/m^2 p<0.005), mean systolic blood pressure (129.12±17.37, 128.42±15.57, 140.36±22.68 mmHg p=0.001) IMT (0.92±0.23, 1.02±0.21, 1.07±0.28 mm p<0.001), hemoglobin (158.05±21.44, 151.12±23.03, 147.46±28.09 g/l p=0.029), creatinine (63.18±14.43, 68.07±17.59, 79.74±40.32 μmol/l p=0.001) in the low, moderate and high groups of CAVI. There were no differences in the HbA1c, fasting plasma glucose, diastolic blood pressure, total cholesterol, HDL-C, LDL-C and triglyceride levels among the three groups. In the study population proteinuria was diagnosed in 58 (29.1%) patients. CAVI value was higher in patients with proteinuria (8.54±1.27) than in those without proteinuria (8.08±1.27) (P=0.022). The presence of proteinuria was also highest in high CAVI group (23.6%, 24.6%, 43.4% in the low, moderate, and high groups, respectively) p=0.028.

Conclusion: This study shows that CAVI is a significantly higher in patients with diabetic nephropathy than in those without in Mongolian patients with type 2 diabetes mellitus. Also, CAVI is influenced to an increase in systolic blood pressure. It's expected that due to atherosclerosis.

PE206 Diabetes complications-clinical & epidemiology

Diabetes mellitus and risk of intracranial atherosclerosis: a meta-analysis of observational studies

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Objective: There is strong association exists between diabetes and cardiovascular disease. Coronary artery disease due to atherosclerosis is the leading cause of death in diabetic patients. So, in this study we are exploring the risk of intracranial atherosclerosis due to diabetes mellitus.

Methods: Literature search was performed in databases including PubMed and Embase from inception to June 2019. Two investigators independently retrieved the literature, extracted the data and assess the study quality using NewCastle Ottawa scale. Primary outcome was to assess the association between diabetes mellitus and risk of intracranial atherosclerosis. Secondary outcomes include subgroup analysis based on ethnicity, study populations and co-morbidities. Review Manager version 5.3 was used for the statistical analysis.

Results: Finally twelve studies qualified for the quantitative analysis with a total of 18067 patients. Included studies were of high quality. A non-significantly higher association was observed for the association between diabetes mellitus and risk of intracranial atherosclerosis with a pooled relative risk (RR) of 1.98 (95% CI: 1.67-2.30), p=0.07 as compared to patients without diabetes mellitus. A significant association was observed among community dwelling diabetes mellitus patients with a RR of 1.95 (95% CI: 1.53-2.50), p=0.01. Subgroup analysis based on stroke patients also revealed no significant association.

Conclusion: Diabetes mellitus could be a risk factor for intracranial atherosclerosis. Significant association was observed in community dwelling people with diabetes. Further relevant research is needed to make the evidence transparent.

PE207 Diabetes education case

A case in which team education positively affected patients with first diagnosis of diabetes

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Case: 45 age (male), 171 cm/77 kg (108 kg 6 months ago), BMI 26.3 kg/m^2 (Obesity). For a month, polydipsia with symptoms of polyurea, but no unusual symptoms. HbA1c:16.7%, BST:424 mg/dL, Total Cholesterol 277 mg/dL. • 1st education (Physician) emphasized the risk of 16.7% HbA1c and the importance of active treatment. When the patient did not recognize the seriousness, he said, "If it is kept in a condition, it will die from the disease". For 10 days, the lifestyle correction and medication were prescribed. (Clinical Nutrition) Usually rice 3 bowls (9 exchange), meat (300 g or more/2-3 times a week), after 10 pm pizza&chicken(alone), 1 bottle of coke (500ml)/day, cigarettes(1 pack a day). It was evaluated that they were ingesting more than 3,000 to 4,000 kcal per day. We emphasized the current dietary habits and emphasized 1/2 (vegetables), 1/4 (protein or carbohydrate) meals of dishes using dish methods, and taught a total of 1,800 calorie intake per day. (Nurse) Basic education on diabetes through blood test analysis, SMBG. Targeted blood glucose & medication, and complication management were trained. Patients felt little change in condition according to high blood glucose levels, but they recognized the severity of their first diagnosis of diabetes and the current blood test and had an active commitment to correct their lifestyle. • 2th education The blood sugar and diet recorded for 10 days were evaluated and total blood sugar was 1,200-1,300 kcal, and blood sugar was FBS(245-211-180-160-130-111) mg/dL and PP2hr(370-310-250-261-180-175) mg/dL.

Conclusion: Patients were able to know the seriousness of the test results and the method of diabetes management through team education, and they are practicing the right life pattern so far. We will continue to strive for continuous health care and plan to increase the intake of insufficient protein.

PE208 Diabetes education case

Pediatric prediabetes

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Background: Diabetes, uncommon 20 years ago in Mongolia, now is taking tall on the young and old, men and women regardless of location of residence. The WHO supported STEPS Survey of 2005 showed increase in diabetes from 3% in 1999 to 7% in 2005. According to the WHO STEPS Survey of 2013, 7% of the population of almost 3 million was detected with apparent diabetes and 8% with hidden diabetes suggesting that 1 in 7 persons were ill with diabetes. Furthermore, early detection of type 1 diabetes is possible through a blood test when people have two or more diabetes-related autoantibodies and glucose levels have become abnormal.

Case Presentation: A 3-year-old child, he vomited suddenly in June of 2021 although he didn't have any symptom of illness since his birth. In that day he ate some candies and random glucose level was 17 mmol\l. 2 -h post prandial glucose level was 13 mmol\l and he received IV fluids at hospital and returned to home. Next morning Endocrinologist performed some blood tests for diabetes screening and every result was normal. However, he did not have any symptom of diabetes, he visited for regular screening in October and insulin, c-peptide result was low (C peptide=0,56 ng\ml, Insulin=1,32 uU\ml). He was on a diet and controlled fasting glucose for 2 months. In December, due to dropping test results (C peptide=0,34 ng\ml, Insulin<0.200 uU\ml) he was diagnosed as prediabetes.

Discussion: Overall, we have focused on the role of early detection of T1DM by using specific antibodies such as ICA, IAA, IA2 which are impossible in our country today. Moreover, based on the above mentioned case, we would like to develop better screening of T1DM, sometime in the future and contribute for science in Mongolia.

PE209 Diabetes education case

Adjunctive therapy for the prevention of frequent nocturnal hypoglycemia using raw cornstarch

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Nocturnal hypoglycemia is a common clinical symptom in patients with metabolic and endocrine abnormalities. Dietary intervention with raw corn starch (RCS) therapy is effective in treating recurrent hypoglycemia, in addition to medical treatment and pharmacotherapy. Mr.A, a 59-year-old Chinese man with hypertension, hypercholesterolemia and insomnia but without diabetes, had persistent nocturnal hypoglycemia for the past one month. His self-monitoring blood glucose records less than 3.0 mmol/L from 2 am to 5 am daily. Besides pharmacotherapy, the medical team and the dietitian challenged this patient with RCS therapy to prevent nocturnal hypoglycemia. His weight was 85.5 kg, and his Body Mass Index (BMI) of 28.9 kg/m^2. The dietary assessment showed an intake of approximately 1500 kcal/day with 185g (49%) of carbohydrates and less than 10g fibre. The nutrition diagnosis was impaired nutrient utilization related to compromised endocrine function as presented with frequent nocturnal hypoglycemia. The patient was prescribed 1600 kcal/day (25 kcal/kg dosing weight). Administration of RCS starting with 30 g and progressively to 45 g (0.7 g/kg dosing weight) before bedtime had been prescribed, and a high fibre (25 g) and low glycemic index (GI) diet to avoid postprandial blood glucose (BG) peaks. The patient reports his 24-hour diet recall via WhatsApp application, with blood glucose measurements taken via capillary daily. Four weeks after initiating RCS therapy, the patient's nocturnal BG ranged between 4.1 and 4.4 mmol/L. The patient reported abdominal discomfort during RCS intake. No hypoglycemic symptoms were observed when the RCS and diet prescriptions were followed. Diet supplemented with RCS is non-invasive and effective in preventing hypoglycemia caused by metabolic and endocrine abnormalities and is non-invasive and effective. Due to the paucity of publications on the RCS dosage guideline, further research is required to determine its efficacy in treating specific clinical conditions that result in frequent hypoglycemia.

PE210 Diabetes education case

Diabetes mellitus treatment - role of education among medical students

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Objective: To assess knowledge regarding diabetes management among medical students

Methods: A cross-sectional study was done among the medical students to assess their knowledge of diabetes treatment and prevention. A questionnaire was provided to each of them and scores are recorded based on their answers.

Results: This study reported that the average student could answer less than half of the questions given in the questionnaire. They had some knowledge regarding non-pharmaceutical part of diabetes care but comparatively could not answer much about the drug usage. Students who filled the questionnaire online had more correct answer compare to pen and paper mode. Post graduate had more correct answers regarding the pharmaceutical part compare to undergraduate students.

Conclusion: This study shows the necessity of providing proper education to medical students so that they can in turn educate the patients and there is an overall improve in diabetes management

PE211 Diabetes education case

COVID-19 complications on diabetic patients

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Background: In Mongolia, diabetes mellitus represents a real and growing public health threat. Diabetes prevalence in 2009 was 9% in urban areas and 4% in rural regions. At the same time, pre-diabetes (IFG) was at 12% and 7.3% respectively [4, 5]. Mongolia is a nation undergoing rapid and widespread epidemiological transition and urbanization: a process that is expected to continue in coming decades and is likely to drive the diabetes burden. Everyone with diabetes, is more vulnerable to developing a severe illness if they do get coronavirus pandemic.

Case Presentation: A 53 years old woman, was diagnosed T2DM eight years ago. In 2021, the patient was infected COVID19 and hospitalized for 14 days. She had post covid symptoms such as severe apnea, fatigue and pulmonary fibrosis was diagnosed by HRCT. (Noted both lungs upper and lower lobes multiple GGO and Halo signs which suspicious post COVID-19 extensive pulmonary fibrosis). Our diabetes team paid attention to decrease not only fasting glucose but also post prandial glucose during corticosteroid and antifibrotic treatment. Then we watched unbelievable change on HRCT. (Noted both lungs upper and lower lobes relatively decreased numbers and sizes of GGO with disappeared both lungs Halo signs compared with previous examination). She improved glucose control and diet as well as exercise routine and HbA1C result was lowered by 2%.

Discussion: Overall, individuals with diabetes re more likely to have serious complications from COVID-19. Your risk of getting very sick from COVID-19 is likely to be lower if your diabetes is well-managed. However we have focused on the role diabetic control in the current pandemic and consideration of human resource especially deficiency of diabetes educators. Moreover, based on the above mentioned case presentation, we would like to pay more attention on prevention and vaccination of diabetic patients.

PE212 Diabetes education case

A case of nutrition education using carbohydrate counting in adolescent patient with newly diagnosed Type 1 Diabetes Mellitus (T1DM)

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A 14-year-old girl was hospitalized for nausea, polyuria and weight loss over the prior three months. Her laboratory results showed BST 632 mg/dl, HbA1c 14.6%, C-peptide 0.84 ng/ml, and Insulin Ab positive. She began insulin intensive therapy after a diagnosis with T1DM and opted to receive diabetes education. Her dietary history included eating 3meals per day regularly but a lack vegetable intake. She occasionally indulged in tteokbokki, and ice cream with her friends after school. She initially presented with complaints of depression due to the notion that her diabetes prevented her from eating the foods that she liked. In order to increase the patient's enjoyment for eating and motivation for self-management, a plan for diabetes diet education using carbohydrate counting was prepared. Because of her mother is a foreigner, to account for potential language barriers, we planned an intensive program that the patient could understand herself. The education program is as follows: Day 1: The basic dietary principles of diabetes Day 2: Recommended daily intake calories and food exchange Day 3: Carbohydrate counting and insulin to carbohydrate ratio Day 4: How to read the nutrition label and write a food diary Day 5: Calculating the carbohydrates in desired foods The patient showed interest and was educated faithfully, and she actively changed her attitude by asking questions. After three months, laboratory results indicated that her HbA1c decreased to 10%. Her treatment with long- and short-acting insulin was reduced from 21 to 13units and 22 to 13units, respectively. Carbohydrate counting has limitations for hypoglycemia or an imbalance in nutrient intake, however, it can enable the joy of eating one's favorite foods and flexible meals. In order to increase compliance in adolescents diagnosed with T1DM, it is necessary to develop and apply various educational materials so that carbohydrate counting can be implemented more easily.

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DIABETES & METABOLISM JOURNAL

Aims and Scope

The aims of the Diabetes & Metabolism Journal are to contribute to the cure of and education about diabetes mellitus, and the advancement of diabetology through the sharing of scientific information on the latest developments in diabetology among members of the Korean Diabetes Association and other international societies.

The Journal publishes articles on basic and clinical studies, focusing on areas such as metabolism, epidemiology, pathogenesis, complications, and treatments relevant to diabetes mellitus. It also publishes articles covering obesity and cardiovascular disease. Articles on translational research and timely issues including ubiquitous care or new technology in the management of diabetes and metabolic disorders are welcome. In addition, genome research, meta-analysis, and randomized controlled studies are welcome for publication.

The editorial board invites articles from international research or clinical study groups. Publication is determined by the editors and peer reviewers, who are experts in their specific fields of diabetology.

General Information

The Diabetes & Metabolism Journal is the official journal of the Korean Diabetes Association. It is published bimonthly, with articles in English accepted through the process of peer review. The official title of the journal is 'Diabetes & Metabolism Journal' and the abbreviated title is 'Diabetes Metab J'. The journal was launched in 1972 and had been published under the title the Journal of the Korean Diabetes Association until 2007 (pISSN 1015-6461). From 2008 to 2010, its title was the Korean Diabetes Journal (pISSN 1976-9180, eISSN 2093-2650). Since 2011, volume 35, the title is now the Diabetes & Metabolism Journal. Index words from the medical subject headings (MeSH) list of Index Medicus are included in each article to facili-tate article searches. The Journal is also published on the official website of the Diabetes & Metabolism Journal (https://e-dmj.org/) and is widely distributed to members of the Korean Diabetes Association, medical schools, libraries, and international institutions. Circulation number of print copies and electronic copies are 560 and 4,300 respectively. It is indexed in KoreaMed, KoMCI, KoreaMed Synapse, MEDLINE, PubMed, PubMed Central, SCOPUS, EMBASE, Ebsco, DOI/CrossRef, Google Scholar, and Science Citation Index Expanded (SCIE).

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