

POSTER PRESENTATION

PBS-01-1

Enhanced VEGF Signaling in Islets Contributes to β -Cell Injury and Consequential Diabetes in SDT Rats

Eri Mukai¹, Takeshi Ohta², Harukiyo Kawamura³, Eun-Young Lee⁴, Asuka Morita⁴, Nobuya Inagaki⁵, Toshihiko Iwanaga⁶ and Takashi Miki⁴

¹Department of Medical Physiology/Department of Diabetes and Clinical Nutrition, Chiba University Graduate School of Medicine/Kyoto University Graduate School of Medicine, Japan; ²Central Pharmaceutical Research Institute, Japan Tobacco Inc., Japan;

³Department of Medical Physiology/Clinical Cell Biology and Medicine, Chiba University Graduate School of Medicine, Japan; ⁴Department of Medical Physiology, Chiba University Graduate School of Medicine, Japan; ⁵Department of Diabetes and Clinical Nutrition, Kyoto University Graduate School of Medicine, Japan; ⁶Laboratory of Histology and Cytology, Hokkaido University Graduate School of Medicine, Japan

OBJECTIVE: Pancreatic islets are rich in vascularization, which is essential for glucose sensing and appropriate insulin secretion in β -cells. Spontaneously Diabetic Torii (SDT) rat, a model of non-obese diabetes with ocular complications, exhibits vascular abnormalities within islets as the initial changes at pre-diabetic stage (8 weeks old), followed by β -cell loss. In the present study, we investigated functional relationship between β -cells and vasculature within islets and its contribution to pathogenesis of diabetes in SDT rats.

METHODS: Male SDT rats aged 5 weeks, which do not show any morphological change in islets, were administered with Habu snake venom (HSV), and excised pancreas were subjected to HE staining and immunostaining. We also administered SDT rats with Streptozotocin or a vascular endothelial growth factor (VEGF) receptor (VEGFR) inhibitor Sunitinib.

RESULTS: HSV injection induced hemorrhage inside and at the periphery of islets in SDT rats, whereas islets in control SD rats showed less bleeding. HSV increased phosphorylation of VEGFR2, and co-injection of soluble VEGFR apparently ameliorated HSV-induced hemorrhage in SDT rat islets. Although saline-treated SDT rats at 13-weeks-old showed hemorrhage, inflammation and fibrosis in islets, β -cell depletion induced by Streptozotocin resulted in neither hemorrhage nor inflammation inside and at the periphery of islets. VEGF secretion from islets was increased in SDT rats compared with in SD rats. Five weeks Sunitinib treatment inhibited hemorrhage in islets, β -cell loss, and diabetes development in SDT rats.

CONCLUSION: Enhanced VEGF signaling in islets contributes to β -cell injury islet vascular failure and consequential β -cell dysfunction in SDT rats.

PBS-01-2

The Experiment Study of Duodenal Jejunal Bypass Surgery in Type 2 Diabetic Rats

Mei-Hua Qu¹, Qingtao Yan², Chun-Yan Fang¹, Xiu-Rong Zhang¹, Ting-Kun Zhao¹, Lin Wang¹ and Hai-Lin Han¹

¹Department of Pharmacology, Weifang Medical University, China; ²Department of Pediatric Surgery, Weifang People's Hospital, Weifang, Shandong, China

The wistar diabetic rats were induced successfully by feeding high- fat, high-sugar diet and injecting low- dose streptozotocin (STZ). The rats were randomly divided into DJB operation group (D), Metformin treat group (M) and sham operation group(S), eight rats in each group. The fasting blood glucose was measured by Onetouch glucose meter. The fasting insulin in the plasma was detected by ELISA kit from D&R Company before DJB operation and 8 weeks after DJB operation. Meanwhile, insulin resistance index and sensitivity index before DJB operation and 8 weeks after DJB operation were calculated.

RESULTS:

1 The fasting blood glucose of group D decreased significantly from 19.53 ± 3.45 to 5.15 ± 0.67 mmol/L ($P < 0.01$) measured by glucose meter at 8 weeks after DJB surgery compared to before surgery, and the fasting insulin decreased significantly from 8.61 ± 0.7 to 3.1 ± 0.61 mIU/L ($P < 0.01$) detected by ELISA kit. Insulin resistance index decreased from 7.68 ± 1.64 to 0.72 ± 0.06 ($P < 0.001$) and the insulin sensitivity index increased from 0.0063 ± 0.0019 to 0.0625 ± 0.0059 ($P < 0.001$) calculated by the formula.

2 Group M fasting glucose decreased from 18.63 ± 1.32 to 5.36 ± 0.26 mmol/L ($P < 0.01$) measured by glucose meter at 8 weeks after metformin treatment compared to T2DM control animals. The fasting insulin decreased from 7.79 ± 1.27 to 3.20 ± 0.46 mIU/L ($P < 0.01$) detected by ELISA at the same period. The insulin resistance index

decreased from 7.00 ± 0.54 to 0.71 ± 0.07 ($P < 0.001$) and the insulin sensitivity index increased significantly from 0.0064 ± 0.0051 to 0.0637 ± 0.007 ($P < 0.001$).

PBS-01-3

Serum Levels of Retinol Binding Protein 4 and its Association with Metabolic Syndrome

Noushin Khalili Boroujeni, Maryam Zare and Masoud Amini

Department of Internal Medicine, Isfahan Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Iran

INTRODUCTION: The dysregulation of adipokines is closely associated with the pathogenesis of insulin resistance and type 2 diabetes. RBP4, a new adipokine, was recently reported to provide a link between obesity and insulin resistance. This study aimed to determine whether plasma RBP4 levels are associated with the metabolic syndrome in first-degree relatives of type 2 diabetes mellitus with different glucose tolerance status. It is also important to investigate whether plasma RBP4 concentration can predict future development of prediabetes.

MATERIALS AND METHOD: This case-control study has been done in the framework of Isfahan Diabetes prevention cohort study in the secondary largest city of Iran. Thirty-four subjects with normal glucose tolerance (NGT) test and 39 subjects with impaired glucose tolerance (IGT) test according to the diagnostic criteria of American Diabetes Association enrolled into the study voluntarily by convenience sampling method. Metabolic syndrome (Mets) was defined according to the updated National cholesterol education program Adult treatment panel III criteria. Plasma RBP4 was evaluated by using ELISA method.

RESULTS: Plasma RBP4 concentrations was 33.3 ± 11.6 μ g/mL in the IGT and 33.3 ± 9.5 μ g/mL in the NGT, respectively. RBP4 level were associated positively with body mass index ($P < 0.05$). There were no associations RBP4 with Metabolic syndrome in the IGT and NGT groups. Elevated serum RBP4 was not associated with components of the Mets.

CONCLUSION: The relationship between RBP4 level and insulin resistance or obesity is now controversial in human. Our results do not support the hypothesis that RBP4 levels are causally related to Mets.

PBS-01-4

Increased Gluconeogenesis from Glycerol Plays a Critical Role in Developing Diabetes Under High Fat Diet

Eun Young Lee¹, Kenichi Sakurai², Chitoku Toda³, Koutaro Yokote², Yasuhiko Minokoshi³ and Takashi Miki¹

¹Department of Medical Physiology, Chiba University, Graduate School of Medicine, Japan; ²Department of Clinical Cell Biology and Medicine, Chiba University, Japan; ³Department of Developmental Physiology, National Institute for Physiological Sciences, Japan

OBJECTIVE: Combination of hereditary insulin resistance and high fat diet feeding has long been considered to contribute to development of diabetes. However, its underlying mechanism has not been fully clarified. We treated mutant IR (mIR) mice, which harbor a loss of function mutation in insulin receptor, with high fat diet, and examined the changes in glucose and energy homeostasis.

METHODS: mIR mice were fed with high fat diet (HFD, 50% fat in calorie) and the changes in expressions of various genes involved in metabolic regulation and other metabolic parameters were examined.

RESULTS: Feeding with HFD for 10 weeks evoked a marked hyperglycemia in mIR but not in wild-type (WT) mice. By contrast, the increase in body weight during HFD feeding was significantly less in mIR mice than in WT mice. Serum insulin levels of mIR mice fed HFD (mIR/HFD) and mIR mice fed normal diet (ND; mIR/ND) were higher than that of WT mice fed HFD (WT/HFD), while that of mIR mice fed HFD (mIR/HFD) was increased. Measurement of mRNA expressions of PEPCK, G6P, and GADPH and glycogen content in the liver revealed that HFD feeding induced vast alteration in glycogen metabolism and gluconeogenesis both in mIR and WT. Notably, gluconeogenesis from glycerol was shown to be increased in mIR mice only under high fat diet.

CONCLUSION: Increased gluconeogenesis from glycerol, possibly through increased lipolysis, plays a critical role in developing diabetes under high fat diet in an insulin resistant mouse model, mIR mouse.

PBS-01-5

Correlation Between Total Testosterone Levels and Abdominal Obesity Among Male Population of Legian Village, Kuta, Bali

I. Made Pande Dwipayana, Arini Junita, A. A. G. Budhiarta, Ketut Suastika, Made Ratna Saraswati and Wira Gotera
Division of Endocrinology and Metabolism, Department of Internal Medicine, Udayana University School of Medicine, Indonesia

OBJECTIVE: Abdominal obesity is frequently associated with metabolic syndrome, insulin resistance, and coronary artery disease. Abdominal obesity is one component of metabolic syndrome. One of the etiologies of abdominal obesity is hormonal factor. In men, decreased of testosterone levels have been thought as a cause of abdominal obesity. The objective of this study is to know the correlation between total testosterone levels and abdominal obesity.

METHODS: This research was a cross sectional study, conducted among 80 healthy men of population in Legian Village, Kuta, Bali.

RESULTS: Among 80 samples, the lowest total testosterone levels was 1.38 nmol/L, and the highest total testosterone levels was 32.44 nmol/L. The means of total testosterone levels was 16.60 nmol/L. We found significant correlation between abdominal obesity and testosterone levels ($r = -0.233$, $P = 0.037$) with spearman correlation.

CONCLUSION: This founding supported the hypothesis that lower testosterone levels maybe play a role in abdominal obesity in men.

KEYWORDS: Total testosterone, abdominal obesity.

PBS-01-6

Alpha Synuclein and the Glucose Metabolism

Gerardo Rodriguez Araujo¹, Hironori Nakagami², Yasufumi Kaneda¹, Masaki Mori¹, Yoshikazu Nakaoka³, Tetsuya Shiuchi⁴ and Yasuhiko Minokoshi⁴
¹Division of Gene Therapy Science, Osaka University School of Medicine, Japan; ²Division of Vascular Medicine and Epigenetics, United Graduate School of Child Development, Osaka University; ³Department of Cardiovascular Medicine, Graduate School of Medicine, Osaka University; ⁴Division of Endocrinology and Metabolism, Department of Developmental Physiology, National Institute for Physiological Sciences, Okazaki, Japan

Alpha synuclein (SNCA) is a protein widely known in Parkinson's disease. However recent evidence has changed this perspective. SNCA is found in several tissues and not exclusively in brain.

OBJECTIVE: Investigate the physiological and pathophysiological role of SNCA in the glucose metabolism.

METHODS: We used population study, *in vitro* and *in vivo* models. Euglycemic hyperinsulinemic clamp was performed in murine model.

RESULTS AND CONCLUSIONS: We demonstrate that SNCA is an important participant in the systemic glucose regulation. Additionally, we have investigated SNCA's role in pathological models such as insulin resistance. This novel perspective will certainly increase the understanding of the mechanism underlying glucose regulation and open the field for new research in diabetes.

PBS-01-7

Serum Proteome Changes in Healthy Subjects with Different Genotypes of NOS1AP in the Chinese Population

Congrong Wang, Feng Jiang, Cheng Hu, Rong Zhang, Weihui Yu, Shanshan Tang, Jingyi Lu and Weiping Jia
Department of Endocrinology and Metabolism, Shanghai Diabetes Institute, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, China

OBJECTIVE: Our previous genetic studies reported that the SNP rs12742393 in NOS1AP was a unique variant for type 2 diabetes susceptibility in the Chinese population for the first time, with C as the risk allele. However, the mechanism on how rs13266634 variant affects type 2 diabetes is still unknown. Therefore, we investigated the different protein profilings according to the 'extreme' genotypes of rs12742393 to elucidate the molecular mechanism of diabetes using proteomics technology.

METHODS: Eight healthy participants, with four CC genotype carriers and four AA genotype carriers were selected for investigation. All the individuals were matched with age, sex, BMI and related clinical traits. Fasting serum samples were collected for proteomics analysis using 2D liquid chromatography coupled with tandem mass spectrometer (2D-LC-MS/MS).

RESULTS: In total, four proteins differed between the two groups ($P < 0.05$, as determined by t-test). Compared with AA group, the levels of apolipoproteinA4 (apoA4) were increased ($P = 0.000265$), whereas the concentration of

alpha-1-antichymotrypsin, KERATIN10 and hyaluronan-binding protein 2 were decreased in CC group ($P = 0.011116$, 0.015661 and 0.021175 , respectively). These for proteins were associated with the lipoprotein metabolism and acute inflammatory response.

CONCLUSION: The protein profiling changes between the 'extreme' genotypes of rs12742393 in NOS1AP indicated that this SNP might play a role in the development of type 2 diabetes in the Chinese population.

PBS-02-1

Deficiency of Interleukin-33 in FLP14 Transgenic Mice Causes Insulin Resistance

Taku Watanabe¹, Tomonori Takeuchi², Naoto Kubota³, Shinji Sakaue¹, Chisa Takashina¹, Takahiro Sato¹, Asuka Yamada¹, Hiroshi Ohira¹, Yoshinori Ohtsuka¹, Ichizo Tsujino¹, Katsuyoshi Kumagai³, Tetsuya Kubota³, Chiaki Hasegawa⁴, Kumpei Tokuyama⁴, Kohjiro Ueki³, Masami Mishina², Takashi Kadowaki³ and Masaharu Nishimura¹

¹First Department of medicine, Hokkaido University School of Medicine, Japan;

²Department of Molecular Neurobiology and Pharmacology, Graduate School of Medicine, University of Tokyo, Japan; ³Department of Diabetes and Metabolic Diseases, Graduate School of Medicine, University of Tokyo, Tokyo, Japan; ⁴Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba, Japan

OBJECTIVE: FLP14 transgenic (Tg) mice unexpectedly developed mature-onset obesity and insulin resistance. The objective of this work was to determine the mechanisms underlying this phenotype.

METHODS: The insertion site of the transgene was analyzed using Southern blot analysis and genome walking. To elucidate whether this genetic alteration induces insulin resistance independent of obesity, we conducted glucose tolerance tests and a hyperinsulinemic-euglycemic clamp study in preobese Tg mice.

RESULTS: Insertion of the FLP14 transgene resulted in complete deletion of the IL33 gene and modification of two other genes. Preobese 3-month-old male mice displayed hyperglycemia, hyperinsulinemia and decreased glucose tolerance. Results from the hyperinsulinemic-euglycemic clamp study showed decreased glucose uptake in skeletal muscle, but no increase in hepatic glucose production. To investigate whether insulin resistance was caused by deletion of the IL33 gene, we treated the mice with a single intraperitoneal or intravenous dose of recombinant IL-33 and observed significant improvement in a number of parameters related to insulin resistance.

CONCLUSION: Insulin resistance in FLP14 Tg mice is caused by deficiency of IL-33.

PBS-02-2

Effect of Adiponectin for Insulin Signaling in 3T3-L1 Adipocytes

Jongdai Kim¹, Jungmook Choi² and Cheolyoung Park¹

¹Department of Internal Medicine, Kangbuk Samsung Hospital, Korea; ²Diabetes research institute, Kangbuk Samsung Hospital, Korea

AIMS: Adiponectin plays an important role in the regulation of glucose and lipid metabolism. Adiponectin secreted from adipocyte has insulin sensitizing effect to hepatocyte and myocyte after circulation. But, there is no study about the role of adiponectin for insulin signaling in adipocytes itself. So, we investigate the role of adiponectin *in vitro* 3T3-L1 adipocyte.

METHODS: 3T3-L1 adipocytes cells were plated in a 6-well plate and cultured. siRNA targeting adiponectin was transfected into adipocytes. Glucose transport was assessed in fully differentiated adipocytes to confluence. Cells were then incubated with 30 min in insulin sensitive model or 24 h in insulin resistant model. Cells were harvested 24 h later and mRNA expression, protein phosphorylation was determined by real-time PCR and western blotting.

RESULTS: In insulin sensitive model, IR-phosphorylation, IRS-phosphorylation, AKT-phosphorylation, and AMPK-phosphorylation were increased. But, in insulin resistant model, this phenomenon were not observed. Adiponectin was decreased in insulin sensitive model. But adiponectin was increased in insulin resistant model. When adiponectin was inactivated by siRNA for adiponectin, insulin induced glucose uptake was decreased in both insulin sensitive and resistant model. GLUT-4 membrane translocation was decreased in both. IRS-1 mRNA, GLUT-4 mRNA level were decreased in both. IR and IRS-1 were decreased in both. Phosphorylated-IR, phosphorylated IRS-1 were decreased in only insulin sensitive model. In both insulin sensitive and resistant model, phospho-AMPK α was decreased by siRNA for adiponectin.

CONCLUSION: Adiponectin activate insulin signaling by both quantitatively and functionally in 3T3-L1 adipocyte.

PBS-02-3

The Role of Tissue-Specific Changes in Fatty Acid Composition on Insulin Resistance Induced by Nutritional Interaction

Hirokazu Ohminami¹, Kikuko Amo¹, Yutaka Taketani¹, Megumi Koganei², Hajime Sasaki², Hironori Yamamoto¹ and Eiji Takeda¹

¹Department of Clinical Nutrition, Institution of Health Biosciences, University of Tokushima, Japan; ²Food Science Research Labs., R&D Div., Meiji Co., Ltd., Japan

Previous our data suggest that a selective combination of dietary carbohydrate and fat may play an important role in the development of insulin resistance, accompanied by changing fatty acid composition in insulin target organ. In the present study, we investigated the effect of dietary carbohydrate and fat composition on the fatty acid composition in insulin target organs.

Male, 11-week-old Zucker fatty (fa/fa) rats were divided into four groups and fed isocaloric diets containing different combinations of sugars (palatinose; P, sucrose; S) and fatty acid (oleic acid; O, linoleic acid; L), i.e. PO, PL, SO, and SL, respectively. Oral glucose tolerance test (2 g/kg B.W.) after 3-week-feeding revealed that SL group had postprandial hyperglycemia and insulin resistance rather than other groups, although there was no significant difference in body weight, hepatic steatosis and dyslipidemia among the groups. The fatty acid composition of the liver and soleus muscle in PO and SO groups was increased the rate of oleic acid (C18:1 n-9) to total fatty acid, those in PL and SL groups was increased that of linoleic acid (C18:2 n-6), respectively. In both tissues, particularly, the rate of arachidonic acid (C20:4 n-6) and the activity of c-Jun N-terminal kinase (JNK) were increased in only SL groups.

We conclude that the disturbance in fatty acid composition could have tissue specific contribution to the development of insulin resistance. It is suggested that there is a potential interaction between dietary carbohydrate and fat known as glucolipotoxicity.

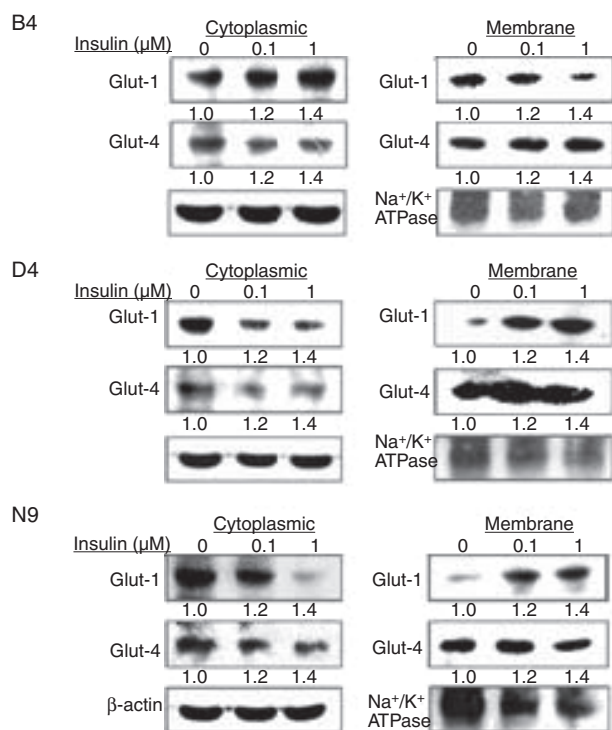
PBS-02-4

Study of Insulin Resistance in Cybrid Cells Harboring Diabetes-Susceptible and Diabetes-Protective Mitochondrial Haplogroups

Hui Lin Huang¹, Pei-Wen Wang², Shao-Wen Weng², Shiao-Mei Kuo², Chia-Wei Liou³ and Tsu-Kung Lin³

¹Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan; ²Department of Internal Medicine Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan; ³Department of Neurology Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

OBJECTIVE: To elucidate the independent role of mitochondria in the pathogenesis of insulin resistance (IR).



METHODS: Cybrid derived from 143B osteosarcoma cell line harboring same nuclear DNA with different mitochondrial haplogroups: B4 (diabetes-susceptible haplogroup in Chinese), D4 (diabetes-resistant haplogroup in Chinese) and N9 (diabetes-resistant haplogroup in Japanese) were studied.

We compared the insulin signaling pathways, intracellular and mitochondrial oxidative stress, and responses to antioxidant n-acetyl cysteine (NAC) treatment. RESULTS: Insulin markedly stimulated translocation of glut4/glut1 from cytoplasm to cell membrane in D4 and N9 cells but not in B4 cells. Ratio of insulin-induced Akt to JNK and P38 phosphorylation was significantly greater in D4 and N9 cells than B4 cells. The levels of oxidative stress were significantly higher in B4 cells in basal and after insulin treatment. Antioxidant NAC improved the imbalance of insulin signaling pathways and increased glut4/glut1 translocation to cell membrane in B4 cells.

CONCLUSION: Mitochondria have an independent role in pathogenesis of IR, possibly through altered intracellular and mitochondrial ROS production.

PBS-02-5

Effect of EPA on Skeletal and Cardiac Muscle of Infants of Diabetic Mother Rats

Akio Nakamura¹, Haruna Masuda¹ and Ritsuko Kawaharada²

¹Department of Molecular and Cellular Pharmacology, Faculty of Medicine, Gunma University Graduate School of Medicine, Japan; ²Department of Health and Nutrition, Takasaki University of Health and Welfare, Takasaki, Japan

OBJECTIVE: Infants of diabetic mothers (IDM) have abnormal circulatory organs. We have already reported that the abnormality of insulin signaling of the infant hearts of diabetic mothers were improved by feeding the pregnant mothers a diet rich in fish oil. In this study, we would like to clarify that which ingredient of fish-oil improves the insulin signaling.

METHODS: Pregnant diabetic (DM) rats induced by streptozotocin fed via gastric tube the eicosapentaenoic acid (EPA) or a control DDW. To examine changes in insulin signaling in the skeletal and cardiac muscle in IDM in relation to diet, we isolated the cardiac and skeletal muscle from the IDM and control infants, and determined the phosphorylation level of Akt473 and the expression levels of mTOR and GLUT4.

RESULTS: The mean blood glucose levels at birth in the IDM was significantly higher than those in the infants from normal mother rat. As time passed, the mean blood glucose levels of IDM have returned to its normal levels on the post-natal day 4. However, the insulin signaling of IDM has changed. In skeletal and cardiac muscle, the phosphorylation levels of Akt473 was increased in IDM feeding the EPA compared with control DDW. The expression level of mTOR and GLUT4 were decreased in the control DDW. However, the intake of EPA reversed these changes.

CONCLUSION: The EPA in the fish oil may improve the impaired signaling pathway of the skeletal and cardiac muscle of infants caused by a diabetic mother's hyperglycemia.

PBS-02-6

Effects of Traditional Herbal Medicine on In Vivo Insulin Action in Streptozotocin-Induced Diabetic Rats

Oyun Khookhor and Yuzo Sato

Department of Health Science, Faculty of Psychological and Physical Science, Aichi Gakuin University, Japan

We investigated the effects of the traditional herbal medicine (THM-5) on *in vivo* insulin action in streptozotocin (i.v.)-induced diabetic rats by means of the euglycemic clamp. In diabetic rats, the glucose metabolic clearance rate (MCR) during 3.0 (low-dose) and 30.0 mU/kg/min (high-dose) insulin infusion was significantly higher in animals administered with THM-5 (500 mg/kg BW, p.o.), compared with saline-administered rats and the insulin signaling in skeletal muscle was evaluated.

Data were analyzed by one-way analysis of variance. When a significant difference was found ($P < 0.05$), values were further compared with the Fisher's PLSD test. The StatView was used for statistical analyses.

The primary goal of this study was to evaluate whether a single treatment with THM-5 could improve glucose metabolism in rats. Outcomes from the euglycemic clamp studies indicated that (1) impaired insulin sensitivity induced by STZ was improved by single and 7 days administration of THM-5 (impaired MCRs of diabetic rats were ameliorated by 80% and 95% as a result of single and 7-days treatment, respectively) However, IR β protein increase and decreased IRS-1 protein expression in diabetes were significantly improved

by THM-5 treatment. THM had effects on the GLUT4 protein content. The increased tyrosine phosphorylation level of IR β , IRS-1, IRS-1 associated with PI3-kinase were significantly inhibited in THM-5 treated diabetes.

These results suggest that the improvement of impaired insulin action in STZ-diabetic rats by a single and chronic administration of THM-5 may be, to enhanced insulin signaling.

PBS-02-7

Assessment of Diabetes Mellitus Through the Mathematical Model for the Glucose-Insulin Regulatory System

Jinwoong Kim¹, Kyungreem Han¹, Hyuk Kang², Jong Hye Cheong¹ and Moo Young Choi³

¹Seoul National University, Korea; ²National Institute for Mathematical Sciences, Daejeon, Korea; ³Department of Physics and Astronomy and Center for Theoretical Physics, Seoul National University, Seoul, Korea

OBJECTIVE: This study is aimed at establishing a mathematical model for the glucose-insulin regulatory system.

METHODS: For the purpose, we propose a mathematical model for the β -cell and incorporate the Sturis model for the glucose dynamics of the brain, liver, muscle, and adipose tissues.

RESULTS: Through extensive numerical simulations and analysis, we are able to observe dynamics of the insulin secretions in the β -cell, coupled with the whole-body level dynamics such as blood glucose, insulin, hepatic glucose output, and glucose uptake rates in the brain, muscle, and adipose tissues. In addition, the insulin resistance and insulin secretory dysfunctions have been successfully evaluated through our mathematical model.

CONCLUSION: This study provides a theoretical basis for the assessment of the β -cell function, simultaneously with insulin resistance/sensitivity.

PBS-02-8

Apple Procyranidins Improve Glucose Tolerance in Diabetic ob/ob Mice

Kasane Ogura¹, Kazuaki Nagashima¹, Toshihiko Shoji², Yuichi Sato¹, Yumiko Tahara¹, Gen Yamano¹, Hiroki Sato¹, Masahito Ogura¹, Eri Mukai¹, Shimpei Fujimoto¹ and Nobuya Inagaki¹

¹Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan; ²National Agriculture and Food Research Organization

OBJECTIVE: It has been reported that several polyphenols including procyanidins show various potential benefits to the human health, such as anti-oxidant, anti-inflammatory, anti-tumor, and longevity effects. Procyanidins, polyphenols extracted from apples, are known to possess an antioxidant effect. Several studies have reported the association of oxidative stress with insulin resistance and hyperinsulinemia in obese and diabetic subjects.

The aim of this study is to investigate whether apple procyanidins (APs) improve glucose tolerance in the diabetic condition and also possess favorable features as an anti-diabetic natural supplements.

METHODS: APs were administrated to diabetic ob/ob mice via drinking water for 3 weeks. After 3-week administration, an oral glucose tolerance test (OGTT), an insulin tolerance test (ITT) and a histological study of pancreatic islets were carried out.

RESULTS: In OGTT, blood glucose levels were significantly lower at 15 and 30 min in APs-treated ob/ob mice compared with controls. In ITT, blood glucose levels were also significantly lower in APs-treated ob/ob mice. In addition, we found that long-term administration of APs suppressed the hypertrophy of pancreatic islets in the diabetic state.

CONCLUSIONS: These results suggest that chronic treatment with APs may ameliorate glucose tolerance and suppress islet hypertrophy by improving insulin sensitivity in ob/ob mice.

PBS-03-1

Trichinella Infection Improves Obesity-Induced Diabetes

Hideyuki Okada, Kazuo Kajita, Taro Usui, Kei Fujioka, Ichiro Mori, Masahiro Yamauchi, Takahide Ikeda, Yoshihiro Uno, Hiroyuki Morita and Tatsuo Ishizuka
Department of General Internal Medicine, Gifu University Graduate School of Medicine, Japan

OBJECTIVE: Inflammation in adipose tissue caused by increase in pro-inflammatory M1 macrophage compared with anti-inflammatory M2 one is associated with obesity-induced insulin resistance. Parasitic helminth infection is known to be able to regulate host immunity via its immunosuppressive

and anti-inflammatory excretory-secretory (ES) products. We investigated the effects of *Trichinella pseudospiralis* infection on blood glucose levels and macrophage functions of the adipose tissue in obese and non-obese mice.

METHODS: Ob/ob and C57/BL mice were divided into infected or non-infected group and followings were compared: 1) plasma glucose and insulin levels, 2) histopathology 3) mRNA levels in adipose tissue. mRNA levels were examined in macrophage (RAW264.7) and 3T3-L1 adipocyte cultured with or without the ES products obtained from *Trichinella pseudospiralis*.

RESULTS: Fasting plasma glucose levels decreased in the infected group of C57/BL and ob/ob mice. Glucose tolerance improved in the infected group of high fat-induced obese mice compared with non-infected ones. mRNA levels of M2 macrophage markers increased, whereas mRNA levels of M1 macrophage ones decreased in the stromal vascular fractions. Macrophages obtained from the peritoneal lavage exhibited lower expression of M1 markers in infected group than in non-infected ones. The ES products reduced pro-inflammatory IL-6 mRNA and increased anti-inflammatory IL-10 mRNA in RAW264.7 macrophages, and reduced IL-6 and MCP-1 mRNA in 3T3-L1 adipocytes.

CONCLUSION: *Trichinella* infection increases ratio of M2/M1 gene expression of macrophage and may play a role in improving adipose tissue inflammation in the obese mice via action of the ES product, which leads to amelioration of glucose tolerance.

PBS-03-2

Endoplasmic Reticulum Stress Regulates Adipogenesis in Adipocytes

Yao-hui Nie, Yong Hou, Alice Kong, Ronald C. W. Ma, Juliana C. N. Chan and Gang Xu
Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

OBJECTIVE: Obesity is the most risky factor causing type 2 diabetes. Endoplasmic Reticulum (ER) stress/unfolded protein response (UPR) has been reported to link with lipid metabolism and adipocyte biology. In this study, we tried to reveal the underlying mechanism of ER stress in adipogenesis.

METHODS: A modified mouse adipocyte cell line 3T3-L1 CAR was used to induce differentiation as a model of adipogenesis. The regulation of adipogenesis was then determined in ER stress initiator (BIP/GRP78) over-expressed 3T3-L1 CAR adipocytes. Adipogenesis was evaluated by oil red o staining and genes expression examined by real-time PCR and immunoblot.

RESULTS: The differentiation of adipocyte was inhibited in BIP over-expressed cells. The accumulation of triglyceride is lower in BIP treated cells, and as well as lipogenic gene expression level. The subsequent analysis of ER stress related gene expression suggested that the UPR was not stimulated in BIP over-expressed cells in the presence of differentiation induced mixture, which might be the reason for failure of the adipogenesis. In another aspect, cAMP-PKA pathway was demonstrated to account for the induction of ER stress during the adipogenesis according to our study, whether BIP over-expression affects cAMP-PKA signaling is still under exploration.

CONCLUSION: Alleviating ER stress by providing sufficient chaperons contributes to the inhibition of adipogenesis. The findings suggest ER stress is required in the development of obesity, which generates a possible target for anti-obesity treatment.

PBS-03-3

The Role of S100B Protein in the Interaction Between Adipocytes and Macrophages

Atsushi Fujiya¹, Hiroshi Nagasaki², Yusuke Seino³, Kouta Ishikawa¹, Hidetada Ogata¹, Tetsuji Okawa¹, Jiro Kato¹, Ayako Fukami¹, Tatsuhito Himeno¹, Eita Uenishi¹, Shin Tsunekawa¹, Hideki Kamiya⁴, Jiro Nakamura⁴, Yutaka Oiso¹ and Yoichi Hamada³

¹Department of Endocrinology and Diabetes, Nagoya University Graduate School of Medicine, Japan; ²Department of Physiology I, School of Medicine, Fujita Health University, Japan; ³Department of Metabolic Medicine, Nagoya University Graduate School of Medicine, Japan; ⁴Division of Diabetes, Department of Internal Medicine, Aichi Medical University School of Medicine, Japan

OBJECTIVE: S100B, a 21 kDa calcium-binding protein reported as an inflammatory marker in the brain, is secreted from adipocytes as well, and a higher concentration of S100B has been observed in the serum of obese patients. To clarify whether S100B is involved in the chronic inflammation of adipose tissues, we examined the role of S100B in the interaction between adipocytes and macrophages.

METHODS: We co-cultured differentiated 3T3-L1 adipocytes and RAW264.7 macrophages as a chronic inflammation model in the adipose tissue. S100B

protein levels and mRNA expression as well as macrophage TNF- α and M1 marker expression were evaluated.

RESULTS: Recombinant S100B upregulated TNF- α and markers for M1 macrophages such as F4/80 or CD11c in RAW264.7. S100B secretion from 3T3-L1 was significantly increased by TNF- α and catecholamines, and decreased by insulin. Conditioned media from 3T3-L1 stimulated TNF- α secretion from RAW264.7 and those from RAW264.7 increased S100B secretion from 3T3-L1. The co-culture of differentiated 3T3-L1 with RAW264.7 resulted in the marked upregulation of TNF- α , MCP-1 and S100B, and also augmented the expression of CCR2, an MCP-1 receptor. The neutralizing antibody against a receptor of advanced glycation endproducts (RAGE), to which S100B binds as an intrinsic ligand, ameliorated TNF- α secretion from RAW264.7 in the presence of 3T3-L1 conditioned media.

CONCLUSION: S100B appears an important adipocyte-derived activator of macrophages and the paracrine loop between adipocytes and macrophages mediated by S100B and TNF- α may establish a vicious cycle that aggravates inflammatory changes in the adipose tissue.

PBS-03-4

Activation of iNOS are Responsible for the Palmitate-Induced Decrease in Adiponectin Synthesis in 3T3L1 Adipocytes

Jaechan Leem¹, Min Jae Jeon², Myoung-Seok Ko², Jung Eun Jang¹, Eun Hee Koh¹, Lee Woo Je¹, Min-Seon Kim¹, Joong-Yeol Park¹ and Ki-Up Lee¹

¹Department of Internal Medicine, University of Ulsan College of Medicine, Korea; ²Asan Institute for Life Sciences, Korea

OBJECTIVE: Mitochondrial dysfunction and endoplasmic reticulum (ER) stress are considered the key determinants of insulin resistance. Impaired mitochondrial function in obese animals was shown to induce the ER stress response, resulting in reduced adiponectin synthesis in adipocytes. The expression of inducible nitric oxide synthase (iNOS) is increased in adipose tissues in genetic and dietary models of obesity. In this study, we investigated the role of iNOS activation in the palmitate-induced decrease in adiponectin synthesis. As excessive NO produced by iNOS was shown to increase mitochondrial damage, we hypothesized that palmitate-induced activation of iNOS would be primarily responsible for mitochondrial dysfunction and ER stress, and the consequent decrease in adiponectin synthesis.

METHODS AND RESULTS: As expected, palmitate increased the expression levels of iNOS and ER stress response markers, and decreased mitochondrial contents. Treatment with iNOS inhibitor increased adiponectin synthesis and reversed the palmitate-induced ER stress response. However, the iNOS inhibitor did not affect the palmitate-induced decrease in mitochondrial contents. Chemicals that inhibit mitochondrial function increased iNOS expression and the ER stress response, whereas measures that increase mitochondrial biogenesis (rosiglitazone and adenoviral overexpression of nuclear respiratory factor-1) reversed them. Inhibition of mitochondrial biogenesis prevented the rosiglitazone-induced decrease in iNOS expression and increase in adiponectin synthesis.

CONCLUSION: These results suggest that palmitate-induced mitochondrial dysfunction is the primary event that leads to iNOS induction, ER stress, and decreased adiponectin synthesis in cultured adipocytes. Excessive NO produced by iNOS links mitochondrial dysfunction to ER stress and decreased adiponectin synthesis.

PBS-03-5

Chronic Effects of Regulatory T Cell Reduction in Adipose Tissue for Insulin Resistance and Obesity

Yusuke Mineoka, Masahiro Yamazaki, Takashi Senmaru, Hiroshi Okada, Mai Asano, Michiaki Fukui, Goji Hasegawa and Naoto Nakamura
Department of Endocrinology and Metabolism, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Japan

OBJECTIVE: This study was conducted to examine the long term effects of adipose Regulatory T cell (Treg) reduction for the development of insulin resistance (IR) and metabolic syndrome in mouse model of obesity.

METHODS: We obtained the mouse model reduced Treg cells with intraperitoneal injection of TH6 once per week. We fed wild-type mice or Treg reduction mice, a high-fat diet for 16 weeks. At week 20, we analyzed the macrophage and lymphocyte fractions in the visceral adipose tissue with flow

cytometry. To examine the development of IR, we performed intraperitoneal glucose tolerance test and insulin tolerance test. We also examined the tissue expression of insulin receptor substrate-1 and -2 (IRS1 and IRS2), insulin receptor, and adiponectin-1 and -2 (AdipoR1 and AdipoR2) mRNA with real-time PCR.

RESULTS: Compared with normal chow diet (NCD) group, diet induced obesity (DIO) group revealed insulin resistance and resulted in increased M1 macrophages and CD8+ cells in visceral adipose tissue. In groups reduced Treg, both of NCD and DIO revealed glucose toxicity whereas insulin sensitivity improved significantly accompanying high serum insulin level ($P < 0.05$). In these groups, the expression of IRS2 in liver was increased ($P < 0.05$) whereas the expression of insulin receptor and AdipoR2 unchanged. The expression of IRS1, insulin receptor and AdipoR1 in muscle was not changed.

CONCLUSIONS: Our experiments indicated that chronically reducing adipose Tregs expressed the differential effect for glucose tolerance and insulin sensitivity via multiple mechanisms despite the development of obesity.

PBS-03-6

Roles of Wilms' Tumor 1-Associating Protein in Development of Obesity and Diabetes

Masatoshi Kobayashi¹, Mitsuru Ohsugi², Takayoshi Sasako¹, Kazuyuki Tobe³, Kohjiro Ueki¹ and Takashi Kadowaki¹

¹Department of Diabetes and Metabolic Diseases, Tokyo University, Japan; ²Mitsui Memorial Hospital, Japan; ³First Department of Internal Medicine, University of Toyama, Japan

We found the elevated gene expressions of Cyclin A2 in pancreatic islets of obese mice, and focused one of its regulators, Wilms' Tumor 1-Associating Protein (WTAP). WTAP has been suggested to have multiple functions, but there has been no report about metabolic function. We hypothesized WTAP may have some roles in development of obesity. We analyzed both 3T3-L1 preadipocytes with knockdown of WTAP and embryonic fibroblasts from *Wtap*^{+/-} mice, and found the impairment of differentiation into adipocytes.

We next analyzed *Wtap*^{+/-} mice since *Wtap*^{-/-} mice are embryonic lethal. *Wtap*^{+/-} mice showed less weight with decreased fat mass than wild-type (WT) mice on both normal chow and high fat diet (HFD).

In adipose tissue, adipocytes were smaller and circulating MCP-1 levels were markedly reduced in *Wtap*^{+/-} mice than those of WT mice on HFD, due to a significant decrease in macrophage infiltration. Similarly, in livers of *Wtap*^{+/-} mice, steatosis was dramatically attenuated with a marked reduction of macrophage. As a consequence, *Wtap*^{+/-} mice exhibited significantly better glucose tolerance, insulin sensitivity and serum lipid profiles compared to WT mice.

Bone marrow transplantation study revealed that reduction of WTAP in hematopoietic cells contributes to the better insulin sensitivity in part, but suppression of body weight gain by haploinsufficiency of WTAP in parenchymal tissues appeared to have more significant impact on the beneficial phenotypes.

In conclusion, these data suggest that WTAP plays a pivotal role in the development of obesity and subsequent insulin resistance, and can be a novel therapeutic target for obesity-induced diabetes.

PBS-04-1

Experimental Study of Change of Glucose and GLP-1 Level after Gastric Bypass

Hongkai Gao¹, Zhang Xiaomei² and Fan Guojun¹

¹Department of General Surgery, The General Hospital of Chinese People's Armed Police Forces, China; ²Department of endocrinology, Dandong No.1 Hospital, Dandong, Liaoning, China

OBJECTIVE: To establish the stomach-preserving Roux-en-Y gastric bypass model in GK rats and investigate the changes of glucose tolerance and glucagon-like peptide-1 after surgery.

METHODS: Thirty GK rats were randomly divided into five groups: group I (sham operation group), group II (traditional Bypass), group III (duodenum bypass), group IV (jejunum bypass), group V (ileum bypass). OGTT and expression of total serum GLP-1 were evaluated at pre-operation and at 4 weeks post operation.

RESULTS: (1) Compared with group I, blood glucose level dropped obviously at OGTT time point after surgery; (2) Compared with group II, blood glucose level changed no significantly after surgery; (3) Comparing with total serum

GLP-1 expression in group I, serum GLP-1 increased at fasting and 30 min after meal; (4) Comparing with total serum GLP-1 expression in group II, serum GLP-1 expression increased at fasting and 30 min after meal, especially in 30 min after meal; (5) Comparing with total serum GLP-1 expression in group III, serum GLP-1 expression increased at fasting and 30 min after meal, especially in group V at 30 min after meal.

CONCLUSIONS: The effective section of GLP-1 expression in gut located in the middle part of small intestine and the remission effect of GBP on T2DM is associated with increase of GLP-1 after GBP.

PBS-04-2

The Effect of High-Fat Diet Induced Obesity on GIP Secretion from K-Cells

Kazuyo Suzuki, Norio Harada, Shunsuke Yamane, Akihiro Hamasaki, Daniela Nasteska, Kazuki Sasaki, Erina Joo, Kimitaka Shibue, Takanari Harada, Atsushi Muraoka, Yaeko Kondo, Yasuhiko Nakamura and Nobuya Inagaki

Department of Diabetes and Clinical Nutrition, Graduate School of Medicine Kyoto University, Japan

OBJECTIVE: GIP is released from enteroendocrine K-cells in response to nutrient ingestion. It is reported that plasma GIP levels are increased in obese state. However, it remains unclear whether it is due to increase of K-cells in number or due to increase of GIP expression in K-cells. We have established the GIP-GFP knock-in (GIP-GFP) mice to visualize K-cells and evaluated the number of K-cells and expression level of GIP mRNA in K-cells under high-fat diet feeding.

METHODS: The intestine of GIP-GFP heterozygous mice was observed by microscope and immunohistochemistry. GIP-GFP heterozygous mice received control fat diet (CFD) or high-fat diet (HFD) for 8 weeks. After food tolerance, OGTT was performed. A number of GFP-positive cells were measured. Quantitative RT-PCR was performed using GFP-positive cells collected by flow cytometry.

RESULTS: In the intestine of GIP-GFP mice, positive emission of GFP fluorescence was confirmed. GFP-positive cells corresponded with GIP-positive cells by immunohistochemistry. Body weight gain of HFD-fed mice was significantly increased compared to that of CFD-fed mice. Plasma GIP and insulin levels during OGTT were significantly higher in HFD-fed mice than those in CFD-fed mice. There was no significant difference in the number of K-cells between CFD-fed mice and HFD-fed mice (immunohistochemistry and flow cytometry analysis). However, the expression levels of GIP mRNA and Pdx1 mRNA in K-cells were significantly higher in HFD-fed mice than those in CFD-fed mice.

CONCLUSION: An increase in GIP mRNA expression might be involved in hypersecretion of GIP from K-cells in the high-fat diet-induced obese mice.

PBS-04-3

Chronic Overexpression of Oxyntomodulin Attenuates Body Fat Gain and Improves Insulin Sensitivity in Mice

Yanyun Chen and Keyun Qing

Department of Endocrine, Eli Lilly & Co, USA

INTRODUCTION: Oxyntomodulin (OXM) is a 37aa preproglucagon-derived peptide hormone that is released along with GLP-1 from the L-cells of the small intestine in proportion to nutrient ingestion. Recent literature reports suggest that OXM is involved in the regulation of food intake and body weight. Unfortunately, native OXM is a very weak anorectic agent and has a short half-life of 8 min because of its rapid degradation in the circulation by dipeptidyl peptidase 4 and other endoprotease. These properties limit our ability to study chronic effects of OXM in animal models.

OBJECTIVE: To investigate the effects of chronically elevated OXM levels in mice.

METHODS: A recombinant adeno-associated virus (AAV) 2 vector containing the mouse OXM gene was constructed and packaged. Approximately 1×10^{10} particles of AAV-OXM or the control vector AAV-GFP were injected through the tail vein into 2-month old C57BL/6 mice.

RESULTS: Throughout the 6-month study period, the AAV-OXM-injected mice had significantly decreased food intake (662.7 ± 7.8 vs 692.1 ± 10.0 g) and body weight gain (11.3 ± 1.0 vs 18.6 ± 0.8 g) when compared with that of

the AAV-GFP-injected mice. Body composition analysis indicated that decreased weight gain was due to lack accretion of fat mass while fat free mass was not affected. Six months post the initial AAV injection, the AAV-OXM group showed significantly improved insulin sensitivity in response to an oral glucose challenge.

CONCLUSIONS: Chronic overexpression of OXM can decrease food intake, body weight, and improve insulin sensitivity. OXM has the potential to be an anti-diabetic agent with weight reduction benefit.

PBS-04-4

Relationship between Obesity and Incretin Effect in Japanese Subjects

Atsushi Muraoka, Akihiro Hamasaki, Norio Harada, Shunsuke Yamane, Kazuyo Suzuki, Daniela Nasteska, Erina Joo, Masahiro Hishizawa, Yaeko Kondo, Kimitake Shibue, Takanari Harada, Kazuki Sasaki and Nobuya Inagaki

Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

OBJECTIVE: Previous studies showed that incretin effect reduces along with worsening of glucose tolerance and negatively correlates to BMI. These findings are, however, almost based on cross-sectional studies, and little is known about the change of incretin effect during weight loss within same subjects. We aimed to investigate the relationship between incretin effect and body weight in Japanese normal glucose tolerance subjects.

METHODS: Isoglycemic 3-h oral [75 g oral glucose tolerance test (OGTT)] and intravenous glucose administration (ivGTT) were performed in 17 Japanese normal glucose tolerance (NGT) subjects [age: 31.2 ± 2.7 years; body mass index (BMI): 24.0 ± 1.9 (mean $\pm$ SD)]. Isoglycemic intravenous glucose infusion was performed using artificial pancreas system STG-22 (Nikkiso, Tokyo, Japan). Incretin effect was calculated by relating the difference in integrated incremental β -cell secretory responses. Incretin effect of obese subjects with BMI above 25 was re-evaluated after at least 5% body weight loss under diet and exercise intervention.

RESULTS: The average incretin effect of 17 NGT subjects was $51.5 \pm 19.6\%$. Incretin effect showed a significant negative correlation with BMI ($r = -0.41$, $P < 0.05$). Since the area under the curve (AUC-) CPR in ivGTT was reduced as much as that in OGTT during body weight loss, the ratio of the differences between AUC-CPR in OGTT and that in ivGTT to AUC-CPR in OGTT was increased. Accordingly, obese subjects showed the improvement of glucose tolerance and the increment of incretin effect after body weight reduction.

CONCLUSION: Body weight change is closely related to numerical incretin effect in Japanese subjects.

PBS-04-5

GLP-1 Response to Oral Glucose Load in Japanese and Caucasians with Glucose Tolerance from Normal to Type 2 Diabetes

Maria Pedersen¹, Jonas B. Moeller², Mitsuru Ohsugi³, Harushiko Tanaka³, Rune V. Overgaard², Jan Lyngø⁴, Nina-Maria Vasconcelos⁵, Kohjiro Ueki³, Takashi Kadowaki³, Bente K. Pedersen⁴, Steen H. Ingwersen² and Jens J. Holst⁶

¹Centre of Inflammation and Metabolism, Rigshospitalet, University of Copenhagen, Denmark; ²Quantitative Clinical Pharmacology, Novo Nordisk A/S, Denmark;

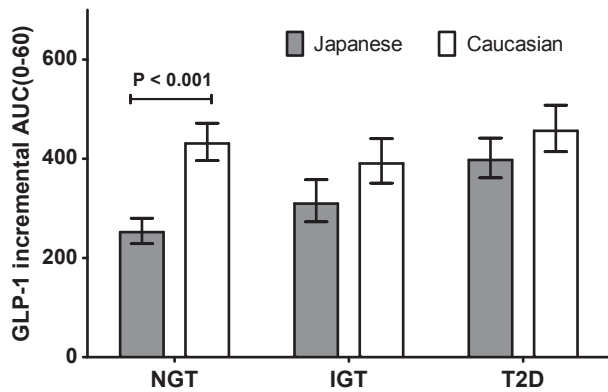
³Department of Metabolic Diseases, Tokyo University Hospital, Japan; ⁴Clinical Pharmacology Diabetes, Novo Nordisk A/S, Denmark; ⁵Medical Writing, Novo Nordisk A/S, Denmark; ⁶Department of Biomedical Sciences, University of Copenhagen, Denmark

OBJECTIVE: We aimed at investigating the total glucagon-like peptide-1 (GLP-1) response following an oral glucose tolerance test (OGTT) in Japanese and Caucasians, and to study its relation to ethnicity, age and body mass index (BMI).

METHODS: One hundred and twenty Japanese and 150 Caucasians aged 40–65 were enrolled to obtain a comparable distribution of high/low BMI across glucose tolerance states (normal [NGT], impaired [IGT], or type 2 diabetes [T2D]). Standard OGTTs were conducted and the total GLP-1 response was obtained using a highly sensitive immunoassay. Evaluable GLP-1 profiles were obtained from 111 Japanese and 134 Caucasians.

RESULTS: The mean GLP-1 response [incremental area under the curve (AUC)] appeared higher in Caucasians compared to Japanese, reaching statistical significance for NGT participants (Figure). The GLP-1 response was positively correlated with age in both ethnic groups, but inversely correlated with BMI in Caucasians only.

Incremental areas under the curve (Δ AUC) during initial GLP-1 responses (0-60 min)



Data are presented as geometric mean and SEM. No interactions between ethnicity and glucose tolerance group were detected.

CONCLUSION: A lower GLP-1 response was obtained in Japanese compared to Caucasians. In both ethnic groups, GLP-1 responses were positively correlated with age.

PBS-04-6

Long-Term Effect of Liraglutide and/or Insulin on Beta Cell Mass in db/db Mice with Long-Standing Hyperglycemia

Kosuke Konishi¹, Jun-ichiro Miyagawa¹, Masayuki Miuchi¹, Etsuko Nagai¹, Toshihiro Matsuo¹, Kazuki Murai¹, Tomoyuki Katsuno¹, Tomoya Hamaguchi² and Mitsuyoshi Namba¹

¹Division of Diabetes and Metabolism, Department of Internal Medicine, Hyogo College of Medicine, Japan; ²Division of Innovative Diabetes Treatment, Department of Internal Medicine, Hyogo College of Medicine

OBJECTIVE: We investigated the long-term effects of the human GLP-1 analogue liraglutide and/or insulin detemir on glucose tolerance and beta cell mass in aged diabetic db/db mice as a model for an advanced stage of type 2 diabetes with long-standing hyperglycaemia.

METHODS: Natural history of glucose tolerance and islet morphology including relative beta cell area were examined in male db/db and db/m+ mice from 6 to 24 weeks of age. Male db/db mice were divided into four groups (insulin detemir monotherapy, liraglutide monotherapy, insulin detemir and liraglutide, and control groups) at 18 week-old when the treatment with liraglutide and/or insulin detemir or physiological saline started as long as 6 weeks.

RESULTS AND CONCLUSION: The proliferation effect on beta cells was not detected in the liraglutide group as compared to control group. On the other hand, significant increase of the relative beta cell area and the beta cell proliferation was observed in the insulin detemir group. Further, synergistic action to the change of beta cell mass and glucose tolerance by the combined treatment with liraglutide and insulin detemir treatment was not confirmed.

The results suggest that GLP-1 receptor agonist showed no apparent stimulatory effect on beta cell proliferation at least in the advanced diabetic stage of db/db mice with hyperglycaemia and markedly decreased beta cell mass. In such condition, insulin treatment may be more effective than GLP-1 to protect beta cells and the progression of the disease in type 2 diabetes mellitus.

PBS-05-1

Changes in Cardiovascular Autonomic Function and Peripheral Nervous System in Type 2 Diabetes Mellitus

Rajesh K. Goit¹, Rita Khadka², Sanjib Sharma³, Nirmala Limbu² and Bishnu Hari Paudel²

¹Department of Physiology, Nepalgunj Medical College, Nepal; ²Department of Physiology B P Koirala Institute of Health Sciences; ³Department of Internal Medicine B P Koirala Institute of Health Sciences

OBJECTIVE: To find the correlation between the autonomic function and peripheral nervous system in type 2 diabetes mellitus.

METHODS: HRV, cardiovascular autonomic reactivity and VPT of 60 patients were assessed. HRV was assessed by FFT of 5 min ECG epoch recorded at spontaneous respiratory rates. Cardiovascular autonomic reactivity was assessed using deep breathing, Valsalva maneuver, hand grip test (HGT) and head up tilt (HUT). VPT was measured at toe, 1st, 3rd, and 5th metatarsals, instep, and heel surfaces of both feet. The degree of correlation was found using Spearman's rank correlation. A *P* value < 0.05 was considered statistically significant.

RESULTS: VPT in right leg was negatively correlated with parasympathetic reactivity [E:I ratio (*r* = -0.338, *P* = 0.008)], and sympathetic reactivity [HGT (*r* = -0.319, *P* = 0.013), HUT (*r* = -0.519, *P* = 0.001)] while VPT in left leg was positively correlated with sympathetic reactivity [HUT (*r* = 0.381, *P* = 0.001)]. Duration of illness was negatively correlated with parasympathetic reactivity [E:I ratio (*r* = -0.464, *P* = 0.001), Valsalva ratio (*r* = -0.469, *P* = 0.001)] and sympathetic reactivity [HGT (*r* = -0.424, *P* = 0.001)] while it was positively correlated with sympathetic reactivity [HUT (*r* = 0.293, *P* = 0.023)]. Age was negatively correlated with sympathetic activity [LF power (*r* = -0.258, *P* = 0.046), SD2 (*r* = -0.268, *P* = 0.038)], sympathetic reactivity [HGT (*r* = -0.444, *P* = 0.001)] while it positively correlated with sympathetic reactivity [HUT (*r* = 0.309, *P* = 0.016)].

CONCLUSION: In T2DM as VPT increases in right leg both parasympathetic and sympathetic reactivity response decreases.

PBS-05-2

Luseogliflozin (TS-071), a Novel SGLT2 Inhibitor, Improves Hyperglycemia and Prevents Diabetic Retinopathy in Rats

Michihito Onishi, Teisuke Takahashi, Haruhiro Yamashita, Emi Gunji, Takuya Takeda, Hideki Tomoike, Saeko Uchida and Kenzo Takahashi

Molecular Function and Pharmacology Laboratories, Taisho Pharmaceutical Co., Ltd., Japan

OBJECTIVE: Luseogliflozin (LUSEO), a novel sodium-dependent glucose co-transporter 2 (SGLT2) inhibitor, increases urinary glucose excretion and reduces hyperglycemia *in vivo*. Diabetic retinopathy is one of the major diabetic complications and a leading cause of blindness. This study is conducted to elucidate the effects of long-term treatment of LUSEO on glycemic control, retinal dysfunction and morphological abnormality in streptozotocin (STZ)-induced diabetic rats.

METHODS: STZ rats were treated with LUSEO as admixture to diet (0.001%, 0.003% and 0.01%) for 9 weeks. Diabetic control and normal control rats were fed a drug-free diet. At the end of the study, electroretinography (ERG) was performed to evaluate retinal functions and histopathological analyses of retinal sections were conducted.

RESULTS: Chronic administration of LUSEO significantly reduced glycated hemoglobin levels. LUSEO also prevented polyuria, glomerular hyperfiltration and kidney hypertrophy. ERG is a used technique to evaluate retinal functions and provides an early warning of retinal abnormalities in diabetes. The peak latencies of oscillatory potential (OP) in the ERG were prolonged as compared with normal control. LUSEO completely prevented the prolongation of peak latencies for OPs. In histopathological analyses, LUSEO prevented the reductions in the thickness of the inner plexiform layer and suppressed the expression of GFAP, a cellular marker for retinal damage, in Muller cells. Furthermore, LUSEO reduced the development of lens opacity as diabetic cataract.

CONCLUSION: These results indicate that LUSEO improves hyperglycemia and diabetic retinopathy in STZ rats. Our data suggest that LUSEO may be an attractive therapeutic option for the treatment of type 2 diabetes.

PBS-05-3

Homocysteine Induce Diabetic Nephropathy by Downregulating CD2-Associated Protein

Wei Ren¹, Jianjin Guo², Jing Xing³, Lu Jia³, Dongming Su³ and Weiping Jia¹

¹Department of Endocrinology and Metabolism, Shanghai Jiaotong University Affiliated Sixth People's Hospital; Shanghai Diabetes Institute, China; ²Department of Endocrinology, the First Affiliated Hospital of Nanjing Medical University, China; ³The Center of Metabolic Disease Research, Nanjing Medical University, China

AIM: To observe the role of homocysteine (Hcy) in the pathogenesis of diabetic renal injury in rat and explore effect of Hcy to the CD2-associated protein (CD2AP).

METHODS: Fourty Sprague–Dawley (SD) rats (about 200 g) were divided into control and diabetic groups. Diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ, 60 mg/kg). Animals with blood glucose levels higher than 16.7 mmol/L 72 h after STZ injection were included in the study. Similar weight rats receiving a single dose of citrate buffer were served as controls. Animals were killed by cardiac venipuncture at the end of the 4th, 8th and 12th week. Plasma Hcy was quantified using ELISA; serum glucose, creatinine, urinary microalbumin excretive rate (UAER) were measured by biochemical analyzer. The concentration of CD2AP in renal cortex was analyzed by Real time PCR and immunohistochemistry. All statistical analyses were performed using SPSS 13.0.

RESULTS: Compared with controls, the plasma Hcy level and UAER were markedly increased ($P < 0.05$) in diabetics rats, while the CD2AP protein level was significantly downregulated ($P < 0.01$). Plasma Hcy level was positively correlated with UAER ($r = 0.72$, $P < 0.01$) and CD2AP ($r = 0.85$, $P < 0.01$).

CONCLUSION: The plasma Hcy level plays an important role in the development of diabetic nephropathy. The mechanisms maybe related to Hcy decreased the expression of CD2AP resulting in the dysfunction of podocyte.

PBS-05-4

Low-Protein Diet Improves Blood and Urinary Glucose Levels and Renal Manifestations of Diabetes in C57BLKS-db/db Mice

Emi Arimura¹, Hiroaki Kawaguchi² and Masahisa Horiuchi³

¹Department of Life and Environmental Science, Kagoshima Prefectural College, Japan;

²Laboratory of Veterinary Histopathology, Joint Faculty of Veterinary Medicine, Kagoshima University, Japan; ³Department of Environmental Medicine, Graduate School of Medical and Dental Sciences, Kagoshima, Japan

PURPOSE: Dietary protein content is related clinically to the development of diabetic nephropathy. Here, we investigated how dietary protein content (12–24% energy) within the range used by humans affected renal manifestations including the expressions of genes involved in the renin-angiotensin (RA) system in control and diabetic mice. Moreover, we examined the effects of dietary protein content on HbA1c and urinary glucose.

METHODS: Control (CT) and leptin receptor-deficient obese (db) mice, 5 weeks old, were fed the diets below. Under ad libitum conditions, mice were fed 12%, 18% and 24% energy from protein (L-, M-, H-diet) for 8 weeks. Under pair-feeding conditions, db mice were supplied H-diet (db-Hp) to the equivalent energy to that consumed by db-L mice. Renal manifestations and values related to glucose and insulin were examined biochemically and pathologically.

RESULTS: Under ad libitum conditions, db mice consumed food and water dose-dependently of the dietary protein content, although they were consumed similarly by CT mice. CT-L mice showed lower urinary albumin and kidney weight, in association with lower mRNA levels of angiotensinogen and renin, than CT-H mice. Under pair-feeding conditions, db-L mice showed a lower ratio of kidney/body weight, HbA1C, and urinary glucose, and a higher β -cell distribution rate in the pancreas than db-Hp mice.

CONCLUSIONS: Low-protein intake in the range used by humans may relieve renal manifestations through the suppressed expression of genes in the renal RA system of CT mice. On the other hand, in db mice, low-protein intake improved hyperglycemia and the renal manifestations of diabetes.

PBS-05-5

The Comparison of Neuroprotective Effect Between DA-9801 and Alpha-Lipoic Acid in the Experimental Diabetes

Heung Yong Jin, Tae Sun Park, Kyung Ae Lee, Jae Moon Kim, Sun Hee Kim and Hong Sun Baek

Department of Internal Medicine, Chonbuk National University School of Medicine, Korea

DA-9801, extract from *Dioscorea japonica* Thunb and *Dioscorea nipponica* Makino, was reported to have neurotrophic activity. Therefore, we investigated that DA-9801 has protective effect on the peripheral nerves in the experimental diabetes comparing with alpha lipoic acid (ALA). Animals were divided into four groups ($N = 10$) and designated as follows according to the DA-9801 (100 mg/kg/day) and ALA (50 mg/kg/day) treatment: Normal, DM, DM + DA-9801, and DM + ALA. After 16 weeks, functional test such as mechanical allodynia using von frey filaments and thermal threshold with hot plate were performed. Biochemical parameters including nerve growth factor (NGF), TNF- α , and IL-6 in sciatic nerve and spinal cord were compared. Intraepidermal nerve fiber (IENF) density, and axonal morphology in sciatic

nerve were assessed for morphometric comparison among groups. Thresholds of von frey filament and hot plate were higher in the DA-9801 treated diabetic group more potently compared with ALA treatment at 8 week, however the pattern was reversed at 16 week. Western blot showed that NGF more increased and TNF- α and IL-6 more decreased in DA-9801 treated DM group compared with DM or DM + ALA group significantly ($P < 0.05$). IENFD was less reduced significantly in the DM + DA-9801 group than other DM groups (7.61 ± 0.32 vs 4.2 ± 0.26 vs 6.5 ± 0.30 , DM + DA-9801, DM, and DM + ALA, respectively $P < 0.05$). Mean myelinated axonal area in the sciatic nerves was higher significantly in the DM + DA-9801 group than other DM groups (69.2 ± 5.76 vs 54.0 ± 6.32 vs 63.1 ± 5.41 , DM + DA-9801, DM, and DM + ALA, respectively $P < 0.05$). Our results demonstrated the therapeutic possibility of DA-9801 in the diabetic peripheral neuropathy in the future.

PBS-06-1

Screening of KCNJ11 Mutation in Shanghai Type 2 Diabetes Mellitus with Poor Beta Cell Function

Shanshan Tang, Rong Zhang, Congrong Wang, Cheng Hu, Feng Jiang, Weihui Yu, Yuqian Bao and Weiping Jia

Shanghai Jiaotong University Affiliated Sixth People's Hospital, China

KEYWORDS: Type 2 diabetes mellitus; potassium inwardly-rectifying channel subfamily J, member 11 (KCNJ11); gene mutation

OBJECTIVE: To investigate the associations between mutations and variants of potassium inwardly-rectifying channel KCNJ11 and type 2 diabetes mellitus.

METHOD: Forty-one patients (30 male, 11 female) with type 2 diabetes mellitus were enrolled, whose average age was (57 ± 12) years old and fasting c-peptide were all <0.2 ng/L in OGTT test and with negative antibody test. PCR-direct sequencing was employed to detect KCNJ11 mutations and the frequencies of the discovered mutations and variants were then analyzed. Then, we recruited 6822 cases Han Chinese in shanghai (3410 patients with type 2 diabetes and 3412 controls). Anthropometric parameters and indices related to glucose and lipid metabolism were tested; all patients were genotyped for KCNJ11 rs5219 by Sequenom. We evaluated the association between the variant and the traits related to glucose metabolism.

RESULT: Only one synonymous mutation (S274S) was found in one participant at KCNJ11. Moreover, we also identified four variants in this study, including rs5215, rs5218, rs5219 and rs1800854. We found that rs5219 was significantly associated with type 2 diabetes. K allele was associated with increased risk of type 2 diabetes, with an odds ratio of 1.1264.

CONCLUSION: In this type 2 diabetes patients with low c-peptide levels, the major cause of pancreatic dysfunction may be not KCNJ11 mutations. K allele of KCNJ11 rs5219 variant was associated with increased risk of type 2 diabetes, with an odds ratio of 1.1264.

PBS-06-2

Genetic Analysis of a Mutant Mouse Progeny Mitigating ER Stress in Akita/Mysterin KO Mice Colony

Hatasu Kobayashi, Wanyang Liu, Junxia Yan, Yukiko Fujii, Hiroko Okuda, Toshiaki Hitomi, H. Kouji Harada and Akio Koizumi

Department of Health and Environmental Sciences, Kyoto University Graduate School of Medicine, Japan

OBJECTIVE: We have established Akita mice (Ins2Akita/+; a C96Y mutation in the Ins2 gene) develop early age-onset diabetes. Diabetes in Akita mouse has been proven to be attributed to ER stress brought by the unfolded mutant insulin. We produce mice lacking mysterin, the susceptibility gene for moyamoya disease (mysterin KO mice, mysterin-/-) and mated them with Akita mice to obtain double KO mouse. In a progeny of Akita/mysterin KO (Ins2Akita/+ and mysterin-/-), we found a male mouse which are resistant to diabetic phenotype. We hereby report phenotype characterization and genetic analysis for this progeny.

METHODS: The mutant male mouse and Akita male mice ($n = 5$) were evaluated by an intraperitoneal glucose tolerance test (IPGTT) after 16 h fasting and measuring of food intake.

RESULTS: In a founder male mouse, IPGTT revealed much improved glucose tolerance than in Akita mouse. Food intake of the mutant mouse was reduced (3.1 g/day) when compared with that of Akita (average: 6.0 g/day). Now we are establishing a progeny of this mouse for genetic analysis.

CONCLUSION: This mutant mouse revealed much less severe diabetic phenotype. The underlying mechanism of alleviation of diabetic phenotype strongly suggests that it mitigates ER stress caused by Akita mutation. Genetic dissection of this progeny may likely elucidate genetic mechanisms to reduce ER stress.

PBS-06-3

The Vascular Smooth Muscle Cell Specific Ablation of Mig-6 Augments the Neointima Formation in Balloon Injury Mouse Model

Koon Soon Kim, Ok Soon Kim, Kyoung Hye Jung, Jun Hwa Hong, Ju Hee Lee, Ye Eun Kang, Hyun Jin Kim, Young Suk Jo, Minho Shong and Jeong Ku Bon
Department of Internal Medicine, Chungnam National University School of Medicine, Korea

BACKGROUND AND AIMS: Mitogen Inducible Gene 6, Mig-6 is identified as a negative feedback inhibitor of epidermal growth factor receptor (EGFR) signal. Molecular target of neointima formation still has not been fully elucidated. We investigated the effect of Mig-6 gene ablation in VSMC and its role in intimal hyperplasia.

MATERIALS AND METHODS: Conditional ablated Mig-6 in the VSMC was generated using the Tagln-Cre mouse model (Taglncre/+Mig-6f/f; Mig-6d/d). To evaluate the neointima formation, we developed balloon injury mouse model in femoral artery. Primary cultured VSMCs were obtained from 10-week-old Mig-6f/f and Mig-6d/d male mice for immunoblotting, proliferation and migration assays.

RESULTS: The neointima formation of injured artery was significantly augmented in the Mig-6d/d mice compared to Mig-6f/f after balloon injury. Primary cultured Mig-6d/d VSMC caused a significant increase in the proliferative and migratory capability of the cells compared to Mig-6f/f. Furthermore, EGFR, PI3K, and MAPK inhibitors reversed these enhanced proliferation and migration of primary cultured Mig-6d/d VSMC. On western blotting, the increased phosphorylation of EGFR was observed in primary cultured Mig-6d/d VSMC compared to Mig-6f/f.

CONCLUSION: Collectively, we found that Mig-6 plays an important role in intimal hyperplasia through enhanced proliferation and migration of VSMC. It will provide a new insight into development of more effective ways for the treatment and prevention of neointima formation.

PBS-06-4

Genetic Variants of IPLA2 Indicate an Association with Type 2 Diabetes in a Chinese Population

Cheng Hu, Zhang Rong, Wang Congrong and Jia Weiping
Shanghai Jiao Tong University Affiliated Sixth People's Hospital, China

OBJECTIVE: Calcium-independent phospholipase A2(IPLA2) plays an important role in mediating glucose and lipid metabolism. In this study, we aimed to investigate the association of IPLA2 variants with type 2 diabetes in the Chinese population.

METHODS: A total of 6822 case-control participants of Han Chinese ancestry were included using a two-stage approach for this study. In the first stage, we enrolled 1892 type 2 diabetic patients and 1808 normal controls. Twelve tagging single nucleotide polymorphisms (SNP) of IPLA2 were genotyped. In the second stage, we additionally recruited 1518 type 2 diabetic patients and 1604 controls for further replication. Meta-analyses were performed after combining the two stages data to confirm the susceptible variants with type 2 diabetes.

RESULTS: In the first stage, we identified that rs2284060, rs132972, rs2076113 and rs5750549 were significantly associated with type 2 diabetes (OR = 1.163, 95% CI 1.053–1.285, $P = 0.0029$; OR = 0.8901, 95% CI 0.8056–0.9834, $P = 0.0220$; OR = 1.164, 95% CI 1.038–1.304, $P = 0.0091$ and OR = 0.8982, 95% CI 0.8071–0.9996, $P = 0.0492$, respectively). In the second stage, only rs5750549 showed a similar effect on type 2 diabetes (OR = 0.8957, 95% CI 0.7952–1.009, $P = 0.0694$). The meta-analyses combining two stages information showed that rs2284060, rs2076113 and rs5750549 were significantly associated with type 2 diabetes (OR = 1.119, 1.1033 and 0.8971, respectively; $P < 0.05$) in the Chinese population.

CONCLUSION: We concluded that genetic variants of IPLA2 were associated with type 2 diabetes in the Chinese population.

PBS-06-5

Plasma Resistin is Associated with Variants of the Decorin Gene, a Possible Resistin Receptor, in the General Japanese Population

Hiroshi Onuma¹, Yasuharu Tabara², Ryoichi Kawamura¹, Jun Ohashi³, Wataru Nishida¹, Yasunori Takata¹, Masaaki Ochi¹, Ryuichi Kawamoto⁴, Katsuhiko Kohara⁵, Tetsuro Miki⁵ and Haruhiko Osawa¹

¹Department of Molecular and Genetic Medicine, Ehime University Graduate School of Medicine, Japan; ²Department of Anti-aging and Genetics, Ehime Proteo-Medicine Research Center, Ehime University, Japan; ³Doctoral Program in Life System Medical Sciences, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Japan; ⁴Department of Community Medicine, Ehime University Graduate School of Medicine, Japan; ⁵Department of Geriatric Medicine, Ehime University Graduate School of Medicine, Japan

OBJECTIVE: Resistin, which antagonizes insulin action, is an adipokine secreted from adipocytes in mice. We previously reported that the G/G genotype of a single nucleotide polymorphism (SNP) at -420 (rs1862513), which was located in the promoter region of the human resistin gene (RETN), was associated with T2DM susceptibility. Recently, the isoform of decorin was identified as a resistin receptor in mice. We examined whether SNPs in the vicinity of the human decorin gene (DCN) were associated with plasma human resistin.

METHODS: In this study, we examined the association between six tag SNPs in the same linkage disequilibrium block around the human decorin gene, rs7139228, rs7956537, rs7308752, rs516115, rs3138167 and rs545666, and plasma human resistin in 2078 subjects in the general Japanese population.

RESULTS: Plasma human resistin was associated with the rs7139228, rs7956537, rs516115, and rs3138167 genotypes in the human decorin gene. A multiple regression analysis revealed that the genotype of rs7139228 (A/A), rs7308752 (G/G), or rs516115 (C/C) was inversely associated with plasma human resistin after adjusting for age, gender, body mass index, and SNP-420 of the human resistin gene. The effect of rs7139228 and SNP-420 appeared to be additive without synergistic interaction.

CONCLUSION: Plasma human resistin was associated with some tag SNPs around the human decorin gene in the general Japanese population. This suggests that decorin or its isoform thereof might also function as a resistin receptor in humans.

PBS-06-6

Melanocortin 4 Receptor Mutations in a Cohort of Obese Adults in China

Rong Zhang, Hu Cheng, Wang Congrong and Jia Weiping
Shanghai Jiao Tong University Affiliated Sixth People's Hospital, China

OBJECTIVE: Melanocortin 4 receptor (MC4R) makes an important contribution in regulating food intake and energy homeostasis and its mutations are the most common causes of monogenetic human obesity. We aimed to detect the mutations in MC4R in a cohort of obese adults in Han Chinese ancestry.

METHODS: A total of 35 unrelated severe obese patients of Chinese Han ancestry residing in Shanghai with BMI &g = 28 kg/m² were enrolled with some exclusion criterion including hypothalamic disease and secondary obesity. We screened the entire encoding regions of MC4R using direct sequencing method for detecting possible mutations in these severe obese patients.

RESULTS: No novel mutations were detected in these patients. One missense heterozygous mutation G231S and one nonsense mutation C277X were identified in two patients, respectively. These two mutation carriers were obese (BMI = 53.96 and 35.24 kg/m², respectively), but without any other endocrine abnormalities. In addition, we also detected three single nucleotide polymorphisms loci including V103I (rs2229616), rs139025325 and rs34114122.

CONCLUSION: We reported two mutations and three SNPs in severe obese adults in the Chinese for the first time. We considered that the mutations of MC4R might be the major cause of obese adults in Chinese. However, further functional studies should be done to elucidate the mechanism.

PBS-06-7

Liraglutide Ameliorate the Ethidium Bromide Induced Mitochondrial Dysfunction of Cultured β -Cell Which are the Model of MIDD

Makiko Ogata, Naoko Iwasaki, Risa Fujimaki, Miho Takizawa and Yasuko Uchigata
Diabetes Center, Tokyo Women's Medical University, Japan

OBJECT: We reported that real-time quantitative mitochondrial pH calculating system in cultured β cells. Using this system, we evaluate the real time

calculate mitochondrial inner membrane pH, and study the effectiveness of high dose (10 nmol/L) Liraglutide to the model of mitochondria induced diabetes and deafness (MIDD) in MIN6 cell.

METHOD: New mitochondrial pH calculating probe (MtpHGV) is transfected in MIN6 cells stably (MtpHGV-MIN6 cells). Mitochondrial pH change by glucose load was calculated by perfusion study. MIDD model was made by loading ethidium bromide. Ethidium bromide (EB) loading was done 0.5, 1, 10 µg/mL for 24 or 48 h in mtpHGV-MIN6 cells. Ten nanomolar Liraglutide was preloaded 3 h before glucose load.

RESULT: PH of outside of mitochondrial inner membrane (mtpH) show acidification by 25 mmol/L glucose load in MIN6 cells as reported previously. EB load inhibit this reaction dose and time dependent manner. 10 µg/mL EB load for 24 h completely inhibit mitochondrial membrane reaction by glucose. 1.0 µg/mL EB load for 24 and 48 h shows weakness of the reaction of glucose load. Ten nanomolar Liraglutide show recovering this weakness by 3 h preloaded, but showing no effect by co-apply with glucose.

CONCLUSION: MIDD model is made for determine mitochondrial function. Mitochondrial damage of MIDD model is ameliorated by 10 nmol/L Liraglutide.

PBS-06-8

Genetic Variations Within the APPL2 are not Associated with Type 2 Diabetes in Chinese Population

Qichen Fang, Shan Jiang, Weihui Yu, Rong Zhang, Cheng Hu, Kun Dong, Yuqian Bao, Chen Wang, Kunsan Xiang and Weiping Jia
Shanghai Jiaotong University affiliated No.6 People Hospital, China

OBJECTIVE: APPL1 and APPL2 are two adaptor proteins, which can mediate adiponectin signaling via binding to N terminus of adiponectin receptors in muscle cells. Our previous studies have demonstrated that genetic variants of APPL1 were correlated with body fat distribution in Chinese type 2 diabetic patients. In this study, we aimed to test the impacts of APPL2 genetic variants on glucose metabolism and insulin resistance in Chinese population.

METHODS: Six SNPs in APPL2 were genotyped in 3697 individuals, including 1808 non-diabetic controls and 1889 type 2 diabetic cases.

RESULTS: Linkage disequilibrium analysis revealed that the five SNPs including rs10861360, rs1196768, rs3751191, rs1107756 and rs2272495 were in modest linkage disequilibrium and formed two haplotype blocks in this region. rs935251 is excluded because of genotyping failure and rs1196744 because of departure from Hardy-Weinberg equilibrium. No individual SNPs showed an allelic association with type 2 diabetes ($P = 0.440-0.903$). None of these SNPs correlated with fasting plasma glucose level and 2-h plasma glucose level in either non-diabetic controls or type 2 diabetic patients. None correlations were found with fasting insulin level and 2-h insulin level in these two groups. None of the SNPs was correlated with plasma lipids including triglycerides, total cholesterol, high-density lipoprotein-, low density lipoprotein-cholesterol. Moreover, there were also no significant differences in HOMA-B and HOMA-IR according to these SNPs.

CONCLUSION: Genetic variations in APPL2 are not associated with type 2 diabetes in Chinese population. The SNPs in APPL2 gene may not play a major role in the development of type 2 diabetes.

PBS-07-1

GSK3- SCF^{βTrCP} Modulates ER Stress-Induced Apoptosis by Targeting ATF4 for Ubiquitination and Degradation in Pancreatic β-Cell

Yuko Nagao, Katsuya Tanabe, Masayuki Hatanaka, Masahiro Emoto and Yukio Tanizawa
The third Department of Medicine, Yamaguchi University Graduate School of Medicine, Japan

OBJECTIVE: ER stress may play a crucial role in loss of pancreatic β-cell mass, contributing to the progression of diabetes. GSK3 is negatively regulated by growth hormone signaling. When activated this kinase inhibits proliferation and promotes apoptosis in pancreatic β-cell. However, role of GSK3 on the induction of β-cell apoptosis under the stress condition is not understood yet. Therefore, we examined potential mechanisms by which GSK3 modulates β-cell apoptosis during ER stress.

METHODS: Mouse primary islets and MIN6 were treated with pharmacological agents provoking ER stress. A β-cell line having one copy of Ins2 C96Y

was established by crossing Akita mice with IT6 mice expressing SV40Tag in β-cells. GSK3 activity was inhibited by SB216763, a chemical inhibitor of GSK3, or by retrovirus mediated overexpression of GSK3β kinase dead mutant.

RESULTS: Pharmacological or genetic inactivation of the GSK3 attenuated ER stress-induced β-cell apoptosis with concomitant augmented ATF4 expression levels. We found that ubiquitination and degradation of ATF4 are governed by SCF^{βTrCP} in a GSK3-dependent manner. ATF4 is constitutively targeted for proteasomal degradation by SCF^{βTrCP}, which recognizes a conserved motif phosphorylated by GSK3. Furthermore, when transcriptional activity of ATF4 was reduced by overexpression of ATF4 dominant negative mutant or utilizing small interfering RNA, the antiapoptotic effect of GSK3 inhibition was significantly attenuated.

CONCLUSION: Our current study illustrates that GSK3 and SCF^{βTrCP} mediated ATF4 degradation is a proapoptotic mechanism in β-cell during ER stress. It may represent a novel area for therapeutic intervention in clinical diabetes.

PBS-07-2

Role of miRNA Regulating Glucose Metabolism in Glucotoxicity-Induced Beta-Cell Dysfunction

Ji-Won Kim, Young-Hye You and Kun-Ho Yoon

Department of Endocrinology, The Catholic University of Korea, Korea

Glucotoxicity plays a major role in the progressive deterioration of beta-cell function and development of type 2 diabetes mellitus. MicroRNAs (miRNAs) have been implicated in the functional regulation of key glucose metabolism pathways and insulin secretion in type 2 diabetes (DM) and may contribute to common disease complications. This study was to search the miRNAs related to glucotoxicity-induced beta-cell dysfunction.

To study the role of miRNAs in glucotoxicity-induced beta-cell dysfunction, we analyzed the miRNA expression patterns of primary rat islet for 3 days after exposure to glucotoxicity and confirmed up-regulated and down-regulated miRNAs. Among the down-regulated miRNAs, we demonstrate that miR-374 and -137 is a key player in glucotoxicity-induced beta-cell dysfunction. miR-374 and -137 expressions are decreased by glucotoxicity, and extrinsic inhibition of miR-374 and -137 by antisense miRNAs induces beta-cell dysfunction. Overexpression of miR-374 and -137 suppresses PGC-1α and Foxo-1 expression in glucolipotoxicity. Here we demonstrate that miR-374 and -137 mediated suppression of PGC-1α and Foxo-1 gene expression is an important initiation step of glucotoxicity induced beta-cell dysfunction and appropriate new target for early treatment.

PBS-07-3

Palmitate Induces Beta-Cell Dysfunction by Activating NADPH Oxidase Through via the Src Kinase Signaling

Yuichi Sato, Shimpei Fujimoto, Eri Mukai, Hiroki Sato, Yumiko Tahara, Kasane Ogura, Gen Yamano, Masahito Ogura, Kazuaki Nagashima and Nobuya Inagaki
Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

OBJECTIVES: Chronic hyperglycemia and hyperlipidemia exert deleterious effects on beta-cell function, respectively referred to as glucotoxicity and lipotoxicity. In pancreatic beta-cells, ATP production in mitochondria plays an essential role in glucose-induced insulin secretion, and reactive oxygen species (ROS) is one of the most important factors that impair the metabolism-secretion coupling in beta-cells. We recently reported that elevated ROS production and impaired ATP production at high glucose in diabetic Goto-Kakizaki (GK) rat islets are effectively ameliorated by Src inhibition. The aim of this study is to investigate the role of ROS in the palmitate-induced dysfunction of pancreatic beta-cells.

METHODS: The rat insulinoma INS-1D cells were exposed to palmitate (0.6 mmol/L) for 24 h, and incubated in low glucose condition with or without the specific Src inhibitor PP2 (10 nmol/L). Then an glucose stimulated insulin secretion (GSIS), an endogenous ROS production, and a NADPH oxidase activity were examined using batch incubation method, CM-H₂DCF fluorescence, and lucigen luminescence, respectively.

RESULTS: GSIS of INS-1D cells was markedly decreased in palmitate-treated condition compared with controls. Endogenous ROS production and NADPH oxidase activity were increased in palmitate-treated INS-1D cells. PP2 decreased the endogenous ROS production, and NADPH oxidase activity, and restored the insulin secretion of palmitate-treated INS-1D cells. Both

antioxidants (Vitamin E +Vitamin C) and ROS scavenger (Tempol and Ebselen) suppressed ROS overproduction and restored GSIS in palmitate-treated INS-1D cells.

CONCLUSION: Palmitate-induced beta-cell dysfunction would be partially caused by the ROS overproduction via activating NADPH oxidase. Palmitate may potentially activate NADPH oxidase via Src kinase signaling.

PBS-07-4

Clock-Controlled Output Gene *Dbp* is a Regulator of *Arnt/Hif-1* Gene Expression in Pancreatic Islet β -Cells

Hiroko Nakabayashi, Yasuharu Ohta, Masayoshi Yamamoto, Yosuke Susuki, Katsuya Tanabe, Manabu Kondo, Masayuki Hatanaka, Yuko Nagao and Yukio Tanizawa
Department of Bio-Signal Analysis, Yamaguchi University, Graduate School of Medicine, Japan

A transcription factor termed aryl hydrocarbon receptor nuclear translocator (ARNT)/hypoxia-inducible factor-1 β (HIF-1 β) has emerged as a potentially important determinant of pancreatic β -cell dysfunction and type 2 diabetes in humans. Eighty-two percent reduction in the *Arnt* expression was observed in islets from type 2 diabetic donors compared to non-diabetic donors. However, only few regulators of *Arnt* gene expression have yet been identified. Meanwhile, it was also revealed that disruption of the clock components CLOCK and BMAL1 leads to hypoinsulinemia and diabetes, but molecular details remain unclear. In this study, we investigated the novel molecular connection between *Arnt* and albumin D-element binding protein (*Dbp*), a clock-controlled output gene, in the development of diabetes. *Wfs1*^{-/-} mice with mild obesity (*Wfs1*^{-/-}Ay/a) develop severe diabetes. Real-time PCR revealed 50% reduction in *Dbp* mRNA, 50% increase in E4-binding protein (*E4bp4*) mRNA, and 30% reduction in *Arnt* mRNA level in isolated *Wfs1*^{-/-}Ay/a mice compared to the wild type. These changes were significant. E4BP4 is known to oscillate anti-phase to DBP, and binds to D-box as a transcriptional repressor. *Arnt* promoter-driven luciferase reporter assay in MIN6 cells revealed DBP activated *Arnt* promoter by 2.5-fold and E4BP4 competitively inhibited the effect. In addition, DBP and E4BP4 directly bound to a D-box element within the *Arnt* promoter when examined by ChIP assay in MIN6 cells. These results suggest down-regulation of *Dbp* and up-regulation *E4bp4* contribute to the β -cell dysfunction through direct suppression of *Arnt* expression.

PBS-07-5

Protective Effect of DPP-4 Inhibitor Vildagliptin on Pancreatic β -Cells in β -Cell Specific C/EBP β Transgenic Mice

Tomokazu Matsuda¹, Hiroaki Takahashi², Yusuke Mieda², Shun-Ichiro Asahara¹, Ayumi Kanno¹, Maki Koyanagi¹, Susumu Seino¹ and Yoshiaki Kido²

¹Division of Diabetes and Endocrinology, Department of Internal Medicine, Kobe University Graduate School of Medicine, Japan; ²Division of Medical Chemistry, Department of Biophysics, Kobe University Graduate School of Health Sciences, Japan

OBJECTIVE: We recently reported that accumulation of the transcription factor C/EBP β in β cells causes ER stress and reduced β cell mass, leading to β cell failure (Matsuda et al., J Clin Invest, 2010). We examined whether the DPP-4 inhibitor vildagliptin (vilda) can preserve pancreatic β cell mass in β cell-specific C/EBP β transgenic mice.

METHODS: β cell-specific C/EBP β transgenic (TG) mice showed a non-fasting glucose level of approximately 200 mg/dL with reduced β cell mass. TG and wild-type (WT) mice were orally treated with or without vilda dissolved in water (0.6 mg/mL) starting at 4 weeks of age.

RESULTS: Treatment of TG mice with vilda markedly ameliorated hyperglycemia and increased serum insulin levels (WT with vilda, 136 $\pm$ 4.0 mg/dL; WT without vilda, 132 $\pm$ 4.8 mg/dL; TG with vilda, 154 $\pm$ 11.1 mg/dL; and TG without vilda, 193 $\pm$ 7.2 mg/dL; *P* < 0.01). TG treated with vilda also showed significantly improved glucose tolerance. Immunostaining analyses of the pancreatic islets showed that TG mice treated with vilda had an 80% increase in β cell mass compared to untreated TG mice. Next, we examined the C/EBP β expression. Vilda had no effect on RNA levels of C/EBP β ; however, it reduced protein levels of C/EBP β . Insulin signaling was reduced in TG mice. Moreover, the expression levels of phospho-CREB and PDX-1 were decreased. However, they were restored by vilda.

CONCLUSION: The DPP-4 inhibitor vilda reduced the β cell failure in β cell-specific C/EBP β TG mice by increasing β cell mass.

PBS-07-6

Adrenomedullin is Induced by ER Stress and Protects β -Cells as Endogenous Antiapoptotic Substance in Islets

Yasuharu Ohta, Hiroko Nakabayashi, Manabu Kondo, Masayuki Hatanaka, Katsuya Tanabe and Yukio Tanizawa

Department of Bio-Signal analysis, Yamaguchi University, Graduate School of Medicine, Japan

Adrenomedullin (AM) is reported to have the cytoprotective role in podocytes, brain, and other tissues. To clarify the cytoprotective role of AM in pancreatic β -cells against ER stress, we investigated up-regulation of AM induced by ER stress and the effect of exogenous AM on ER stress. Our group and others have shown that *Wfs1*^{-/-} β -cells are susceptible to ER stress and that WFS1 deficiency itself evokes the UPR. We have also shown that selective β -cell loss and severe diabetes developed in *Wfs1*^{-/-} mice with mild obesity (*Wfs1*^{-/-} Ay/a). Real-time RT-PCR using isolated islets revealed significant upregulation by 7.5-fold in *Wfs1*^{-/-} mice and by 9.4-fold in *Wfs1*^{-/-} Ay/a mice compared to wild type. Twenty-four hour culture in the presence of 1 μ mol/L thapsigargin significantly increased AM mRNA expression in Min6 cells by 12.5-fold and AM secretion from Min6 cells by 2.2-fold. MIN6 cells were cultured in medium containing thapsigargin in the presence or absence of 100 nmol/L AM peptide for 24 h. Exogenous AM significantly suppressed Caspase-3 cleavage by 22%. pcDNA3-AM or pcDNA3-LacZ was transfected into Min6 cells 24 h prior to culture with thapsigargin and the apoptosis was detected by Caspase-3 cleavage and DNA ladder assay. The apoptosis of pcDNA3-AM-transfected cells was significantly suppressed compared with pcDNA3-LacZ-transfected cells. These findings suggest that ER stress-induced up-regulation of AM could counteract ER stress-induced apoptosis. We also find that pioglitazone induce AM expression in islets. Exogenous AM and inducer of endogenous AM may be used as a therapeutic agents to prevent β -cell apoptosis and the development of diabetes.

PBS-08-1

SIRT5 Regulates Urea Cycle by Deacetylation and Activation of Carbamoyl Phosphate Synthetase 1

Masahito Ogura, Yasuhiko Nakamura, Daisuke Tanaka, Xiaotong Zhuang, Yoshihito Fujita, Akio Obara, Akihiro Hamasaki, Masaya Hosokawa and Nobuya Inagaki
Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

OBJECTIVE: SIRT5 protein, an NAD-dependent deacetylase, is localized in nucleus and involved in life span extension by calorie restriction in yeast. SIRT5 is a mammalian SIRT2 homolog and the SIRT5 protein is localized in mitochondria. Since the function of SIRT5 in metabolism was unclear. The physiological role of SIRT5 was investigated.

METHODS: Total RNA was extracted from organs including liver, kidney, muscle, and heart in C57BL/6 mice fed, fasted for 24 h, or refed for 24 h after 24-h fasting, and quantitative RT-PCR was carried out. We established SIRT5-overexpressing transgenic (SIRT5 Tg) mice in which expression of mouse SIRT5 fused with FLAG tag at the C terminus was driven by the CAG promoter. Mitochondrial proteins prepared from livers of SIRT5 Tg mice and wild-type mice were analyzed using two-dimensional electrophoresis and MALDI-TOF-MS.

RESULTS: SIRT5 mRNA levels in liver and muscle were increased by fasting and were decreased to the levels in the fed condition by refeeding, but were unchanged in kidney or heart. Carbamoyl phosphate synthetase 1 (CPS1), a key enzyme of the urea cycle that catalyzes condensation of ammonia with bicarbonate to form carbamoyl phosphate, was identified as the target protein of SIRT5 in liver using two-dimensional electrophoresis and MALDI-TOF-MS. CPS1 was deacetylated and CPS1 activity was significantly increased in the liver of SIRT5 Tg mice. In hepatocytes of SIRT5 Tg mice, urea synthesis was upregulated compared to that in wild-type mice.

CONCLUSION: SIRT5 may regulate urea cycle in liver by deacetylation and activation of carbamoyl phosphate synthetase 1.

PBS-08-2

FTO Enhances Oxidative Stress and Lipogenesis in Non Alcoholic Fatty Liver Disease

Jianjin Guo¹, Wei Ren², Kuanfeng Xu¹, Dongming Su³ and Tao Yang¹

¹Department of Endocrinology and Metabolism, the First Affiliated Hospital of Nanjing Medical University, China; ²Department of Endocrinology and Metabolism, Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai Diabetes Institute, Shanghai Clinical Center of Diabetes, China; ³The Center of Metabolic Disease Research, Nanjing Medical University, China

OBJECTIVES: Nonalcoholic fatty liver disease (NAFLD) is strongly associated with obesity, hyperlipidemia, and type 2 diabetes mellitus (DM). Numbers of individual studies have found fat mass and obesity-associated (FTO) gene linked to obesity recently. We planned to investigate the expression and function of FTO in liver with lipid metabolism diseases.

METHODS: NAFLD rat model was established by feeding the animals with a high-fat diet for 12 weeks. Biomedical and oxidative stress indicators were detected.

RESULTS: A significant increase of FTO mRNA and protein levels was found in NAFLD group. Compared to the control group, AST and ALT levels were significantly raised by 1.4 and 3.1-fold by the high-fat diets feeding ($P < 0.01$). The elevated MDA level was increased by about 2.5-fold ($P < 0.01$) and the SOD levels reduced by 30% in the HFD group ($P < 0.01$). In addition, the FTO levels were positively associated with MDA and SOD contents.

CONCLUSIONS: This study demonstrates that increased FTO in liver could be involved in oxidative stress and lipid deposition that characterize the NAFLD.

PBS-08-3

Astaxanthin Reduces Hepatic Insulin Resistance and Inhibits the Progression of Lipotoxic Model of NASH

Yinhua Ni, Lili Zhan, Mayumi Nagashimada, Shuichi Kaneko and Tsuguhito Ota
Frontier Science Organization, Kanazawa University, Kanazawa, Japan

OBJECTIVE: Nonalcoholic steatohepatitis (NASH) and insulin resistance frequently coexists in subjects with obesity and type 2 diabetes. NASH can be defined as a lipotoxic liver injury caused by excess body adiposity. Hepatic inflammation and/or fibrosis could be caused by lipid peroxidation preceded by excessive hepatic lipid accumulation. Astaxanthin is a carotenoid compound that is known to be approximately 500 times more potent in inhibiting lipid peroxidation than vitamin E *in vitro*. Here, we examined the inhibitory effect of astaxanthin against the progression of NASH to clarify the significance of lipid peroxidation-mediated lipotoxicity and insulin resistance in the pathogenesis of NASH.

METHODS: Seven-week-old C57BL/6 mice were fed on a high-cholesterol/high-fat diet (CL) or a CL diet containing 0.02% astaxanthin.

RESULTS: After 12 weeks of CL feeding, the levels of TBARS in liver were significantly increased and histological examination revealed hepatic steatosis, inflammation and fibrosis. They showed hyperinsulinemia and glucose intolerance, indicating that mice fed on a CL diet developed NASH associated with insulin resistance. Astaxanthin administration markedly reduced hepatic lipid peroxidation, TG and cholesterol accumulation, and improved insulin sensitivity in CL group. Furthermore, astaxanthin inhibited fibrosis, lowering the TGF- β and collagen I mRNA expression, and hydroxyproline content. Astaxanthin administration in CL-fed mice led to enhanced insulin signal assessed by IR- β and Akt phosphorylation in the liver, associated with reduction of ER stress (CHOP/GRP78), attenuation of MAPK (JNK/p38MAPK) and NF- κ B activation in liver.

CONCLUSION: Astaxanthin, a strong antioxidant, inhibits the progression of NASH by attenuating lipid accumulation, lipid peroxidation, and insulin resistance.

PBS-08-4

Changes of Hepatic Cellular Retinol-Binding Protein-I (CRBP-I) in Relation to Fatty Liver Diseases

Md. Morshedul Alam, Sang Ah Lee, Gwanpyo Koh and Dae Ho Lee
Department of Internal Medicine, Jeju National University School of Medicine and Jeju National University Hospital, Korea

CRBP-I is a cellular binding protein for retinol and retinal, and involved in the regulation of adipogenesis and shown to be elevated in fatty liver diseases. Hepatitis B is also associated with hepatic steatosis.

AIM: We aimed to examine the hepatic and white adipose tissue (WAT) CRBP-I levels in control chow-fed (Control), high fat-fed (HF), db/db, and hepatitis B virus X antigen (HBx)-transgenic (HBx Tg) mice.

METHODS: C57BL/6J mice were fed control chow and high fat diet for 20 weeks, respectively. Age- and sex-matched whole body HBx Tg and db/db mice were also included. Immunoblotting study was done for CRBP-I measurement in study groups. The gene expression involved in retinoid metabolism, and tissue retinol and retinoic acid (RA) were also measured in the liver of HBx Tg and Control mice.

RESULTS: CRBP-I protein expressions in the liver and WAT of control, HF, and db/db mice was comparable between the groups. CRBP-I expression in liver, but not in WAT, of HBx Tg mice was significantly elevated compared with other three groups. The genes that involved in hepatic retinoid metabolism and signaling pathway, including CRBP-I, RXR α , and RAR α , and the tissue levels of retinol and RA were also elevated in the live of HBx Tg mice compared with Control mice.

CONCLUSION: Hepatic and WAT CRBP-I levels were not elevated obese animal models whereas the changes of CRBP-I and retinoid metabolism seem to be involved in hepatitis B-related liver diseases.

PBS-08-5

Metformin Attenuates Proteasome 26S Activity and Exerts Tumor Suppressing Effects in Human Hepatoma Cells

Akio Obara, Yoshihito Fujita, Abulizi Abudukadir, Toru Fukushima, Masaya Hosokawa and Nobuya Inagaki

Department of Diabetes and Clinical Nutrition, Kyoto University Graduate School of Medicine, Japan

OBJECTIVE: Although several clinical studies show that metformin reduces the risk of hepatocellular carcinoma, the effect of metformin on suppressing cell proliferation in liver remains unknown. Recent studies have suggested that mTOR signaling is involved in the anti-carcinogenic effect, and is regulated by the proteasome degradation system. The aim of this study was to investigate the effect of metformin on cell proliferation and the role of the proteasome degradation system in liver cancer cells.

METHODS: HepG2 cells were incubated in DMEM with metformin, regular insulin, or proteasome inhibitor (MG132). Cell proliferation rate was determined by MTT assay. Proteasome 26S activity was measured by fluorogenic proteasome substrate assay. Protein expressions of AMPK α , phospho-AMPK α , phospho-p70 S6 kinase, and DEPTOR were analyzed by western blotting.

RESULTS: Metformin activated AMPK and suppressed cell proliferation of HepG2 cells over 72-h incubation, but insulin did not. Suppression of mTOR signaling by metformin was confirmed by attenuation of phospho-p70 S6 kinase, a downstream target of mTOR. Metformin attenuated proteasome 26S activity and MG132, a proteasome inhibitor, suppressed cell proliferation, suggesting that metformin regulated the target molecule which was degraded by the proteasome 26S and was associated with the mTOR signaling. We evaluated the expression of DEPTOR, an mTOR suppressing substrate known to be degraded by the proteasome system, and found that it was increased in the presence of metformin.

CONCLUSION: Metformin suppressed cell proliferation of HepG2 cells. The proteasome degradation system may have an important role in suppression of cell proliferation of liver cancer by metformin.

PBS-08-6

SIRT5 Deacetylates and Activates Urate Oxidase in Mouse Liver Mitochondria

Yasuhiko Nakamura, Masahito Ogura, Kasane Ogura, Daisuke Tanaka and Nobuya Inagaki

Department of Diabetes and Clinical Nutrition, Graduate school of Medicine, Kyoto University, Japan

OBJECTIVE: Recently, we reported that carbamoyl phosphate synthetase 1 is deacetylated and activated by SIRT5 which is located at mitochondria. Our objective is to identify a novel protein which is deacetylated and the activity of which is regulated by SIRT5.

METHODS: Mitochondria-enriched fractions from livers of wild-type and SIRT5-overexpressing transgenic (SIRT5 Tg) mice were electrophoresed two-dimensionally, and western blot analysis was performed. The acetylated protein spots were detected using anti-acetylated-lysine antibody. The protein at the spot in which acetylation level was decreased in SIRT5 Tg mice

compared to that in wild-type mice was picked up and identified by MALDI-TOF-MS. Then, the acetylation levels and enzyme activity of the protein were compared between wild-type and SIRT5 Tg mice. To confirm the function of SIRT5, acetylation levels of in-vitro synthesized UOX protein by incubation with liver mitochondrial fraction of wild-type mice and SIRT5 Tg mice were examined.

RESULTS: Urate oxidase (UOX), a key enzyme of the purine base catabolism from urate to allantoin, was identified by MALDI-TOF-MS. The acetylation levels of UOX in SIRT5 Tg mice were approximately half as much as those in wild-type mice and the UOX activity was significantly increased by 1.4-fold in SIRT5 Tg mice compared to those in wild-type mice. Furthermore, in-vitro synthesized UOX protein was acetylated by incubation with liver mitochondrial fraction of wild-type mice, and the acetylation levels were significantly decreased by incubation with that of SIRT5 Tg mice.

CONCLUSION: It is suggested that SIRT5 activates UOX through deacetylation in mitochondria of mouse hepatocytes.

PBS-08-7

The Effect of Clusterin on Hepatic Lipogenesis

Hye-Young Seo¹, Mi-Kyung Kim¹, Yun-A Jung¹, Gwon-Soo Jung², Mi-Kyung Choi¹, Jung-Guk Kim², Ji-Yun Jeong², Kwi-Hyun Bae², Keun-Gyu Park² and In-Kyu Lee²

¹Department of Internal Medicine, Keimyung University School of Medicine, Korea;

²Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea

AIMS: Fatty liver is common in obese subjects with insulin resistance. Sterol regulatory binding protein-1c (SREBP-1c) is a master regulator of lipogenic gene expression in liver. Clusterin is an 80 kDa disulfide-linked heterodimeric protein and plays a role in cholesterol transport from peripheral tissues to the liver. However, little is known about the effects of clusterin on hepatic lipogenesis. Here, we examined whether clusterin regulates SREBP-1c expression in liver.

METHODS: The effect of adenovirus-mediated overexpression of clusterin (Ad-Clu) on the expression of SREBP-1c stimulated by insulin or liver X receptor (LXR) agonist (TO901317) in liver cell lines (AML12, H4IIE) were determined by Northern and Western blot analysis. The *in vivo* effects of Clusterin on hepatic lipogenesis were verified by tail vein injection of Ad-Clu into high fat diet-fed mice. Transient transfection study was performed to assess the effect of clusterin on SREBP-1c promoter activity. The effect of Clusterin on LXR-DNA binding activity was examined by electrophoretic mobility shift assay (EMSA).

RESULTS: Ad-Clu inhibited insulin or LXR agonist-stimulated SREBP-1c expression and its promoter activity. *in vivo* model, Ad-Clu in liver of HFD-fed mice by tail vein injection inhibited hepatic steatosis through inhibition of SREBP-1c expression.

Additionally, Clusterin inhibited LXR-agonist-stimulated LXR-DNA binding to its response consensus element on SREBP-1c promoter.

CONCLUSION: This study shows that Clusterin inhibits hepatic lipogenesis *in vitro* and *in vivo* through downregulation of SREBP1c. The present study suggested that clusterin plays a critical role in the regulating hepatic lipogenesis.

PBS-08-8

Elovl6 Promotes Nonalcoholic Steatohepatitis in Mice and Humans

Takashi Matsuzaka¹, Tang Nie¹, Noriko Suzuki-Kemuriyama¹, Motoko Kuba¹, Yoshimi Nakagawa¹, Kiyooki Ishii¹, Masako Shimada¹, Kazuto Kobayashi¹, Shigeru Yatoh¹, Akimitsu Takahashi¹, Hirohito Sone¹, Naoya Yahagi¹, Hiroaki Suzuki¹, Makoto Nakamura², Nobuhiro Yamada¹ and Hitoshi Shimano¹

¹Department of Internal Medicine (Endocrinology and Metabolism), Faculty of Medicine, University of Tsukuba, Japan; ²Department of Gastroenterology, Kyusyu Medical Center, National Hospital Organization, Japan

Nonalcoholic steatohepatitis (NASH) is associated with obesity and type 2 diabetes, and increase potential for liver cirrhosis and cancer. ELOVL family member 6, elongation of very long chain fatty acids (Elovl6) is a microsomal enzyme, which regulates the elongation of C12-16 saturated and monounsaturated fatty acids. We have shown previously that Elovl6 is a major target for sterol regulatory element binding proteins in the liver, and that it plays a critical role in development of obesity-induced insulin resistance by modifying fatty acid composition. To further investigate role of Elovl6 in development of NASH and its underlying mechanism, we utilized three independent mouse

models with loss or gain of function of Elovl6, and human liver samples isolated from patients with NASH in this study. Our results demonstrated that (1) Elovl6 is a critical modulator for atherogenic high-fat diet-induced inflammation, oxidative stress, and fibrosis in the liver, that (2) ELOVL6 expression is positively correlated with severity of hepatosteatosis and liver injury in NASH patients, and that (3) deletion of Elovl6 reduces palmitate-induced activation of the NLRP3 inflammasome; this could be at least one of the underlying mechanisms, by which Elovl6 modulates a progress of NASH. In conclusion, Hepatic long-chain fatty acid composition is a novel determinant in NASH development, and Elovl6 could be a potential therapeutic target for prevention and treatment of NASH.

PBS-08-9

Metformin Suppresses Gene Expression for Selenoprotein P in Hepatocytes via an AMPK-FoxO3a Pathway

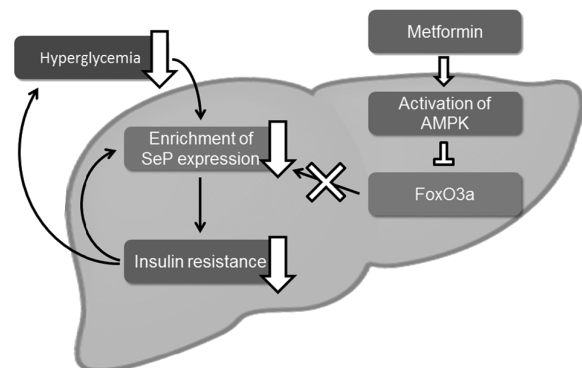
Hiroaki Takayama¹, Hirofumi Misu¹, Atsushi Teraguchi², Natsumi Hirose¹, Reina Saito¹, Ken-Ichi Miyamoto², Hisakazu Iwama³, Koji Murao⁴, Shuichi Kaneko¹ and Toshinari Takamura¹

¹Department of Disease Control and Homeostasis, Kanazawa University Graduate School of Medical Sciences, Japan; ²Department of Hospital Pharmacy, Kanazawa University, Japan; ³Life Science Research Center, Kagawa University, Japan; ⁴Departments of Advanced Medicine, Kagawa University, Japan

OBJECTIVE: Selenoprotein P is a hepatokine that induces insulin resistance (Misu *et al.*, Cell Metabolism, 2010). In this research, we investigated the regulatory mechanism for SeP expression in hepatocytes.

METHODS: Selenoprotein P gene (*SEPP1*) promoter activity was assessed by using luciferase assay in H4IIEC hepatocyte.

RESULTS: (1) Metformin treatment suppressed *SEPP1* promoter activity dose- and time- dependently ($P < 0.001$). (2) Co-administration of an AMPK inhibitor compound C cancelled metformin-induced suppression of *SEPP1* promoter activity ($P < 0.001$). (3) An AMPK activator AICAR treatment suppressed *SEPP1* promoter activity similarly to metformin ($P < 0.001$). (4) Putative FoxO3a binding site was conserved among various species in metformin-responsible element of *SEPP1* promoter. (5) FoxO3a knockdown by siRNA cancelled metformin-induced suppression of *SEPP1* promoter.



CONCLUSION: Metformin suppresses *SEPP1* promoter activity via an AMPK-FoxO3a pathway in hepatocytes. Hypoglycemic effects of metformin might be mediated partly by selenoprotein P suppression in the liver.

PBS-09-1

Depeptidyl Peptidase-4 Inhibitors Improved Glycemia by Suppression of α -Cell Proliferation in a STZ Diabetic Model

Tsuyoshi Yangimachi, Yukihiro Fujita, Yasutaka Takeda, Jun Honjo, Hiroya Kitsunai, Hidemitsu Sakagami, Yumi Takiyama, Atsuko Abiko, Yuichi Makino and Masakazu Haneda

Department of Internal Medicine, Asahikawa Medical University, Japan

OBJECTIVE: Dipeptidyl peptidase-4 (DPP-4) inhibitors have been reported to delay the occurrence of hyperglycemia in animal models of diabetes by enhance of endogenous incretins, but the mechanism is not well elucidated. In the present study, we assessed whether DPP-4 inhibition suppresses the progression to hyperglycemia in low-dose streptozotocin (STZ)-induced diabetic mice, and then investigated how DPP-4 inhibition affects islet function and morphology.

METHODS: The DPP-4 inhibitor, des-fluoro-sitagliptin (SITA) was administered to mice during and after STZ injections, and in some mice also prior to STZ. We measured metabolic variables, examined immunohistochemical analysis, and quantified pancreatic hormone contents.

RESULTS: In control animals, STZ resulted in hyperglycemia associated with impaired insulin secretion and excess glucagon secretion. In SITA-treated STZ mice, especially in mice administered SITA earlier and longer, these metabolic abnormalities were improved. We observed β -cell loss and dramatic α -cell expansion associated with decreased insulin content and increased glucagon content following STZ administration. In SITA-treated mice, islet architecture and insulin content was preserved, and no significant increase in glucagon content was observed despite injection with STZ. Interestingly, we observed α -cell proliferation prior to hyperglycemia after STZ exposure and SITA treatment reduced its proliferation. In STZ mice, we observed increased α -cell GIP and reduced islet GIPR expression concomitantly with α -cell expansion, which was substantially recuperated the treatment by SITA.

CONCLUSION: Our results indicate that the ability of DPP-4 inhibition to suppress the progression to STZ-induced hyperglycemia involves both alleviation of β -cell death and α -cell proliferation.

PBS-09-2

Effect of GLP-1 Analogue, Exendin-4 on Inhibition of Islet Fibrosis

Shin-Young Park, Ji-Won Kim and Kun-Ho Yoon

Department of Endocrinology and Metabolism, The Catholic University of Korea, Seoul, Korea

OBJECTIVE: Pancreatic islet fibrosis might be to lead the β -cell loss and dysfunction in type 2 diabetes. Pancreatic stellate cell (PSC) are known to be related to pancreatic fibrosis and inflammation, and are the result of extracellular matrix protein synthesis. Therefore, we investigated the effect of GLP-1 analogues on activated PSCs *in vitro*, and pancreatic islets fibrosis *in vivo*.

METHODS: PSCs cultured in 5.5, 27.7 mmol/L glucose and 27.7 mmol/L with 10 nmol/L Ex-4 for 3 and 9 days. Western blot analyses for the expressions of α -SMA and ECM proteins, such as CTGF, α -collagen I and fibronectin, were performed. Level of Transforming growth factor- β in culture media are measured.

For *in vivo* study, saline, Ex-4 (2.5 nmol/L/kg/twice a day) and Insulin were injected into OLETF rats for 12 weeks. We analyzed pancreatic islet morphology, quantified β -cells mass and the severity of islet fibrosis.

RESULTS: GLP-1 receptor expression was strongly induced with high glucose stimulation in PSCs. The protein level of α -SMA was increase by high glucose however attenuated by Ex-4 treatment for 3 days. After 9 days culture of PSCs in high glucose, the expressions of CTGF and α -collagen I synthesis were increased and also attenuated by Ex-4 treatment. Islet fibrosis in OLETF rats was significantly attenuated by Ex-4 treatment than control group of glucose matched insulin treated group.

CONCLUSION: The data suggesting the effects of Ex-4 on high glucose induced PSCs activation and the prevention of islet destruction by fibrosis in the animal model of type 2 diabetes.

PBS-09-3

Assessment of Gene Expression in Enteroendocrine K-Cells

Kazuki Sasaki, Norio Harada, Shunsuke Yamane, Akihiro Hamasaki, Kazuyo Suzuki, Daniela Nasteska, Atsushi Muraoka, Erina Joo, Yaeko Kondo, Kimitaka Shibue, Takanari Harada and Nobuya Inagaki

Department of Diabetes and Clinical Nutrition, Kyoto University, Japan

OBJECTIVE: Gastric inhibitory polypeptide (GIP) is an intestinal hormone secreted from enteroendocrine K-cells in response to meal ingestion that potentiates insulin secretion. Gene expression of transporters, channels, receptors, and co-expressing other hormones in K-cells is unclear, because separating these cells from intestinal other epithelial cells *in vivo* is difficult. For the purpose, we isolated K-cells from the intestinal epithelial cells of GIP-GFP knock-in mice which were generated to visualize K-cells by EGFP and evaluated gene expression of GIP co-expressing intestinal hormones and molecules which might be involved in GIP secretion.

METHODS: GFP-positive cells and GFP-negative cells were collected from the small intestine of GIP-GFP knock-in mice by flow cytometry system, and mRNA was extracted. Then, mRNA expression levels of some molecules and intestinal hormones were evaluated by semi-quantitative RT-PCR.

RESULTS: The expression levels of GFP and GIP mRNA were significantly higher in GFP-positive cells than those in GFP-negative cells. Additionally, the expression levels of SUR1, GLUT2, GLUT5, free fatty acid receptors (GPR40 and GPR120) and Pax6 transcriptional factor were significantly higher in GFP-positive cells than those in GFP-negative cells. Furthermore, the expression levels of some intestinal hormones, such as secretin and cholecystokinin, were higher in GFP-positive cells than those in GFP-negative cells.

CONCLUSION: Some glucose transporters and free fatty acid receptors are expressed in K-cells, indicating that they might be involved in GIP secretion from K-cells. In addition, some intestinal hormones are co-expressed in K-cells.

PBS-09-4

Withdrawn

PBS-09-5

Effects of the Supplement Contain Glutamine, Fiber, and Oligosaccharide on Colitis and Glucagon-Like Peptide in Mice

Erina Joo¹, Shunsuke Yamane¹, Akihiro Hamasaki¹, Norio Harada¹, Tetsuro Matsunaga², Atsushi Muraoka¹, Kazuyo Suzuki¹, Daniela Nasteska¹, Toru Fukushima¹, Tatsuya Hayashi³, Hidemi Tsuji¹, Kenichiro Shide¹, Kinsuke Tsuda⁴ and Nobuya Inagaki¹

¹Department of Diabetes and Clinical Nutrition, Kyoto University, Graduate School of Medicine, Japan; ²AJINOMOTO Integrative Research for Advanced Dieting, Graduate School of Agriculture, Kyoto University, Japan; ³Laboratory of Sports and Exercise Medicine, Graduate School of Human and Environmental Studies, Kyoto University, Japan; ⁴Laboratory of Metabolism, Graduate School of Human and Environmental Studies, Kyoto University, Kyoto, Japan

OBJECTIVE: The supplementation product enriched with glutamine, dietary fibers, and oligosaccharide (GFO), is widely used for enteral nutrition support. Given the intestinotrophic effects, GFO is also expected to attenuate the symptoms of ulcerative colitis (UC). In this study, we investigated whether GFO has suppressive effects on mucosal damage in UC in a mouse experimental model. We also investigated the effect of GFO on glucagon-like peptide secretion.

METHODS: C57BL/6 mice received 2.5% of dextran sulfate sodium (DSS) in drinking water for 5 days to induce colitis. They were given 0.25 mL of GFO or 20% of glucose solution as control twice daily for 10 days. In addition, we evaluated the effect of single oral administration of GFO on plasma GLP-1 levels in mice.

RESULTS: The body weight loss and disease activity index (DAI) were significantly lower in GFO-treated mice compared to glucose-treated mice. The colon length was significantly longer in GFO-treated mice compared to glucose-treated mice. Histological findings indicated that intestinal inflammation was significantly attenuated in GFO-treated mice. Furthermore, GFO treatment significantly inhibited the DSS-induced increase in mRNA expression of IL-1 β . In a single oral administration, plasma GLP-1 levels were significantly higher in GFO-administered mice compared to those in glucose-administered mice.

CONCLUSION: These results suggest that GFO is effective in preventing the progression of mucosal damage in UC. We speculate that GFO stimulates GLP-2 secretion concomitantly with GLP-1 secretion and attenuates the development of mucosal damage of UC via enhancement of GLP-2 secretion.

PBS-10-1

Beta-Cell Surrogates for the Cure of Type 1 Diabetes Mellitus from Neonatal Pig Liver-Derived Hepatocytes via Viral Transduction of PDX-1/VP16, BETA2/NeuroD and MafA and Chemically Defined Medium

Dong-sik Ham, Ji-Won Kim, Min-Jung Kim and Kun-Ho Yoon

Department of Endocrinology & Metabolism, College of Medicine, The Catholic University of Korea, Seoul, Korea

Generation of beta-cell surrogate from non-beta cells is urgently needed to treat diabetes mellitus because current therapies, organ or islet cell transplantation, have some limitations such as shortage of donors, immune suppression. Liver-derived cells could be attractive source for generating beta cell surrogates because of their differentiating and proliferating capacity. Also, liver and pancreas share common characteristics such as glucose sensing ability. Therefore, liver-derived cells can be transdifferentiated to beta-like cells in optimal culture condition.

We Isolated hepatocytes from neonatal pig livers, and adenovirally transduced Ad-PDX-1/VP-16, BETA2/NeuroD and MafA to induce trans-

differentiation into insulin-producing cells and chemically defined medium. We note that cells highly expressed GLUT-2 and insulin as well as other endocrine related markers. Then, we quantified insulin positive cells in induced hepatocytes. Also, we evaluate the function of glucose-responsiveness in transduced cells. As a result, they could not only secrete insulin and c-peptide by glucose stimulation *in vitro* but also improve hyperglycemia in diabetic nude mice after renal capsular transplantation. At 6 weeks after transplantation, glucose tolerance test were statistical significantly improved by transplantation. Engrafted cells highly expressed insulin and c-peptide in the kidney graft.

In conclusion, we generated functional insulin-producing cells from neonatal pig derived hepatocytes via sequential transduction of Ad-PDX-1/VP-16, BETA2/NeuroD and MafA. These results suggest that neonatal pig derived hepatocytes could be useful source for the beta cell surrogates and could provide the basis of generating for transplantable beta cell source for the treatment of diabetes mellitus.

PBS-10-2

Studies on Polyvinyl Alcohol-Macro-Encapsulated Islets for Diabetes Therapy

Shoichiro Sumi¹, Yuanjun Gu², Meirigeng Qi³, Naoaki Sakata⁴, Zhi Qi⁵, Yasumasa Shirouzu¹, Kaichang Yang⁶, Goichi Yanai¹, Akihito Hiura¹ and Kazutomo Inoue⁷
¹Institute for Frontier Medical Sciences, Kyoto University, Japan; ²Jumpsun Bio-medicine (shanghai) Co., Ltd, Shanghai, China; ³University of Illinois, Chicago, IL, USA; ⁴Tohoku University, Sendai, Japan; ⁵Nankai University, Tianjin, China; ⁶Taipei Medical University, Taipei, Taiwan; ⁷Inoue Clinic Diabetes Center, Kyoto, Japan

Micro-encapsulated islets used in recent clinical trials are not fully retrievable after intraperitoneal transplantation (Tx). We studied retrievable and exchangeable macro-encapsulated islets. Polyvinyl alcohol (PVA) is a hydrophilic polymer and its aqueous solution becomes gel through micro crystallization by freezing and thawing. Utilizing this feature we developed PVA-macroencapsulated islets (PVA-MEIs).

Rat islets suspended in Euro-Collins solution containing 3% PVA were encapsulated as mesh-reinforced sheet-shape PVA-MEIs by freezing and thawing.

Insulin secretion, *in vitro*, was increased by high glucose (16.7 mmol/L) followed by returning to basal levels in low glucose (3.3 mmol/L) in PVA-MEIs even after 14-day culture, whereas it was no longer observed after 7-day culture in free islets. When cultured in media containing 10% heat-inactivated FBS, 10% or 20% fresh human plasma (FHP), free islets were destroyed by FHP, but no changes were observed in PVA-MEIs, in which insulin content was also preserved.

PVA-MEIs containing 750 rat islets were transplanted intraperitoneally to the streptozotocin (STZ; 220 mg/kg, i.p.)-induced diabetic mice. Nonfasting blood glucose showed a rapid decrease from pre-Tx levels (approximately 580 mg/dL) to the levels between 155 and 273 mg/dL and stayed lower than DM control up to 30 days with a consistent increase in body weight. PVA-MEIs Tx prevented exacerbation of metabolic and renal function and pathology in STZ-diabetic mice. PVA-MEIs cryo-preserved for 1, 7 and 30 days showed similar function *in vitro* and corrected hyperglycemia when transplanted with a slight impairment in the 30-day group.

PVA-MEIs seem to be a promising modality for future DM therapy.

PBS-10-3

Attenuated Primary Graft Failure of PEGylated Islet as Assessed by Quantitative Islet MR Imaging

Sang-Man Jin, Sunghwan Suh, Se Won Kim, Hye Jeong Kim, Ji Cheol Bae, Kyu Yeon Hur, Myung-Shik Lee, Moon Kyu Lee and Jae Hyeon Kim
 Division of Endocrinology and Metabolism, Department of Internal Medicine, Samsung Medical Center, Korea

Surface camouflage of islets using poly (ethylene glycol; PEG) has been reported to attenuate the immune response in islet allotransplantation and xenotransplantation. However, little is known about the role of islet PEGylation in primary islet graft failure in intra-portal islet transplantation. We aimed to determine whether PEGylation could protect islets from primary graft failure.

Using rat syngeneic marginal mass intra-portal islet transplantation model, post-transplant glycemic level of recipient rats transplanted with PEGylated and non-PEGylated islets were compared. Using magnetic resonance (MR) imaging of ferucarbotran-labeled islet, the area of hypointense spots representing PEGylated and non-PEGylated islets were compared.

PEGylation of islet improved glycemic control of syngeneic intraportal marginal mass islet transplantation recipients. Quantitative islet MR imaging revealed higher area of hypointense spots in PEGylated islet group in immediate post-transplant period. The higher area of hypointense spots in PEGylated islet group was translated to the better post-transplant outcome.

In conclusion, PEGylation protects islets from primary graft failure in intraportal islet transplantation. The protective effect of PEGylation on the primary graft failure was demonstrable with ferucarbotran labeling of islet before PEGylation.

PBS-10-4

Anti-Hypoxia Effect of Perfluorocarbon Carried Alginate Microcapsule

Heon Seok Park, Ji-Won Kim, Haiyan An and Kun-Ho Yoon
 The Catholic University of Korea, Korea

BACKGROUND: Microencapsulated islets is a promising approach for the final solution of Type 1 diabetes. Failure was often ascribed to the lack of biocompatibility generating inflammatory response, or limited immunobARRIER competence or hypoxia. The aim of this study is to optimize microencapsulation of islets with perfluorocarbon and to observe the anti-hypoxia effect on PFC *in vivo* and *in vitro*.

METHODS: To optimize the microencapsulated of SD-rat islets and perfluorocarbon ratio, we adjusted the polymerization solution. Microencapsulated SD-rat islets with perfluorocarbon were incubated in hypoxia chamber at 6 h. PFC-alginate microencapsulated islets were transplanted into a peritoneal cavity of STZ-induced SD-rat. And the PFC-alginate capsulated islets were harvested on 24 h after transplantation. We performed AO/PI to confirm the cell death.

RESULTS: We used 20% of perfluorocarbon ratio with alginate. Perfluorocarbon reduced the islet damage by hypoxia. PFC-alginate capsule harvested at 24 h after transplantation in STZ-induced SD-rat. the anti-hypoxia effect of perfluorocarbon was confirmed in the alginate encapsulated islets. PI-positive cells in PFC-alginate microencapsulated islets were significantly lower than alginate only microencapsulated islets.

CONCLUSIONS: We conclude that these new methods can be applied to islets encapsulated in materials as complex as PFC-alginate. Measurements made with these materials revealed that PFC emulsion improves survival of encapsulated islets under hypoxic conditions.

PBS-10-5

Development of 123I-Labeled Exendin Derivative Targeting to GLP-1 Receptor for Insulinoma SPECT Imaging

Xiaotong Zhuang¹, Kentaro Toyoda¹, Hiroyuki Fujimoto¹, Hiroyuki Kimura², Yuu Ogawa², Eri Mukai¹, Masashi Ueda², Takashi Temma², Mitsuharu Hirai³, Mikako Takagi³, Asami Kon³, Hirokazu Matsuda³, Masahiro Ono², Hideo Saji² and Nobuya Inagaki¹

¹Department of Diabetes and Clinical Nutrition, Graduate School of Medicine Kyoto University, Japan; ²Department of Patho-Functional Bioanalysis, Graduate School of Pharmaceutical Science, Kyoto University, Japan; ³Arkay, Inc., Kyoto, Japan

OBJECTIVE: Insulinomas are the most common pancreatic neuroendocrine tumors. Insulinomas express glucagon-like peptide-1 receptor (GLP-1R) with high density and incidence. Thus, a radiolabeled compound bound to GLP-1R has been expected as a useful tool for imaging insulinomas. In this study, we designed [Nε-(3-[123I]iodobenzoyl)lysine12]-Exendin(9-39)-NH₂ ([123I]IB12-Ex(9-39)) targeting GLP-1R on insulinoma cells, and evaluated its utility as a probe for single-photon emission computed tomography (SPECT) imaging of insulinomas in the mouse model.

METHODS: The binding affinity of IB12-Ex(9-39) to human GLP-1R was evaluated by competitive binding assay using the prepared membranes of GLP-1R expressing cells. To assess the *in vivo* selectivity, biodistribution studies were conducted with INS-1-xenografted mice at 15, 30, 60, 120, and 360 min after [125I]IB12-Ex(9-39) injection. SPECT scans were performed after intravenous administration of [123I]IB12-Ex(9-39). In addition, stability of [123I]IB12-Ex(9-39) *in vivo* was evaluated by analysis of the extracted tumor homogenate with reverse phase HPLC analysis.

RESULTS: IB12-Ex(9-39) had a high binding affinity for GLP-1R (IC₅₀ = 1.6 nmol/L). The *in vivo* biodistribution of [125I]IB12-Ex(9-39) in INS-1-

xenografted mice showed a high uptake in the tumor (12% ID/g at 6 h) and high tumor-to-blood (T/B), tumor-to-muscle (T/M), and tumor-to-pancreas (T/P) ratios (T/B = 30, T/M = 75, T/P = 2.4 at 6 h). SPECT studies using [123I]IB12-Ex(9-39) in xenografted mice showed the clear image of the tumor 30 min after injection. Furthermore, [123I]IB12-Ex(9-39) showed high stability *in vivo*.

CONCLUSION: These results show that [123I]IB12-Ex(9-39) targeting GLP-1R would be useful as a radiolabeled probe for imaging insulinomas with SPECT.

PBS-10-6

Mechanical Immune Isolation System Using Nanofilter for Pancreatic Islet Transplantation

Hae Kyung Yang, Jae Hyoung Cho, Ji Won Kim, Heon Seok Park, Shin Young Park, Jin Sun Chang, Joung Ah Shin and Kun Ho Yoon
Division of Endocrinology and Metabolism, College of Medicine, Catholic University of Korea, Seoul, Korea

Pancreatic islet transplantation has recently emerged as an alternative therapy for cure of type 1 diabetes and some type 2 diabetes patients. But widespread clinical application of islet transplantation is currently limited by immune rejection of transplanted islets, the need for lifelong immunosuppression and hypoxic injury. To minimize both cellular and humoral immune attack on the islet graft, microencapsulation using biomaterials for immunoisolation has been introduced. However hypoxia and immune rejection still remains as major problems. Here, we introduce a special filter blocking immune cells while permitting passage of glucose and insulin.

We designed a PEO (polyethylene oxide)-functionalized straight nanochannel array filter, based on porous alumina. To prevent immune rejection by human IgG, the pore size of the nanochannel should be smaller than hydrodynamic diameter of IgG (15 nm). PEO was coated on oxide surface to prevent protein adhesion. This novel biofilter showed superior immunoprotection, high permeability for nutrients and antifouling property. We examined how the diffusion of glucose and IgG varies with the various pore sizes of the nanochannel.

IgG was effectively blocked by the filter with pore size <26 nm and glucose passed more effectively with increasing pore size. Based on the hydrodynamic size of IgG and the employment of PEO, we were able to design an ideally optimized biofilter to block IgG and to be permeable to nutrients.

A novel PEO-coated biofilter with 18–26 nm sized pores was effective in immune isolation by blocking immunoglobulins while permitting the passage of nutrients.

PBS-10-7

Targeting the PGC-1 α to Overcome the Harmful Effects of Glucocorticoid on Expansion and Transdifferentiation of Neonatal Porcine Pancreas Cell Clusters

Young-Hye You, Ji-Won Kim, Seung-Hyun Ko and Kun-Ho Yoon
Department of Endocrinology, Catholic University School, Korea

AIMS: PGC-1 α has recently been implicated in a crucial factor in glucocorticoid-suppressed expansion and transdifferentiation of porcine NPCCs. We investigated whether the suppression of PGC-1 α expression protects against β -cell dysfunction by dexamethasone (Dx) treatment *in vitro* and *in vivo* determined the mechanism of action of PGC-1 α in porcine NPCCs.

METHODS: Porcine NPCCs were treated with Dx (1 μ mol/L) in monolayer culture. The expression of transcription factors was determined by RT-PCR and staining. For *in vivo* study, Ad-siPGC-1 α infected porcine NPCCs were transplanted into kidney subcapsule of normal nude mice and Dx (1 mg/kg) was injected daily for 4 weeks.

RESULTS: Suppression of Dx or PGC-1 α -induced Pdx-1 gene level was normalized by siPGC-1 α . Nucleic-Foxo-1 and cytoplasmic-Pdx-1 were shown by Dx treatment. However, these were translocated by siPGC-1 α . Dx-induced PGC-1 α positive cells were suppressed by siPGC-1 α . As a consequence of that, reduction of Pdx-1 and insulin cell by Dx treatment increased by siPGC-1 α . *in vivo* study, expression of insulin in the graft tissue disappeared in the Dx injected group. However, siPGC-1 α + Dx injected group showed strong insulin expression in the graft.

CONCLUSION: Our results suggest that transdifferentiation of the porcine NPCCs into β -cells are influenced by Dx treatment which might be resulted by suppression of pancreas key transcription factors and PGC-1 α plays an important role in the expansion and transdifferentiation of porcine NPCCs. PGC-1 α is an attractive target for modulating the deleterious effects of glucocorticoid on the pancreas stem cells.

PBS-11-1

Critical Role of Malate-Aspartate Shuttle in Induction of Incretin Responsiveness by Formation of Pseudoislets

Ghupurjan Ghani¹, Masahiro Iwasaki², Masahito Ogura², Norihide Yokoi², Tadao Shibasaki², Kohtaro Minami² and Susumu Seino³

¹Division of Diabetes and Endocrinology, Department of Internal Medicine, Kobe University Graduate School of Medicine, Japan; ²Division of Cellular and Molecular Medicine, Kobe University Graduate School of Medicine, Kobe, Japan; ³Divisions of Cellular and Molecular Medicine, and Diabetes and Endocrinology, Department of Internal Medicine, CREST, Kobe University Graduate School of Medicine, Kobe, Japan

OBJECTIVE: Cell-cell interactions are involved in the regulation of cellular functions. It is well known that insulin secretion from intact pancreatic islets is much greater than that from dispersed beta-cells. We aimed to clarify the role of beta-cell-beta-cell interaction in insulin secretion.

METHODS: Pseudoislets (PIs) were formed from clonal beta-cells (designated MIN6-K20 β -cells) by culture on gelatin-coated dishes for 7 days. Insulin secretion was measured by batch incubation method with stimulation of glucose and glucagon-like peptide-1 (GLP-1). Metabolome analysis was performed using capillary electrophoresis/mass spectrometry (CE/MS).

RESULTS: Monolayer-cultured MIN6-K20 β -cells secreted insulin in a glucose-dependent manner, but did not respond to GLP-1, an incretin that potentiates insulin secretion through cAMP signaling. Interestingly, formation of PIs drastically induced potentiation of insulin secretion by GLP-1. While cAMP content was only slightly increased by GLP-1 in monolayer-cultured MIN6-K20 β -cells (MCCs), it was markedly increased in PIs. The intracellular ATP level was significantly higher in PIs than that in MCCs. Metabolome analysis revealed glutamate and aspartate to be major metabolites contributing to cAMP responsiveness in PIs. Since these metabolites are intermediate metabolites of the malate-aspartate (MA) shuttle, activity of the shuttle might be enhanced in PIs. Glucose-induced insulin secretion (GIIS) itself was not affected by aminooxyacetate (AOA), an inhibitor of the MA shuttle, in PIs, whereas the potentiation of GIIS by GLP-1 was markedly abolished in PIs by AOA.

CONCLUSION: Activation of the MA shuttle by beta-cell-beta-cell interaction is critical in normal regulation of insulin secretion.

PBS-11-2

HMG-CoA Reductase Inhibitors Ameliorate Palmitate-Induced Inhibition of GSIS by Reducing SREBP2 Expression and Cellular Cholesterol Levels

Hyun Min Kim¹, Mi-Ra Yun², Hyung Jun Kim², Byung Hun Jeon², Hanna Seok¹, Ji Hye Huh¹, Byung-Wan Lee¹, Eun Seok Kang¹, Hyun Chul Lee¹ and Bong Soo Cha¹

¹Department of Internal Medicine, Yonsei University College of Medicine, Korea; ²Brain Korea 21 project for Medical Science, Yonsei University College of Medicine, Seoul, Korea

BACKGROUND: SREBP-2 plays a crucial role in the regulation of cholesterol metabolism in many cells and activation of SREBP-2 in β -cells is known to cause loss of β -cell mass with accumulation of cholesterol. Here, we investigated the change of gene expression involved in cellular cholesterol homeostasis in palmitate-induced β cell dysfunction and the effects of pravastatin, atorvastatin, and simvastatin on cellular cholesterol level and insulin secretion from INS-1 cells.

METHODS: INS-1 cells were incubated in high palmitate condition (300 μ mol/L) with or without pravastatin, atorvastatin, and simvastatin for 24 h. SREBP2 expression was assessed by PCR and immunoblot. Glucose-stimulated insulin secretion was conducted. Intracellular cholesterol content was measured.

RESULTS: Palmitate induced SREBP2 expression in INS-1 cells in a dose-dependent manner. SREBP2 expression was reduced in INS-1 cells incubated in high palmitate condition with pravastatin treatment. As expected, palmitate treatment results in impaired glucose-stimulated insulin secretion. Addition of pravastatin prevented the deleterious effects in INS1 cells. To investigate the underlying mechanism, we measured intracellular cholesterol level. Palmitate treatment significantly increased cellular cholesterol level, however, pravastatin reduced intracellular cholesterol level, both free and esterified form. The more lipophilic statins, atorvastatin and simvastatin, showed the same results

showed the same results on SREBP2 expression, GSIS, and intracellular cholesterol levels as pravastatin did.

CONCLUSION: In summary, we have observed that various HMG-CoA reductase inhibitors ameliorate palmitate-induced inhibition of GSIS and the decreased expression of SREBP2 and intracellular cholesterol levels may be related with this effect.

PBS-11-3

Interaction of Incretin and Sulfonylurea Through Epac2 in Insulin Secretion

Harumi Takahashi, Tadao Shibasaki, Shihomi Hidaka, Toshimasa Takahashi, Aika Ono and Susumu Seino

Division of Cellular and Molecular Medicine, Kobe University Graduate School of Medicine, Japan

OBJECTIVE: We recently found that cAMP sensor Epac2 is a target of sulfonylurea (SU). To investigate the interaction of incretin and SU through Epac2 in insulin secretion, we examined the effects of combination of SU and incretin or cAMP analog on insulin secretion and activation of Epac2/Rap1 signaling.

METHODS: We examined the effects of combination of SUs and GLP-1 or 8-pCPT-2'-O-Me-cAMP (8-CPT), an Epac-selective cAMP analog, on insulin secretion from isolated mouse pancreatic islets. Activation of Rap1 by SUs and 8-CPT in insulin-secreting MIN6 cells was examined by GTP-Rap1 pull-down assay. Next, we examined dynamics of insulin secretion by SUs and GLP-1 or 8-CPT from perfused mouse pancreata.

RESULTS AND CONCLUSION: In pancreatic islets, GLP-1 and 8-CPT potentiated glibenclamide (GLB)-induced insulin secretion in the presence of 8.8 mmol/L glucose. At low concentration of glucose (4.4 mmol/L), GLP-1 also potentiated GLB-induced insulin secretion. Similarly, glimepiride (GLM)-induced insulin secretion was potentiated by GLP-1 and 8-CPT at both 4.4 and 8.8 mmol/L glucose. In MIN6 cells, activation of Rap1 was enhanced by combination of 8-CPT and GLB or GLM. In perfusion experiment, GLB induced biphasic (early and late phases) insulin secretion similar to that induced by glucose. GLP-1 markedly potentiated both early and late phases of insulin secretion induced by GLB at 4.4 mmol/L glucose. 8-CPT also potentiated GLB-induced insulin secretion in both early and late phases. These results suggest that combined incretin and SU augments insulin secretion through Epac2/Rap1 signaling.

PBS-11-4

Grb10 Inhibits Glucose-stimulated Insulin Release from Pancreatic β -Cells Associated with Suppressing of Insulin/IGF-1 Signaling Pathway

Ling Li¹, Yunxia Zhu², Mingliang Zhang², Dechao Yin², Junxi Lu¹, Feng Liu³, Chen Wang¹ and Weiping Jia¹

¹Diabetes Institute, Shanghai Jiao Tong University, China; ²Department of Endocrinology and Metabolism, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, China; ³Departments of Pharmacology, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA

OBJECTIVE: Grb10 is an adaptor protein that interacts with insulin receptor and insulin like growth factor-1 receptor. Grb10 transgenic mice showed impaired glucose tolerance. The aim of the study was to explore the effect of Grb10 on β -cell function.

METHODS: Grb10 protein expression was detected in islets from rats fed with chow or high fat and high sugar (HFHS) diet. The effects of Grb10 on glucose-stimulated insulin secretion and insulin/IGF-1 signaling pathway in islets were investigated in rat islets overexpressing Grb10 by adenovirus transfection.

RESULTS: Grb10 was expressed in both rat and human islets. In addition, Grb10 expression in islets was increased in rats fed with HFHS diet (relative expression: 2.03 ± 0.29 vs 0.98 ± 0.13 , $P < 0.05$) compared to rats fed with chow. *in vitro* study showed Grb10 expression was significantly increased in islets treated with palmitate (0.4 and 1 mmol/L), IL-1 β (50 U/mL) or high levels of glucose (20 mmol/L). Twenty millimolar glucose-induced insulin release was impaired in Grb10 overexpressed cells compared with control (islets: 2.23 ± 0.37 vs 3.54 ± 0.66 μ g/mg protein, $P < 0.05$; dispersed islet cells: 6.16 ± 0.59 vs 10.20 ± 1.29 ng/10⁵ cells, $P < 0.05$). Moreover, insulin- and IGF-1-induced Akt and ERK1/2 phosphorylation in rat dispersed islet cells was reduced and even abolished by Grb10 overexpression.

CONCLUSION: Grb10 expression was up-regulated in rat islets treated with higher levels of glucose, free fat acid and IL-1 β . In addition, Grb10 overexpression in islets impaired glucose-stimulated insulin secretion and insulin/IGF-1-stimulated Akt and ERK1/2 signaling pathway. Taken together, our study demonstrates that Grb10 is a potential target to improve β -cell function.

PBS-11-5

Regulation of Actin Dynamics by N-WASP and Cofilin in Pancreatic Beta-Cells and its Role in Insulin Secretion

Tadao Shibasaki¹, Eitai Uenishi¹, Harumi Takahashi¹, Hitomi Hamaguchi¹, Yutaka Oiso² and Susumu Seino¹

¹Division of Cellular and Molecular Medicine, Kobe University Graduate School of Medicine, Japan; ²Division of Endocrinology and Diabetes, Nagoya University Graduate School of Medicine, Japan

OBJECTIVE: Actin dynamics in pancreatic beta-cells is involved in insulin secretion. However, how actin dynamics are regulated by intracellular signaling is not known. The objective of this study is to clarify the role of actin dynamics regulated by N-WASP and cofilin in glucose-induced insulin secretion (GIIS).

METHODS: N-WASP and cofilin activities by glucose stimulation were examined in insulin-secreting MIN6 cells. The effect of dominant-negative (DN) mutant of N-WASP on actin dynamics was also investigated in primary cultured mouse pancreatic beta-cells infected with adenovirus carrying AcGFP1-labeled actin. The effects of DN-N-WASP and DN-cofilin on GIIS were evaluated using perfusion of MIN6 cells.

RESULTS: We found that N-WASP, which promotes actin polymerization through activation of actin nucleation factor Arp2/3 complex, is activated by glucose stimulation in MIN6 cells. The activation of N-WASP was essential for glucose-induced F-actin remodeling in living pancreatic beta-cells. Introduction of DN-N-WASP into MIN6 cells significantly suppressed GIIS, especially the second phase. We also found that cofilin, which severs F-actin in its dephosphorylated (active) form, is converted to the phosphorylated (inactive) form by glucose stimulation in MIN6 cells, thereby promoting F-actin remodeling. In addition, DN-cofilin markedly reduced the second phase of GIIS.

CONCLUSION: Actin dynamics regulated by the balance of N-WASP and cofilin activities determine a biphasic response of GIIS.

PBS-11-6

Chronic Effects of NERP-1 and 2 on Insulin Secretion and Insulin Gene Expression in Pancreatic Beta-Cells

Marie Rhee¹, Ji-Won Kim¹, Hideki Yamaguchi², Masamitsu Nakazato² and Kun-Ho Yoon¹

¹Department of Internal Medicine, Catholic University School of Medicine, Korea; ²Neurology, Respiratory, Endocrinology, and Metabolism, Division of Internal Medicine, Faculty of Medicine, University of Miyazaki, Miyazaki, Miyazaki, Japan

AIMS: Neuroendocrine regulatory peptides NERP-1 and NERP-2 are novel amidated peptides derived from VGF, a polypeptide secreted from neurons and endocrine cells through a regulated pathway. It was reported that NERP-1 and 2 may have local modulator function on human endocrine system and clearly expressed in human pancreas islets.

METHODS: We confirmed the expression of NERP-1 and 2 on human diabetes patient's pancreas as well as diabetic animal models. And we investigate the alteration of pancreas specific transcription factors, insulin secretion, and insulin granule-related proteins by NERPs expression.

RESULTS: In normal/diabetic human and mice models, NERP2 levels were dramatically increased in diabetic pancreas. When the INS1 cells were incubated with 10 nmol/L NERPs during 3 days, translocated FOXO1 and decreased PDX1, BETA2/NeuroD and insulin levels were shown by NERP2 treatment. Glucose stimulated insulin secretion levels were blunted when the INS1 cells and primary rat islets were incubated with NERP-1 and 2. In the readily releasable pool which is associated with the first phase of glucose-stimulated insulin release, the number of granules was decreased by NERP1 and 2. The insulin granule-related protein and mRNA were down-regulated by NERP2 treatment.

CONCLUSION: NERP-2 expression was increased in diabetic conditions. Also, NERP2 might play an important role in the insulin secretion through regulation of insulin secretory granule and beta-cell transcription factors. Therefore, we suggest that NERPs may be potent endogenous suppressors of glucose-dependent insulin secretion.

PBS-11-7

Src Regulates Insulin Secretion by Modulating Glucokinase Activity in INS-1 Cells

Hiroki Sato, Shimpei Fujimoto, Kazuaki Nagashima, Eri Mukai, Masahito Ogura, Yuichi Sato, Gen Yamano, Yumiko Tahara, Kasane Ogura, Kazu Sugizaki and Nobuya Inagaki
Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

OBJECTIVE: Impaired glucose-stimulated insulin secretion (GSIS) is an important feature of diabetes mellitus. We recently reported that high glucose-induced ROS production in islet cells is elevated in diabetic Goto-Kakizaki (GK) rats, and Src (c-Src) inhibition effectively ameliorates ATP production and insulin secretion by improving mitochondrial function. However the precise role of Src in glucose metabolism in pancreatic beta cells is not fully elucidated. In the present study, we investigated the role of Src in glucose metabolism in pancreatic beta cells using the rat insulinoma cell line INS-1 cells.

RESEARCH DESIGN AND METHODS: INS-1 cells are transfected with Src siRNA or scramble siRNA as control. After 48-h incubation, real-time PCR, western blotting, and measurements of insulin secretion, cellular ATP content, glucose utilization and glucokinase activity were carried out.

RESULTS: Forty-eight hours after transfection of Src siRNA, suppression of Src expression was confirmed by real-time PCR and western blotting. Compared to control, Src siRNA reduced glucose-induced increase in insulin secretion and intracellular ATP content. On the other hand, Src siRNA did not suppress insulin secretion induced by combination of ketoisocaproate and monomethyl succinate, or by high potassium stimulation significantly. Src siRNA also suppressed glucose utilization in glycolysis pathway, and in addition, activity of glucokinase, a key enzyme of glycolysis pathway, was also reduced by Src siRNA.

CONCLUSIONS: Src plays an important role in insulin secretion by regulating glucokinase activity in INS-1 cells.

PBS-11-8

The Rab27a Effector Exophilin7 Promotes Fusion of Insulin Granules Without Stable Docking to the Plasma Membrane

Hao Wang, Ray Ishizaki, Xu Jun, Kazuo Kasai, Hiroshi Gomi and Tetsuro Izumi
Laboratory of Molecular Medicine, Institute for Molecular and Cellular Regulation, Gunma University, Japan

OBJECTIVE: The Rab27a effector granuphilin mediates the docking of insulin granules to the plasma membrane through interactions with Rab27a on the granule membrane and the syntaxin-1a/Munc18-1 complex on the plasma membrane. However, phenotypes of insulin exocytosis differ considerably between Rab27a- and granuphilin-deficient pancreatic β cells, suggesting that other Rab27a effectors function in those cells. We found that one of putative Rab27a effector, exophilin7 is expressed in pancreatic β cells.

METHODS: (1) Glucose and insulin tolerance tests. (2) Islet perfusion assays to examine insulin secretory ability. (3) Electron microscopy to examine the intracellular distribution of insulin granules. (4) Immunoprecipitation and immunoblotting. (5) TIRF microscopic analysis for direct observation of the fusion events.

RESULTS: (1) Exophilin7-null mice exhibit no gross alterations in glucose tolerance or insulin secretion. (2) Exophilin7-null islets exhibit decreased insulin secretion in response to strong stimulation. (3) Exophilin7 has no effect on intracellular distribution or plasma membrane-docking of insulin granules. (4) In contrast with granuphilin, exophilin7 has no affinity to Munc18-1 or syntaxins on the plasma membrane. (5) Exophilin7 affects exocytosis of insulin granules without stable docking to the plasma membrane.

CONCLUSION: Exophilin7 is expressed in the pancreatic β cells and promotes fusion of insulin granules without stable docking to the plasma membrane.

PBS-12-1

The JAK/STAT Signaling is Essential for Human *REG I α* Transcription in Pancreatic β Cells

Akiyo Yamauchi, Asako Itaya-Hironaka, Sumiyo Sakuramoto-Tsuchida, Kiyomi Yoshimoto, Tomoko Miyaoka, Takanori Fujimura, Hiroki Tsujinaka, Chikatsugu Tsuchida, Hiroyo Ota and Shin Takasawa
Department of Biochemistry, Nara Medical University, Japan

OBJECTIVE: Human *regenerating gene* (*REG*) *I α* gene, which encodes an autocrine/paracrine growth factor, was induced in pancreatic β cells by the

combined addition of interleukin (IL)-6 and dexamethasone (Dx). Here, we have investigated how the *REG I α* gene is induced by IL6/Dx in β cells.

METHODS: The reporter plasmids containing several length of 5'-flanking region of human *REG I α* gene were transfected into pancreatic β cell derived cell lines (rat RINm5F, hamster HIT-T15, and human 1.1B4). After IL-6/Dx stimulation, the promoter activity was measured by luciferase assay. The interaction of nuclear proteins with the promoter DNA was assayed by electrophoretic mobility shift assay (EMSA).

RESULTS: The progressive deletion of the promoter down to position -146 retained enhancement of human *REG I α* promoter activity by IL-6/Dx, but an additional deletion to position -74 caused the loss of the inducibility, suggesting that the minimal region responsive to IL-6/Dx is -146 to -75. Analysis of the responsive region revealed a potential Signal Transducer and Activator of Transcription (STAT)-binding site at position -142 to -134. The disruption of the STAT-binding sequence completely blocked the IL-6/Dx-induced *REG I α* transcription. The addition of AG490, a Janus kinase (JAK) 2 inhibitor, significantly inhibited the IL-6/Dx-induced *REG I α* transcription. EMSA revealed that IL-6/Dx stimulation increased activated STAT in β cell nuclei.

CONCLUSION: These results indicated that the JAK/STAT signaling is involved in the IL-6/Dx-induced human *REG I α* gene transcription for pancreatic β cell regeneration.

PBS-12-2

The Effects of T3 and TR- β Selective Thyromimetics (KB-141) on the Proliferation of Pancreatic β -Cells

Jeonghyun Park¹, Taekyun Kim¹, Na Han¹, Seungman Kim¹, Eunjo Lee¹, Taenyun Kim¹, Minjung Kwon¹, Soonhee Lee¹, Mikyung Kim¹, Byungdoo Rhee¹ and G. J. Grover²

¹Department of Internal Medicine, Inje University, Korea; ²Department of Pharmacology, Eurofins-Drug Safety Laboratories, Dayton, NJ, USA

BACKGROUNDS: Thyroid hormone (T3) influences a variety of physiological processes, including cell growth, differentiation and metabolisms in mammals. KB-141, the TR β -selective thyromimetics would show its favorable benefits on β -cells without untoward systemic side effects. The aim of our study is to clarify the effects of KB-141 on the proliferation of insulin secreting β cells by KB-141T3.

MATERIALS AND METHODS: RINm5, INS-1 cells and isolated primary rodent islets (SD rats) were used in our experiments. Triiodothyronine (T3) and KB-141 were applied to cultured cell lines and isolated primary rodent islets in various concentrations and time intervals along with vehicle only control. At 24, 48 and 72 h of continuous exposure, viable cells were harvested and counted. In isolated rodent islets, Ki-67, insulin and glucagon counterstaining were performed. TR β 1 expression, viability, proliferation were analyzed by Western blot and RT-PCR, CCK-8, BrDU, FACS, TUNNEL assay and Trypan Blue negative cell number in a Thomas's hemacytometer. Insulin secretory function of exposed β -cells were verified by the amount of insulin mRNA and GSIS.

RESULTS: T3 and KB-141 significantly promoted the growth of RINm5, INS-1 cells, and the β -cells in isolated primary islets and improved glucose stimulated insulin secretion.

CONCLUSION: KB-141 would be used as a fundamental diabetes treatment to increase functioning β -cell mass without untoward systemic side effects caused by non-specific thyroid hormone receptor stimulation.

KEYWORDS: KB-141, thyromimetics, β -cells, stimulation, proliferation.

PBS-12-3

Reduction in Pancreatic β -Cell Mass Caused by Enhanced Expression of *Cdkn1c* as a Result of Interaction Between *C/EBP β* and Epigenetic Control

Shun-Ichiro Asahara¹, Kyoko Teruyama², Hiroaki Etoh², Hiroyuki Inoue², Yuka Ihara², Yukina Kawada², Tomokazu Matsuda¹, Kazuki Yasuda³, Masato Kasuga³, Susumu Seino¹ and Yoshiaki Kido²

¹Department of Internal Medicine, Kobe University Graduate School of Medicine, Japan;

²Department of Biophysics, Kobe University Graduate School of Health Sciences, Japan;

³Reserch Institute National Center for Global Health and Medicine, Japan

BACKGROUND: The relationship between pancreatic β cell mass and the onset of type 2 diabetes mellitus has received a lot of attention recently. Our

research focused on the Cdkn1c gene, because it is involved in the regulation of pancreatic β cell mass. The Cdkn1c gene is an imprinting gene whose expression is controlled by the non-coding RNA Kcnq1ot1. We found that when the expression of Kcnq1ot1 decreased, epigenetic alterations induced an increase in the expression of Cdkn1c, which, in turn, led to a decrease in the pancreatic β cell mass. We have already reported that the transcription factor C/EBP β accumulates in the pancreatic β cells of high fat-fed mice. It has been reported that a binding motif of C/EBP β is present in the Cdkn1c promoter. So we hypothesize that the accumulation of C/EBP β in pancreatic β cells with reduced expression of Kcnq1ot1 causes further enhancement of Cdkn1c expression and promotes pancreatic β cell failure.

METHODS: Kcnq1ot1 truncated C/EBP β overexpressing mice (KT) were produced by crossbreeding Kcnq1ot1 truncated mice with pancreatic β cell specific C/EBP β overexpressing mice.

RESULTS: *in vivo* studies have shown that compared to C/EBP β overexpressing mice and wild type mice, KT mice show significantly higher blood glucose levels, smaller pancreatic β cell mass, and enhanced expression of Cdkn1c in the pancreatic islets.

CONCLUSIONS: The findings suggest that the introduction of epigenetic modifications into MIN6 cells or pancreatic β cells may lead to enhanced binding of C/EBP β to the Cdkn1c promoter, then an increase in the expression levels of Cdkn1c, and a decrease in pancreatic β cell mass.

PBS-12-4

Development of Non-Invasive PET Probe for Quantifying Pancreatic β -Cell Mass Using Fluorine-18-Labeled Exendin-4

Hiroyuki Fujimoto¹, Kentaro Toyoda¹, Hiroyuki Kimura², Yuu Ogawa², Eri Mukai¹, Zhuang Xiaotong¹, Masashi Ueda³, Takashi Temma², Mitsuharu Hirai⁴, Hirokazu Matsuda², Hideo Saji² and Nobuya Inagaki¹

¹Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan; ²Department of Patho-Functional Bioanalysis, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan; ³Radioisotopes Research Laboratory, Kyoto University Hospital, Faculty of Medicine, Kyoto University, Kyoto, Japan; ⁴Arkray, Inc., Kyoto, Japan

OBJECTIVE: The volume of pancreatic β -cells is known to decrease during development and progression of diabetes. A technique for measurement of β -cell volume *in vivo* is required, but a non-invasive method to detect pancreatic β -cells has not been developed. The aim of this study is to address whether the mass of pancreatic β -cells can be quantified non-invasively by positron emission tomography (PET) targeting glucagon-like peptide-1 receptors (GLP-1R), using fluorine-18-labeled exendin-4 ([18F]exendin-4).

METHODS: For developing PET imaging probe, the lysine residue of exendin-4 at 12 was labeled with [18F]. For evaluating GLP-1R specificity, binding assay *in vitro* was performed. For assessment of *in vivo* selectivity, biodistribution study was performed by intravenous administration of [18F]exendin-4 to mice. At appropriate time points after administration, selected organs and blood were harvested and their weight and radioactivities were measured. Furthermore, [18F]exendin-4 (3MBq) was systematically administered and its accumulation in pancreas was imaged by PET using microPET system.

RESULTS: The binding assay analysis showed competitive inhibition of [125I]exendin(9-39) binding by specific non-radioactive [19F]exendin-4 and its IC₅₀ was 4.4 nmol. Biodistribution study showed that radioactivity of pancreas was 20.4%dose/g and highest at 60 min. The ratio of radioactivity in pancreas to that in blood, liver, intestine, and kidney were 30.9, 35.9, 8.0, 2.4, respectively. MicroPET imaging revealed clear, remarkable accumulation of radioactivity of [18F]exendin-4 in pancreas.

CONCLUSION: The [18F]exendin-4 could serve as a useful probe for non-invasive PET imaging for the evaluation of pancreatic β -cell mass.

PBS-12-5

The Importance of 6-O-Sulfate Groups in Heparan Sulfate in the Mouse β -Cell Proliferation During Pregnancy

Iwao Takahashi, Tomomi Sato, Fumi Sato, Nina Yoshida, Kazuaki Ohashi and Koji Nata
Department of Medical Biochemistry, Iwate Medical University School of Pharmacy, Japan

OBJECTIVE: Maternal pancreatic islet proliferation in pregnancy is one of the interesting phenomena for β -cell expansion in physiological conditions. However, the molecular mechanisms underlying these events are only partially understood. Heparan sulfate (HS) is linear polysaccharides consisting

of repeating disaccharide unit backbone onto which is superimposed a complex pattern of modifications, most notably addition of sulfate groups. The produced polymorphic sulfated sequence motifs are responsible for binding to a variety of signaling molecules and modulating their biological functions. Recently, we found that HS is localized exclusively around β -cells in islets of adult mice and required for islet morphogenesis, β -cell proliferation and insulin secretion. Furthermore, we found that the 3-O-sulfate modification is necessary for glucose-induced insulin secretion (GIIS). The aim of this study is to clarify the effect of the modification in HS including sulfation for β -cell proliferation during pregnancy.

METHODS: Quantitative RT-PCR was used for analyzing mRNA expression of HS biosynthesis enzymes in islets from pregnant (gestational days 13.5) mice. Expression of HS 6-O-sulfotransferase isoform-1 (Hs6st1) was silenced and GIIS and cell proliferation were examined in MIN6, mouse β -cell line.

RESULTS: In pregnant mouse islets, increased expression of C5-epimerase, Hs6st1 and HS 3-O-sulfotransferase isoform-3B1 mRNAs were detected (fold change 3- to 4-fold) by real-time PCR analysis. Silencing of Hs6st1, one of these upregulated enzymes, by RNA interference reduced MIN6 cell proliferation to 77% of control treatment ($P < 0.001$), whereas GIIS was unaffected.

CONCLUSION: Our data suggest that 6-O-sulfate groups modified by Hs6st1 play important role(s) in the β -cell proliferation during pregnancy.

PBS-12-6

Elucidation of Pancreatic Beta-Cell Fate After Birth Using Ins2-CreER/R26R-YFP Double Knock-in Mouse

Kanako Tamura¹, Kohtaro Minami¹, Keisuke Iemoto¹, Korefumi Nakamura¹ and Susumu Seino²

¹Division of Cellular and Molecular Medicine, Kobe University Graduate School of Medicine, Japan; ²Division of Cellular and Molecular Medicine and Division of Diabetes and Endocrinology, Kobe University Graduate School of Medicine, Kobe, Japan

AIMS: Pancreatic beta-cell mass is maintained dynamically throughout lifetime to control blood glucose levels. Although it has been shown that the major mechanism of the maintenance of beta-cell mass after birth is self-replication of pre-existing beta-cells, pancreatic beta-cells might also be generated from non-beta-cells. We have addressed this issue by using the inducible Cre/loxP system to trace beta-cells.

METHODS: We crossbred Ins2-CreER knock-in mice with R26R-YFP mice to generate Ins2-CreER/R26R-YFP double knock-in mice, in which pancreatic beta-cells can be labeled specifically and permanently upon injection of tamoxifen, and traced the beta-cells by pulse and chase experiment. For tracing beta-cells from neonate to youth, we injected tamoxifen to pregnant mothers 1 day before they gave birth. We then trace beta-cells from postnatal day 0 (P0) to day 56.

RESULTS: The labeling index (a percentage of YFP-labeled beta cells) was decreased significantly from P14 to P28, suggesting that beta-cells were generated from non-beta-cells in this period. Indeed, YFP-negative beta-cell clusters, an indication of neogenesis of beta-cells, were detected. We found that the labeling index was not changed between P28 and P56, which suggests no more neogenesis after P28. However, the number of YFP-negative beta-cell cluster was decreased significantly. We have noticed that the labeling index in mature islets (excluding YFP-negative clusters) was stable from P0 to P28 but decreased at P56.

CONCLUSION: Taken together, these results suggest that neogenic beta-cell clusters do not differentiate into mature islets but might migrate to pre-existing mature islets with aging.

PBS-12-7

Intermittent Hypoxia Stimulates β Cell Proliferation via Up-Regulation of Reg Family Genes

Shin Takasawa¹, Hiroyo Ota², Asako Itaya-Hironaka¹, Akiyo Yamauchi¹, Sumiyo Sakuramoto-Tsushima¹, Tomoko Miyaoka¹, Takanori Fujimura¹, Hiroki Tsujinaka¹, Kiyomi Yoshimoto¹, Chikatsugu Tsuchida¹, Shinji Tamaki² and Hiroshi Kimura²

¹Department of Biochemistry, Nara Medical University, Japan; ²Department of Internal Medicine, Nara Medical University, Japan

OBJECTIVE: Accumulating evidence suggests the associations between sleep apnea syndrome (SAS) and type 2 diabetes. However, the direct effect of intermittent hypoxia (IH) on pancreatic β cell proliferation remains a missing piece of the puzzle.

METHODS: Pancreatic β cell-derived cell lines (rat RINm5F, hamster HIT-T15, and human 1.1B4) were exposed either to 64 cycles/24 h of IH [5 min hypoxia (1% O₂)/10 min normoxia (21% O₂)], sustained hypoxia or normoxia for 24 h. After the treatment, the expression of regenerating gene (*Reg*) family and *IL-6* was determined by real-time RT-PCR. Cellular proliferation and apoptosis were measured by WST-8 assay and TUNEL method, respectively. **RESULTS:** The cellular proliferation of HIT-T15, RINm5F, and 1.1B4 cells was significantly increased by IH, whereas apoptosis of these cells were unchanged, suggesting that IH stimulates β cell proliferation. Real-time RT-PCR showed that *Reg I*, *PAP II/Reg III*, *PAP III*, and *Reg IV* mRNAs in rat RINm5F and *REG 1 α* mRNA in human 1.1B4 cells were significantly increased by IH. The knockdown experiments revealed that *Reg I*, *PAP II/Reg III*, *PAP III* and *Reg IV* were involved in IH-induced β cell proliferation. In addition, IH significantly increased the mRNA levels of *IL-6*, which was reported to increase *Reg* family gene expression. **CONCLUSION:** The cyclic change of hypoxia-reoxygenation, which occurs in SAS patients, stimulates pancreatic β cell proliferation. In this process, up-regulation of *Reg* family genes could be involved. The IH-induced expression of *IL-6* may be a trigger for the up-regulation of *Reg* family genes.

PBS-12-8

Expression of Gastrin in Pancreatic Islets of a Mouse Model of Beta Cell Regeneration

Kohtaro Minami¹, Hisato Kitanoya¹, Kanako Tamura¹, Maya Kudo¹, Harumi Takahashi¹ and Susumu Seino²

¹Division of Cellular and Molecular Medicine, Kobe University Graduate School of Medicine, Japan; ²Division of Diabetes and Endocrinology/Division of Cellular and Molecular Medicine, Kobe University Graduate School of Medicine, Japan

OBJECTIVE: We previously reported that pancreatic beta cells are spontaneously regenerated in mice expressing a dominant negative form of Kir6.2 gene specifically in the beta cells (Kir6.2G132S Tg mice). However, the mechanism of regeneration of pancreatic beta cells in Kir6.2G132S Tg mice has remained unclear. The aim of this study is clarify the mechanism of the regeneration.

METHODS: Changes in body weights, blood glucose levels, and serum insulin levels were measured. Pancreatic islets were obtained from mice at 4 (hyperglycemic state) and 25 weeks of age (improved glycemic state) and were subjected to GeneChipTM analysis and immunohistochemistry.

RESULTS: At 4 weeks of age, the number of insulin-positive cells was reduced significantly in Kir6.2G132S Tg mice compared to wild-type mice. However, the number gradually increased with age, and the Tg pancreas at 25 weeks of age was histologically indistinguishable from wild-type pancreas. We found that expressions of 81 genes were increased in Kir6.2G132S Tg islets at both 4 and 25 weeks of age. Among these, gastrin gene expression in the Tg islets was increased more than 100-fold when compared to that in wild-type islets at 4 weeks of age. Immunoreactivity of gastrin was clearly detected in the Tg islets. There was no significant difference in either CCK receptor (CCKAR) or gastrin receptor (CCKBR) expression between wild-type and the Tg islets as judged by GeneChipTM analysis.

CONCLUSIONS: Autocrine/paracrine signals of gastrin may have roles in regeneration of pancreatic beta cells in Kir6.2G132S Tg mice.

PBS-12-9

Assessment and Prediction of Beta-Cell Mass Through the Animal Study and Mathematical Model

Jinwoong Kim¹, Kyungreem Han¹, Segun Goh², Min Jee Hong¹ and Moo Young Choi²

¹Seoul National University, Korea; ²Department of Physics and Astronomy and Center for Theoretical Physics, Seoul National University, Seoul, Korea

OBJECTIVE: This study aims to develop a mathematical model for the pancreatic β -cell mass to assess and predict the β -cell mass via the blood glucose level.

METHODS: We develop a mathematical model of the beta-cell mass based on animal study such as the oral glucose tolerance test, quantification of pancreatic β -cell mass, and measurements of the apoptosis and replication rates.

RESULTS: Through the extensive simulations, the correlations among the β -cell mass, glucose tolerance test, and whole-body glucose level have been obtained. In addition, the various degrees of β -cell function of the experimentally induced diabetic rats have been successfully evaluated and predicted through our mathematical model.

CONCLUSION: This study provides an integrative approach to the assessment and prediction of the β -cell mass.

PBS-13-1

The Vascular Protective Effect of GLP-1 on HMVEC in Hyperglycemic conditions

Dong-Mee Lim, Ji-Young Kim, Keun-Young Park, Hee-Kwan Won and Byung-Joon Kim

Department of Internal Medicine, Konyang University School of Medicine, Korea

OBJECTIVES: The major complication of diabetes mellitus is cardiovascular problem. But the aspects of vascular complication are some different in macrovascular and microvascular features. So, this study was conducted to investigate the different response and mechanism of human microvascular endothelial cell (HMVEC) and human aortic endothelial cell (HAEC) in high glucose and in pretreatment with exendin-4 (Ex-4), a GLP-1 receptor agonist. **RESEARCH DESIGN AND METHODS:** The different response of HMVEC and HAEC in high glucose (30 mmol/L) after pretreatment with Ex-4 (25 nmol/L) was evaluated based on real-time PCR, western blot analysis, immunocytochemistry, wound healing assay and angiogenesis assay and the signaling of Notch-1 in HMVEC and HAEC using Notch-1 siRNA.

RESULTS: GLP-1 receptor, notch 1 and 4 were expressed in HMVEC and HAEC. Although, there was no angiogenesis and wound healing effect in high glucose stressed HAEC and/or pretreatment with VEGF or Ex-4, but in HMVEC, angiogenesis and wound healing effect were shown. Also, Notch-1 signaling was changed in HMVEC. MMP-2, PECAM-1 and TIMP-2 were increase in HMVEC with pretreatment Ex-4. To investigate whether the angiogenesis effects of Ex-4 are related Notch-1, the effect of down-regulation Notch was examined using a siRNA method in HMVEC. Branch number of angiogenesis, wound healing effect and MMP-2 were significantly decreased in Notch-1 siRNA treated HMVEC.

CONCLUSIONS: Our findings suggested that regulation of Notch-1 signaling in Ex-4 treated HMVEC induce angiogenesis and wound healing effect. Modulation of Notch 1 signaling may hold promise as a novel therapeutic strategy for the treatment of diabetic microvascular complications.

PBS-13-2

Glucose Fluctuations Aggravate the Vulnerability of Diabetic Heart Against Ischemia/Reperfusion Mediated via MicroRNAs Modulation

Yasushi Teshima, Naohiko Takahashi, Shotaro Saito, Hidekazu Kondo, Akira Fukui, Satoru Nishio, Mikiko Nakagawa and Tetsunori Saikawa

Department of Laboratory Examination and Diagnostics, Oita University, Japan

OBJECTIVE: We investigated whether glucose fluctuations may increase the susceptibility to ischemia/reperfusion in diabetic rat heart.

METHODS AND RESULTS: In *in vitro* experiments, cultured cardiomyocytes were alternately exposed to high (450 mg/dL) and low (30 mg/dL) concentrations of glucose for 5 days. Exposure to glucose fluctuations increased level of reactive oxygen species (ROS) and made cardiomyocytes more vulnerable to oxidative stress. In *in vivo* experiments, rats were divided into three groups: control, diabetes mellitus (DM), and DM with glucose fluctuations (DM + GF). DM was induced by streptozotocin i.v. and glucose fluctuation was induced by 24 h-fasting and insulin injection. Isolated hearts were subjected to 20 min ischemia/30 min reperfusion. The infarct size was significantly larger in DM + GF than DM. Electron microscopy disclosed that mitochondria were swollen and structure of cristae was destroyed in the heart of DM, which were aggravated in DM + GF. The level of ROS and activities of intracellular antioxidant enzymes were analyzed in search of possible mechanisms. Level of ROS was increased, and activities of catalase and superoxide dismutase were down-regulated in the heart of DM + GF compared to DM. Further, microarray analysis was performed to explore the expression profiles of microRNAs in each group. Expressions of mir-200c and -141 were more abundant in DM + GF than DM. We also confirmed that these microRNAs seem to contribute to the decreased activities of antioxidant enzymes and subsequent ROS increase.

CONCLUSIONS: Glucose fluctuations increased ROS level and enhanced ischemia/reperfusion injury in diabetic heart. Up-regulations of mir-200c and -141 may account for ROS increase by suppressing antioxidant enzymes.

PBS-13-3

Vaspin Increases NO Bioavailability Through Reduction of Asymmetric Dimethylarginine in Vascular Endothelial Cells

Chang Hee Jung¹, Woo Je Lee¹, Jenie Yoonoo Hwang¹, So Mi Seol², Yun Mi Kim², Yu La Lee² and Joong-Yeol Park¹

¹Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Korea; ²Asan Institute of Life Science, Asan Medical Center

Vaspin has been suggested to have antiatherogenic effect. Decreased activity of endothelial nitric oxide synthase (eNOS) plays an important role in the pathogenesis of atherosclerosis. Asymmetric dimethylarginine (ADMA) is a well-known endogenous competitive inhibitor of eNOS and risk factor of cardiovascular diseases. In this study, we aimed to find out whether vaspin could increase eNOS activity by reducing the level of ADMA through the activation of dimethylarginine dimethylaminohydrolase (DDAH) II, the responsible enzyme for the degradation of ADMA, in cultured endothelial cells. Furthermore, we studied whether signal transducer and activator of transcription (STAT)3, a transcription factor which has a putative binding site at the promoter region of DDAH II, was involved in the regulation of DDAH II by vaspin. Vaspin significantly decreased the level of ADMA and increased NO level in culture media of endothelial cells. Vaspin increased the serine site's phosphorylation of eNOS (Ser 1177) and phosphorylation of STAT3. The effect of vaspin on the increased phosphorylation of eNOS was abolished by knocking down STAT3 protein level expression using small interfering RNA. Vaspin increased the promoter activity and gene expression of DDAH II. Transfection of STAT3 increased the gene expression of DDAH II and vaspin amplified it. Vaspin-induced increase in DDAH II gene expression was attenuated by the DDAH II promoter that had mutation in putative STAT3-binding site. Furthermore, vaspin stimulated the STAT3-DNA binding activity. These results suggest that vaspin increases eNOS activity by reducing ADMA level through the activation of STAT3-mediated DDAH II gene expression.

PBS-13-4

Adipose Triglyceride Lipase is Downregulated in *db/db* Mouse Heart, an Aggravating Mechanism of Diabetic Cardiomyopathy

Tomoaki Inoue¹, Kunihisa Kobayashi², Toyoshi Inoguchi¹, Noriyuki Sonoda¹ and Ryoichi Takayanagi¹

¹Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University, Japan; ²Department of Endocrinology and Diabetes Mellitus, Fukuoka University Chikushi Hospital, Japan

Adipose triglyceride lipase (ATGL) was recently identified as a rate limiting triglyceride (TG) lipase and its activity is stimulated by comparative gene identification-58 (CGI-58). Mutations in ATGL or CGI-58 gene are associated with neutral lipid storage diseases characterized by accumulation of TG in multiple tissues. The cardiac phenotype, known as triglyceride deposit cardiomyopathy, shows TG accumulation in both coronary atherosclerotic lesions and the myocardium. Recent reports show that myocardial TG content is significantly higher in patients with diabetes and is associated with impaired left ventricular diastolic function. Therefore, we investigated roles of ATGL and CGI-58 in the development of myocardial steatosis in the diabetic state.

Triglyceride contents in the hearts of diabetic fatty *db/db* mice are higher than in those of *db/+* control mice. Histological examinations assessed with oil red O staining showed marked lipid deposition within the hearts of *db/db* mice. Next, we determined expression of genes and proteins that affect triglyceride metabolism and found that ATGL and CGI-58 expression were decreased in the hearts of *db/db* mice. Also, we found increased expression of genes that affect triglyceride synthesis (SREBP1c, monoacylglycerol acyltransferases and diacylglycerol acyltransferases). In addition, we analyzed the expression levels of key modulators of apoptosis, PKC activity and oxidative stress. It was found that Bcl-2 levels were lower and phosphorylation of PKC and 8-hydroxy-2'-deoxyguanosine were increased in diabetic hearts. These results suggest that reduced ATGL and CGI-58 expression with increased TG synthesis may exacerbate myocardial steatosis and oxidative stress thereby leading to cardiac apoptosis in diabetes.

PBS-13-5

Mechanism on Proliferation of Vascular Smooth Muscle Cells Through Glucose-Induced PKC-Delta Activation

Seok-Man Son, Byung-Jin Kang, A-Ra Jo, Dong-Won Yi and Yang-Ho Kang

Department of Internal Medicine, Pusan National University School of Medicine, Korea

BACKGROUND: We hypothesized that protein kinase C (PKC) isozymes contribute to diabetic vascular diseases and determined their roles in the critical intermediary signaling events in high glucose-induced proliferation of vascular smooth muscle (VSM) cells.

METHODS: Primary cultured rat aortic smooth muscle cells were treated for 72 h with media containing 5.5 mmol/L D-glucose (normal glucose), 30 mmol/L D-glucose (high glucose) or 5.5 mmol/L D-glucose plus 24.5 mmol/L mannitol (osmotic control). Cell number and cell cycle were then measured. Immunoblotting of PKC isozymes using phosphospecific antibodies was performed, and PKC activity was also measured.

RESULTS: High glucose increased VSM cell number and displayed significantly greater percentages of S and G2/M phases compared to 5.5 mmol/L glucose and osmotic control. High glucose also markedly increased activity of PKC-delta isozyme. When VSM cells were transfected with PKC-delta siRNA, VSM cell number was significantly attenuated in the high glucose-treated VSM cells.

CONCLUSION: These results suggest that high glucose-induced VSM cell proliferation is dependent upon activation of PKC-delta, which may responsible for stimulated intracellular redox sensitive signal pathways in VSM cells.

PBS-13-6

Cardiac Lipid Accumulation and Gene Expression Profile in Response to Streptozotocin-Diabetes

Jinya Suzuki, Mika Yamada, Mai Ichikawa, Michiko Imagawa, Satsuki Sato, Yasuo Zenimaru and Sadao Takahashi

Third Department of Internal Medicine, University of Fukui Faculty of Medical Science, Japan

OBJECTIVE: Diabetic cardiomyopathy is characterized by intracellular lipid accumulation (steatosis) which generates lipotoxicity and eventually leads to cardiac dysfunction. Cardiac steatosis and gene expression were analyzed to address the pathophysiology of the disease.

METHODS: C57BL/6 mice were treated with streptozotocin to induce diabetes. The hearts were collected 3-weeks afterwards to investigate cardiac steatosis, function, and gene expression profile using Affymetrix microarrays. Comparison analyses were performed between control and diabetic condition to screen the altered genes (>2-fold). The gene ontology (GO) classification and the pathway analysis were carried out using GO Slim and KEGG database, respectively. The selected genes were analyzed by qRT-PCR.

RESULTS: The induction of diabetes led to cardiac steatosis; cardiac triglyceride content was increased 75% and the electron microscopy showed many lipid droplets around the clusters of mitochondria. With diabetes the expression of 426 genes were increased while that of 384 genes were decreased (>2-fold), and the echocardiography showed slightly impaired systolic function. GO classification for the altered genes identified 24 functional groups including lipid metabolic process and response to stress. KEGG pathway analysis revealed that 17 pathways were significantly affected with diabetes. The pathways included PPAR α signaling, Ca signaling, and several cardiomyopathies. The qRT-PCR analysis confirmed the increased expression of PPAR α and its target gene HMG-CoA synthase 2 in the diabetic hearts.

CONCLUSION: Diabetes induces many axes of transcriptional changes including PPAR α -pathway. Controlling those changes could be a target to regulate diabetic cardiomyopathy.

PBS-14-1

Curcumin Attenuates Migration of Cytokine-Induced Human Aortic Smooth Muscle Cells

Hsing-Chun Lin¹, Chien-Ning Huang¹ and Ya-mei Yu²

¹Institute of Medicine, Chung Shan Medical University, Taiwan; ²Institute of Nutrition, Chang Jung Christian University, Taiwan

In the United States and other Western countries, atherosclerosis is the leading cause of illness and death. The migration and matrix metalloproteinases (MMPs) activation of vascular smooth muscle cells (VSMCs) may play a key role in the development of atherosclerosis. Curcumin, which is consumed daily by millions of people, is a polyphenol derived from the plant Curcuma

longa. In general, curcumin has been associated with a large number of biological and cellular activities, including antioxidative, anti-inflammatory, anticarcinogenic, and hypocholesterolemic properties. In this study, we investigated the inhibitory effect of curcumin on tumor necrosis factor- α (TNF- α)-induced human aortic smooth muscle cells (HASMCs) migration and MMP-9 activity. Curcumin lowered the secretion and protein expression of MMP-9 by gelatin zymography and western blot assays. They also decreased nuclear translocation of nuclear factor- κ B (NF- κ B) P50, P65, and ROS production. In addition, the migration assay showed that curcumin effectively inhibited the TNF- α -induced migration of HASMCs as compared with the control group. In conclusion, curcumin inhibit TNF- α -induced nuclear translocation of P50 and P65, thereby suppressing the secretion and protein expression of MMP-9, resulting in decreased HASMCs migration. Thus, curcumin have anti-inflammatory properties and may play an important role in the prevention of atherosclerosis.

PBS-14-2

Evaluation of Brain Redox Status and Association of Cognitive Dysfunction in Diabetic Mice by Overhauser-Enhanced MRI

Yohei Minami¹, Toyoshi Inoguchi², Noriyuki Sonoda², Eiichi Hirata¹, Fuminori Hyodo², Kazuhiro Ichikawa², Hideo Utsumi² and Ryoichi Takayanagi¹

¹Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University School of Medicine, Japan; ²Innovation Center for Medical Redox Navigation, Kyushu University, Japan

Oxidative stress contributes to the development of diabetic complications. Increasing epidemiologic evidence suggested that diabetes mellitus is associated with dementia and cognitive decline. However, underlying mechanism is not fully understood. Overhauser-enhanced MRI (OMRI) is a newly developed non-invasive technique for imaging of redox status in living animals by Overhauser effect.

We evaluated brain oxidative stress of the mice following 9 weeks streptozotocin (STZ) injection and 12-week aged db/db mice by OMRI. OMRI can measure ROS production quantitatively as intensity decay of imaging reacted with radical probe. In addition, we evaluated cognitive impairment of the mice following 9, 14, 22 weeks STZ injection and 10, 20, 30-week aged db/db mice in radial arm water maze (RAWM) and other oxidative stress markers.

Cognitive function in RAWM were not impaired in mice following 9 weeks STZ-injection and 10-week aged db/db mice but were impaired in mice following 14, 22 weeks STZ injection and 20, 30-week aged db/db mice compared to the control mice. However, Oxidative stress of mice following 9 weeks STZ injection were markedly increased compared to the control mice by OMRI (0.0139 ± 0.0015 vs 0.0087 ± 0.0006 , $P < 0.01$) and of 12-week aged db/db mice were also increased (0.0126 ± 0.0005 vs 0.0104 ± 0.0006 , $P < 0.05$) compared to the control.

Taken together, our results suggested that OMRI is a powerful tool to evaluate brain redox status. Furthermore, elevation of oxidative stress might be a causative pathogenic mechanism in diabetes-associated cognitive impairment and that regulation of redox state may open up new approaches to augmenting diabetes-associated dementia.

PBS-14-3

Withdrawn

PBS-14-4

Metformin Prevents High-Fat Diet-Induced Liver Tumorigenesis in C57Bl/6 Mice

Kazuki Tajima¹, Akinobu Nakamura¹, Jun Shirakawa¹, Kazuki Orime¹, Yu Togashi¹, Yoji Nagashima² and Yasuo Terauchi¹

¹Department of Endocrinology and Metabolism, Yokohama-City University, Japan;

²Department of Molecular Pathology, Yokohama-City University, Japan

OBJECTIVE: Metformin has recently increased attention because of its anti-tumor effects. We investigated the effects of metformin on high-fat (HF) diet-induced liver tumorigenesis using mouse model for NASH and liver tumor.

METHODS: We challenged C57Bl/6J mice with standard chow diet, a HF diet (HF group) or a HF diet with metformin (250 mg/kg/day; HF + Met group) for 60 weeks. Histological and phenotypical analyses were performed.

RESULTS: After 60 weeks, although the body weight of HF + Met group was comparable to the HF group, metformin treatment significantly decreased liver weight and plasma ALT levels. The hepatic triglyceride content was comparable

between the HF and HF + Met group. Scoring of the pathological findings showed that metformin treatment significantly improved the scores for inflammation and fibrosis, but not steatosis compared with the HF group. The incidence of hepatic nodular lesions was significantly decreased in the HF + Met group compared with the HF group (25% vs 70%). Metformin treatment increased the phosphorylation level of AMPK in liver, however the phosphorylation levels of mTOR and S6K were comparable between the HF and HF + Met group. We next investigated whether metformin prevented NASH model mice that had already been administered HF diet for 30 weeks from the development of liver tumors. Addition of metformin failed to reduce the incidence of hepatic nodular lesions compared with the HF group (75% vs 83%).

CONCLUSION: Metformin prevented HF diet-induced liver tumorigenesis in C57Bl/6J mice in an mTOR/S6K-independent pathway. It seems likely that the anti-tumor effect of metformin worked at early stage before the onset of NASH.

PBS-14-5

Association Between Alzheimer's Disease, Hyperglycemia and Lipid Metabolism: Evidence from an Animal Model

Yi Jing Sheen¹, Hui-Ting Yang² and Jaiinn-Liang Lin³

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Hospital Department of Health, Executive Yuan, Taiwan; ²Department of Nutrition, China Medical University, Taiwan

OBJECTIVE: Various epidemiological studies had shown that type 2 diabetes and metabolic syndrome were highly correlated to Alzheimer's disease. The present study was to clarify which of the risk factors in metabolic syndrome affected the progress to Alzheimer's disease.

METHODS: Thirty-two five-week-old male spontaneously hypertensive rats (abbreviated to SHR) and eight Wistar Kyoto rats (abbreviated to WKY) were divided into five groups: normal controls (WKY group), control, streptozotocin (called STZ for short), high fat diet (HFD), and high fat diet with STZ (DM group) groups. In STZ group, rats were injected 40 mg/kg BW/day streptozotocin for three consecutive days a week. In HFD group, subjects were given 10% (w/w) lard diet whereas the animals in DM group were both given high fat diet and STZ injection during the experiment. Eight weeks later, 12-h fasting blood samples, liver, and brain tissues were collected.

RESULTS AND CONCLUSION: Animals in DM group have the highest serum amyloid precursor protein (abbreviated to APP) concentration with the highest fasting blood glucose levels. The HFD group has the highest serum amyloid β 42 (abbreviated to A β 42) protein level with the highest serum and hepatic triglyceride amounts. A significant correlation between fasting blood glucose and serum APP concentrations ($R^2 = 0.6197$, $P < 0.001$) was found. A high correlation was also shown in hepatic triglyceride and serum A β 42 protein level ($R^2 = 0.6223$, $P < 0.001$). Conclusively, the study provided evidences of a strong linkage between high blood sugar and APP in the animal model of metabolic syndrome.

PBS-14-6

Willow Bark Extract is a Robust Natural Indirect Antioxidant Through the NRF2 Activation

Atsushi Ishikado¹, Yoko Sono¹, Motonobu Matsumoto¹, Stacey Robida-Stubbs², Aya Okuno¹, George L. King³, T. Keith Blackwell² and Taketoshi Makino¹

¹R&D Department, Sunstar Inc., Japan; ²Joslin Diabetes Center, Harvard Stem Cell Institute, Harvard Medical School, Boston, MA, USA; ³Section on Vascular Cell Biology, Joslin Diabetes Center, Harvard University, Boston, MA, USA

Nuclear factor erythroid 2-related factor 2 (NRF2) is a redox-sensitive master regulatory transcriptional factor that plays an important role in the protection against oxidative stress in vascular tissue, and several studies have shown that activation of NRF2 may prevent some diabetic vascular complications such as nephropathy. In the present study, we evaluated the approximately 150 botanical extracts to screen the materials for activating NRF2 using antioxidant response element (ARE)-luciferase assay system in human umbilical vein endothelial cells (HUVECs). We discovered that willow bark extract (WBE) listed in European Pharmacopoeia induced a robust phase II response as indicated by NRF2 activation. WBE also dose-dependently increased mRNA and protein expressions of NRF2 target genes, HO-1, GCLM, GCLC or p62, accompanied with increase in intracellular glutathione (GSH) content in HUVECs. WBE increased the intranuclear expression and DNA binding of NRF2 as well as a dose-dependent ARE-luciferase activity. The siRNA of NRF2 significantly reduced mRNA and protein expressions of HO-1, GCLM, GCLC or p62, and intracellular GSH content increased by

WBE. Furthermore, pretreatment with WBE rescued the *tert*-butyl hydroperoxide-induced cell toxicity, while the cytoprotective effect of WBE was deleted by the siRNA of NRF2. Salicin or its related compounds, active anti-inflammatory ingredients of WBE had no effects on NRF2 activation. Thus, these results provide the first evidence that WBE increases antioxidative activity through the activation of NRF2 and may contain active substances rather than salicin that can protect against the development of diabetic vascular complications and other oxidative stress-induced diseases.

PBS-14-7

Lipophilic Statins Induced Vascular Endothelial Cell Apoptosis

Hyun Jung Yang¹, Hyung Kyung Jim¹, Su Jin Oh², Won Chul Ha², Tae Seo Sohn² and Hyun Shik Son²

¹Department of Clinical Research Center, Ui Jeong Bu St. Mary's Hospital, Catholic University Medical Center, Korea; ²Department of Internal Medicine, Ui Jeong Bu St. Mary's Hospital, Catholic University Medical Center, Korea

OBJECTIVE: To observe the effect of statins on vascular endothelial cell apoptosis, we studied the association of AKT and caspase 3 in human aortic endothelial cells (HAECs) after treatment of statins.

METHODS: We observed morphological change of HAECs after treatment of statins. We also observed AKT phosphorylation and caspase 3 cleavage. And we compared the effect according to lipophilic statins and hydrophilic statin.

RESULTS: Lipophilic statins (simvastatin and atorvastatin) but not hydrophilic statin, induced vascular endothelial cell apoptosis dose dependently. They also induced caspase 3 activation by decrease of AKT phosphorylation.

CONCLUSION: We observed lipophilic statins induced vascular endothelial apoptosis through66 interfering of AKT phosphorylation.

PBS-14-8

Impact of Insulin on Experimental Periodontitis in Diabetic Rats

Nobuhisa Nakamura¹, Toru Nishikawa², Keiko Naruse¹, Yasuko Kobayashi¹, Makoto Mizutani³, Shinichi Miyajima², Kei Adachi², Takeshi Kikuchi², Norikazu Ohno³, Toshihide Noguchi² and Tatsuaki Matsubara¹

¹Department of Internal Medicine, School of Dentistry, Aichi-Gakuin University, Japan;

²Department of Periodontology, School of Dentistry, Aichi-Gakuin University, Japan;

³Department of Oral Anatomy, School of Dentistry, Aichi-Gakuin University, Japan

BACKGROUND AND AIMS: Periodontal disease is highly prevalent and severe in diabetic patients. Unlike other diabetic complications, periodontal disease and diabetes mellitus have bidirectional interactions. We previously showed the involvement of nitrosative stress in periodontitis in diabetic rats. In this study, we examined the impact of insulin on the ligature-induced periodontitis in diabetic rats.

MATERIALS AND METHODS: Diabetes was induced by an intraperitoneal injection of streptozotocin into 5 week old male Sprague-Dawley rats. Two weeks after the induction of diabetes, surgical nylon thread was ligated around the cervical portion of the maxillary 2nd molar to induce periodontitis. The 2nd molar on the opposite side remained without ligation as the control side. At the same time, the half of the diabetic rats were implanted insulin pellet into the back skin as the insulin-treated group. Periodontitis was evaluated at 2 weeks after the ligation.

RESULTS: Insulin treatment significantly improved blood glucose and HbA1c in diabetic rats. Ligation induced severe periodontitis in the diabetic rats, which were apparently shown by the increase of TNF- α and iNOS mRNA expressions and inflammatory cell infiltration in the gingiva and alveolar bone loss. The treatment of insulin significantly suppressed these abnormalities. The number of nitrotyrosine positive cells was significantly higher in the periodontitis in the diabetic rats compared with that in the normal rats, which was abolished by the insulin treatment.

CONCLUSION: These results suggest the beneficial effects of insulin on the periodontitis in diabetic patients.

PBS-14-9

Irbesartan Attenuates HMGB1 Production in Macrophages

Yoshiro Kato, Koichi Kato, Hideki Kamiya, Atsuko Watarai, Ena Naito, Chika Kojima, Yukako Sugiura, Sami Sato, Takahiro Ishikawa and Jiro Nakamura

Division of Diabetes, Department of Internal Medicine, Diabetes Center, Aichi Medical University, Japan

BACKGROUND AND AIMS: High-mobility group box 1 (HMGB1) is released into the extracellular space by activated macrophages and acts as an

inflammatory mediator through RAGE or toll-like receptor (TLR). Recent studies reported that the number of HMGB1-producing macrophages significantly increased in human atherosclerotic lesions and the serum HMGB1 concentrations were significantly increased in diabetic patients, suggesting that HMGB1 plays an important role in the development of diabetic complications through inflammatory processes. An IRMA 2 substudy demonstrated that irbesartan treatment reduced biomarkers of inflammatory activities in diabetic patients. However, the effects of irbesartan on HMGB1 production are still unknown. In the present study, we investigated the effects of irbesartan on HMGB1 production and the molecular mechanisms of its effects in macrophages to evaluate the anti-inflammatory effects of irbesartan.

RESULTS: Irbesartan inhibited LPS-induced HMGB1 production (101.9 ± 9.6 vs 36.9 ± 8.1 ng/mL, $P < 0.005$), IFN- β production (162.7 ± 0.7 vs 58.4 ± 1.3 pg/mL, $P < 0.01$) and NO production (18.3 ± 2.1 vs 9.5 ± 0.4 μ mol/L, $P < 0.01$) in RAW264.7 cells. Losartan did not inhibit LPS-induced HMGB1 production.

CONCLUSION: We examined the effects of irbesartan on LPS-induced production of HMGB1, IFN- β and NO in macrophages. Previous studies indicated that LPS exploited TLR4/IFN- β signaling pathway to induce HMGB1 release, and that NO played a role as a downstream molecule of IFN- β signaling pathway. Irbesartan inhibited HMGB1 production via the inhibitory effect on IFN- β signaling pathway in macrophages. Our data indicates that irbesartan would have beneficial effects on diabetic complications through its anti-inflammatory effects.

PBS-15-1

Glucagon Receptor and Incretin Receptors mRNA Expression are Inversely Regulated by Glucose Through ChREBP Activation

Katsumi Iizuka, Reiko Tomita, Wu Wudelehu, Yukio Horikawa and Jun Takeda

Department of Diabetes and Endocrinology, Graduate School of Medicine, Gifu University, Japan

In patients with type 2 diabetes mellitus, normalization of fasting glucose levels restores insulin response to glucagon-like peptide-1 (GLP-1) and glucose-dependent insulintropic polypeptide (GIP). Decreased insulin response to GLP-1 occurs partly because of decreased GLP1 and GIP receptor expression in pancreatic beta-cells. In pancreatic islets, hyperglycemia causes a decrease in GLP-1 receptor (Glp1r) and GIP receptor (Gipr) mRNA expression and an increase in glucagon receptor (Gcgr) mRNA expression, but the precise mechanism remains unknown. We studied the role of glucose activated transcription factor, ChREBP, in the glucose-regulation of these genes expression. In the rat pancreatic insulinoma cell line INS-1E cells, glucose caused a dose- and time-dependent increase in Gcgr mRNA and decrease in Glp1r and Gipr mRNA expression. On the basis of these results, adenoviral overexpression of dominant active ChREBP in INS-1E cells caused an increase in Gcgr mRNA and decrease in Glp1r and Gipr mRNA expression. We then determined the carbohydrate response element (ChoRE) in rat Gcgr promoter. Deletion study and CHIP assay against anti-ChREBP antibody revealed that ChoRE (-554 bp/-538 bp) is a functional glucose response element in rat Gcgr promoter. In contrast, glucagon partly suppresses glucose-induced Gcgr mRNA expression. In conclusion, Gcgr and incretin (GLP-1 and GIP) receptors mRNA expression are inversely regulated by glucose through ChREBP activation.

PBS-15-2

Preparation and Evaluation of Rat Islet β -Cell-Rich Fractions by Flow Cytometry

Xiao Wen Li¹, Dechao Yin¹, Ling Li², Mingliang Zhang², Shihong Wang², Kaida Mu², Chen Wang¹ and Weiping Jia²

¹Shanghai Key Laboratory of Diabetes Mellitus, Shanghai Clinical Center for Diabetes, Shanghai Jiaotong University Affiliated Sixth People's Hospital, China; ²Department of Endocrinology and Metabolism, Shanghai Key Laboratory of Diabetes Mellitus, Shanghai Clinical Center for Diabetes, Shanghai Jiaotong University Affiliated Sixth People's Hospital, China

OBJECTIVE: To establish the method on purification of rat pancreatic β -cells by flow cytometry.

METHODS: Rat islets were digested by collagenase and fished under microscopy. After dissociated with trypsin and deoxyribonuclease, single islet cells were analyzed and sorted according to their autofluorescence intensity and side scatter (SSC) properties by flow cytometry. Cell viability was detected by Hoechst 33342 and propidium iodide. B-cell purity was identified by

immunocytochemistry analysis. Insulin was measured with enzyme-linked immunosorbent assay.

RESULTS: β -cell enriched population had higher autofluorescence intensity and SSC than non- β -cell enriched population. The proportion of insulin positive staining cells in β -cell enriched-population was 94.5% ($\pm 0.95\%$), while that in non- β -cell enriched population was 10.0% ($\pm 0.82\%$). The death rate of β -cell enriched-population was low ($<5\%$). Insulin release from β -cell enriched-population was increased with the increase of glucose concentration from 2.8 to 20 mmol/L ($r = 0.8$, $P < 0.001$), and reached statistic significance at 20 mmol/L glucose condition compared with that at 2.8 mmol/L glucose condition ($P < 0.001$). Moreover, Forskolin and Exendin-4 significantly enhance insulin secretion ($P_{FK} < 0.001$, $P_{EX4} < 0.05$).

CONCLUSION: β -cells purified by flow cytometry according to cell autofluorescence and side scatter have a low mortality, high purity rate and good function.

PBS-15-3

Effects of Combining Luseogliflozin, a Novel SGLT2 Inhibitor, with Glimepiride or Pioglitazone in Diabetic Mice

Saeko Uchida, Hideki Tomoike, Takuya Takeda, Naoki Kojima, Emi Gunji, Michihito Onishi, Kiyokazu Kitano, Teisuke Takahashi and Kenzo Takahashi
Molecular Function and Pharmacology Laboratories, Taisho Pharmaceutical Co., Ltd., Japan

OBJECTIVE: Luseogliflozin (LUSEO, TS-071), a novel, potent and selective SGLT2 inhibitor, provides insulin-independent glucose-lowering effects and causes a reduction of body weight (BW) *in vivo*. The aims of this study are to examine the effect of combining LUSEO with glimepiride (GLI) or pioglitazone (PIO) on hyperglycemia, and to explore the additional benefit of combination therapy on plasma insulin level or BW.

METHODS: LUSEO (10 mg/kg) and GLI (0.5 mg/kg) were orally administered either alone or in combination to diabetic KKAY and non-diabetic C57BL mice. To study the effect of LUSEO on PIO-induced BW gain, KKAY mice were fed a diet containing LUSEO (0.01%), PIO (0.1%) or in combination of both drugs for 2 weeks.

RESULTS: In KKAY mice, the combination of LUSEO and GLI additively decreased plasma glucose (PG) level as compared with either alone. A decrease in plasma insulin level was observed in LUSEO-treated mice. The plasma insulin level in LUSEO + GLI-treated mice was significantly lower than that in GLI-treated mice, which was the same as that in LUSEO-treated mice. In C57BL mice, GLI, but not LUSEO, significantly decreased PG level, and the glucose-lowering effect of GLI was not affected by coadministration with LUSEO. The combination of LUSEO and PIO additively decreased non-fasting PG level as compared with either alone. LUSEO significantly reduced PIO-induced BW and subcutaneous fat mass gains.

CONCLUSION: These results show that combination of LUSEO and GLI or PIO improves hyperglycemia, and has the additive benefit on plasma insulin level or BW in diabetic mice.

PBS-15-4

Glucose Regulates Secretion of Exogenously Expressed Insulin from HepG2 Cells and in a Diabetic Mouse Model

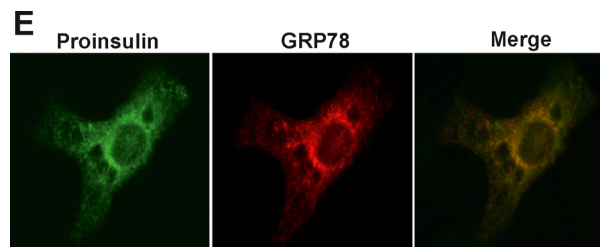
Yuan-Yuan Liu¹, Wendy Jia², Irene Wanke², Daniel Muruve², Haipeng Xiao¹ and Norman Wong²

¹Department of Endocrinology, First Affiliated Hospital of Sun Yat-sen University, China; ²Departments of Medicine and Biochemistry & Molecular Biology, the Faculty of Medicine, University of Calgary, Canada

OBJECTIVE: To examine whether hepatocyte secretion of insulin derived from an engineered construct can be regulated by glucose.

METHODS: Adenovirus constructs were designed to express proinsulin or mature insulin containing the conditional binding domain (CBD). This motif binds GRP78 an endoplasmic reticulum (ER) protein that enables the chimeric hormone to enter into and stay within the ER until glucose regulates its release.

RESULTS: Infected HepG2 cells expressed proinsulin containing the CBD. Immunocytochemistry studies suggested proinsulin and GRP78 colocalized and most likely in ER. The amount of hormone released from infected cells was glucose-dependent. Glucose regulated release of the chimeric hormone



was rapid and sustained. When infected with adenovirus that expresses mature insulin, the glucose levels of diabetic mice were lower.

CONCLUSIONS: Our data suggest that a chimeric CBD-proinsulin expressed in hepatocytes localizes to the ER. Release of the chimeric hormone from the ER is regulated by glucose. In a diabetic mouse model, infection with adenovirus that expresses mature insulin lowered blood glucose.

PCS-01-1

The Relationship Between Serum Total Bilirubin and White Blood Cell Count in an Adult Population

Wan-Ni Tsai¹, Ya-Yu Wang², Shih-Yi Lin¹, Wayne Huey-Herng Sheu³ and Wen-Dau Chang²

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Veterans General Hospital, Taiwan; ²Department of Family Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; ³Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

OBJECTIVE: Several studies have shown that serum bilirubin has a protective effect against cardiovascular disease and that inflammation plays an important role in its pathogenesis. This cross-sectional study investigated whether there was an association between serum white blood cell (WBC) count, a simple indicator of inflammation, and serum total bilirubin level in a cohort of an adult population in Taiwan.

METHODS: A total of 2458 apparently healthy adults (1246 men and 1212 women) who attended health examination from August 2000 to April 2002 were enrolled.

RESULTS: Total serum bilirubin levels showed a significantly negative correlation with WBC counts and triglyceride levels while significantly positively with high density lipoprotein cholesterol levels in both genders. When total bilirubin levels were divided into quartiles ($0 < Q1 < 0.5$, $0.5 < Q2 < 0.7$, $0.7 < Q3 < 0.9$, $0.9 < Q4 < 1.2$ mg/dL for men; $0 < Q1 < 0.4$, $0.4 < Q2 < 0.6$, $0.6 < Q3 < 0.8$, $0.8 < Q4 < 1.2$ mg/dL for women), individuals in the lower bilirubin quartiles had higher blood WBC counts. Using multivariate linear regression analysis with WBC count as the dependent variable, total bilirubin showed an independent negative correlation with WBC count after adjusting for age, BMI, fasting blood glucose, lipids, ALT, eGFR, antihypertensive, antidiabetic, and antihyperlipidemic medications, smoking status, physical activity level, alcohol consumption and blood pressure in both genders.

CONCLUSION: In conclusion, results from our study demonstrated that higher total bilirubin concentrations within the normal range were associated with lower blood WBC counts, regardless of other classical cardiovascular risk factors.

PCS-01-2

Carotenoid Intake and Serum Carotenoid Levels in Non-Alcoholic Fatty Liver Disease Patients with Diabetes

Bunzo Matsuura¹, Kumiko Toshimitsu², Yoshiko Nagai², Shin Yamamoto³, Teruki Miyake³, Shinya Furukawa³ and Morikazu Onji³

¹Department of Lifestyle-related Medicine and Endocrinology, Ehime University Graduate School of Medicine, Japan; ²Division of Nutrition, Ehime University Hospital, Japan; ³Department of Gastroenterology and Metabolism, Ehime University Graduate School of Medicine, Japan

AIMS: We previously reported that in patients with non-alcoholic steatohepatitis (NASH) there was an excess intake of carbohydrates/energy, especially simple carbohydrates, and low intakes of protein/energy, polyunsaturated fatty acid and zinc. In this study, we identified carotenoid intake and serum carotenoid concentration in NASH patients.

SUBJECTS: Forty eight NASH patients and 30 simple steatosis (SS) patients diagnosed from histological findings and 15 healthy volunteers (C) were enrolled. 37% of SS patients and 42% of NASH patients have diabetes. Their dietary habits and intake of nutrients were analyzed by detailed questioning by physicians and dieticians. Serum carotenoid levels were analyzed by high performance liquid chromatography (HPLC).

RESULTS: About intake of carotenoids, beta-cryptoxanthin intake in female patients with NASH was significantly lower than that with SS. Serum level of beta-cryptoxanthin in female patients with NASH was significantly lower than that with SS.

CONCLUSIONS: Lower intake and lower serum concentration of beta-cryptoxanthin may be related to the progression of non-alcoholic liver disease with diabetes.

PCS-01-3

Circulating Osteocalcin Level is not Associated with Incident Type 2 Diabetes in Middle-Aged Male Subjects: Mean 8.4 Year Retrospective Follow-Up Study

You-Cheol Hwang¹, Jae-Hwan Jee², In-Kyung Jeong¹, Kyu Jeung Ahn¹, Ho Yeon Chung¹ and Moon-Kyu Lee³

¹Department of Medicine, Kyung Hee University School of Medicine, Korea; ²Center for Health Promotion, Samsung Medical Center; ³Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine

OBJECTIVE: Recent human studies suggested that serum osteocalcin is associated with the cross-talk between bone and energy metabolism. The aim of this study was to determine whether serum osteocalcin level is independently associated with the development of type 2 diabetes.

RESEARCH DESIGN AND METHODS: A retrospective cohort study was performed of 1229 non-diabetic men, aged 25–60 years, who were recruited from the Health Promotion Center, Samsung Medical Center, between January 1997 and December 1997. They were followed regularly at the center, on an out-patient basis and during hospitalization for a mean of 8.4 years and the development of type 2 diabetes were determined.

RESULTS: In the baseline analysis, body mass index, body fat percentage, triglyceride, homeostasis model assessment of insulin resistance value, and plasminogen activator inhibitor-1 levels varied inversely with the osteocalcin tertiles, and serum high-density lipoprotein cholesterol levels increased with the osteocalcin tertiles. However, no differences were observed in fasting glucose and glycated hemoglobin levels across the osteocalcin tertiles. Incident type 2 diabetes occurred in 90 (7.3%) of the study subject. In Cox proportional hazards models, however, no statistical differences in the development of type 2 diabetes across the osteocalcin tertiles were evident after adjustment of other risk factors for incident diabetes.

CONCLUSIONS: Despite baseline associations with favorable metabolic parameters, the serum osteocalcin level was not associated with the development of type 2 diabetes in middle-aged males.

PCS-01-4

The Relationship Between Plasma Levels of Homocysteine and Omentin-1 in Obese and Type 2 Diabetic Patients

Jianjin Guo¹, Wei Ren² and Liu Jie³

¹Department of Endocrinology and Metabolism, the First Affiliated Hospital of Nanjing Medical University, China; ²Department of Endocrinology and Metabolism, Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai Diabetes Institute, Shanghai Clinical Center of Diabetes, China; ³Department of Endocrinology and Metabolism, Shanxi Provincial People's Hospital, China

OBJECTIVES: The association between the plasma homocysteine (Hcy) concentration and diabetes has more recently been confirmed. Omentin-1 is a novel adipokine expressed in visceral adipose tissue and negatively correlated with insulin resistance and obesity. We planned to investigate the relationship of plasma levels of Hcy and omentin-1 in obese and type 2 diabetic subjects. **METHODS:** We performed a cross-sectional randomized study including 42 patients with T2DM and 46 subjects with normal glucose regulation (NGR). Each group was divided into obese and non-obese subgroups according to BMI ≥ 25 or < 25 kg/m². Fasting serum concentrations of Hcy and omentin-1 were measured using ELISA. The association of omentin-1 with Hcy was evaluated.

RESULTS: After age and sex adjustment, Hcy level in T2DM was significantly higher than that of NGR [(16.81 $\pm$ 5.08 vs 12.51 $\pm$ 3.46) μ mol/L, $P < 0.05$].

The omentin-1 levels in overall subjects was 17.69 $\pm$ 4.41 vs 22.8 $\pm$ 4.8 μ g/L, ($P < 0.01$). Hcy level of obese subjects are increased in both NGR and T2DM groups [(11.27 $\pm$ 2.87 vs 13.46 $\pm$ 3.62) μ mol/L, (14.28 $\pm$ 2.91 vs 18.71 $\pm$ 5.56) μ mol/L, both $P < 0.05$]. The contrary tendency was observed for the omentin-1 level [(25.79 $\pm$ 4.11 vs 21.73 $\pm$ 4.78) μ g/L, (18.94 $\pm$ 3.04 vs 16.75 $\pm$ 5.08) μ g/L, both $P < 0.05$]. Correlation analysis showed that plasma Hcy and omentin-1 levels were correlated to BMI ($r = 0.251$ and -0.242 , $P < 0.01$). The serum level of Hcy is negatively correlated to omentin-1 level ($r = -0.378$, $P < 0.01$).

CONCLUSIONS: Serum Hcy levels in obese and type 2 diabetic subjects are increased, while the omentin-1 levels are decreased. Omentin-1 level is inversely related to BMI and Hcy level.

PCS-01-5

TOHO-Lipid Intervention Trial Using Pitavastatin (TOHO-LIP) in Patients with High Risk Hypercholesterolemia – 96 Weeks Reports Diabetes Sub-Analysis-

Teruo Shiba¹, Sumie Okahata¹, Kentaro Sakamoto¹, Takako Mitsumatsu¹, Fumihiko Hara², Shuui Nanjo², Shinji Hisatake², Atsushi Namiki², Shohei Yamashina², Kenji Wagatsuma², Junichi Yamazaki², Gen Yoshino³, Yasuo Iwasaki⁴, Shigeo Yamamura⁴, Hidehiko Hara⁵, Kaoru Sugi⁵, Toshiki Fujioka⁶, Mao Takahashi⁷, Hirofumi Noike⁷ and Kohji Shirai⁸

¹Division of Diabetes and Metabolism, Toho University Ohashi Medical Center, Tokyo, Japan; ²Department of Cardiovascular Medicine, Toho University Omori Medical Center, Tokyo, Japan; ³Department of Internal Medicine, Shin-Suma General Hospital, Hyogo, Japan; ⁴Department of Neurology, Toho University Omori Medical Center, Tokyo, Japan; ⁵Division of Cardiovascular Medicine, Toho University Ohashi Medical Center, Tokyo, Japan; ⁶Department of Neurology, Toho University Medical Center Ohashi Hospital, Tokyo, Japan; ⁷Department of Cardiovascular Center, Sakura Hospital, Toho University, Chiba, Japan; ⁸Department of Internal Medicine, Sakura Hospital, Toho University, Chiba, Japan

BACKGROUND: HDL-C has been paid attention for its anti- atherosclerotic properties and recently, non HDL-C is recognized as a useful surrogate marker for prediction of atherosclerotic events. There have been few clinical reports comparing effects of strong statins on lipid profiles of diabetic subjects with hyperlipidemia in the long-term treatment.

OBJECTIVE: We have evaluated TOHO-LIP (TOHO-Lipid Intervention trial using Pitavastatin) database regarding effects of pitavastatin (P) in lipid profiles, laboratory parameters and safety as compared with atorvastatin (A) for anchored 96 weeks.

METHOD: TOHO-LIP has been conducted at TOHO University three hospitals, which enrolled 652 patients with high risk hypercholesterolemia. TOHO-LIP sub-analysis was conducted in 414 diabetic patients treated with pitavastatin (2 mg/day) or atorvastatin (10 mg/day).

RESULTS: TC, LDL-C and non HDL-C, levels significantly improved at 96 weeks with statin treatments. The rate of reaching target for non HDL-C levels (JAS Guideline 2012) was also comparable in two groups, 77% (P) and 81% (A) at 96 weeks. In general, HDL-C levels slightly increased after treatment, the patients with hypo-HDL-C, defined as HDL-C below 40 mg/dL, at baseline showed significant increase by +14.5% at 96 weeks only by pitavastatin treatment. Adverse effect on glucose metabolism represented by FPG or HbA1c levels was not observed in both groups at 96 weeks.

CONCLUSION: Both strong statin showed comparable effects on lipid profile of diabetic subjects while in subjects with hypo-HDL Cholesterol, pitavastatin solely improved HDL-C level, suggesting effective prevention for events. Future, we need to investigate the relationship between cardiovascular events and improvement of lipid profiles by statins.

PCS-01-6

Increased Peripheral White Blood Cell Counts are Associated with Lower HDL Cholesterol: Potential Role of Systemic Inflammation in Regulating HDL-C Metabolism

Hsin May Chang¹, Wen-Dau Chang², Ya-Yu Wang², Pi-Hwa Liu², Shin-Yi Lin¹ and Wayne H.-H. Sheu¹

¹Department of Metabolism and Endocrinology, Taichung Veterans General Hospital, Taiwan; ²Department of Family Medicine, Taichung Veterans General Hospital, Taiwan

OBJECTIVE: Large epidemiological evidences have shown that low high density lipoprotein cholesterol (HDL-C) level is a strong predictor of cardiovascular disease. Previous human and experimental studies have demonstrated that pro-inflammatory cytokines can affect concentration of plasma lipoproteins,

including HDL-C. The study aimed to validate the relationship between peripheral white blood cell (WBC) counts, a clinical marker of inflammation, and HDL-C in an apparently healthy Chinese population.

MATERIALS AND METHODS: 2520 healthy adult subjects (1264 men and 1256 women, mean age of 48.6 ± 12.0 years), who attended health examination at our hospital from 2000 to 2002, were enrolled. Their body weight (kg) and height (m) were measured to compute body mass index (BMI). A venous blood sample was drawn after overnight fasting to determine fasting plasma glucose (FPG), alanine aminotransferase (ALT), creatinine, triglycerides (TG), total cholesterol (TC), HDL-C levels, and total WBC counts. The medical history and lifestyle habits were self-reported using a structured questionnaire.

RESULTS: The subjects with lower blood HDL-C concentrations had higher BMI, FPG, TG levels, and WBC counts (all $P < 0.01$). Univariate analysis showed that WBC counts were correlated positively with BMI, TC, and negatively with HDL-C values. Using multiple linear regression analysis, WBC counts remained a significant determinant of HDL-C level after adjusting for age, gender, BMI, FPG, TC, TG, blood pressure, and lifestyle habits.

CONCLUSION: Higher WBC counts were associated with lower HDL-C levels in an apparently healthy general population. Inflammation might be involved in the regulation of HDL-C metabolism.

PCS-01-7

Effect of Age and Sex on HbA1c Levels in Non-Diabetic Korean Subjects

Ji Cheol Bae, Sunghwan Suh, Se Won Kim, Hye Jeong Kim, Sang-Man Jin, Jae Hyeon Kim, Myung-Shik Lee, Moon Kyu Lee and Kwang-Won Kim
Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea

OBJECTIVE: There are well known confounders that influence the HbA1c values independent of glycemia. The relationship between mean glycemia and HbA1c value may not be the same in all people. We examined the relationship between HbA1c with age and sex in non-diabetic Korean subjects.

RESEARCH DESIGN AND METHODS: We performed cross-sectional analyses of 87,742 non-diabetic subjects who participated in comprehensive health check-ups. Age was categorized into 5-year groups. After excluding anemia (Hgb < 11.5 and < 13.5 in men and women, respectively), we examined HbA1c levels by age and by sex, with adjustment for fasting plasma glucose level. **RESULTS:** HbA1c level increased with increasing age groups after adjustment for fasting plasma glucose levels ($P < 0.001$). Also, after adjustment for fasting plasma glucose level, HbA1c level was higher in woman across all age groups ($P < 0.001$). The gap between HbA1c level between man and woman widen with increasing age after groups aged more than 50 years ($P < 0.001$ for interaction).

CONCLUSION: In non-diabetic populations, HbA1c levels were positively associated with age and higher in woman than man after adjustment for fasting plasma glucose. Also, there was gender difference in the relationship between HbA1c and age.

PCS-02-1

Association with Plasma Macrophage Inhibitory Cytokine-1 (MIC-1) in the Type 2 Diabetes Mellitus Patients

Osamu Ebisui, Hitto Tokunaga, Yasuhiko Hara, Ayako Ochi, Kazuyuki Akasaka and Mizune Tamaki
Department of Diabetes and Endocrinology, Ehime Prefectural Central Hospital, Japan

OBJECTIVE: We examined whether plasma MIC-1 levels were increased in the type 2 diabetes mellitus (DM) patients relative to controls.

METHODS: Sixty-five patients with type 2 DM were compared with 65 age- and BMI-matched normal glucose tolerance controls. Blood samples were obtained in the fasting state for measurement of clinical chemistry parameters. Plasma levels of MIC-1 were measured by ELISA. These parameters of both groups were analyzed by Mann-Whitney's U test. Multiple regression models were used to assess the relationship between sex, body weight, systolic blood pressure, diastolic pressure, total cholesterol, HDL cholesterol, TG, a waist circumferences, Cr, BMI, the presence of DM, and plasma MIC-1 concentration by Stepwise analysis.

RESULTS: Plasma MIC-1 levels, waist circumferences, systolic blood pressure, FBS, HbA1c, and HOMA-R were significantly higher in the type 2 DM than the control groups. Multiple regression analysis resulted in ANOVA

$P < 0.0001$, $R^2 = 0.431$. DM, age, and Cr were significant factors and $\beta = 0.464, 0.459, 0.153$, all P values were $P < 0.001$, partial correlation coefficients were 0.417, 0.397, 0.382 in each factors.

CONCLUSION: These results suggest that MIC-1 are contributed to pathogenesis of the type 2 DM.

PCS-02-2

Similar Disposition Indices in Japanese and Caucasians – Despite Differences in Insulin Secretion and Sensitivity

Jonas Bech Moeller¹, Chiara Dalla Man², Rune V. Overgaard¹, Steen H. Ingwersen¹, Christoffer W. Tornøe¹, Maria Pedersen³, Harushiko Tanaka⁴, Mitsuru Ohsugi⁴, Kohjiro Ueki⁴, Jan Lynge⁵, Nina-Maria Vasconcelos⁶, Bente K. Pedersen³, Takashi Kadowaki⁴ and Claudio Cobelli²

¹Quantitative Clinical Pharmacology, Novo Nordisk A/S, Denmark; ²Department of Information Engineering, University of Padova, Italy; ³Center of Inflammation and Metabolism, Rigshospitalet, Denmark; ⁴Department of Metabolic Diseases, Tokyo University Hospital, Japan; ⁵Clinical Pharmacology Diabetes, Novo Nordisk A/S, Denmark; ⁶Medical Writing, Novo Nordisk A/S, Denmark

OBJECTIVE: Differences between Japanese and Caucasians are perceived in Type 2 diabetes (T2D), although direct comparative studies are rare. Our study aimed at assessing beta-cell function, insulin sensitivity, hepatic extraction and disposition index in Caucasians and Japanese ranging from normal (NGT) to impaired glucose tolerance (IGT) and T2D. This paper presents results obtained using oral minimal models (OMMs).

METHODS: 150 Caucasians and 120 Japanese underwent oral glucose tolerance tests (OGTT). Subjects were stratified according to glucose tolerance (NGT, IGT, and T2D) and into high and low BMI groups. Basal, dynamic, and static beta-cell function, insulin sensitivity, hepatic extraction, and disposition indices were assessed by OMMs.

RESULTS: Japanese generally had lower insulin and C-peptide secretion as compared to Caucasians at basal conditions as well as following OGTT. At all glucose tolerance states, basal beta-cell function was lower in Japanese ($P < 0.01$). Dynamic and static beta-cell indices were significantly lower in the Japanese IGT group compared to Caucasians ($P < 0.05$). In contrast, insulin sensitivity appeared higher in Japanese IGT subjects. Hepatic extraction at basal and during OGTT were similar in the NGT and IGT groups, but significantly higher in the Japanese T2D subjects compared to Caucasians ($P < 0.01$). Disposition indices were similar in Japanese and Caucasians at all disease states.

CONCLUSION: We confirm existence of differences in beta-cell function, insulin sensitivity and hepatic extraction between Caucasians and Japanese. However, Japanese and Caucasians have similar ability to compensate for insulin resistance with increased beta-cell function as indicated by similar disposition indices at all disease states.

PCS-02-3

Pancreatic Fat is Correlated with Indexes for Insulin Resistance but not Those for Insulin Secretion in Normoglycemic Subjects

Hisako Komada, Kazuhiko Sakaguchi, Yushi Hirota, Naoko Hashimoto, Tomoaki Nakamura, Michinori Takabe, Yoshinori Inoue, Yoko Okuno, Tomokazu Matsuda, Hidenori Fukuoka, Genzo Iguchi, Yutaka Takahashi, Wataru Ogawa and Susumu Seino

The Division of Diabetes, Metabolism, and Endocrinology, Department of Internal Medicine, Kobe University School of Medicine, Japan

OBJECTIVE: Evidence suggests that ectopic fat accumulation leads to organ dysfunctions. Previous studies have shown that pancreatic fat contents (PFC) were greater in type 2 diabetic subjects than in normoglycemic controls. However, it is unclear how increased PFC contributes to β -cell dysfunction. We investigated the relationship between PFC and various clinical parameters including those for β -cell function and insulin resistance in normal glucose tolerance (NGT) subjects.

METHODS: PFC was determined by measuring triglyceride contents in pancreas with the use of ¹H-magnetic resonance spectroscopy (¹H-MRS) in 31 Japanese NGT subjects. We also measured hepatic lipid content (HLC) and intramyocellular lipid content (IMCL) with the use of ¹H-MRS, and quantitated visceral fat (VF) and subcutaneous fat (SF) accumulation by magnetic resonance imaging.

RESULTS: PFC was positively correlated with age and body mass index (BMI). PFC was also correlated positively with HOMA-R, HLC and VF, and negatively with the Matsuda index even after adjustment for age and BMI. However, PFC was not correlated with SF and IMCL. PFC was also not

correlated with indexes for β -cell function including HOMA- β , insulinogenic index, and the ratio of the area-under-the insulin curve to the area-under-the glucose curve during OGTT. Multiple regression model analysis revealed that HLC was the strongest determinant of PFC ($\beta = 0.43$, $P = 0.014$).

CONCLUSION: Pancreatic fat content is correlated with parameters for insulin resistance but not with those for insulin secretion in Japanese NGT subjects.

PCS-02-4

Increased Interleukin 18 and Decreased Lung Function are Associated with 2 h Glucose on OGTT in Japanese Nondiabetic Males

Kazuko Nin¹, Mitsuo Fukushima², Ataru Taniguchi³, Yoshikatsu Nakai⁴, Shigeo Muro⁵, Daisuke Yabe⁶, Masaya Hosokawa⁷, Sae Aoyama², Naoya Watanabe⁸, Ryoichi Otsubo⁸, Takahide Okumura⁹, Fusanori Nishimura¹⁰, Shinji Sato¹¹, Tomoyuki Kurashina¹² and Shoichiro Nagasaka¹²

¹Human Health Sciences, Faculty of Medicine, Kyoto University, Japan; ²Division of Clinical Nutrition and Internal Medicine, Okayama Prefectural University, Japan; ³Division of Diabetes and Endocrinology, Kyoto Preventive Medical Center, Japan; ⁴Kyoto Institute of Health Science, Japan; ⁵Department of Respiratory Medicine, Graduate School of Medicine, Kyoto University, Japan; ⁶Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, Japan; ⁷Faculty of Human Sciences, Tezukayama Gakuin University, Osaka, Japan; ⁸Health Care and Promotion Center, Yodogawa Christian Hospital, Japan; ⁹Department of Pharmacy, Saiseikai-Nakatsu Hospital, Japan; ¹⁰Department of Dental Science for Health Promotion, Hiroshima University Graduate School of Biomedical Sciences, Japan; ¹¹Department of Sport and Health Science, Osaka Sangyo University, Japan; ¹²Division of Endocrinology and Metabolism, Jichi Medical University, Japan

OBJECTIVE: Although 2 h glucose but not fasting glucose on 75 g oral glucose tolerance test is a risk factor for coronary heart disease (CHD), it is unclear whether which factors contributing to 2 h glucose after 75 g oral glucose stimuli are associated with CHD events. Increased inflammatory biomarkers and decreased lung function are associated with CHD events in humans. The aim of the present study is to investigate whether 2 h glucose after 75 g oral glucose stimuli is associated with increased inflammatory biomarkers or decreased lung function.

METHODS: Two hundred and twenty healthy nondiabetic Japanese males with current nonsmoking and without prior lung disease were recruited from medical checkup. High molecular weight (HMW) adiponectin, tumor necrosis factor (TNF), leptin, high sensitive C-reactive protein (hsCRP), interleukin 18 (IL-18), forced vital capacity (FVC), and forced expiratory volume at 1 s (FEV1) were measured. Multiple regression analysis was used for statistical analysis.

RESULTS: Fasting glucose was independently associated with body mass index ($\beta = 0.501$, $P = 0.004$). In contrast, 2 h glucose after 75 g oral glucose stimuli was independently associated with FVC ($\beta = -10.46$, $P = 0.002$) and IL-18 ($\beta = 0.047$, $P = 0.012$).

CONCLUSIONS: From these results, it can be suggested that FVC and IL-18 are important factors associated with 2 h glucose after 75 g oral glucose stimuli in nondiabetic Japanese males.

PCS-02-5

Circulating TNF Receptor 2 is Associated with Chronic Kidney Disease in Non-Obese Japanese Patients with Type 2 Diabetes

Yoshio Izumi¹, Daisuke Yabe², Ataru Taniguchi³, Mitsuo Fukushima⁴, Yoshikatsu Nakai⁵, Masaya Hosokawa⁶, Takahide Okumura⁷, Kazuko Nin⁸, Kazunari Matsumoto⁹, Fusanori Nishimura¹⁰, Shoichiro Nagasaka¹¹ and Yutaka Seino²

¹Department of Internal Medicine, Osaka North Postal Services Agency Hospital, Japan; ²Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, Osaka, Japan; ³Division of Diabetes and Endocrinology, Kyoto Preventive Medical Center, Kyoto, Japan; ⁴Division of Clinical Nutrition and Internal Medicine, Okayama Prefectural University, Okayama, Japan; ⁵Kyoto Institute of Health Sciences, Kyoto, Japan; ⁶Faculty of Human Sciences, Tezukayamagakuin University, Osaka, Japan; ⁷Department of Pharmacy, Saiseikai Nakatsu Hospital, Osaka, Japan; ⁸Human Health Sciences, Graduate School of Medicine, Kyoto University, Japan; ⁹Diabetes Center, Sasebo Chuo Hospital, Nagasaki, Japan; ¹⁰Department of Dental Science for Health Promotion, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan; ¹¹Division of Endocrinology and Metabolism, Jichi Medical University, Tochigi, Japan

OBJECTIVE: Chronic low-grade inflammation and/or obesity are suggested to induce chronic kidney disease (CKD) in patients with type 2 diabetes. The aim of the current study is to investigate the relationship between inflammatory biomarkers and CKD in non-obese patients with type 2 diabetes.

METHODS: One hundred and six non-obese Japanese patients with type 2 diabetes were recruited for the measurement of GFR, tumor necrosis factor

(TNF), high molecular weight (HMW) adiponectin, high sensitive C-reactive protein (hsCRP), and some variables including urinary albumin. Body mass index, serum creatinine, and urinary albumin levels were $21.2 \pm 0.2 \text{ kg/m}^2$ (range, 17.1–24.9 kg/m^2), $0.76 \pm 0.02 \text{ mg/dL}$ (range 0.39–1.38 mg/dL), $41.5 \pm 4.0 \text{ mg/gCr}$ (range 1.6–195.0 mg/gCr), respectively. They were stratified into two groups based on the value of estimated GFR (eGFR): low eGFR (eGFR < 60 mL/min/1.73 m^2) and normal eGFR (eGFR > 60 mL/min/1.73 m^2). Logistic regression analysis was used for statistical analysis.

RESULTS: Whereas univariate logistic regression analysis showed that gender, diabetes duration, HDL cholesterol, uric acid, urinary albumin, and soluble TNF receptors (sTNF-R1, sTNF-R2) are associated with the development of stage 3 CKD, multivariate logistic regression analysis revealed that sTNF-R2 (Odds ratio 1.003, 95% confidence interval 1.000–1.005, $P = 0.030$) showed significant associations with the development of stage 3 CKD.

CONCLUSIONS: Whereas longitudinal studies are needed, our cross-sectional study may suggest that circulating TNF receptor 2 is an independent risk factor for chronic kidney disease in non-obese Japanese patients with type 2 diabetes.

PCS-02-6

Circulating TNF Receptor 2 is Associated with Early Decline in GFR in Nondiabetic Japanese Subjects

Ataru Taniguchi¹, Mitsuo Fukushima², Naoya Watanabe³, Yoshikatsu Nakai⁴, Daisuke Yabe⁵, Kazuko Nin⁶, Masaya Hosokawa⁷, Sae Aoyama², Ryoichi Otsubo³, Takahide Okumura⁸, Yoshio Nomura⁹, Fusanori Nishimura¹⁰, Shinji Sato¹¹, Tomoyuki Kurashina¹² and Shoichiro Nagasaka¹²

¹Division of Diabetes and Endocrinology, Kyoto Preventive Medical Center, Japan; ²Division of Clinical Nutrition and Internal Medicine, Okayama Prefectural University, Japan; ³Health Care and Promotion Center, Yodogawa Christian Hospital, Japan; ⁴Kyoto Institute of Health Science, Japan; ⁵Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, Japan; ⁶Human Health Sciences, Graduate School of Medicine, Kyoto University, Japan; ⁷Faculty of Human Sciences, Tezukayama Gakuin University, Japan; ⁸Department of Pharmacy, Saiseikai-Nakatsu Hospital, Japan; ⁹Department of Oral Health, Kobe Tokiwa Junior College, Japan; ¹⁰Department of Dental Science for Health Promotion, Hiroshima University Graduate School of Biomedical Sciences, Japan; ¹¹Department of Sport and Health Science, Osaka Sangyo University, Japan; ¹²Division of Endocrinology and Metabolism, Jichi Medical University, Japan

OBJECTIVE: Chronic kidney disease (CKD) is associated with cardiovascular events. The factors associated with the early decline in CKD are not fully clarified. Diabetic state per se may be such a powerful effect on the factors underlying the reduction in GFR that other factors responsible for the reduction in GFR might be masked. We therefore recruited nondiabetic subjects.

METHODS: Four hundred and 20 nondiabetic Japanese subjects with estimated GFR (eGFR) >60 mL/min/1.73 m^2 were enrolled to explore the factors associated with initial decline in GFR. Along with hemoglobin A1c (HbA1c), tumor necrosis factor (TNF) system (TNF- α , soluble TNF receptor 1 (sTNF-R1), sTNF-R2) and some variables including high sensitive C-reactive protein (hsCRP), high molecular weight (HMW) adiponectin, or leptin were measured. They were stratified based on the classification of CKD: stage 1 CKD (eGFR > 89 mL/min/1.73 m^2) and stage 2 CKD (90 > eGFR > 60 mL/min/1.73 m^2).

RESULTS: Whereas no significant differences were observed in some variables including gender, BMI, blood pressure, insulin, TNF- α , hsCRP, HMW adiponectin, or leptin between the two groups, age, HbA1c, sTNF-R1, sTNF-R2, and triglycerides were significantly higher in subjects with stage 2 CKD as compared to those with stage 1 CKD. Multiple logistic regression analysis revealed that only sTNF-R2 showed significant associations with the development of stage 2 CKD (Odds ratio 1.092, 95% confidence interval 1.013–1.177, $P = 0.021$).

CONCLUSIONS: Whereas longitudinal analyses are needed, our cross sectional study may suggest that circulating TNF receptor 2 is associated with early deterioration in CKD in nondiabetic Japanese subjects.

PCS-03-1

Vegetarian Diet in Taiwan has NO Specific Benefit to Type 2 Diabetes Patients

Chih-Ming Sun, Yu-Hung Chang, Hui-Chun Hsu and Yau-Jiunn Lee
Lee's Endocrinology Clinic, Taiwan

OBJECTIVES: Comparing to these difference within the different diet habits (vegetarian, breakfast vegetarian and omnivore) and all the metabolic index in type 2 diabetes patients in southern Taiwan.

METHODS AND SUBJECTS: Include criteria: (1) maintain the same diet habit over 3 years; (2) regular remedy for type 2 diabetes over 1 year in the same clinic. Collecting patient's anthropometric data, include blood pressure, height weight, age, duration, waist circumference and hip circumference, drug history, fasting blood and measuring the metabolic index, include fasting blood glucose, hemoglobin A1C (HbA1C), creatine (Cr), triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL) and low-density lipoprotein cholesterol (LDL). Using UKPDS risk engine to calculate the relative cardiovascular risk.

RESULTS: There are 69 patients with vegetarian (vegan, lacto-ovo-vegetarian, lacto-vegetarian and ovo-vegetarian), 132 patients with breakfast vegetarian (BV), and 207 patients with omnivore in all 2868 patients. Vegetarian habit accounts for 2.4% in type 2 diabetes patients. Patients with vegetarian have significantly higher systolic blood pressure (SBP; 147.1 ± 19.9 , 143.1 ± 19.9 , and 140.1 ± 17.6 , $P = 0.037$), TG (173.1 ± 68.2 , 153.5 ± 95.5 , and 140.0 ± 68.5 , $P < 0.001$) and significantly lower HDL (45.7 ± 10.3 , 50.0 ± 11.3 , and 53.0 ± 14.6 , $P = 0.001$). The body mass index, fasting blood glucose, HbA1C, TC and LDL levels were no statistically different among three groups. There are not any difference in cardiovascular risk.

CONCLUSION: The metabolic index include TG and SBP in type 2 diabetes significantly higher in vegetarian than in BV and in omnivore. Other metabolic index include blood sugar, creatine, TC and LDL have no difference among three group. Using UKPDS risk engine to predict cardiovascular risk, there is no difference among three group.

PCS-03-2

A High-Fiber Diet Improves Vascular Dysfunction Together with M1/M2 Phenotype in Patients with Type 2 Diabetes Mellitus

Keiko Kondo¹, Yoshihiko Nishio², Katsutaro Morino¹, Atsushi Ishikado¹, Motoyuki Kondo¹, Keiko Nakao¹, Takeshi Yoshizaki¹, Osamu Seikine¹, Satoshi Ugi¹, Atsunori Kashiwagi¹ and Hiroshi Maegawa¹

¹Department of Medicine, Shiga University of Medical Science, Japan; ²Department of Diabetes and Endocrine Medicine, Kagoshima University Graduate School of Medical and Dental Sciences, Japan

A high-fiber diet (HFD) shows anti-atherogenic effect, although underlying mechanism remains unclear. The inflammation is associated with atherosclerosis, and the increase in the ratio of M1/M2 phenotype of monocyte-macrophage is a marker of activated inflammation. In this study, we investigated whether HFD affects M1/M2 phenotype of peripheral blood monocytes (PBM) as well as vascular function in patients with T2DM.

We evaluated mRNA expression levels of CD11c/CD163 as a marker of M1/M2 phenotype of PBM and vascular function in 10 patients with T2DM (59.2 years, M/F = 3/7, diet/OHA = 8/2) and 8 age-matched subjects with normal glucose tolerance (NGT; 58.0 years, M/F = 4/4). In addition, the diabetic patients were followed for 16 weeks assigned to two periods of 8 weeks of either a HFD or a control diet (CD) in a crossover design. Before and after each period, vascular function and CD11c/CD163 ratio in PBM were evaluated.

The vascular function assessed with either peak forearm blood flow (FBF; $P = 0.026$) or flow debt repayment (FDR; $P = 0.015$) was significantly low in the diabetic patients as compared with NGT. The ratio of CD11c/CD163 expression levels was higher in the diabetes patients. During the intervention with HFD, the intake of total fiber was increased by two-fold compared with the CD. Body weight ($P = 0.007$) and HbA1c ($P = 0.036$) levels were decreased after the HFD. HFD improved 39.2% of FBF ($P = 0.075$), and 63.5% of FDR ($P = 0.006$), and 20% of CD11c/CD163 ratio ($P = 0.022$), but not with CD.

A high-fiber diet improved vascular function, and altered M1/M2 phenotype of PBM in patients with T2DM.

PCS-03-3

The Effects of Caloric Restriction on Fetuin-A and Cardiovascular Risk Factors in Rats and Humans: A Randomized Controlled Trial

Hae Yoon Choi¹, Jae Hee Ahn¹, Ho Cheol Hong¹, Yoon Jung Kim¹, Joo Hyung Kim¹, Chai Ryoung Eun¹, Nam Hoon Kim¹, Sae Jeong Yang¹, Hye Jin Yoo¹, Hee Young Kim¹, Ji A. Seo¹, Nan Hee Kim¹, Sin Gon Kim¹, Kyung Mook Choi¹, Sei Hyun Baik¹, Dong Seop Choi¹ and Kyung Wan Min²

¹Department of Internal Medicine, College of Medicine, Korea University, Korea;

²Department of Internal Medicine, Eulji University School of Medicine, Korea

The secreted liver protein fetuin-A is associated with insulin resistance, metabolic syndrome, type 2 diabetes, and atherosclerosis. We examined the effect of caloric restriction (CR) on fetuin-A level and concomitant changes in hepatic steatosis and cardiovascular risk factors in rats and humans.

We performed a randomized controlled clinical trial to examine the circulating fetuin-A level and cardiovascular risk parameters including visceral fat area (VFA), atherogenic lipid profile, inflammatory markers, adipokines and brachial artery endothelial function in 76 overweight women with type 2 diabetes before and after 12 weeks of CR. In addition, the effects of CR on hepatic steatosis and fetuin-A mRNA expression were evaluated in obese OLETF rats, an animal model of obesity and type 2 diabetes.

Circulating fetuin-A levels were significantly decreased after 12 weeks of CR, accompanied by improvements in VFA, blood pressure, glucose, lipid profiles, and liver function. The CR group also showed significantly decreased apolipoprotein B, leptin, and insulin resistance compared to those in the control group, although endothelial function were not different. Multiple regression analysis showed that the changes in fetuin-A were independently associated with CR and changes in hsCRP, adiponectin, and HOMA-IR ($R^2 = 24.6\%$). Moreover, CR significantly reduced hepatic steatosis and fetuin-A expression, as well as weight, glucose, total cholesterol and triglyceride levels in OLETF rats.

CR significantly reduced the hepatic expression of fetuin-A and its circulating levels and improved several cardiovascular risk factors in obese rats and humans with type 2 diabetes.

PCS-03-4

Effects of Consumption of Side Dishes with White Rice on Postprandial Glucose Metabolism in Healthy Men

Noriko Kameyama¹, Chizuko Maruyama¹, Sadako Matsui², Risa Araki² and Taro Maruyama³

¹Division of Food and Nutrition, Graduate School of Human Sciences and Design, Japan Women's University, Japan; ²Department of Food and Nutrition, Japan Women's University, Japan; ³Department of Internal Medicine, Saitama Social Insurance Hospital, Japan

OBJECTIVE: Co-ingestion of protein, fat, and fiber with carbohydrate reportedly affects postprandial glucose responses. However, the effects of dish-based combinations reflecting Japanese dietary style on postprandial glucose metabolism remain unclear. We evaluated effects of the consumption of side dishes with white rice in the same meal on postprandial glucose metabolism.

METHODS: Nine healthy Japanese male volunteers participated in this randomized, cross-over study. The subjects consumed four different meals on separate days. The test meals were: (A) white rice; (B) addition of protein-rich main dishes (egg and *tofu*) to meal A; (C) addition of a fat-rich food item (mayonnaise) to meal B; (D) addition of vegetable dishes (spinach and broccoli) to meal C. Blood samples were collected before and 30, 60, 120 and 180 min after consumption of the test meal. Plasma glucose (PG), serum insulin (IRI) and plasma total glucose-dependent insulinotropic polypeptide (GIP) were measured.

RESULTS: The increase in PG at 30 min was less after meal D than after meal B ($P < 0.05$). The incremental area under the curve (IAUC) for PG after meal D was smaller than those after meals A (0–120 min) and B (0–30 and 0–60 min; $P < 0.05$). IRI responses did not differ among the test meals. IAUC for GIP (0–180 min) was the largest after meals C and D, followed in order by those after meals B and A ($P < 0.05$).

CONCLUSION: Consumption of side dishes with white rice in the same meal has an effect on postprandial glucose and GIP responses.

PCS-03-5

Association Between Dietary Nutrients and Impaired Fasting Glucose in Korean Adults: Analysis of the Korea National Health and Nutrition Examination Survey in 2009–2010

Jae Woong Kim¹, Seok Hong Lee², Sangmi Ock³, Eun Young Kim³, Jin Nam Kim³, Hye Sook Yoo⁴, Ji Yeon Park⁴, Jaetaek Kim² and Jihyun Ahn²

¹Department of Internal Medicine, Chung-Ang University Hospital, Korea; ²Department of Internal Medicine, Diabetes Center, Chung-Ang University Hospital, Seoul, Korea;

³Diabetes Center, Chung-Ang University Hospital, Seoul, Korea; ⁴Department of Food Service and Nutrition, Chung-Ang University Hospital, Seoul, Korea

BACKGROUND: The impaired fasting glucose is a high risk factor of type 2 diabetes and cardiovascular disease. The aim of this study is to determine the relationship between dietary nutrients and impaired fasting glucose in Korean adults.

METHODS: The data was obtained from the Korean National Health and Nutrition Examination Survey in 2009–2010. Total 9484 aged 20–70 years

adults without previously diagnosed diabetes were included in this study. IFG was defined as fasting glucose of 100–125 mg.

RESULTS: Among participants, 1036 (27.1%) men and 977 (17.3%) women showed IFG. Age, blood pressure, weight, BMI, waist circumference, total cholesterol, LDL-cholesterol, triglyceride, AST, ALT, total daily energy intake (kcal), daily carbohydrate intake (%), daily sodium intake (mg) were significantly higher in subjects with IFG than those with normal glucose level ($P < 0.001$). In multiple regression analysis with adjusted covariates such as age, sex, smoking status, physical activity, house income, marital status, alcohol consumption IFG was significantly associated with high carbohydrate intake ($>70\%$; OR: 1.14, 95% confidence interval (CI): 1.02–1.28, $P < 0.018$), high sodium intake (>4000 mg; OR: 1.17, 95% confidence interval (CI): 1.06–1.30, $P < 0.002$).

CONCLUSIONS: The reduction of dietary carbohydrate and sodium intake will prevent IFG associated with cardiovascular disease risk factors in Korean adults.

PCS-03-6

Effect of High-Intensity Progressive Resistance Training on Glycemic Control in Japanese Men with Type 2 Diabetes

Minemori Watanabe¹, Takeshi Sato², Kazuhiro Magawa², Tomoya Oda², Taku Tsunekawa¹, Risako Watanabe¹ and Ataru Okumura¹

¹Department of Endocrinology and Diabetes, Okazaki City Hospital, Japan; ²Department of Physical Medicine and Rehabilitation, Okazaki City Hospital, Japan

OBJECTIVE: Several lines of evidence indicate that high-intensity progressive resistance training (PRT) improves glycemic control in Western countries, while there are little evidences regarding the relation between PRT and type 2 diabetes mellitus (T2DM) in Japan. Therefore, we examined the effect of high-intensity PRT on glycemic control in Japanese men with T2DM.

METHODS: Nine Japanese men with T2DM ranging from 21 to 59 years of age and $23.2\text{--}34.8$ kg/m² body mass index (BMI; treated with oral hypoglycemic agents: two subjects, naive: seven subjects) participated in a supervised 12-week high-intensity (75–80% of the one-repetition maximum) PRT program. Clinical and laboratory measurements were assessed before and after the program.

RESULTS: A 12-week high-intensity PRT significantly decreased HbA1c (0 week: $11.0 \pm 0.8\%$, 12 weeks: $7.4 \pm 0.4\%$) and increased HDL-cholesterol (0 week: 43.0 ± 6.0 mg/dL, 12 weeks: 50.0 ± 6.0 mg/dL). Whole-body lean mass (0 week: 57.5 ± 5.1 kg, 12 weeks: 60.9 ± 4.5 kg), whole-body muscle mass (0 week: 53.2 ± 4.5 kg, 12 weeks: 56.0 ± 3.7 kg) and basal metabolic rate (0 week: 1382 ± 135 kcal, 12 weeks: 1454 ± 162 kcal) were significantly increased by the program. On the other hand, there were no significant changes in BMI (0 week: 27.7 ± 1.6 kg/m², 12 weeks: 29.0 ± 3.6 kg/m²) and body fat percentage (0 week: $27.4 \pm 3.4\%$, 12 weeks: $25.4 \pm 5.3\%$).

CONCLUSION: This study suggests the possibility that high-intensity PRT improves glycemic control in Japanese men with T2DM as Western countries.

PCS-04-1

Impact of Gender on Glycemic Control and Safety in Managing Asian Patients with T2DM: A FINE-Asia Registry Subanalysis

Linong Ji¹, Karim Admane², Jay Lin³, Edward Wang⁴ and Jian Wang⁵

¹Department of Endocrinology and Metabolism, Peking University People's Hospital, China; ²Sanofi, Paris, France; ³Novosys Health, Flemington, NJ, USA; ⁴Sanofi, Bridgewater, NJ, USA; ⁵Jinling Hospital, Nanjing, Jiangsu, China

OBJECTIVE: The First Basal Insulin Evaluation (FINE) Asia study was a prospective, observational registry evaluating basal insulin initiation in Asian patients with type 2 diabetes mellitus (T2DM) inadequately controlled by oral antidiabetic drugs (OAD). The aim of this *post-hoc* analysis was to determine the impact of gender on the efficacy and safety of treatment.

METHODS: Basal insulin was initiated with or without concomitant OADs. Follow-up duration was 6 months. Primary efficacy endpoint was change in HbA1c from baseline following insulin initiation. Secondary endpoints included HbA1c and fasting blood glucose (FBG) response rates and hypoglycemic events.

RESULTS: A total of 1334 (49.8%) male and 1345 (50.2%) female patients were included in the analysis. There were no differences between genders with respect to HbA1c and FBG levels at baseline, while females had significantly

greater body mass index (mean $\pm$ SD, 26.4 ± 5.0 vs 25.9 ± 4.9 ; $P = 0.008$). HbA1c was reduced in both groups at follow up, but change from baseline was significantly less in females, ($-2.0 \pm 1.8\%$ vs $-2.2 \pm 1.7\%$; $P < 0.001$). Fewer females reached HbA1c $<8\%$ (62.9% vs 72.2%; $P < 0.001$) and FBG <7.2 mmol/L (60.8% vs 70.7%; $P < 0.001$). There were no differences in the hypoglycemia incidence (14.8% vs 13.9%, $P = 0.49$) or severe hypoglycemia (0.6% vs 0.3%, $P = 0.25$) between the genders.

CONCLUSIONS: Following basal insulin initiation, there was greater HbA1c reduction in males than females, and more males reached the real-life targets of HbA1c $<8\%$ and FBG <7.2 mmol/L after 6 months. The incidence of hypoglycemia and severe hypoglycemia was similar in both genders.

This study was supported by Sanofi.

PCS-04-2

Therapeutic Efficacy of Premixed Insulin Aspart 70/30 Insulin in Glycemic Control in the Type 2 Diabetic Patients

Aki Ikoma, Hodaka Yamada, Masashi Yoshida, Tomoko Asano, Atsushi Aoki, Hideo Toyoshima, Masafumi Kakei and San-e Ishikawa

Department of Internal Medicine, Jichi Medical University Saitama Medical Center, Japan

Selection of insulin for type 2 DM is variable according to developing various kinds of insulin agents. Premixed insulin aspart 70/30 (70Mix) is a new type of insulin. But its clinical indication remained undetermined yet.

The present study was undertaken to elucidate glycemic control by 70Mix in type 2 diabetic patients.

Thirty type 2 diabetic patients were enrolled. They were 18 males and 12 females with the ages of 64.0 ± 13.2 years. 70Mix was administrated three times a day, and glycemic control has been evaluated after the start of 3 and 6 months. Before the start of 70Mix, glycemic control was carried out with anti-hyperglycemic oral agents (eight patients), intensive insulin therapy (eight patients), rapid type insulin therapy (seven patients), premixed-type insulin therapy (nine patients), long-acting insulin therapy in BOT (three patients). The treatment with 70Mix was effective in 21 patients (70Mix group). HbA1c (JDS) was improved from $9.0 \pm 1.7\%$ to $8.0 \pm 1.5\%$ in 3 months, and $7.5 \pm 1.2\%$ in 6 months. In contrast, the 70Mix became withdrawn in 2.34 months (mean) in nine patients because of worsening of glycemic control (interruption group). HbA1c (JDS) was changed from $9.1 \pm 2.4\%$ to $8.3 \pm 2.0\%$, and FPG changed from 237.9 ± 185.3 to 162.6 ± 67.0 mg/dL when 70Mix was withdrawn. Hypoglycemia was more frequent in the interruption group than in the 70Mix group.

These findings indicate that plasma glucose is controlled well by the 70Mix in most of patients with type 2 DM. However, the efficacy of 70Mix is individually variable among the patients, and thus its effectiveness should be evaluated at early period of usage.

PCS-04-3

Insulin Degludec does not Increase Antibody Formation Compared to Insulin Glargine: An Evaluation of Phase 3a Trials

Priscilla Hollander¹, Jiten Vora², Marcus Niemeyer³, Thue Johansen⁴ and Richard Bergenstal⁵

¹Baylor University Medical Center, Dallas, TX, USA; ²Royal Liverpool University Hospitals, Liverpool, UK; ³Novo Nordisk A/S, Bagsvaerd, Denmark; ⁴Novo Nordisk A/S, Soeborg, Denmark; ⁵International Diabetes Center at Park Nicollet, Minneapolis, MN, USA

OBJECTIVES: Here we present antibody data from all phase 3a trials in patients with T1D or T2D where insulin antibody development was analyzed for insulin degludec (IDeg) and compared to insulin glargine (IGlar).

METHODS: Insulin antibodies were measured in six randomized, controlled, open-label, treat-to-target trials (26–52 weeks duration): two in T1D (IDeg: $n = 801$; IGlar: $n = 315$) and four in T2D (IDeg: $n = 1734$; IGlar: $n = 860$). IDeg and IGlar were dosed once-daily. Insulin aspart was used as bolus insulin in the T1D trials. Antibody levels were measured using specific radioimmunoassays and expressed as percent bound/total radioactivity (%B/T).

RESULTS: Across all trials, very few subjects developed IDeg- and IGlar-specific antibodies and mean levels of antibodies cross-reacting to human insulin remained low for subjects with T1D (10–15% B/T) and T2D ($<6\%$ B/T). Spearman correlation coefficients were calculated on an individual trial basis to investigate the influence of cross-reacting antibodies on change from baseline in HbA1c and HbA1c and total daily insulin dose at end-of-trial. All correlation coefficients were low indicating no clinically relevant influence of

insulin antibodies on HbA_{1c} or dose. Based on scatter plots, there was no difference in HbA_{1c} or total insulin dose at end-of-trial between subjects having cross-reacting antibody levels >10% B/T and those with levels <10% B/T. Adverse events in subjects with an antibody titer >10% B/T were similar to the overall trial population.

CONCLUSION: The immunogenic responses to long-term treatment with IDeg and IGlare are similar and low, with no clinically relevant impact on HbA_{1c} or total daily insulin dose.

PCS-04-4

Ultrastructural Visualisation of Insulin Degludec Multi-Hexamers *In Vivo* Supports a Unique Mechanism of Protraction

Torben Seested, Svend Havelund, Ib Jonassen, Thomas Hoeg-Jensen, Charles Pyke and Erica Nishimura
Novo Nordisk A/S, Malov, Denmark

OBJECTIVE: Insulin Degludec (IDeg) is a novel basal insulin engineered to form a depot of soluble multi-hexamers at the injection site from which there is a slow and steady absorption into the circulation to provide an ultra-long half-life of over 24 h.

METHODS: In the present study we visualise at the ultra-structural level the *in vivo* formation of IDeg multi-hexamers in the subcutis. IDeg or NPH insulin (120 nmol/20 U) was subcutaneously injected in the neck of anesthetized pigs. After 10 min, a biopsy of the injection site was fixed in paraformaldehyde and embedded in epoxy resin.

RESULTS: Micrographs from ultra-thin sections revealed filament-like structures, measuring approximately 5–20 nm in width. The size and shape of these filament-like structures resemble that of IDeg multi-hexamers previously observed by *in vitro* electron microscopy. Immuno-gold labelling was performed using two antibodies directed against the insulin backbone and two antibodies specific for the acylated linker on IDeg. When applied to separate tissue blocks, all four antibodies showed the same pattern of immuno-reactivity, confirming the presence of IDeg in the filament-like structures located in the subcutis. Anti-insulin antibodies pre-absorbed with insulin and a non-relevant antibody showed no gold labelling over the filament-like structures. In contrast to IDeg, large (approximately 200–500 nm in width) crystalline, rod-like structures were observed after injection of NPH. Immuno-gold reactivity was only observed with the two antibodies directed against the insulin backbone.

CONCLUSION: These data visualize the formation of IDeg multi-hexamers at the injection site and support IDeg's unique mechanism of protraction.

PCS-04-5

Significance of Nadir Fasting Plasma Glucose Levels Achieved by Mealtime Dosing of a Rapid-Acting Insulin Analog in Patients with Type 2 Diabetes

Akiko Shimizu, Toshinari Takamura, Ken-Ichiro Kato, Masafumi Uno, Yumie Takeshita, Hirofumi Misu and Shuichi Kaneko
Department of Disease Control and Homeostasis, Kanazawa University School of Medical Science, Japan

OBJECTIVE: We previously showed that strict control of postprandial glucose levels improves fasting plasma glucose (FPG) levels in patients with type 2 diabetes (Diabetes Res Clin Pract 2007). The present study investigated clinical indices predicting a steady state FPG achieved by mealtime dosing of a rapid-acting insulin analog (Nadir FPG).

METHODS: A rapid-acting insulin analog was administered at each mealtime to 147 Japanese patients with type 2 diabetes. The insulin dose was adjusted to attempt to achieve plasma glucose levels of 80–120 mg/dL before lunch, dinner and bedtime each day. The primary endpoint was the proportion of patients achieving a nadir FPG of <140 mg/dL. The secondary endpoint was clinical indices predicting nadir FPG.

RESULTS: Appropriate nadir FPG level (<140 mg/dL) was achieved by 63% of the patients. The body mass index was significantly higher in the achiever group than the non-achiever group (24.2 ± 4.1 vs 21.8 ± 3.2 kg/m²; *P* < 0.05). Nadir FPG was negatively associated with various indices of residual δ -cell function. The response of C-peptide immunoreactivity (δ CPR) to arginine loading was the best predictor among other parameters. When the δ CPR to arginine loading was more than 2.3 ng/mL, the sensitivity and the specificity of the achievement of appropriate nadir FPG were both 71% and 71%, respectively.

CONCLUSIONS: 63% of the patients with type 2 diabetes achieved appropriate nadir FPG without basal insulin replacement. Indices of residual δ -cell function, especially δ CPR to arginine loading would predict the necessity of basal insulin replacement.

PCS-04-6

Predictors of Hypoglycemia in the Real-World Management of Asian Patients with T2DM: A FINE-Asia Registry Analysis

Jian Wang¹, Karim Admane², Edward Wang³, Jay Lin⁴ and Linong Ji⁵

¹Department of Endocrinology, Jinling Hospital, China; ²Sanofi, Paris, France; ³Sanofi, Bridgewater, NJ, USA; ⁴Novosys Health, Flemington, NJ, USA; ⁵Peking University, Beijing, China

BACKGROUND/OBJECTIVES: FINE-Asia was a multinational (11 countries), 6-month observational study. Basal insulin use was assessed in 2921 insulin-naïve Asian patients with T2D uncontrolled on OADs. Analyses aimed to identify demographic-/treatment-based predictors of hypoglycemia (all, moderate, severe).

METHODS: Analyses were conducted using multivariate logistic regression models with all, moderate or severe hypoglycemia as dependent variables. Covariates included, but not limited to, baseline A1C, age, gender, BMI, diabetes/OAD duration, and country; covariates associated with significantly higher risk of hypoglycemia, compared with reference group, are shown (Table).

RESULTS: Treatment with detemir and NPH was associated with significantly higher risks of any/moderate and any/moderate/severe hypoglycemia, respectively, vs glargine. Treatment in China, Korea, Pakistan and Thailand was associated with higher risks than in India. Preparatory education and higher insulin dosage at baseline were associated with higher risk of any/moderate hypoglycemia.

Parameter	Any Hypoglycemia 0-6 months (n = 384)		Moderate Hypoglycemia 0-6 months (n = 374)		Severe Hypoglycemia 0-6 months (n = 12)	
	Odds Ratio (CI)	P-value	Odds Ratio (CI)	P-value	Odds Ratio (CI)	P-value
Insulin Type¹						
Detemir (n=61)	2.4 (1.1,5.1)	0.025	2.4 (1.1,5.1)	0.025	NA*	NA
NPH (n=589)	2.2 (1.6,2.9)	<0.0001	2.2 (1.7,3.0)	<0.0001	8.8 (1.7,44.7)	0.008
Baseline BMI						
Per kg/m ²	1.0 (1.0,1.0)	0.114	1.0 (1.0,1.0)	0.2	0.8 (0.7,1.0)	0.022
Education levels²						
Preparatory (n=329)	1.8 (1.2,2.8)	0.008	1.8 (1.2,2.8)	0.008	0.7 (0.0,9.2)	0.789
Country/Region³						
China (n=491)	4.5 (3.0,6.7)	<0.0001	4.6 (3.1,6.9)	<0.0001	0.2 (0.0,1.3)	0.09
Korea (n=291)	1.8 (1.1,3.1)	0.032	1.9 (1.1,3.2)	0.022	NA	NA
Pakistan (n=139)	4.2 (2.3,7.5)	<0.0001	4.1 (2.2,7.4)	<0.0001	NA	NA
Thailand (n=448)	2.2 (1.4,3.5)	0.0005	2.2 (1.4,3.5)	0.0006	0.0 (0.0,1.0)	0.048
Insulin Dose at Baseline						
Per 1 U/kg	42.2 (11.9,149.1)	<0.0001	47.2 (13.2,168.7)	<0.0001	0.1 (0.0,263.9)	0.553

P-value obtained via analysis of maximum likelihood estimates (P<0.05 considered significant). Odds ratio >1 indicated higher hypoglycemia risk.

CI = 95% Wald Confidence Interval (Lower-Upper bound)

* NA: Odds ratio not estimable due to lack of sample size (eg, low# of events in corresponding group)

¹Reference group: Insulin glargine (n=2016)

²Reference group: Tertiary education (n=569)

³Reference group: India (n=681)

CONCLUSIONS: Choice of basal insulin, insulin dose, education level, BMI, and country/region may impact hypoglycemia risk in real-world settings.

This study was supported by Sanofi.

PCS-04-7

The Effectiveness of Starting Biphasic Insulin Aspart 30 (Premix) in Older Versus Younger Adults with Type 2 Diabetes

Siddharth Shah¹, Yuxiu Li², Zanariah Hussein³, Mohammad Hasan⁴, Praful Chakkarwar⁵ and Pradana Soewondo⁶

¹Department of Medicine, Bhatia Hospital, Mumbai, India; ²Peking Union Medical College Hospital, Beijing, China; ³Medical Department, Hospital Putrajaya, Putrajaya, Malaysia; ⁴Miracles, Diabetic Institute Pakistan (DIP), Lahore, Pakistan; ⁵Novo Nordisk Pharma Gulf FZ-LLC, Dubai, United Arab Emirates; ⁶Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Indonesia, Jakarta, Indonesia

OBJECTIVES: The management of type 2 diabetes (T2DM) becomes more complex in older people, due to increased comorbidities and risk of

hypoglycaemia. We have therefore investigated the effectiveness and safety of beginning the premix biphasic insulin aspart (oral glucose-lowering drugs) in older (>65 years) and younger (≤65 years) adults.

METHODS: A₁chieve was a 24-week, non-interventional study in 28 countries, evaluating safety and effectiveness of insulin analogues in T2DM ($n = 66,726$) in routine clinical practice. This subgroup analysis used data on previously insulin-naïve adults.

RESULTS: Introducing premix aspart was associated with similar improvement in glycaemic control in both age groups at similar insulin doses (Table). Overall and major hypoglycaemic events remained infrequent in both age groups (Table). Body weight showed no clinically significant difference but was numerically greater in older adults. Quality of life improved significantly in both groups ($P < 0.001$; Table).

Table. Clinical outcomes after 24 weeks of treatment with premix.

		>65 years	≤65 years
Insulin dose (U/kg/day)	Day 1	0.42 (0.19)	0.42 (0.17)
	Final visit	0.47 (0.20)	0.47 (0.21)
HbA _{1c} (%)	Baseline	9.5 (1.9)	9.5 (1.7)
	Change	-2.2 (1.8)*	-2.2 (1.6)*
FPG (pre-breakfast) (mmol/l)	Baseline	10.7 (3.5)	11.2 (3.4)
	Change	-3.7 (3.6)*	-4.1 (3.3)*
PPG (post-breakfast) (mmol/l)	Baseline	15.3 (4.5)	15.7 (4.1)
	Change	-5.2 (4.9)*	-5.9 (4.3)*
Hypoglycaemia (overall) (event/person-year [% with event])			
Overall	Baseline	0.99 (3.8)	0.94 (4.0)
	Final visit	1.49 (6.1)*	0.98 (4.0) [‡]
Major	Baseline	0.15 (0.8)	0.08 (0.4)
	Final visit	0.00 (0.0)*	0.00 (0.3)*
Body weight (kg)	Baseline	67.5 (12.3)	70.6 (12.6)
	Change	1.0 (3.9)*	0.2 (3.4)*
Quality of life (VAS 0–100)	Baseline	63.7 (16.6)	62.6 (17.0)
	Change	13.1 (16.6)*	15.4 (17.0)*

Mean (SD) or %; * $p \leq 0.001$, [‡] $p = 0.961$; FPG, fasting plasma glucose; PPG, postprandial plasma glucose; SD, standard deviation; VAS, visual analogue scale

CONCLUSION: In the A₁chieve study, use of insulin aspart premix was well-tolerated and effective in younger and older insulin-naïve adults with T2DM.

PCS-04-8

The Omission Ratio of Different Insulin Injection Strategies

Chung-Chia Liao^{1,2} and Chen Shu-Fen¹

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Cheng-Ching Hospital, Taiwan; ²Institute Biochemistry and Biotechnology, College of Medicine, Chung Shan Medical University, Taichung, Taiwan

OBJECTIVE: This study was to investigate the omission ration of different insulin injection strategies and its related factors.

METHODS: 147 outpatients in a regional teaching hospital in Taichung city were included from January 2012 to April 2012. The data was collected when these patients had their routine OPD visit.

RESULTS: This study included 147 patients receiving insulin injection. 76 male and 71 female patients had a mean age of 60.57 years. 30% of the subjects were on basal insulin injection in conjunction with noninsulin agents and 70% on twice daily insulin injection. The ratio of patients using insulin injection pen was 36%. The insulin omission ratio was 21.77%. The patients using insulin pen had lower omission ratio than those using insulin syringes. The omission ratio of basal insulin with noninsulin agents was higher than that of twice daily insulin injection. In the twice daily insulin injection group, the omission ratio was highest in the split-mixed insulin injection group, followed by the pre-mixed insulin injection with insulin syringes and finally, the pre-mixed insulin injection with insulin pen. The most common cause of missed insulin injection was interference of insulin injections by daily activities.

CONCLUSION: From our study, the more complex insulin regimen had a larger insulin omission ratio and those patients using insulin injection pen had better insulin injection adherence. Diabetes educators should give extensive insulin regimen training to diabetic patients so as to guarantee the efficacy of their diabetes regimen, regardless of whether at home or outside the home.

PCS-05-1

Effect of Insulin Switching on A1C in Inadequately Controlled Asian Pacific Diabetes Patients

Gabriel V. Jasul Jr¹, Chih-Yuan Wang², Edward Wang³ and Karim Admane⁴

¹St. Luke's Medical Center, Philippines; ²National Taiwan University Hospital, Taipei, Taiwan; ³Sanofi, Bridgewater, NJ, USA; ⁴Sanofi, Paris, France

OBJECTIVE: Effects of switching from 1 insulin regimen to another in real-world patients with inadequately controlled type 1 (T1D) or type 2 diabetes (T2D) were examined prospectively in a non-interventional, open-label registry in 10 Asia Pacific countries.

METHODS: Inclusion required diabetes duration ≥5 years, A1C ≥8% and prescribed switch in insulin regimen. Change in A1C and FBG over 6 months was measured.

RESULTS: Of 1765 patients, 115 had T1D and 1650 had T2D. At study entry, 435 (24.6%) were using insulin only and 1330 (75.4%) insulin + OAD. In total, 787 (44.6%) were using premixed insulin, 730 (41.4%) basal insulin and 116 (6.6%) prandial + basal insulin. At baseline, 70.0% (1236/1765) switched between insulin classes, with 73.2% (576/787) switching from premixed insulin to glargine (T1D: 33.9%, 39/115; T2D: 32.5%, 537/1650). Mean ± SD baseline daily dose of all switched insulin was 27.7 ± 18.8 U. A1C and FBG declined significantly over 6 months in both diabetes types. At Month 6, 17.5% (17/97) of T1D and 27.6% (402/1456) of T2D patients reached A1C < 7%. The most common reason for not achieving A1C < 7% was insufficient up-titration of insulin dose (377/958, 39.4%). This study's real-world nature precluded outcome optimization. Seventy-four adverse drug reactions (all hypoglycemia: 85.1% of mild severity) were reported by 2.8% (49/1765) of patients. Most hypoglycemic events at Months 3 (87.7%, 50/57) and 6 (94.1%, 16/17) were non-serious.

CONCLUSION: Insulin switching in this non-interventional, open-label registry was safe and effectively lowered A1C in T1D and T2D patients.

This study was supported by Sanofi.

PCS-05-2

Improved Glycemic Control of Biphasic Insulin Aspart in Chinese T2D Patients Poorly Treated on Oral Anti-Diabetic Drugs

Wenying Yang¹, Yuxiu Li², Liming Chen³, Yongquan Shi⁴, Yongde Peng⁵ and Minxiang Lei⁶

¹Department of Endocrinology, China-Japan Friendship Hospital, China; ²Department of Endocrinology, Peking Union Medical College Hospital, China; ³Department of Endocrinology, Tianjin Medical University Metabolic Diseases Hospital, China; ⁴Department of Endocrinology, Shanghai Changzheng Hospital, China; ⁵Department of Endocrinology, Shanghai First People's Hospital, China; ⁶Department of Endocrinology, The First Xiangya Hospital of Central South University, China

OBJECTIVE: To evaluate clinical safety and effectiveness of biphasic insulin aspart (BIAsp 30) in patients with type 2 diabetes (T2D) poorly treated on oral anti-diabetic drugs (OADs).

METHODS: A₁chieve was a multinational, prospective, open-label, non-interventional study in patients with T2D initiating insulin analogues in 28 countries across Asia, Africa, Europe, and Latin America. Data were collected at baseline and Week 24 (end of study).

RESULTS: In China, 4100 patients previously treated only with OADs initiated BIAsp 30 + OADs (54.2% males, mean ± SD age 56.2 ± 13.6 year, BMI 24.7 ± 3.2 kg/m², duration of T2D 6.8 ± 5.4 year). Glycemic control was significantly improved after 24 weeks treatment as measured by HbA_{1c} (from 9.3 ± 2.1% to 7.0 ± 1.0%, change -2.3 ± 2.0%), fasting plasma glucose (FPG, from 10.2 ± 3.3 to 6.8 ± 1.3 mmol/L, change -3.5 ± 3.4 mmol/L), and postprandial plasma glucose (PPPG, from 14.4 ± 4.6 to 8.8 ± 1.8 mmol/L, change -5.6 ± 4.7 mmol/L; all $P < 0.001$). The proportion of patients achieved HbA_{1c} target <7.0% increased from 9.7% to 54.2%. Total daily insulin dose was 0.44 ± 0.18 U/kg at baseline and 0.47 ± 0.18 U/kg at Week 24. Rates of total, major, nocturnal hypoglycemic events (events/patient/year) were 1.47, 0.10, 0.31 at baseline and 1.35, 0.00, 0.22 at Week 24.

CONCLUSION: BIAsp 30 improved glycemic control with low risk of hypoglycemia in Chinese patients with T2D inadequately controlled on OADs in the A₁chieve study.

PCS-05-3

Diabetic Complications and Glycemic Control in Patients Treated by Glargine and Oral Agents in a Real-Life Setting: ALOHA Study Subanalysis

Tetsuya Ohtani¹, Takashi Kadowaki² and Masato Odawara³

¹Sanofi-aventis K.K., Japan; ²Department of Diabetes and Metabolic Diseases, Graduate School of Medicine, The University of Tokyo, Japan; ³Department of Diabetology, Metabolism, and Endocrinology, Tokyo Medical University, Japan

OBJECTIVE: To investigate the association of diabetic microvascular complications with the effectiveness and safety outcomes regarding basal supported oral therapy using insulin glargine and oral antidiabetic drugs, we analyzed data from patients in the Add-on Lantus to Oral Hypoglycemic Agents (ALOHA) study that is a observational, non-interventional, 24-week follow-up study.

METHODS: Change in hemoglobin A1c (A1C) including the attainment of A1C < 7.0%, fasting and postprandial plasma glucose (FPG and PPG), daily dose of glargine and weight were evaluated at 24 weeks or at glargine discontinuation. Information on dose and hypoglycemic episodes was obtained from medical records. Data were analyzed according to the classification of the combination of three diabetic microvascular complications, i.e. any levels of retinopathy, neuropathy, and nephropathy at baseline.

RESULTS: Out of 3631 patients, 1889 (52.0%) were without any diabetic complications. Patients with all three complications accounted for 8.3% ($n = 301$). Levels of A1C, FPG, and PPG improvement and glargine daily dose were similar among patients with and without diabetic complications. Response rate achieving A1C < 7.0% was the highest in patients without any diabetic complications (19.1%). Patients with both retinopathy and nephropathy had the lowest response rate (8.8%) and the highest hypoglycemic rate (3.2%).

CONCLUSION: Our results suggest that type-2-diabetes patients without any diabetic complications can most probably attain a good glycemic control by insulin glargine therapy with oral antidiabetic drugs in 24 weeks. Insulin glargine initiation might be more beneficial in patients prior to than after suffering from diabetic retinopathy and nephropathy.

PCS-05-4

Ultra-Long Acting Insulin Degludec Reaches Steady State Within 2-3 Days of Once-Daily Administration

Tim Heise¹, Leszek Nosek¹, Hans-Veit Coester¹, Carsten Roepstorff², Marcus Niemeier³, Nathan Lassota² and Hanne Haahr²

¹Profil Institut fuer Stoffwechselforschung, Neuss, Germany; ²Novo Nordisk A/S, Soeborg, Denmark; ³Novo Nordisk A/S, Bagsvaerd, Denmark

OBJECTIVES: Insulin degludec (IDeg) is a new basal insulin with an ultra-long duration of action >42 h leading to a flat, stable and consistent action profile at steady-state. Clinical use and dose titration requires an understanding of the time it takes for IDeg to reach steady-state.

METHODS: In three randomized, double-blind clinical pharmacology trials, subjects with type 1 and 2 diabetes (T1DM/T1DM/T2DM; $n = 27/66/49$) received IDeg once-daily at 0.4, 0.6 and/or 0.8 U/kg. Blood samples were obtained before each dosing to determine serum IDeg concentration relative to Day 10/6/4 after first dose. The time to steady-state was estimated as time from first dose until serum IDeg trough concentrations exceeded 90% of the final plateau level.

RESULTS: For all subjects, independent of dose or diabetes type, steady-state was reached after 2-3 days of IDeg dosing. At steady-state, exposure of IDeg was consistent from day-to-day.

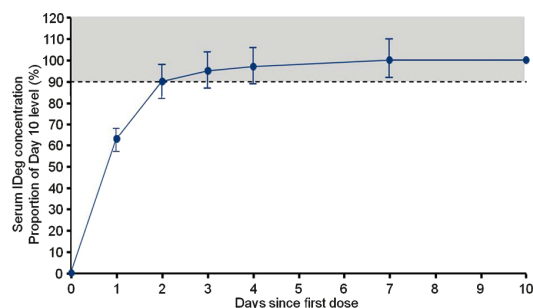


Figure 1: Relative serum IDeg trough concentrations (estimated ratios and 95% CIs) during initiation of once-daily dosing in subjects with T1DM

CONCLUSION: IDeg achieves steady-state levels after 2-3 days of once-daily administration without further increases in exposure thereafter.

PCS-05-5

Clinical Experience with Insulin Detemir in Insulin Naive Patients: Results from the South Korean Cohort of Global A1chieve Study

Sei Hyun Baik¹, Keun Yong Park², Kang Seo Park³, Kyu Jeung Ahn⁴, Kyung Wan Min³, Jeong H. Park⁵, Sang Ah Chang⁶, Bong Soo Cha⁷, Dong-Jun Kim⁸, Yong Seong Kim⁹, Tae Keun Oh⁹, Suk Chon¹⁰, Hyeonjin Kim¹¹, Il Sueong Nam-Goon¹², Seok Woo Kang¹³, Mi Jin Kim¹⁴, Hye-Soon Kim¹⁵, Young Sik Choi¹⁶, You Hern Ahn¹⁷ and Sora Lee¹⁸

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Korea University College of Medicine, Korea; ²Konyang University College of Medicine, Korea; ³Eulji University School of Medicine, Korea; ⁴Kyung Hee University School of Medicine, Korea; ⁵Inje University College of Medicine, Korea; ⁶The Catholic University of Korea College of Medicine, Korea; ⁷Yonsei University College of Medicine, Korea; ⁸Inha University College of Medicine, Korea; ⁹Chungbuk National University College of Medicine, Korea; ¹⁰Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine, Korea; ¹¹Kwandong University College of Medicine, Korea; ¹²Ulsan University Hospital, Korea; ¹³Seoul Red Cross Hospital, Korea; ¹⁴Hongik Hospital, Korea; ¹⁵Keimyung University School of Medicine, Korea; ¹⁶Kosin University College of Medicine, Korea; ¹⁷Hanyang University College of Medicine, Korea; ¹⁸Medical, Novo Nordisk Pharma Korea, Korea

OBJECTIVE: A1chieve was a non-interventional, observational study of 66,726 people with type 2 diabetes, started on insulin detemir (IDet), insulin aspart or biphasic insulin aspart in 28 countries. The present abstract is to demonstrate a subgroup analysis from insulin naive South Korea patients with type 2 diabetes who were treated with IDet in the study ($N = 1453$).

METHODS: The clinical information on safety and effectiveness of IDet was collected for 24 weeks. The primary endpoint was the number of serious adverse drug reactions (SADRs) occurred during the study period. Several effectiveness parameters including HbA1c, fasting plasma glucose (FPG), postprandial plasma glucose (PPG) levels as well as the quality of life (QoL) were evaluated as secondary endpoints. Information on body weight, daily insulin dose, and dosing frequency was also collected.

RESULTS: In total, two SADRs and nine ADRs were reported in 0.1% and 0.6% patients, respectively. No major hypoglycaemic episode occurred. HbA1c, FPG, PPG levels were significantly reduced after 24 weeks by $1.6 \pm 2.0\%$, 3.5 ± 4.0 and 4.7 ± 6.3 mmol/L (Mean $\pm$ SD), respectively. The QoL was also improved that the EQ-5D index increased by 7.5 ± 18.3 at Week 24 compared to the baseline. Body weight was slightly increased 0.7 ± 2.9 kg. Daily IDet dose was 0.27 ± 0.14 IU/kg at baseline and was 0.36 ± 0.18 IU/kg at Week 24. The majority of patients remained on once daily injection during the whole study period.

CONCLUSIONS: In insulin naive South Korea patients participating in A1chieve study, IDet treatment can improve glycaemic control without causing safety concerns.

PCS-05-6

Pooled Clinical Trial Analysis of Insulin Glargine vs NPH in Insulin-Naive Asian Patients with Type 2 Diabetes Mellitus

Changyu Pan¹, Karim Admane², Quanwu Zhang³, Jay Lin⁴, Edward Wang³ and Guang Ning⁵

¹Department of Endocrinology, Chinese PLA General Hospital, China; ²Sanofi, Paris, France; ³Sanofi, Bridgewater, NJ, USA; ⁴Novosys Health, Flemington, NJ, USA; ⁵Ruijin Hospital, Shanghai, China

OBJECTIVE: This analysis evaluated the efficacy and safety of insulin glargine vs NPH insulin in Asian patients with type 2 diabetes (T2DM), utilizing pooled data from 2 randomized, multicenter clinical trials.

METHODS: Data were pooled from 720 insulin-naive Asian patients from 11 countries/regions. Study duration was 24 or 28 weeks. Insulin was titrated to achieve a target FBG of ≤ 6.7 or ≤ 7.7 mmol/L. HbA1c, FBG, and demographics were measured at baseline and study end. Hypoglycemia was defined in each study.

RESULTS: There were 357 patients initiated on glargine and 363 on NPH. Overall, mean (SD) age was 56.1 (8.5) years, BMI was 24.2 (3.1) kg/m², and duration of diabetes was 11.2 (6.2) years. Baseline characteristics were similar between groups. At study end, there was a significant reduction in HbA1c in both groups ($P < 0.001$ for both groups). The *post-hoc* analysis target HbA1c < 7% was achieved by 18.5% and 15.2% with glargine and NPH, respectively. More patients achieved target FBG < 6.1 mmol/L with glargine (36.4%) than

NPH (25.8%). Insulin dose increased in both groups (both $P < 0.001$); the difference between groups was not significant. The low incidence of severe hypoglycemia was less with glargine than with NPH ($P = 0.03$), as was the incidence of severe nocturnal hypoglycemia ($P = 0.02$).

CONCLUSION: In insulin-naïve Asian patients with T2DM, HbA1c reduction was similar with glargine or NPH but severe (nocturnal) hypoglycemia was less with glargine. HbA1c reduction was limited by inadequate insulin titration to lower FBG.

This study was supported by Sanofi.

PCS-05-7

Utility of Indices Using Postprandial C Peptide Levels for Indication of Insulin Therapy to Achieve Good Glycemic Control in Japanese Patients with Type 2 Diabetes

Shogo Funakoshi, Tomonao Hirobata, Aya Iwashashi and Gen Inoue
Japan Red Cross Wakayama Medical Center, Japan

AIM: To elucidate the relationship between residual endogenous insulin secretion and the necessity of insulin therapy to achieve good glycemic control, indices using serum C-peptide immunoreactivity (CPR) were analyzed in patients with type 2 diabetes.

METHODS: Beta-Cell function was evaluated by fasting CPR (FCPR), 2-h postprandial C peptide levels after breakfast (PPCPR), the increment of CPR (DeltaCPR). Indices using CPR were compared between the group requiring insulin (insulin group, including patients taking oral hypoglycemic agents plus insulin at discharge) and the group not requiring insulin (non-insulin group). A receiver-operator characteristic (ROC) curve was made, and optimal cut-off point and likelihood ratio were determined for each index.

RESULTS: Likelihood ratios at the optimal point of FCPR, PPCPR, DeltaCPR, CPI, and PPCPI were 2.4, 3.0, 1.7, 3.4, and 2.0, respectively. Optimal cut-off point of CPI was 1.0 ng/mg. Sensitivity and specificity at optimal point of CPI were 58% and 83%, respectively.

Analysis of indices using serum C peptide of patients with mean preprandial capillary plasma glucose levels at discharge of < 150 mg/dl.

		FCPR	PPCPR	ΔCPR	CPI	PPCPI
area under the ROC curve		0.75	0.78	0.68	0.68	0.72
Cut-off values		(ng/ml)	(ng/ml)	(ng/ml)	(ng/mg)	(ng/mg)
	Optimal	2.00	4.25	2.25	1.0	2.0
	90% specificity	1.25	2.75	1.25	0.9	1.2
	90% sensitivity	2.50	5.75	3.25	1.8	3.0
Values at optimal cut-off point						
	Sensitivity (%)	87	74	68	58	77
	Specificity (%)	63	76	61	83	61
	likelihood ratio	2.4	3.0	1.7	3.4	2.0

CONCLUSION: The advantage of CPI of the indices of CPR to select insulin therapy was shown.

PCS-05-8

Patient and Physician Satisfaction with Lantus SoloSTAR in Asia Pacific

Chao-Hung Wang¹, Sidartawan Soegondo², Edward Wang³ and Karim Admane⁴

¹Mackay Memorial Hospital, Taiwan; ²University of Indonesia, Depok, Indonesia;

³Sanofi, Bridgewater, NJ, USA; ⁴Sanofi, Paris, France

OBJECTIVES: To evaluate real-world patient satisfaction with and perception of the Lantus SoloSTAR insulin pen in Asian patients with diabetes.

METHODS: An observational, open-label, multicountry (India, Indonesia, Pakistan, Philippines, Singapore, Taiwan), multicenter, prospective Asian registry study – the SoloSTAR study – was executed. Data are presented using descriptive statistics.

RESULTS: A total of 2402 patients were enrolled (98.1% [$n = 2356$] had type 2 diabetes; 1.9% [46] had type 1 diabetes). A total of 83% had had diabetes for

≥ 5 years (mean duration $\pm$ SD: 11.8 ± 7.0 years). Mean $\pm$ SD age was 59.2 ± 12.9 years. Males (51.3%, $n = 1232$) and females (48.7%, $n = 1170$) were equally distributed. A total of 2182 patients were followed-up. Among those using SoloSTAR, 87.0% ($n = 1898$) were very satisfied or satisfied, 11.9% (259) were neither satisfied nor unsatisfied, and 1.1% (24) were not satisfied. Data from first time insulin users and those with prior injection device experience demonstrated a similar trend in favor of Lantus SoloStar. All physicians agreed that SoloSTAR made it easier and faster to train patients. The most beneficial, physician-cited features of SoloSTAR were ease of use, ease of training, and ease in selecting desired dose.

CONCLUSION: In this observational open-label study, SoloSTAR was found to be well accepted by both patients and physicians in the Asian region. The enhanced ease and convenience and high rate of satisfaction attributed to Lantus SoloSTAR could aid in overcoming some of the perceived barriers to insulin therapy.

This study was supported by Sanofi.

PCS-06-1

Pioglitazone 7.5 vs 15 mg Daily Added to Sulfonyleurea Plus Metformin Therapy in Taiwanese with Type 2 Diabetes

Shu-Hwa Hsiao¹, Ming-Chao Lee², Shu-Chun Hu² and Ta-Jen Wu²

¹Department of Pharmacy, National Cheng Kung University Hospital, Taiwan;

²Department of Internal Medicine, National Cheng Kung University Hospital, Taiwan

BACKGROUND: All reported adverse reactions of pioglitazone, such as bladder cancer, osteoporosis, congestive heart failure, and weight gain, are considered dose-related. Pioglitazone 7.5 mg daily was recently reported to be effective in Japanese with type 2 diabetes.

OBJECTIVES: To investigate the efficacy of pioglitazone (Actos) 7.5 mg daily vs 15 mg daily add-on therapy in type 2 diabetic patients who are not well controlled with sulfonyleurea plus metformin combination therapy in the real world practice.

METHODS: Twenty one patients (10 male and 11 female) were added pioglitazone 15 mg daily and 21 sex- and age-matched patients with pioglitazone 7.5 mg daily as add-on therapy in an open case-controlled study for 24 weeks. The changes of HbA1c and weight gain were assessed at baseline and at 24-week.

RESULTS: Treatment with pioglitazone for 24 weeks resulted in significant decreases in HbA1c (from 8.96 ± 1.46 to 8.23 ± 1.08 , $P < 0.05$, in 7.5 mg daily group and from 9.26 ± 1.29 to 8.43 ± 1.56 , $P < 0.01$, in 15 mg daily group). Both groups showed significant small increases in weight (from 67.0 ± 10.5 kg to 67.6 ± 10.8 kg, $P < 0.0001$ in 7.5 mg daily group and from 69.8 ± 10.0 to 71.1 ± 10.1 kg, $P < 0.0001$ in 15 mg daily group).

CONCLUSION: Both pioglitazone 7.5 mg daily and 15 mg daily significantly improved HbA1c and induced mild weight gain in type 2 diabetes patients with poor glycemic control. Pioglitazone 7.5 mg daily is a choice for initial add-on therapy.

PCS-06-2

Is an Initial Treatment with Metformin and Lifestyle Interventions Effective and Safe for Long Terms in Japanese Patients with Newly Diagnosed Type 2 Diabetes Mellitus?

Satoru Sumitani¹, Shinya Morita², Yoshihiko Utsu², Reiko Deguchi², Kosuke Fujimoto², Masahiro Koseto², Shunji Miki², Bunzo Sato², Hideji Nakamura¹ and Soji Kasayama²

¹Center for Preventive Medicine, Nissay Hospital, Japan; ²Department of Medicine, Nissay Hospital, Japan

OBJECTIVE: To examine the long-term effectiveness and safety of metformin and lifestyle interventions (LSI) as an initial treatment in Japanese patients with newly diagnosed type 2 diabetes mellitus (T2DM).

METHODS: Twenty patients with newly diagnosed T2DM (18 men and two women, age 53 ± 11 (mean $\pm$ SD) years, BMI 25.9 ± 4.8 kg/m²) were followed for 48 weeks in outpatient clinical settings. Metformin and LSI were given to all patients at the time of diagnosis. Metformin was started at the dose of 500 mg/day and was increased every 2 weeks up to 1500 mg/day. When HbA1c $< 7.0\%$ was not achieved at 16 weeks, another oral hypoglycemic agent (OHA) was added. Primary outcomes were the change of HbA1c and the percentage of patients who achieved HbA1c $< 7.0\%$ at 48 weeks. The change of fasting plasma glucose (FPG) and that of body weight (BW) were also measured. Adverse events including hypoglycemia were recorded.

RESULTS: Seven patients (35.0%) did not achieve HbA1c < 7.0% at 16 weeks and required the second OHA. The level of HbA1c decreased from $9.1 \pm 2.1\%$ at baseline to $6.5 \pm 0.8\%$ ($P < 0.001$) at 48 weeks. Sixteen patients (80.0%) achieved HbA1c < 7.0% at 48 weeks. FPG decreased from 182 ± 80 mg/dL to 120 ± 14 mg/dL ($P < 0.001$), while BW decreased from 74.7 ± 12.8 kg to 71.8 ± 12.7 kg ($P = 0.004$). Four patients (20.0%) were unable to take 1500 mg/day of metformin due to diarrhea. No hypoglycemia was observed in any patients during the study periods.

CONCLUSION: Metformin and LSI as an initial treatment are effective and safe for long terms in Japanese patients with newly diagnosed T2DM.

PCS-06-3

An Evaluation of the Glycemic Control in Patients with Type 2 Diabetes Switching from Rosiglitazone to Gliptins

Ric Fung¹, Vincent Tok Fai Yeung², Mary Lau¹ and Orla Cassidy³

¹Pharmacy Department, Our Lady of Maryknoll Hospital, Hong Kong; ²Department of Medicine, Our Lady of Maryknoll Hospital, Hong Kong; ³University of Sunderland, UK

OBJECTIVES: DPP-4 inhibitors (gliptins) are a new class of drugs first approved for treatment of type 2 diabetes in 2006. Following the FDA/EMA decision on rosiglitazone in September 2010, rosiglitazone-containing medications were suspended from the Hospital Authority's drug formulary in Hong Kong and patients on rosiglitazone had to be switched to alternative medications. This study aimed to assess diabetic control after switching from rosiglitazone to gliptins and to compare their therapeutic efficacy with that of other alternative medications.

METHOD: In this retrospective clinic-based study, we recruited type 2 DM patients on oral combination therapies who had rosiglitazone changed to alternative treatments from September to December 2010 and HbA1c checked within 3 months before the switching, and reviewed their treatment regime and HbA1c values 3–6 months after switching treatment.

RESULTS: A total of 36 patients (17 male, 19 female, mean age = 66, duration of rosiglitazone treatment = 94 weeks) were reviewed. Amongst them, 21 patients were switched to gliptins, 5 pioglitazone, 6 insulin, and 4 miscellaneous treatments. There was no significant difference in HbA1c levels pre- and post-switching (overall: 8.1% vs 8.1%; gliptin group: 7.9% vs 8%; other treatments: 8.5% vs 8.3%), nor significant change in percentage of patients achieving HbA1c target < 7%. A significant reduction in mean body weight of 1.5 kg ($P < 0.05$), however, was observed in the gliptin group.

CONCLUSION: Gliptins have comparable efficacy to glitazones and other treatment modalities for type 2 DM, and compare favourably in terms of potential benefits in weight reduction.

PCS-06-4

Alfa Glucosidase Inhibitor Reduces the Risk of Hypoglycemia in Elderly Japanese Type 2 Diabetes Patients

Kentaro Watanabe, Tatsuya Suzuki, Hiroshi Nakano and Kenzo Oba

Division of Geriatric Medicine, Department of Internal Medicine, Nippon Medical School, Japan

OBJECTIVE: This study aimed to evaluate the relationship between the daily profiles of the plasma glucose level and the use of alfa glucosidase inhibitor (AGI) in elderly Japanese type 2 diabetes patients.

METHODS: The study subjects were 114 type 2 diabetes patients aged 65 years old or more, who were treated with an oral hypoglycemic agent. Plasma glucose concentrations measured at 10 time points (08.00 h (before breakfast); 10.00; 12.00 (before lunch); 14.00; 18.00 (before dinner); 20.00; 0.00; 03.00; 06.00; and 08.00 h the next day yielded a daily profile of plasma glucose levels. The low plasma glucose level was <80 mg/dL ($PG < 80$). We evaluated the occurrence of low plasma glucose in a daily profile. Then, the study subjects were divided two groups: those receiving AGI (AGI group; $n = 44$), and those not receiving AGI (Non-AGI group; $n = 70$). We evaluated the relationship between the daily profiles of the plasma glucose level and of AGI in the two groups.

RESULTS: The incidence and frequency of $PG < 80$ in the AGI group was significantly lower than those of the Non-AGI group. Multivariate linear regression analysis assuming the frequency of $PG < 80$ as a dependent variable, and the administration of AGI adjusted for the clinical characteristics of the subjects as independent variables showed a significant correlation between the frequency of $PG < 80$ and AGI ($\beta = -0.224$, $t = -2.251$; $P = 0.027$).

CONCLUSION: The results of this study demonstrated that an alfa glucosidase inhibitor may reduce the risk of hypoglycemia in elderly Japanese type 2 diabetes patients.

PCS-06-5

Pioglitazone 15 mg Daily as Add-on Therapy to Sulfonylurea Plus Metformin in Patients with Type 2 Diabetes

Ta-Jen Wu, Horng-Yih Ou and Hao-Chang Hung

Department of Internal Medicine, National Cheng Kung University Hospital, Taiwan

BACKGROUND: Pioglitazone therapy is associated with several risks, such as weight gain, heart failure, osteoporosis, and bladder cancer. As most adverse effects are dose-related, a low and effective dose is desirable.

OBJECTIVES: To investigate pioglitazone 15 mg daily add-on therapy on glycemic control and adverse reactions in type 2 diabetic patients who were not well controlled with sulfonylurea plus metformin combination therapy.

METHODS: Forty-two patients with type 2 diabetes mellitus, were randomly assigned pioglitazone (Diazone) 15 mg daily or a placebo in a double-blinded, placebo-controlled study for 12 weeks. The major outcomes were differences in baseline HbA1c, fasting plasma glucose, and homeostasis model assessment-insulin resistance (HOMA-IR) index at week 12 (Trial Registration: ClinicalTrials.gov number: NCT00991055.)

RESULTS: Forty-one patients (21 with pioglitazone and 20 with placebo) completed the study. Treatment with pioglitazone 15 mg daily for 12 weeks resulted in a significant decrease in HbA1c (from $8.99 \pm 1.14\%$ to $7.98 \pm 0.76\%$, $P < 0.001$), fasting plasma glucose (from 183.9 ± 39.3 to 144.8 ± 19.9 mg/dL, $P < 0.0001$), and HOMA-IR (from 2.97 ± 1.71 to 1.94 ± 1.25 , $P < 0.0001$). The differences between the two groups were statistically significant in both glycemic control and insulin resistance. The pioglitazone group had a significant increase in weight and a mild decrease in hemoglobin.

CONCLUSION: Pioglitazone 15 mg daily significantly improved both glycemic control and insulin resistance with mild weight gain and hemodilution in patients with type 2 diabetes.

PCS-06-6

Analysis of Severe Hypoglycemia Leading to Hospitalization in Diabetic Patients Treated with Sulfonylureas or Insulin

Eri Ikeguchi¹, Takao Taniguchi¹, Yo Aramaki¹, Miki Araki¹, Motozumi Okamoto¹ and Akihiro Hamasaki²

¹Department of Internal Medicine, Otsu Red Cross Hospital, Japan; ²Department of Diabetes and Clinical Nutrition, Kyoto University, Japan

OBJECTIVE: As numbers of elderly diabetic patients are increasing, we are of the opinion that prolonged hypoglycemia, especially due to sulfonylureas, is also increasing. In order to prevent hypoglycemia, we analyzed the clinical features of diabetic patients hospitalized for drug-induced hypoglycemia.

METHODS: Between January 2008 and March 2012, 53 diabetic patients were admitted to our hospital for hypoglycemia due to sulfonylureas or insulin. We analyzed them based on clinical records retrospectively.

RESULTS: Forty-one patients were treated with sulfonylureas (SU group) and 12 received insulin (insulin group). The SU group was older than the insulin group, with mean ages of 82.95 ± 8.69 and 74.75 ± 10.78 years, respectively. The mean HbA1c (NGSP) was lower in the SU group than the insulin group ($6.56 \pm 1.19\%$ vs $7.64 \pm 1.20\%$, respectively, $P = 0.02$). The SU group needed a significantly longer time for recovery from hypoglycemia than the insulin group. The majority of the SU group were aged over 80 years, with serum creatinine over 1.0 mg/dL or eGFR below 50 mL/min/1.73 m².

CONCLUSION: We should use sulfonylureas carefully for elderly patients, and consider dosage reduction or change to other oral antidiabetic drugs or insulin therapy, because their actual renal function is estimated to be worse than indicated by the serum creatinine level, and their diet is easily disrupted. We should reconsider the target HbA1c level according to patients' age, and provide intensive education on coping methods when they are in poor health.

PCS-06-7

Preserved Beta Cell Function may be a Major Determinant for Long-Term Durability of Pioglitazone Effect

Hyun Min Kim, Sun Ok Song, Eun Young Lee, Hanna Seok, Eun Young Choi, Ji Hye Huh, Byung-Wan Lee, Eun Seok Kang, Hyun Chul Lee and Bong Soo Cha
Department of Internal Medicine, Yonsei University College of Medicine, Korea

The glycemic response to TZD is variable among individuals. Thus, we investigated the patient factors associated with long-term hypoglycemic effect of pioglitazone in routine clinical practice.

This was a retrospective analysis of type 2 diabetic patients who were newly initiated on pioglitazone in 2006, and maintained for more than 48 months without dose-up of another medication. Baseline glycemic and lipid profile, pancreatic β -cell function, and insulin resistance levels using the homeostasis model assessment (HOMA) were checked. HbA1c concentrations were measured every 6 months after pioglitazone treatment. A total of 158 patients (M:F = 76:82, mean age: 59.1 ± 9.3 years) were enrolled. The mean HbA1c was $7.7 \pm 1.4\%$ at baseline, $6.8 \pm 0.9\%$ after 6 months, and $6.6 \pm 0.6\%$ after 48 months of pioglitazone treatment. When stratified according to tertile of baseline HOMA-IR, although the baseline HbA1c was higher in the 3rd tertile, the degrees of glycemic control were comparable. However, regarding HOMA-B, HbA1c level after 48 months were lower in the highest HOMA-B group (6.79 ± 0.60 vs 6.78 ± 0.66 vs 6.41 ± 0.53 , $P = 0.002$) as well as the proportion of patients who achieved a target HbA1c of $<7\%$, were higher (69.8% vs 66.0% vs 88.5% , $P = 0.029$). In multiple logistic regression analysis, HOMA-B retained their significance as the independent predictors for long term glycemic control.

These results suggest that preserved beta cell function instead of insulin resistance, can be a better predictive parameter for long-term hypoglycemic effect of pioglitazone.

PCS-07-1

Effect of Exenatide on Body Weight and Glucose Control in Japanese Type 2 Diabetic Subjects in Clinical Settings

Natsuko Oshitani¹, Masafumi Matsuda¹, Yoshitaka Akiyama¹, Tomoko Morita¹, Chieko Morisawa¹, Yoshimi Abe¹, Mitsugu Tokunaga¹, Shinya Minagawa¹, Masako Yazawa¹, Eiji Omura¹ and Shoji Kawazu²
¹Department of Endocrinology and Diabetes, Saitama medical Center, Saitama Medical University, Japan; ²The Institute for Adult Diseases, Asahi Life Foundation

Exenatide, GLP-1 analogue has been shown to be effective in glucose control and suppression of weight gain in type 2 diabetic subjects. Clinical use of exenatide often needs concomitant administration of sulfonylureas, pioglitazone, and metformin which is not approved to use concomitantly with liraglutide. Therefore, we investigated effectiveness of exenatide on body weight and glucose control in Japanese type 2 diabetic subjects in clinical settings. Exenatide has been introduced as a clinical choice of treatment as decided by physicians in charge in our clinic. Clinical practices have been guided by 'Treatment Guide for Diabetes 2010'. We obtained the clinical data from the electronic medical records system, and the data from subjects who were treated with exenatide more than 3 months were analyzed by SPSS ver.19. Forty-three type 2 diabetic subjects (M/F = 17/26, 54 ± 13 y.o., duration of diabetes = 12 ± 9 years, BMI = 29 ± 5 kg/m², HbA1c = $8.9 \pm 2.4\%$) received exenatide. At the start of administration of exenatide, Body weight before (75 ± 15 kg) and after (71 ± 15 kg) the treatment of exenatide was decreased ($P < 0.01$), and HbA1c was significantly decreased to $7.9 \pm 2.1\%$ ($P < 0.05$). In clinical settings in our institute, type 2 diabetic subjects including those who were treated with insulin as much as 120 units per day, had been successfully switched from insulin treatment to exenatide. More than 60% of patients had benefit in both body weight reduction and lowering plasma glucose concentration. Incremental doses of exenatide, and the concomitant use of metformin would be required for body weight reduction.

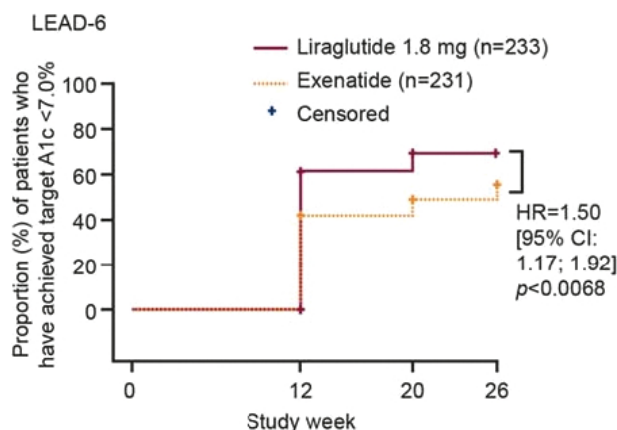
PCS-07-2

Patients Likelier to Reach A1c Target During 26 Weeks' Treatment with Liraglutide Compared with Sitagliptin or Exenatide

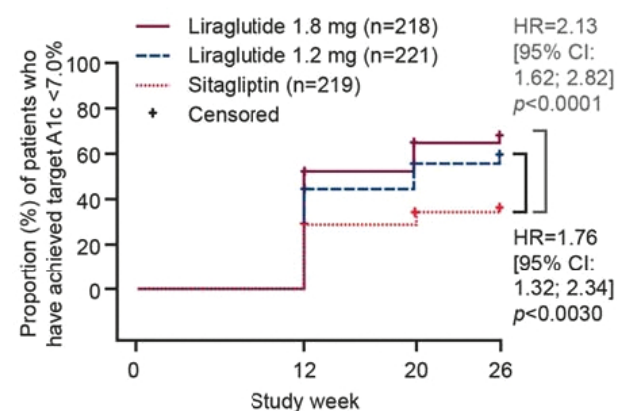
Morten Donsmark¹, Eduard Montanya², Claus Svendsen¹ and Robert Ratner³
¹Medical Affairs, Novo Nordisk A/S, Denmark; ²IDIBELL-Hospital Universitari Bellvitge, Barcelona, Spain; ³MedStar Research Institute, Hyattsville, MD, USA

OBJECTIVE: Rapid attainment of target A1c levels improves adherence to therapy in patients with T2D. This *post-hoc* analysis covered target A1c attainment during two phase 3b trials (NCT00518882, NCT00700817).

METHODS: Patient proportions reaching target A1c $<7.0\%$ at 12, 20 and 26 weeks were analyzed for two clinical trials in patients with T2D: liraglutide OD vs exenatide BID (LEAD-6) and liraglutide vs sitagliptin (LIRA-DPP-4). The 'time to A1c target' was analyzed by a Cox proportional hazards model, with treatment and previous OAD treatment as fixed effects; baseline A1c as covariate. **RESULTS:** In both trials, patient proportions reaching target for their first time was higher with liraglutide respectively at each timepoint. In LEAD-6, patient proportions reaching target overall was greater for liraglutide 1.8 mg compared with exenatide.



LIRA-DPP-4



CONCLUSION: Timely achievement of target A1c level is more likely with liraglutide compared with sitagliptin or exenatide BID.

PCS-07-3

Perioperative Liraglutide Therapy in Japanese Patients with Type 2 Diabetes

Naoko Katagiri, Kohei Yoshimi, Yumiko Tahara, Yuichi Sato and Shizuka Kaneko
Division of Diabetes/Endocrinology/Lifestyle-Related Disease, Takatsuki Red Cross Hospital, Japan

OBJECTIVE: To investigate the efficacy and safety of perioperative liraglutide therapy, glycemic control using liraglutide was retrospectively analysed in Japanese patients with type 2 diabetes.

METHODS: Liraglutide therapy was initiated before elective operations (10 orthopedic, seven diagnostic cardiac catheterizations for ischemic heart disease, six cataract, one uterus cancer, one breast cancer, and one prostate cancer operation) in 26 patients (M/F:18/8, Age: 67.7 ± 12.8 , HbA1c: $7.8 \pm 1.3\%$, BMI: 25.6 ± 3.9) with type 2 diabetes. In case of hyperglycemia during operation, regular insulin was added. The change in BMI, blood pressure, and perioperative complications were retrospectively analysed.

RESULTS: Twenty-two out of 26 patients achieved target blood glucose level before operation, and didn't need additional regular insulin. One patient with knee osteoarthritis lost weight with preoperative Liraglutide therapy, and eventually the operation became unnecessary because the pain disappeared. Three patients, who had nausea as a side effect, could not achieve target glycemic control and needed additional regular insulin therapy. Hypoglycemic episodes, wound healing retardations or other complications were not observed during any of the operations.

DISCUSSION: Liraglutide therapy is especially helpful for diabetic patients with limited exercise ability and at risk of hypoglycemia in the perioperative period. As liraglutide decreases gastrointestinal motility, we avoided using liraglutide for patients undergoing gastrointestinal surgery. In cases of hyperglycemia during operations, which is thought to be induced by overactive stress hormones, additional regular insulin should be considered.

CONCLUSION: Liraglutide provides an optional way to safely achieve good glycemic control for patients with type 2 diabetes in perioperative period.

PCS-07-4

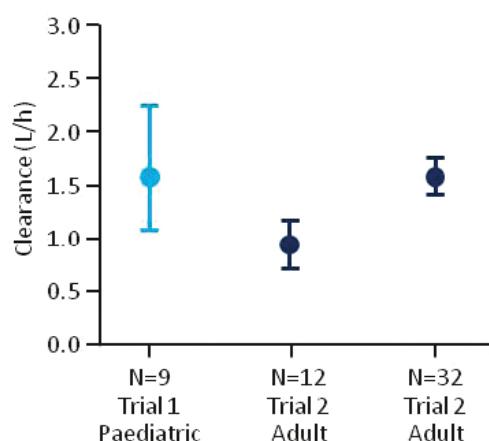
Population PK Analysis of Liraglutide in Paediatric Subjects and Comparison with Adults with T2D

Steen H. Ingwersen¹, Kristin Petri¹, Lisbeth Jacobsen¹ and David Klein²

¹Qualitative Clinical Pharmacology, Novo Nordisk A/S, Denmark; ²Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

BACKGROUND: Only metformin and insulin are approved for treating paediatric subjects with T2D (10–17-year-olds). This analysis investigated pharmacokinetics of liraglutide in paediatric subjects compared with adults.

METHODS: A 1-compartment model with 1st-order absorption and elimination was used to estimate clearance (CL/F) and distribution volume (V/F) for liraglutide in data pooled from three trials. AUC_{0–24 h}^{SS} derived from CL/F and dose was used to investigate dose-proportionality in paediatric subjects. Covariate analysis investigated effects of dose, bodyweight, gender and age (paediatric/adult) on liraglutide exposure.



Geometric mean (95%CI) of post hoc estimated clearance (CL/F) for liraglutide 1.8 mg in Trial 1 (paediatric T2D subjects) and Trials 2 and 3 (adult T2D subjects)

	Age	n (M:F)	Weight, median (range) (kg)	Liraglutide dose (mg/day)
Trial 1	Paediatric (10–17 years)	13 (5:8)	106 (57–214)	0.3, 0.6, 1.2, 1.8 (sequential weekly increase)
Trial 2	Adult (≥18 years)	12 (6:6)	83 (72–104)	1.8
Trial 3	Adult (≥18 years)	32 (23:9)	96 (58–140)	1.8

The differences between Trials 2 and 3 were partly due to differences in body weight and gender distribution.

RESULTS: PK data indicated dose-proportionality for model-derived AUC_{0–24 h}^{SS} in Trial 1. Bodyweight and gender were significant covariates for exposure in both age-groups. AUC_{0–24 h}^{SS} decreased with increasing bodyweight. Mean AUC_{0–24 h}^{SS} was 63% higher at lowest bodyweight (53 kg), 56% lower at highest bodyweight (216 kg) compared with median (90 kg). Males had 31% lower exposure (independent of bodyweight) than females. CL/F estimates were comparable for children and adults.

CONCLUSION: The regimen used for liraglutide treatment of T2D in adults achieved a comparable exposure in the paediatric population studied.

PCS-07-5

In Japanese Patients with Type 2 Diabetes, Clinical Predictors for Effectiveness of Liraglutide Treatment are Different Between Obese and Non-Obese Patients

Shuji Sasaki¹, Yasuhiro Sako², Noriyuki Sonoda³, Toyoshi Inoguchi³ and Ryoichi Takayanagi⁴

¹Department of Endocrinology, Metabolism and Diabetes, Kyushu University Hospital, Japan; ²Saiseikai Fukuoka General Hospital; ³Innovation Center for Medical Redox Navigation, Kyushu University; ⁴Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University

We compared the clinical characteristics of Japanese patients with type 2 diabetes who were either responders or non-responders to LIRA. In total, 171 patients who were treated with LIRA were involved in the study, with 61% classified as responders (>0.3% decrease in HbA1c) and 26% classified as non-responders (>0.3% increase in HbA1c). The average duration of follow-up was 126.8 days. Both groups lost 2.0 kg of body weight on average with the treatment. The responders had significantly higher HbA1c levels, and 73% of non-responders had already received metformin prior to the treatment. The efficacy of LIRA in combination with oral antidiabetic agents was 72%, and the efficacy upon switching from insulin to LIRA alone was 51%. The efficacy was also not different between a group of non-obese patients (BMI < 25) and a group of obese patients (BMI > 25). In the non-obese patients, the fasting C-peptide was significantly lower in the non-responders than in the responders (1.2 vs 1.8 ng/mL; *P* < 0.05). In the obese patients, the C-peptide in the urine was significantly higher in the non-responders than in the responders (153.3 vs 103.8 µg/day; *P* < 0.05). Based on multivariate analysis, the efficacy of LIRA was independently correlated with the HbA1c level (Odds ratio [OR] 1.58), the BMI (OR 0.89) and the fasting C-peptide/glucose level (OR 2.94). These data indicate that a reduction of the endogenous insulin secretion in non-obese patients and a resistance to insulin in obese patients are associated with a resistance to LIRA treatment.

PCS-07-6

Case Note Survey of T2D Patients Prescribed Incretin Therapies According to Current Recommendations in Clinical Practice

Marc Evans¹, Phil McEwan², Richard O'Shea³, Lindsay George¹ and Alison Clarke¹

¹Diabetes and Endocrinology, Llandough Hospital, United Kingdom; ²Swansea University, Swansea, UK; ³University of Wales College of Medicine, Heath Park, Cardiff, UK

OBJECTIVE: Assess the clinical and cost-effectiveness and patient preference for incretin-based therapies when initiated according to National Institute for Health and Clinical Excellence (NICE) recommendations in UK clinical practice.

METHODS: In a retrospective chart audit, anonymised data were collected for patients receiving incretin-based therapy in clinical practice according to NICE recommendations. Parameters assessed included HbA1c, weight, proportion of patients achieving NICE treatment continuation criteria, adverse events, and treatment discontinuation. Based on observed treatment effects, drug cost-effectiveness was also assessed. Treatment preference for a dipeptidyl peptidase-4 (DPP-4) inhibitor or glucagon-like peptide-1 receptor agonist (GLP-1RA) was assessed prospectively.

RESULTS: One thousand one hundred and fourteen patients were followed up for a median of 48 weeks (256 received liraglutide, 148 exenatide, 710 DPP-4 inhibitor). Liraglutide reduced HbA1c significantly more vs exenatide or DPP-4 inhibitor (both *P* < 0.05). Weight changes were similar for both GLP-1RAs but were significantly greater vs DPP-4 inhibitors (both *P* < 0.05). NICE treatment continuation criteria were met by 32% and 24% of liraglutide 1.2 mg- and exenatide-treated patients (≥1% HbA1c reduction, ≥3% weight loss) and 61% of DPP-4-inhibitor-treated patients (≥0.5% HbA1c reduction). Life-years/patient gained were 0.12, 0.08, and 0.07, and costs/quality-adjusted life-year were £16,505, £16,648, and £20,661 for

liraglutide, exenatide and DPP-4 inhibitors, respectively. Most patients preferred the GLP-1RA profile, with these patients having higher BMI, HbA1c and diabetes duration than those preferring the DPP-4 inhibitor profile.

CONCLUSIONS: Liraglutide provided the greatest reductions in HbA1c and bodyweight, with a more cost-effective profile than exenatide or DPP-4 inhibitors. Patients with more advanced disease preferred GLP-1RAs vs DPP-4 inhibitors.

PCS-08-1

Effects of Sitagliptin, Acarbose and Sulfonylureas on Postprandial Levels of GLP-1 and GIP in Japanese Patients with Type 2 Diabetes
Daisuke Yabe, Hitoshi Kuwata, Koin Watanabe, Kenji Sugawara, Yuka Kitamoto, Kazu Sugizaki, Shuichi Fujiwara, Takanori Hyo, Kyoko Kuwabara, Kayo Yokota, Masahiro Iwasaki, Naomi Kitatani, Ryota Usui, Minoru Matsumoto, Takeshi Kurose and Yutaka Seino

Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, Japan

OBJECTIVES: We evaluated effects of sitagliptin, acarbose and sulfonylureas (SU) on postprandial levels of GLP-1 and GIP in Japanese patients with type 2 diabetes (T2DM).

METHODS: Japanese T2DM were subjected to meal-tolerance tests using a 480-kcal Japanese standard breakfast with or without drug administration, and incretin levels as well as glucose, insulin, and glucagon levels were determined.

RESULTS: Two week administration of 100 mg sitagliptin in 27 patients [Age (years), 62 ± 2 ; BMI (kg/m^2), 25.1 ± 1.2 ; HbA1c (NGSP, %), 7.4 ± 0.2] significantly elevated fasting and postprandial levels of intact GLP-1, and the area under the curve (AUC) of intact GLP-1 after meal ingestions, while total GLP-1 and GIP did not change. One time administration of 100 mg acarbose in 21 patients [Age (y), 61 ± 1 ; BMI (kg/m^2), 23.2 ± 0.5 ; HbA1c (NGSP, %), 7.0 ± 0.1] significantly increased both total and intact GLP-1 levels 60 and 120 min after meal ingestions as well as total GLP-1 AUC. The acarbose administration significantly decreased total GIP levels 30 and 60 min after meal ingestions as well as total GIP AUC. Postprandial incretin levels in 23 untreated and 18 SU-treated patients [Age (y), untreated 59 ± 2 and SU 67 ± 1 ; BMI (kg/m^2), untreated 22.0 ± 0.5 and SU 23.0 ± 0.8 ; HbA1c (NGSP, %), untreated 7.0 ± 0.1 and SU 7.3 ± 0.1] did not differ between two groups.

CONCLUSION: In Japanese T2DM, sitagliptin, through inhibition of DPP-4-dependent degradation, increased intact GLP-1 without affecting secretion of GLP-1 and GIP. Acarbose enhanced GLP-1 secretion and suppressed GIP secretion after meal ingestions. Sulfonylureas had little effects on meal-induced secretion of GLP-1 and GIP.

PCS-08-2

Anti-Inflammatory Effects of Sitagliptin in Japanese Patients with Type 2 Diabetes

Yukiko Kawasaki¹, Yoshiyuki Hamamoto¹, Sachiko Honjo¹, Kanta Fujimoto¹, Hisato Tatsuoka¹, Atsuko Matsuoka¹, Kanako Mori¹, Yoshiharu Wada¹, Jun Minamikawa², Minoru Imbe³, Yoshio Nakamura⁴, Hiroki Ikeda⁵, Koichiro Nabe⁶ and Hiroyuki Koshiyama¹

¹Center for Diabetes & Endocrinology, Tazuke Kofukai Medical Research Institute Kitano Hospital, Japan; ²Minamikawa Clinic, Japan; ³Imbe Clinic, Japan; ⁴Division of Diabetes & Endocrinology, Department of Internal Medicine, Hyogo Prefectural Amagasaki Hospital, Japan; ⁵Ikeda Hospital, Japan; ⁶Tamura Clinic, Japan

OBJECTIVE: We prospectively investigated the effects of sitagliptin, a DPP4 inhibitor, on beta cell function and high sensitivity C-reactive protein (hsCRP) in the Japanese patients with type 2 diabetes (T2DM).

METHODS: Subjects included a total of 56 T2DM patients uncontrolled on diet and exercise and/or oral hypoglycemic agents with HbA1c $\geq 6.9\%$ in six clinics in Japan. They received additional treatment with sitagliptin 50 mg/day for 24 weeks. HbA1c, proinsulin-to-insulin ratio (P/I ratio), and hsCRP were determined before and after sitagliptin treatment.

RESULTS: Sitagliptin significantly improved HbA1c from 8.3 ± 1.0 to $7.6 \pm 1.2\%$, ($P < 0.01$). As a total, P/I ratio showed no significant change before and after sitagliptin treatment. However, when we compared the two groups, high basal P/I ratio group (>0.4) and low basal P/I ratio group (<0.4), P/I ratio showed a significant decrease from 0.72 ± 0.22 to 0.57 ± 0.21 ($P < 0.01$) among the high P/I ratio group, while P/I ratio showed no significant change in the low P/I ratio group. On the other hand, hsCRP

improved significantly from 0.74 (0.34 – 1.28) mg/L to 0.62 (0.35 – 1.08) mg/L ($P = 0.02$) in total subjects. There was no significant improvement in the low hsCRP group ($n = 28$), while hsCRP improved significantly from 1.39 (0.94 – 2.14) mg/L to 0.92 (0.45 – 1.49) mg/L ($P < 0.01$) in the high hsCRP group ($n = 28$).

CONCLUSION: Sitagliptin may have protective effects on beta cell function and anti-inflammatory effects.

PCS-08-3

Effects on HbA1c Reduction by Combination Therapy of Sitagliptin and Other Oral Antidiabetic Drugs

Shinsuke Tokumoto¹, Yoshiyuki Hamamoto¹, Yukiko Kawasaki¹, Sachiko Honjo¹, Kanako Mori², Yoshiharu Wada¹, Hiroki Ikeda¹ and Hiroyuki Koshiyama¹

¹Center for Diabetes and Endocrinology, The Tazuke Kofukai Foundation Medical Research Institute Kitano Hospital, Japan; ²Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

PURPOSE: While sitagliptin (Sita), the first clinically available incretin enhancer in Japan, rarely causes hypoglycemia, it has been reported that combination therapy of Sita with oral hypoglycemic agents may have more glucose lowering effects than monotherapy with Sita. We aimed to evaluate the association between the effects of Sita on HbA1c levels and the combination with other oral antidiabetic drugs.

METHODS: Subject included a total of 97 patients with type 2 diabetes, who were received Sita 50 mg/day. We studied HbA1c levels before treatment and 3 months after.

RESULTS: The mean age of total patients was 66.9 ± 9.3 years, and male-to-female ratio was 57:40. We found that higher HbA1c before treatment resulted in a greater HbA1c reduction at 3 months. Mean reduction in HbA1c was -0.64% for Sita alone (five cases), -0.84% for Sita and sulfonylurea (SU; 33 cases), -0.55% for Sita and metformin (11 cases), and -1.20% for Sita and SU and metformin (48 cases). There was no significant difference between monotherapy and combination therapy, but reduction in combination therapy (-0.21%) was greater. When analyzed by SU agents used in combination therapy, reduction of HbA1c was -1.29% for glibenclamide, -0.94% for glimepiride, and -0.58% for glizalide. But because pre-therapeutic HbA1c level in descending order was $8.10 \pm 0.61\%$ for glibenclamide, $7.47 \pm 0.69\%$ for glimepiride, and $6.74 \pm 0.51\%$ for glizalide, pre-therapeutic HbA1c might have effects on HbA1c reduction. Moreover, the replacement of α -glucosidase inhibitors by Sita reduced HbA1c by 0.89% .

CONCLUSIONS: Sita in combination with SU or metformin may have a good hypoglycemic effect and be more potent than α -GI alone.

PCS-08-4

Safety and Efficacy of Saxagliptin in Combination with Submaximal Sulfonylurea vs Uptitration of Sulfonylurea in Korean Patients with Type 2 Diabetes

So Hee Kim, C. H. Kyung, M. K. Kim, J. Y. Ha, E. J. Kwon, Y. M. Lee, H. J. Lee, J. W. Kim, T. W. Noh, S. A. Kang, J. S. Park, C. W. Ahn and K. R. Kim

Department of Internal Medicine, Yonsei University College of Medicine, Gangnam Severance Hospital, Korea

Saxagliptin is a potent and selective DPP-4 inhibitor and a few studies have been reported. Because there are genetic and environmental differences, it may result in differences in response to antidiabetic drugs. This *post-hoc* subanalysis assessed the safety and efficacy of saxagliptin added to sulfonylurea in Korean patients with type 2 diabetes.

Forty-five patients (32–76 years; HbA1c 7.2–10.7%) were randomly assigned to be treated with saxagliptin 2.5 mg ($n = 14$), 5 mg ($n = 15$) or placebo and blinded glyburide 2.5 mg ($n = 16$) added to glyburide 7.5 mg OL. Patients in the placebo group could uptitrate blinded glyburide to a maximal glyburide dose of 15mg for 24 weeks. Efficacy was assessed as the change from baseline to week 24 in HbA1c, fasting plasma glucose, and the proportion of patients achieving HbA1c $< 7.0\%$.

At week 24, adjusted changes from baseline HbA1c vs placebo + uptitrated glyburide for saxagliptin 2.5 and 5 mg were -0.68% (95% CI -1.35 , -0.01) and -0.37% (-1.03 , 0.29). Reductions from baseline to week 24 in FPG vs placebo + uptitrated glyburide were also observed by -4.8 mg/dL (-32.8 , 23.1) and -22.4 mg/dL (-49.9 , 5.0). The proportion of patients achieving an HbA1c $< 7.0\%$ was greater for saxagliptin groups vs placebo + uptitrated glyburide (7.1% and 26.7% vs 0%). Reported hypoglycemia and other adverse events were similar in all groups (Hypoglycemia: 1 and 2 cases vs 1 case).

Saxagliptin added to submaximal glyburide therapy led to improvements across key glycemic parameters compared with uptitration of glyburide alone in Korean patients and was generally safe.

PCS-08-5

Variation of Serum Adiponectin Concentrations in Patients with Type 2 Diabetes Mellitus Treated with DPP-4 Inhibitor

Yasumi Shintani, Kanako Nakauchi, Yu Miyai, Sayo Ueda, Hiroki Inoue, Yo Nakai, Eiji Yamamoto, Naotsugu Murakami, Sunao Shimada and Yoshiko Kanezaki
Division of Metabolism and Endocrinology, Tokushima Red Cross Hospital, Japan

OBJECTIVE: Total (T)- and high-molecular weight (HMW)- adiponectin (Ad) levels were measured in sera of Japanese patients with type 2 diabetes treated with DPP-4 inhibitor to investigate its long-term effect on insulin sensitivity.

METHODS: (1) 19 patients (11 men, eight women) with type 2 diabetes were enrolled in the study. They were 61 ± 9 year (mean $\pm$ SD) in age and 24.8 ± 4.4 kg/m² in BMI. Sitagliptin (50 mg/day, $n = 13$) or alogliptin (25 mg/day, $n = 6$) was started in combination with sulfonylurea ($n = 10$, with reduced doses), α -glucosidase inhibitors ($n = 10$) and metformin ($n = 6$), and the patients were followed up for 6 months. Patients treated with pioglitazone were not included. (2) Serum T-Ad and HMW-Ad levels were measured by specific immunoassays. Serum leptin (Lep) was measured as a marker for adiposity and energy status. Metabolic parameters of glycemic control, insulin secretion/resistance and serum lipids (LDL-C, TG, HDL-C) were also evaluated.

RESULTS: (1) HbA1c (NGSP) was rapidly reduced from 9.8 ± 2.0 (before treatment: 0M) to 8.3 ± 1.2 (1 month: 1M), 7.0 ± 0.7 (3 months: 3M), $6.9 \pm 0.9\%$ (6 months: 6M). Body weight, Lep and lipids were almost unchanged during treatment. (2) Serum T-Ad gradually increased from 6.6 ± 2.9 (0M) to 7.0 ± 3.0 (1M), 8.1 ± 3.7 (3M), 9.4 ± 4.1 μ g/mL (6M). Serum HMW-Ad varied in parallel with T-Ad: 1.3 ± 0.8 (0M), 1.6 ± 1.2 (1M), 1.8 ± 1.1 (3M), 2.1 ± 1.4 μ g/mL (6M).

CONCLUSIONS: Serum T- and HMW-Ad concentrations gradually increased in patients with type 2 diabetes when treated with DPP-4 inhibitor, implying an insulin-sensitizing effect. This may contribute to the long-term effectiveness of DPP-4 inhibitor and a possible reduction in cardiovascular events during treatment.

PCS-08-6

Efficacy of Switching to Alogliptin in Patients with Poorly-Controlled Blood Glucose After Sitagliptin Treatment

Koutarou Nagai¹, Hisashi Daidou¹, Yukie Saio¹ and Hidenao Nishimura²

¹Department of Endocrinology and Diabetes, Hashima City Hospital, Japan; ²Department of Pharmacy/Hashima City Hospital, Japan

OBJECTIVE: To examine the efficacy of switching to alogliptin (A) in patients with HbA1c levels of 6.9% (NGSP) or higher after administration of sitagliptin (S).

METHODS: Type 2 diabetic outpatients having HbA1c levels of 6.9% or higher, 32.3 $\pm$ 12.7 weeks after the start of S 50 mg in our hospital were randomly assigned to a group switching to A 25 mg (group A) and a group continuing S 50 mg (group S), and HbA1c levels were evaluated 12 and 24 weeks after drug switching.

SUBJECTS: The group A consisted of 26 patients (13 males, 13 females; age, 65.2 ± 9.8 years; BMI, 25.2 ± 4.1 ; duration of S treatment, 32.3 ± 12.7 weeks; and drugs, single/combination was 3/25), and the group S included 28 patients (18 males, 10 females; age, 62.4 ± 12.7 years; BMI, 24.6 ± 4.1 ; duration of S treatment, 31.0 ± 7.3 weeks; drugs, single/combination was 3/25).

RESULTS: The group A had a significant reduction ($P < 0.05$) from HbA1c $7.4 \pm 0.5\%$ to $7.1 \pm 0.7\%$. The group S showed little change from HbA1c $7.4 \pm 0.5\%$ to $7.3 \pm 0.8\%$. The patients with HbA1c levels $< 6.9\%$ in both groups had relatively low levels of HbA1c at the time of drug switching, and both groups included many patients without SU treatment.

CONCLUSION: Switching to A was considered to be one of the treatment options in patients with no sufficient improvement in HbA1c level after S therapy.

PCS-08-7

Analysis of Therapeutic Effect of Sitagliptin in Type 2 Diabetes

Yuka Kitamoto¹, Motoya Koie¹, Sei Morita¹, Tomohiro Santou¹, Mitsuo Fukushima² and Koichiro Yasuda¹

¹Department of Diabetology and Endocrinology, Saiseikai Noe Hospital, Osaka, Japan, Japan; ²Department of Nutrition, Faculty of Health and Welfare Science, Okayama Prefectural University, Okayama, Japan

OBJECTIVE: In order to examine the character of type 2 diabetic patients having short term effects from sitagliptin, we measured daily profile of plasma glucose level and insulin secretion before and after taking sitagliptin.

METHODS: Twenty-two Japanese patients with type 2 diabetes mellitus without insulin treatment were enrolled in this study. In patients, mean age were 64 ± 7 years. We made glucagon tolerance test 2 days after admission to evaluate insulin secretory capacity. We measured plasma glucose (PG) and serum insulin seven times of days, at before meals, 2 h after meals and before bedtime 3 and 9 days after admission. We started sitagliptin 50 mg from 4 days after admission.

RESULTS AND CONCLUSION: All measuring points in day, mean PG levels, especially post prandial glucose levels were reduced after taking sitagliptin ($P < 0.01$). But there was no significant difference in serum insulin at all measuring points. At 2 months after taking sitagliptin, there was no body weight gain compared with beginning period. Mean HbA1c (NGSP) was reduced from 10.2% at the beginning to 8.5% at 2 months after taking sitagliptin ($P < 0.001$). The difference between the sum of PG of day 3 and that of day 9 was positively correlated with the difference between the C-peptide reactive of before and after glucagon tolerance test ($r = 0.475$). Glucagon tolerance test may be useful to select type 2 diabetic patients having benefit from sitagliptin.

PCS-08-8

Long-Term Efficacy and Tolerability of Sitagliptin in Japanese Patients with Type 2 Diabetes Mellitus

Eitaro Nakashima¹, Mariko Narita², Rui Imamine¹, Yu Kouchi¹, Minoru Kusama¹, Mariko Kawai¹, Makiko Watanabe¹, Chiai Tanaka³, Akio Kanai⁴, Takahiko Kawamura⁴, Takahisa Sano¹ and Nigishi Hotta¹

¹Department of Diabetes and Endocrinology, Chubu Rosai Hospital, Japan; ²Department of Pharmacy, Chubu Rosai Hospital, Japan; ³Department of General Internal Medicine, Chubu Rosai Hospital, Japan; ⁴Center for Preventive Medicine, Chubu Rosai Hospital, Japan

OBJECTIVE: To evaluate the long-term efficacy and tolerability of sitagliptin in Japanese patients with type 2 diabetes mellitus who were inadequately controlled.

METHODS: A total of 155 type 2 diabetic outpatients (baseline HbA1c was 8.1%) in our hospital were enrolled retrospectively in this study. Patients were treated with sitagliptin to control their blood sugar levels for at least 3 months up to 18 months. Key endpoints were the change from baseline in HbA1c, body weight, systolic and diastolic blood pressure, lipid profiles, serum level of creatinine, and estimated glomerular filtration rate (eGFR) and the incidence rate of adverse effects.

RESULTS: Sitagliptin produced significant reductions in HbA1c (-0.8% vs baseline) after 6 months of treatment, and resulted in no significant change in body weight, blood pressure, or lipid profiles in follow-up periods. Moreover, there was a significant increase of serum creatinine levels and a significant decrease of eGFR. Twenty-three patients treated with sitagliptin with inadequately controlled or renal dysfunction were switched to vildagliptin after approximately 6 months of treatment. This substitution reduced HbA1c levels significantly (-0.35% vs baseline at the time of the switch) and resulted in no significant but tendency of improvement in eGFR measured at average 5.5 months after the switch.

CONCLUSION: Sitagliptin is effective and generally well tolerated in Japanese patients with type 2 diabetes mellitus. Our results suggest that switch from sitagliptin to vildagliptin may be another option for patients who show ineffective or intolerance for sitagliptin. Further studies are needed to verify these results.

PCS-09-1

α -Lipoic Acid Prevents Nonalcoholic Fatty Liver Disease in OLETF Rats

Soo Kyong Kim¹, Tae Sik Jung¹, Jong Ryul Hahm¹, Hwa Jung Jung¹, Soon Il Chung¹ and Roh Gu Seob²

¹Department of Internal Medicine, Gyeongsang National University School of Medicine, Korea; ²Department of Anatomy and Neurobiology, Gyeongsang National University School of Medicine, Korea

BACKGROUND: Insulin resistance, oxidative stress, inflammation, and innate immune system activation contribute to the development of non-

alcoholic fatty liver disease (NAFLD) through steatosis and inflammation in the liver. The powerful antioxidant alpha-lipoic acid (ALA) has been shown to improve insulin sensitivity and suppress inflammatory responses. This study explores how ALA administration protects against NAFLD.

METHODS: Otsuka Long-Evans Tokushima Fatty (OLETF) rats were divided into two groups (treated with 200 mg/kg/day of ALA or untreated) at 12 weeks of age and sacrificed at 28 weeks of age.

RESULTS: Serum levels of glucose, insulin, free fatty acids, total cholesterol, triglyceride, and leptin were decreased in ALA-treated rats. Serum adiponectin levels were higher in ALA-treated rats. ALA treatment decreased the expression of sterol regulatory element binding protein-1 and acetyl CoA carboxylase and increased glucose transporter-4 expression in the livers of OLETF rats. Expression of the antioxidant enzymes heme oxygenase-1 and Cu/Zn-superoxide dismutase was increased in the livers of ALA-treated rats. The lipid peroxidation marker 4-hydroxynonenal was decreased in the liver of ALA-treated rats. Proteins associated with innate immune activation (Toll-like receptor-4 and high-mobility group protein box-1) and inflammatory markers (vascular cell adhesion molecule-1, intercellular adhesion molecule-1, and cyclooxygenase-2) were decreased in the livers of ALA-treated rats.

CONCLUSIONS: Chronic ALA supplementation prevents NAFLD through multiple mechanisms by reducing steatosis, oxidative stress, immune activation, and inflammation in the liver.

PCS-09-2

Effects of Lifestyle Intervention on Weight Control and the Follow-Up Results in Overweight and Obesity Staffs

Hsiao-Shan Lin¹, Hsiao-Lien Chen², Dia-Sue Wu¹ and Pei-Chen Hsu¹

¹Department of Dietitian, Lotung Poh-Ai Hospital, Taiwan; ²Department of Endocrinology and Metabolism, Lotung Poh-Ai Hospital, Ilan, Taiwan

OBJECTIVE: To evaluate the effects of lifestyle intervention on anthropometry and exercise duration during 10 weeks weight loss period and whether that can assist in long-term weight control in staffs.

METHODS: The program included 10-week weight loss period and 24-week weight loss maintenance period. The intervention of weight loss consisted of nutrition and exercise classes during working hours 1 h per week. The subjects with body weight loss more than 5 kg would include into weight loss maintenance period. Anthropometric tests were measured before and after the weight loss period and weight loss maintenance period.

RESULTS: In an intention-to-treat analysis from pre to post tests, the group significantly reduced average body weight with 3.3 kg ($P < 0.05$), BMI with 1.3 kg/m² ($P < 0.05$), body fat percentage with 2.4 ($P < 0.05$), waist circumference 6.5 cm ($P < 0.05$), and upper-arm circumference from 1.5 cm ($P < 0.05$) and significantly increased exercise duration from 24.3 to 40.6 min per week ($P < 0.05$). After the weight loss maintenance period, the group had significantly decrease average body weight with 1.4 kg ($P < 0.05$) and BMI with 0.5 kg/m² ($P < 0.05$) compared to the 10-week. There were no significant difference in body fat percentage, waist circumference, and upper-arm circumference ($P > 0.05$).

CONCLUSION: The significantly reduced body weight, body fat, waist circumference and upper-arm circumference as well as increased the exercise duration show great essential for lifestyle intervention in overweight and obesity staffs. And continuous self-control may also important in maintaining weight loss.

PCS-09-3

Body Fat Distribution, Insulin Resistance, and Metabolic Syndrome in Non-Overweight Korean Adults: 2009–2010 Korean National Health and Nutrition Examination Survey

Jihyun Ahn¹, Jae Woong Kim¹, Seok Hong Lee¹, Jaetaek Kim¹, Sangmi Ock², Eun Young Kim² and Jin Nam Kim²

¹Department of Internal Medicine, Chung-Ang University Hospital, Korea; ²Diabetes Center, Chung-Ang University Hospital, Seoul, Korea

BACKGROUND: Our objective was to investigate the relationship between body fat distribution, insulin resistance (IR), and components of the metabolic syndrome (MS).

METHODS: Data were obtained from the Korean National Health and Nutrition Examination Survey in 2009–2010. Total 5294 Korean adults (1835 men and 3459 women) who were more than 19 years old participated. Body mass index (BMI), waist circumference (WC), blood pressure (BP), levels of

total cholesterol, triglycerides, high density lipoprotein (HDL)-cholesterol, glucose, and insulin were measured by standard methods. Overweight was defined as BMI over 23 kg/m². IR was defined as homeostasis model assessment (HOMA)-IR over 2.5. The high body fat distribution was defined as above 35% in women and above 25% in men.

RESULTS: The prevalence of IR was 15.4% in normal fat group and 24.3% in high fat group ($P < 0.001$). The percentage of subjects with MS was significantly increased ($P < 0.001$) in high fat group than in normal fat group (11.8% vs 6.4%). In multiple regression analysis with adjusted covariates such as age, sex, smoking, alcohol intake, regular exercise, the high fat is an indicator of IR with an odds ratio of 1.74 (95% CI 1.11–2.73, $P < 0.015$).

PCS-09-4

The Effectiveness of Continuous Individualized Medical Nutrient Therapy on Weight Reduction in Community-Based groups

Dia-Sue Wu¹, Hsien-Cheng Chang², Hsiao-Shan Lin¹, Pei-Chen Hsu¹ and Pei-Fen Liu¹

¹Department of Dietitian, Lotung Poh-Ai Hospital, Taiwan; ²Chief, Family Medicine, Lotung Poh-Ai Hospital, Taiwan

OBJECTIVE: Medical Nutrient Therapy (MNT) represents an effective intervention strategy to weight reduction in obesity. The aim of this study was to evaluate the effects of MNT on weight reduction in the community-based groups.

METHODS: The intervention period included 8 weeks and the maintenance period included 6 weeks. Dietitians provided continuous individualized MNT to the participants weekly. And then follow up again the effectiveness of weight reduction at 6 months after the maintenance period. We measured height, body weight, BMI, and waist circumference at baseline, 8-week, 14-week, and 38-week. We also checked blood sample which included blood sugar and lipid profile at baseline, 8-week, 14-week and collected KAP questionnaires of diet to estimate the effectiveness.

RESULTS: There 60 participants were completed in both of intervention and maintenance period. It was noted that there were several significant average reductions in body weight with 3.53 kg, waist circumference with 5.97 cm, BMI with 1.34 kg/m², total cholesterol with 18.3 mg/dL, LDL-C with 12.06 mg/dL, and scores of KAP questionnaires at 8-week compared to baseline ($P < 0.001$). However, there were no significant differences in anthropometric tests, blood data, and scores of KAP questionnaires at 14-week compared to 8-week.

CONCLUSION: Our study showed that it was effective on weight reduction by continuously individualized MNT. Furthermore, it could improve metabolic syndrome and prevention of obesity-related chronic diseases.

PCS-09-5

Weight Loss Intervention for Newly Diagnosed Obese Diabetic Patients

Yanjimaa Sankhuu¹, Sainbileg Sonomtseren², Suvd Junai² and Bolormaa Vandanmagsar³

¹Department of Endocrinology, State Central Clinical Hospital, Mongolia; ²Department of Endocrinology, School of Medicine, Health Sciences University of Mongolia; ³Laboratory of Gene – Nutrient Interaction, Pennington Biomedical Research Center, Louisiana State University System, USA

AIMS: Aims of this study were evaluate results of weight loss intervention for newly diagnosed obese diabetic patients.

METHODS: Prospective cohort study included 92 newly diagnosed DM patients. Weight loss intervention included small group diet and physical activity counseling. Weight (kg), body fat (%), waist and hip circumferences (cm), blood pressure (mm Hg), fasting blood glucose (mmol/L), HbA1C (%), total cholesterol (mmol/L) and triglyceride (mmol/L) were measured before and after 6 months weight loss intervention.

RESULTS: Eighty (86.9%) DM patients completed weight loss intervention. Mean age of DM patients was 47.78 ± 6.32 years old. Results of prospective cohort study showed mean body weight (84.41 ± 13.08 vs 80.11 ± 12.42; $P < 0.0001$), BMI (31.57 ± 4.2 vs 29.87 ± 3.72; $P < 0.0001$), waist circumference (104.18 ± 10.51 vs 99.78 ± 8.52; $P < 0.0001$), hip circumference (107.04 ± 8.66 vs 105.38 ± 7.79; $P < 0.009$), WHR (0.96 ± 0.07 vs 0.94 ± 0.05; $P < 0.0001$), body fat (36.19 ± 5.64 vs 34.26 ± 6.57; $P < 0.0001$), systolic blood pressure (133.03 ± 22.5 vs 127.54 ± 17.5; $P < 0.009$), diastolic blood pressure (81.18 ± 13.14 vs 77.61 ± 11.03; $P < 0.03$), fasting blood glucose (11.57 ± 4.06 vs 7.99 ± 2.64; $P < 0.0001$), HbA1C (8.45 ± 2.70 vs 5.95 ± 1.70;

$P < 0.0001$) and total cholesterol (3.9 ± 1.05 vs 3.15 ± 0.96 ; $P < 0.0001$) were significantly improved, except triglyceride (2.11 ± 0.82 vs 1.73 ± 1.8 ; $P < 0.052$).

CONCLUSIONS: Weight loss intervention by diet and physical activity counseling for newly diagnosed obese DM patients was effective. Mean weight loss of DM patients was ± 4 kg, after 6 months.

PCS-09-6

Changes in Correlation Coefficients Between Obesity Indices, Insulin Resistance, Cardiovascular Risk Factors and Visceral Fat in Women According to Each Cut-Off Values of Obesity Indices

Yeoup Lee Sang

Department of Family Medicine, Pusan National University Yangsan Hospital, Korea

BACKGROUND: Some controversy surrounds the effects of moderate weight loss on metabolic and cardiovascular risk factors in severe obese patients. The purpose of this study was to investigate the influence of severity of obesity on correlation of obesity indexes, insulin resistance and cardiovascular risk in women.

METHODS: Subjects of this study were obesity women who were examined at three university hospitals from January 2003 to December 2004. The study group consisted of 113 women older than 18 years. Body mass index (BMI), waist circumference, fasting insulin, fasting glucose, lipids, visceral adipose tissue (VAT) area were measured. The correlations of obese patients group between obesity factors and risk factors were analyzed after varying the cut off value of the obese group.

RESULTS: When BMI was above 28 kg/m^2 , the correlation with triglyceride (TG)/high density lipoprotein cholesterol (HDL-C) was no longer existed and when it was above 29 kg/m^2 , AI, the correlations with total cholesterol (TC)/HDL-C and VAT were no longer existed. When BMI was above 30 kg/m^2 , the correlation with homeostasis model of insulin resistance (HOMA-IR) index. HOMA-IR was no longer existed. When waist circumference was above 85 cm, the correlations with HOMA-IR and atherogenic index were no longer existed and when it was above 90 cm, the correlations with TG/HDL-C, TC/HDL-C and VAT were no longer existed.

CONCLUSION: Our data suggest that more than moderated weight loss may be needed to achieve improvement of metabolic and cardiovascular risk factors in severe obese women.

PCS-09-7

A Study of Weight Reduction Among Overweight and Obese Employees by Lifestyle Modification

Pei-Fen Liu, Hsiao-Lien Chen, Pei-Chen Hsu, Hsia-Shan Lin, Shou-Pang Huang and Dia-Sue Wu

Dietitian, Lotung Poh-Ai hospital, Taiwan

OBJECTIVE: The prevalence of obesity is growing up fast in the worldwide and obesity associated with many chronic diseases closely. In this study, we investigated the effects of changing eating habits and increasing exercise durations on the weight reduction of the hospital employees.

METHODS: Fifty-six overweight and obesity employees were recruited. During 8 weeks intervention period, we gave nutritional educations, regular exercises and set a low-fat diet environment at hospital canteen. We collected questionnaires of eating habits and analysis body weight, waist circumference (WC), body mass index (BMI), body fat, arm circumference, blood pressure (BP), frequency of low-fat diet and exercises by paired t-test and Pearson product-moment correlation.

RESULTS: Fifty-six participants (age 33.3 years; body weight 73.8 kg ; BMI 27.9 kg/m^2). We found the body weight, BMI, WC, arm circumference were significantly decreased (3.1 kg , 1.1 kg/m^2 , 4.4 cm , 1.0 cm , respectively; $P < 0.001$), BP significantly decreased from $121.6/75.8$ to $116/73.3 \text{ mmHg}$ ($P < 0.01$) and increased intake low-fat diet ($0.7\text{--}1.7$, $P < 0.01$), but body fat and exercises no significant differences. The questionnaires data showed that nutritional education can help to improve eating habits (-1.5 ± 4.0 , $P < 0.01$), but between weight and nutrition knowledge, attitudes and behavior of diet no significantly correlation.

CONCLUSION: After lifestyle modifications, such as diet, regular exercise shown beneficial effects of weight reduction. The change of dietary environment and nutrition education to low fat diet may success of weight reduction. Therefore, it can help to prevent risk of metabolic syndrome and chronic disease such as diabetes mellitus and cardiovascular disease.

PCS-10-1

Prevalence and Risk Factors of Diabetic Retinopathy Among T2DM Patients

Erdenechimeg Dulamjav and Altaisaikhan Khasag

Department of Endocrinology, Health Sciences University of Mongolia, Mongolia

AIMS: The aims of this study were to determine prevalence and risk factors of Diabetic Retinopathy among T2DM patients.

METHODS: Cross-sectional study included 645 T2DM patients of six districts of Ulaanbaatar, Mongolia. Diabetic Retinopathy was diagnosed by questionnaire and clinical examination including ophthalmoscopy and fundus photography.

RESULTS: The prevalence of Diabetic Retinopathy among registered diabetes type 2 patients was 29.3%. Risk factors for Diabetic Retinopathy were identified as low intake of vegetable; high level of blood glucose, HbA1C and total cholesterol and longer duration of diabetes ($P < 0.05$). Progression of Diabetic Retinopathy positively associated with high level fasting blood glucose, total cholesterol, systolic and diastolic blood pressure, triglyceride and low level HDL ($P < 0.05$).

CONCLUSIONS: The prevalence of Diabetic Retinopathy among T2DM patients was 29.3%. Risk factors for diabetic retinopathy were high level blood glucose, HbA1C, total cholesterol and longer duration of diabetes. Diabetes poor control was significantly associated with progression of Diabetic Retinopathy.

PCS-10-2

Comparison of Frequency of Risk Factors in Diabetic Patients with and without Retinopathy in Ahvaz South West of Iran

Rashidi Homeira¹, Ali Kasiri², Hajieh Bibi Shahbazian¹, Seyed Mahmoud Latifi¹ and Ferdos Zaman¹

¹Diabetes Research Center, Ahvaz Jundishapur University of Medical Sciences, Iran, Islamic Republic of; ²Ophthalmology, Ahvaz Jundishapur University of Medical Sciences Iran

OBJECTIVE: To determine several risk factors in type 2 diabetic patients with and without retinopathy.

METHODOLOGY: In a prospective study 256 type 2 diabetic patients who referred to Golestan Hospital diabetes clinic were evaluated. All patients underwent physical & retina examination and laboratory assay including duration of diabetes mellitus, CVD, CKD, smoking, and BP, BMI, HbA1C, total cholesterol, HDL & LDL cholesterol, TG, FBS, creatinine, 24-h urine microalbumin. Data were analyzed by SPSS 17, chi square, independent t test, logistic regression.

RESULTS: Mean age of patients (81 male, 175 female) was 54 ± 10.27 . Prevalence of any diabetic retinopathy was 22.3% (clinical significant macula edema 0.5%, proliferative retinopathy 6%, nonproliferative retinopathy 15.8%). In multiple logistic regression, longer duration of diabetes (OR = 0.98, 95% CI: 0.98–0.99, $P < 0.001$), and BMI (OR = 0.93, CI: 0.86–0.99, $P = 0.043$) were the independent risk factors of DR. Mean of FBS, HbA1C, 24 h urine microalbumin, systolic blood pressure in any retinopathy diabetic subjects compared with others were (191 ± 83 vs 165.7 ± 74.5 , $P = 0.03$), (9.1 ± 2 vs 8.5 ± 1.9 , $P = 0.02$), (181.2 ± 404.7 vs 60.2 ± 236 , $P = 0.03$), (124.3 ± 21.3 vs 118.5 ± 17.8 , $P = 0.04$) respectively. There were no significant difference between patients with and without diabetic retinopathy in total cholesterol, LDL, HDL, TG, creatinine, diastolic BP, types of treatment, CVD, CKD and smoking.

CONCLUSION: This study determined prevalence of diabetic retinopathy was high & it associated with FBS, HbA1C, 24 h urine microalbumin, systolic blood pressure. Longer duration of diabetes and BMI were the independent risk factors of DR.

PCS-10-3

Follow-Up Study of Japanese Patients with Overt Diabetic Nephropathy (CKD Stage 3)

Hiroki Ikeda¹, Kenichi Ida¹, Msaru Usami¹, Hiroyuki Koshiyama² and Masaki Ikeda¹

¹The Seimeikai Ikeda Hospital, Japan; ²Center for Diabetes & Endocrinology, The Tazuke Kofukai Medical Research Institute Kitano Hospital, Japan

In order to compare the prognostic values of the chronic kidney diseases (CKD) staging by KDOQI and the staging of diabetic nephropathy according to the Ministry of Health, Labour and Welfare of Japan (Jpn DN Staging), we

performed a follow-up study about the clinical course of diabetic nephropathy in Japanese patients with diabetes. Subjects included a total of 177 Japanese patients with diabetic nephropathy corresponding to CKD KDOQI stage 3, ie those with eGFR of 30–60 mL/min/1.73 m², and who could be followed up for more than 5 years. They were divided into the four groups according to the Jpn DN Staging; those with stage 1, 2, 3A and 3B are defined as those with casual urinary albumin/creatinine excretion ratio (ACR) of the <30 mg/g creatinine (*n* = 59), those with ACR of 30–299 mg/g Cre (*n* = 54), those with proteinuria of 300–999mg/day (*n* = 37), and those with proteinuria more than 1000mg/day (*n* = 27), respectively. The average eGFR of the first visit was not significantly different between the stage 1, 2, 3A and 3B (48.6, 45.9, 47.6, 47.5 mL/min/1.73 m², respectively). However, the average eGFR showed a significant decrease in stage 2, 3A and 3B compared to those of the first visit value (46.3, 39.5, 36.7, 21.4 mL/min/1.73 m², *P* < 0.01, respectively). Those findings suggest that the Jpn DN Staging may have some prognostic value, but the measurement of eGFR as well as ACR is mandatory for follow-up of diabetic nephropathy in Japanese patients with diabetes.

PCS-10-4

Urinary Cystatin C as Predictive Marker for Progression of Type 2 Diabetic Nephropathy

Ji Hyun Kang¹, Sang Soo Kim², Sang Heon Song², In Joo Kim², Yun Kyung Jeon², Bo Hyun Kim², Ihm Soo Kwak² and Yong Ki Kim³

¹Department of Internal Medicine, Dong-eui Medical Center, Korea; ²Department of Internal Medicine, Pusan National University Hospital, Busan, Korea; ³Kim Yong Ki Internal Medicine Clinic, Busan, Korea

OBJECTIVE: The aim of this study was to evaluate the association of urinary cystatin C as tubular damage marker with progression of type 2 diabetic nephropathy.

RESERCH DESIGN AND METHODS: Serum and urinary cystatin C as primary parameters and nonalbumin proteinuria (NAP) as secondary parameter were measured at baseline. In this prospective observational study, 237 type 2 diabetic patients were followed up for 29 months (range, 13–44 months). The baseline and last eGFR were used in the calculation for the annual decline in eGFR.

RESULTS: Both urine CCR (cystatin C-to-creatinine ratio) and NAPCR (NAP-to-creatinine ratio) were significantly different according to albuminuria status and have strongly positive correlation between two markers at baseline (*r* = 0.597, *P* < 0.001). After adjusting for several clinical factors, both urinary CCR and NAPCR had significant association with the decline of eGFR (*r* = 0.151, *P* = 0.025; *r* = 0.377, *P* < 0.001, respectively). In addition, both urine CCR and NAPCR have positive correlations with the decline of eGFR in the patients with eGFR > 60 mL/min/1.73 m². In the normoalbuminuric patients, the urine NAPCR only remained significant association with the decline of eGFR, whereas urine CCR lost significant correlation.

CONCLUSIONS: Urinary cystatin C as a tubular damage marker as well as NAP have predictive values for progression of type 2 diabetic nephropathy.

PCS-10-5

Identified the Role of T Complex Protein-1 Subunit β in Early Diabetic Nephropathy

Chung-Ze Wu¹, Jin-Shuen Chen², Yuh-Feng Lin³, Li-Chien Chang⁴ and Yi-Jen Hung⁵

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, Taiwan; ²Division of Nephrology, Department of Internal Medicine, Tri-service General Hospital, National Defense Medical Center, Taipei; ³Division of Nephrology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, Taipei; ⁴School of Pharmacy, National Defense Medical Center, Taipei; ⁵Division of Endocrinology and Metabolism, Department of Internal Medicine, Tri-service General Hospital, National Defense Medical Center, Taipei

BACKGROUND: T-complex polypeptide 1 subunit β (TCP-1β) has been suggested to be associated with early diabetic nephropathy (DN) by *in vitro* cell model in our laboratory. In this study, the relationship between the expression of TCP-1β and *in vivo* models, included mice models and clinical cases, was explored.

MATERIALS AND METHODS: As for mice models, IDDM and NIDDM was established by streptozotocin (STZ)-induced and STZ-Nicotinamide-induced high fat-fed mice, respectively. During induction, at given time, as the progression of serum glucose, mice models were divided into three stages, stage 1 is baseline, stage 2 is first day of hyperglycemia development and stage 3 is 14th day. As for clinical case, the levels of urine TCP-1β in different stages

of DN designed by the difference of estimated glomerular filtration rate (eGFR) were measured by competitive ELISA.

RESULTS: As for mice models, the expression of TCP-1β in kidney tissues and urine samples of IDDM stage 3 was significant higher than that in stage 1 and 2. In regard to NIDDM, expression of TCP-1β presented in all stages, but they showed no significant difference. In clinical subjects, TCP-1β can be detected in urine by competitive ELISA. The levels of urine TCP-1β was significant high in hyperfiltration phase (eGFR > 120 cc/min) than other stages.

CONCLUSION: TCP-1β may be a potential marker to predict the development of early DN.

PCS-10-6

Regression and Progression of Diabetic Retinopathy in Type 2 Diabetes Patients: A 4-Year Follow-Up Study at Diabetes Clinics in Japan

Yuko Watanabe, Hitomi Fujii and Takaichi Miyakawa
Internal Medicine, Tama-center Mirai Clinic, Japan

We conducted a 4-year observational study to reveal changes of diabetic retinopathy. A total of 162 consecutive adult type 2 diabetic patients seen at three diabetes clinics in the Tokyo Metropolitan Area were enrolled in 2007. Eligible patients had regular dilated eye examinations by ophthalmologists, and had spot urine albumin to creatinine ratio (ACR) measured at least two times in each year. An estimated glomerular filtration rate (eGFR) was calculated by the 3-variable equation for Japanese. We excluded patients with kidney failure. Patients had a mean age (SD), 60.4 (10.5); female, 43%; mean BMI, 24.8 kg/m² (4.0); mean HbA1c, 7.53% (1.24). 75% of patients were on oral antidiabetic agents (OADs) and/or insulin; 30% of patients were on ARBs. Percentage of patients having nonproliferative and proliferative retinopathy was 17% and 9%, respectively. Progression of retinopathy was determined if diabetic retinopathy increased more than one stratum (no retinopathy; nonproliferative diabetic retinopathy; and proliferative diabetic retinopathy) after 4 years; regression was determined vice versa. Patients whose retinopathy progressed (*N* = 25) tended to be young and have high eGFR at start; had high HbA1c at the end (*P* = 0.03). Patients whose retinopathy regressed (*N* = 10) tended to be old and have lower HbA1c at start, and were more on insulin (*P* = 0.002). They showed a mean ACR decrease of 158 (*P* = 0.01) after 4 years.

CONCLUSIONS: In this cohort, 60% of patients remained without having retinopathy and 6% of patients showed improvement, by treating diabetes and its consequences vigorously.

PCS-10-7

Arylhydrocarbon Receptor Transactivating Activities are Elevated in Type 2 Diabetic Subjects with Nephropathy

Jin Taek Kim¹, Sang Soo Kim¹, Young Hwan Hwang¹, Youngmi Kim Pak², Wook-Ha Park² and Hong Kyu Lee¹

¹Internal Medicine, Division of Endocrinology, Eulji University Hospital, Korea;

²Department of Physiology, College of Medicine, Kyung Hee University, Seoul, Korea

OBJECTIVE: Evidence is emerging that exposure to persistent organic pollutants (POP) is a risk factor for obesity-related diseases and for diabetes mellitus (DM). We hypothesized that POP will be a risk factor for diabetic nephropathy, a common long-term complication of diabetes, in people with type 2 diabetes.

METHODS: We enrolled diabetic subjects with normoalbuminuria (*n* = 36), microalbuminuria (*n* = 29), macroalbuminuria (*n* = 8), and end stage renal disease who were on hemodialysis (*n* = 31). POP exposure status was assessed based on Chemically Activated Luciferase gene expression (CALUX) assay which is a cell-based measurement of AhR ligand mixtures using an AhR-dependent reporter assay. Their plasma's AhR transactivating (AHRT) activities were converted to well known AhR ligand 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) equivalents (TCDDeq pM).

RESULTS: Plasma AHRT activities were higher in the microalbuminuria (40.1 ± 7.1 pmol/L), macroalbuminuria (37.4 ± 5.5 pmol/L), and ESRD (59.1 ± 20.0 pmol/L) than in the normoalbuminuria group (12.7 ± 5.4 pmol/L; *P* < 0.05). Plasma AHRT activity were correlated with estimated glomerular filtration rate (eGFR; *r* = −0.663, *P* < 0.001) and serum creatinine level (*r* = 0.635, *P* < 0.001). In addition, systolic blood pressure (SBP; *r* = 0.223, *P* = 0.026), HbA1c (*r* = 0.339, *P* < 0.001), and diabetic duration (*r* = 0.394, *P* < 0.001) were found to be the correlates of the AHRT activities. Furthermore, AHRT activities were found to be an independent risk factor for

overt proteinuria and ESRD after controlling for potential risk factors such as age, diabetic duration, SBP, HbA1c.

CONCLUSION: Our findings support the hypothesis of POP being a risk factor for diabetic nephropathy. Further studies are warranted.

PCS-11-1

Relationship Between Urine Albumin and Creatinine Clearance in Patients with Type 2 Diabetes Mellitus

Veerasak Sarinnapakorn and Anchana Kongchai

Internal Medicine, Rajavithi Hospital, Rangsit University, Thailand

BACKGROUND: Urine microalbumin is parameter to assess early renal dysfunction in DM because glomerular filtration rate (GFR) is well preserved in early renal dysfunction but the measurement of urine microalbumin excretion is not available in some hospitals. Some hospitals can assess renal dysfunction by measurement of serum creatinine and calculate glomerular filtration rate (GFR) that can not assesses early renal dysfunction. The study was conducted to find correlation of albuminuria and eGFR in Thai type 2 diabetic patients.

OBJECTIVE: To assess relationship between urine albumin and glomerular filtration rate (GFR) in type 2 diabetes mellitus patient.

METHODS: A retrospective reviewed of 95 patients with type 2 diabetes mellitus between January 1 and December 31, 2010. Baseline characteristic data was collected gender, age, BMI, hypertension, dyslipidemia, urine albumin and glomerular filtration rate (calculated by Cockcroft-Gault equation)

RESULTS: Total 95 patients with type 2 diabetes mellitus were classified to three groups: Group 1 normoalbuminuria (urine albumin <30 mg/gmcr) 39 patients, Group 2 microalbuminuria (urine albumin between 30 and 300 mg/gmcr) 34 patients, Group 3 macroalbuminuria (urine albumin >300 mg/gmcr) 22 patients. The relationship between urine albumin and glomerular filtration rate (GFR) found that in normoalbuminuria patients (71.69 ± 24.61 mL/min) was significantly higher than in microalbuminuria (54.69 ± 22.64 mL/min) and macroalbuminuria (44.71 ± 19.72 mL/min; *P* value < 0.001*). Urine albumin negatively correlated with GFR and can calculated by equation: Albuminuria (mg/gmcr) = eGFR * (-8.741) + 831.636, (*P* value = 0.002*). The GFR correlated with hypertension.

CONCLUSIONS: Urine albumin have negatively correlated with eGFR and can calculated by equation: Albuminuria (mg/gmcr) = eGFR*(-8.741) + 831.636

PCS-11-2

Relationship Between LDL Subfraction and CAN in Type 2 Diabetes Mellitus

Hyuk-Sang Kwon, Eun-Hee Jang, Mee-Kyoung Kim, Ki-Hyun Baek, Ki-Ho Song, Kwang-Woo Lee and Bong-Yun Cha

Department of Internal Medicine, The Catholic University of Korea, Korea

OBJECTIVES: This study was performed to investigate the relationship between low-density lipoprotein (LDL) subfraction and cardiac autonomic neuropathy (CAN) in the patients with type 2 diabetes mellitus.

METHODS: Total 175 type 2 diabetic patients (96 men and 79 women) who have not taken lipid-lowering agents previously were consecutively enrolled in this study. LDL subfraction was determined with LipoPrint LDL system which fractionates LDL into seven parts (LDL1 through 7) according to the size and the extent of charge. And we analyzed mean LDL size and small LDL proportion from the percent of LDL3 through 7 over whole LDL.

RESULTS: LDL subfraction showed the different trend according to gender, men had smaller mean LDL size than that of women (26.2 ± 0.8 nm vs 26.5 ± 0.7 nm, *P* = 0.05) and larger proportion of small dense LDL (23.51 ± 18.3% vs 18.58 ± 16.4%, *P* = NS). Subjects with CAN revealed significantly smaller mean LDL size and larger proportion of small dense LDL compared with those without CAN in women, but not in men. After adjusting other confounding risk factors, small dense LDL was still remained the independent risk factors for CAN (i.e. mean LDL size OR = 0.882, *P* -value = 0.029; small LDL proportion OR = 1.062, *P* -value = 0.033) in women, but not in men.

CONCLUSIONS: In this study, more atherogenic, small dense LDL is related to CAN in type 2 diabetic female patients.

PCS-11-3

Evaluation of Diabetic Neuropathy Using Pupillary Light Reflex Test in Patients with Diabetes Mellitus

Shuichi Fujiwara, Daisuke Yabe, Takeshi Kurose, Minoru Matsumoto, Ryota Usui, Hitoshi Kuwata, Koin Watanabe, Hyo Takanori and Yutaka Seino

Kansai Electric Power Hospital, Japan

In this study we evaluated the efficacy of pupillary light reflex test in the detection of early diabetic neuropathy. A total of 282 (189/93, M/F) patients were recruited in this study. The pupillary light reflex test was performed using Iriscorder Dual C10641. The measured parameters are as follows: D1, initial diameter before light (mm); D2, minimum diameter after light (mm); CR, constriction ratio [CR = (D1-D2)/D1]; VC, the maximum velocity of constriction (mm/s). Mean age was 62, mean duration of diabetes was 11.2 years, and mean HbA1c level was 8.6%. CR was significantly associated with coefficient of variation of R-R interval of 100 heart beat at rest (CV R-R; *P* < 0.01) and during deep breathing (*P* < 0.01), however, CR showed no association with orthostatic hypotension. On the other hand, VC was significantly associated with both of CV R-R and orthostatic hypotension. Accordingly VC may represent the autonomic neuropathy more precisely than CR. We evaluated vibration perception threshold using C-64 tuning fork as a marker of somatic nerve dysfunction. VC showed significant correlation with vibration perception threshold (*P* < 0.01), and from the regression analysis VC which corresponds to the lower limit of normal vibration sensation was 3.52. The frequency of abnormal Achilles tendon reflex in group of <3.6 VC was more than the group of over or equal to 3.6 VC (*P* < 0.01). Since the somatic nerve dysfunction appears earlier than autonomic neuropathy, cut-off point of 3.6 VC may represent the early stage of autonomic neuropathy.

PCS-11-4

Peripheral Arterial Stiffness is Associated with Progression of Estimated Glomerular Filtration Rate Among Patients with Type 2 Diabetes

Yi Jing Sheen¹, Jaiinn-Liang Lin¹, Cho-Tsan Bau¹, Tsai-Chung Li² and Wayne H.-H. Sheu³

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Hospital Department of Health, Executive Yuan, Taiwan; ²Institute of Biostatistics, China Medical University, Taichung, Taiwan; ³Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

OBJECTIVE: Prevalence of peripheral arterial disease (PAD) are higher in subjects with chronic kidney disease (CKD). However, the associations between peripheral artery stiffness and progression of CKD are largely unexplored. We examined several indexes of PAD and progression of estimated glomerular filtration rate (eGFR) in 1 year in patients with type 2 diabetes.

METHODS: A total of 577 (male/female:294/283) patients with mean age of 63.0 ± 11.3 years (mean ± SD) and baseline eGFR 91.5 ± 28.4 mL/min/1.73 m² were enrolled. Baseline clinical characteristics and indexes of PAD including brachial-ankle Pulse Wave Velocity (ba-PWV) were collected. Following up calculated eGFR were obtained at the 6th and the 12th month.

RESULTS AND CONCLUSION: One hundred and seventeen patients (20.3%) experienced continuously worsened eGFR progression (progressively worsen lower eGFR were detected both at the following data) and rest of them (*n* = 460) did not get worse within 1 year. Baseline HbA1C and ba-PWV values were significantly higher in the worsened eGFR progression group than those non-worsen group. Receiver operating characteristic (ROC) curve of these factors in predicting eGFR worsened progression were constructed, the area under curve were HbA1C (0.566) and ba-PWV (0.590, cutoff point at 1819.5 cm/s had a sensitivity of 61%, specificity of 54%). In conclusion, ba-PWV is associated with the eGFR decline in 1 year. This simply constructed and non invasive examination may assist in the early detection of CKD progression in patients with type 2 diabetes.

PCS-11-5

The Importance of Resting Heart Rate as Early Diagnosis of Diabetic Cardiovascular Autonomic Neuropathy

Masakazu Shii, Takashi Matsuoka, Sato Takekawa, Shiho Nakai, Yuko Wada, Yukako Nakashima, Daisuke Fujiwara, Atsushi Yoshida, Takahiro Suzuki and Kenji Takahashi

Department of Diabetic Medicine, Kurashiki Central Hospital, Japan

BACKGROUND: Diabetic polyneuropathy is most frequent in diabetic microangiopathic complications, and impaired autonomic neuropathy spoils

QOL (quality of life). Cardiovascular autonomic neuropathy (CAN) should be one of CVD risk factor, and clinically most important in diabetic autonomic neuropathy. CAN is usually indicated by orthostatic hypotension, decreased CVR-R, and resting tachycardia ((100 bpm), but resting tachycardia is not popular in Japan.

AIM: Resting heart Rate (HR) over 100bpm is really compatible to early diagnosis of CAN.

SUBJECT AND METHOD: Subjects were 787 patients with type 2 diabetes mellitus admitted in our hospital during recent 2 years. Diabetes mellitus due to steroid hormone, liver cirrhosis, pancreas disease, and thyroid diseases was excluded from subjects. CVR-R and resting HR on admission were examined and compared between a group with polyneuropathy and a group without polyneuropathy. A hundred of resting heart rates were recorded for CVR-R excluding of atrial fibrillation and other arrhythmias.

RESULTS: (1) Resting HR showed a negative correlation with CVR-R, and it was statistically significant ($P < 0.001$). (2) The false negative of autonomic neuropathy increased, when a cutoff value of HR defined to be over 100 bpm. (3) CVR-R (<1.5) was observed at higher rate in HR (≥ 90 bpm) than in HR (<90 bpm). (4) Most of patients with orthostatic hypotension showed HR (<90 bpm).

CONCLUSION: Simultaneous evaluation of resting HR and CVR-R is useful in diagnosis of CAN, and our data suggests that resting HR over 90 bpm as a cutoff value is more appropriate than over 100 bpm in early diagnosis of diabetic CAN.

PCS-11-6

Clinical Implication of Plasma and Urine YKL-40, as a Proinflammatory Biomarker, on Early Stage of Nephropathy in Type 2 Diabetic Patients

Bo Gwang Choi¹, Min Jung Bae², Won Jin Kim², Yang Seon Yi², Sang Soo Kim², In Joo Kim², Sang Heon Song², Yong Ki Kim³, Yun Kyung Jeon², Ju In Kim⁴, Bo Hyun Kim², Ihm Soo Kwak², Jong Han Kim⁵ and Jun Ho Lee⁶

¹Department of Internal Medicine, Kim Yong Ki Internal Medicine Clinic, Korea;

²Department of Internal medicine, Pusan National University Hospital, Korea; ³Kim Yong Ki Internal Medicine Clinic, Busan, Korea; ⁴Biomedical Research Institute, Pusan National University Hospital, Busan, Korea; ⁵Department of Internal Medicine, Young-Do Hospital, Korea; ⁶Department of Internal Medicine, Haedong Hospital, Busan, Korea

OBJECTIVE: Chronic inflammation has emerged as being a key pathophysiology in the early stages of diabetic nephropathy. YKL-40 has been established as an inflammatory marker in chronic inflammation. The aim of this study was to evaluate the association of plasma and urine YKL-40 with albuminuria in the early stage of type 2 diabetic nephropathy.

DESIGN AND METHODS: A total of 75 type 2 diabetic patients and 22 non-diabetic controls with estimated glomerular filtration (eGFR) > 60 mL/min/ 1.73 m² were enrolled. Plasma and urine concentrations of YKL-40 were analyzed by ELISA kit.

RESULTS: The plasma levels of YKL-40 were significantly higher in the normoalbuminuric group with diabetes than in the control group, and increased with increasing severity of albuminuria among diabetes. However, urine YKL-40 was only increased in macroalbuminuric state. Plasma YKL-40 was positively correlated with urine YKL-40 ($r = 0.291$, $P = 0.011$). Urinary albumin significantly correlated with both plasma and urine YKL-40 in a univariate analysis. After adjusting for several confounding factors, plasma YKL-40 was significantly correlated with albuminuria ($r = 0.359$; $P = 0.001$), whereas urine YKL-40 did not show significant correlation with albuminuria ($r = 0.128$, $P = 0.241$).

CONCLUSIONS: Although urine YKL-40 have a limited role, plasma YKL-40, as a proinflammatory marker, was an independent factor affecting albuminuria in early stage of nephropathy in type 2 diabetes and might have an useful role and as a noninvasive marker for the early diabetic nephropathy detection.

PCS-11-7

Diabetic Nephropathy: Old Pathways, New Candidate Early Risk Predictors

Christina Gertrude Yap¹, Anuar Zaini² and Iekhsan Othman²

¹Department of Medicine, Monash University, Sunway Campus, Malaysia; ²School of Medicine and Health Sciences, Monash University, Sunway Campus, Malaysia

OBJECTIVE: The aim of this investigation was to determine up- or down-regulated biomolecules in diabetes which correlates to diabetic nephropathy.

METHODS: A cross-sectional cohort study was carried out among Malaysians, consisting of a control cohort ($n = 28$), diabetes ($n = 50$), diabetic nephropathy ($n = 35$) and non-diabetic nephropathy ($n = 15$). Whole blood samples were collected, lymphocytes were isolated from peripheral blood, RNA was extracted from lymphocytes and applied to the Illumina microarray gene expression platform. Statistical significance tests were done using the ANOVA and Benjamini Hochberg FDR multiple testing corrections at P -value cut-off of $P < 0.001$

RESULTS: The up-regulated genes are PGK1, GPI, ENO1, and TPI1 from the glycolysis pathway; ANGPTL4, AKR1B1 and SORD from the polyol pathway; MGST1, CYP2C19, AKR1C4, CYP1A1, CYP2E1 and EPHX1 from the xenobiotic metabolism pathway. These genes corresponded to the pathogenesis pathway of diabetes towards early nephropathy. Elevation of CYP2E1 expression in diabetes and nephropathy has been reported, and it is contributed by reactive oxygen species generated by the polyol pathway. Theoretically, CYP2E1 is the earliest biomolecule to be elevated in the DN pathogenesis pathway.

CONCLUSION: Findings of this study suggest that besides the CYP2E1 gene, genes involved in glucose metabolism and associated pathways may be candidate early predictors of diabetic nephropathy. Analytical methods may be developed for quantitating products of these signature genes, and may serve as useful candidate early predictors of diabetic nephropathy.

PCS-12-1

Effect of Anti-Platelet Agents on Arterial Stiffness in People with Type 2 Diabetes Mellitus

Chong Hwa Kim, Su-Jin Jeong and Joo Yong Hyun

Department of Internal Medicine, Sejong General Hospital, Korea

Arterial stiffness is an independent risk factor for cardiovascular events in diabetic patients, and it can be assessed by measuring pulse wave velocity (PWV). Pulse wave velocity also predicts the mortality of coronary artery disease (CAD). We investigated whether pharmacological interventions with anti-platelet agents can affect arterial stiffness in people with type 2 diabetes. In this study, 637 people with type 2 diabetes were divided into 3 groups in the use of anti-platelet agents: aspirin treated group ($n = 125$), cilostazol treated group ($n = 253$), and combination of aspirin and cilostazol treated group ($n = 259$). Pulse wave velocity (aortic, upper, and lower PWV) was measured before treatment and at 24 week follow up in the 3 groups. Aortic pulse wave velocity in the cilostazol treated group and combination of aspirin and cilostazol treated group were slightly reduced (from 8.03 ± 1.96 to 7.84 ± 1.75 m/s, and from 7.98 ± 1.66 to 7.86 ± 1.78 m/s, respectively) after 12 week treatment. Furthermore, upper PWV was decreased in the cilostazol treated group compared with aspirin and combination of aspirin and cilostazol treated group after 12 weeks (difference of 1st PWV-2nd PWV, 0.39 ± 0.26 , 0.06 ± 0.11 and 0.09 ± 0.13 m/s, respectively). Lower PWV in the 3 groups were decreased after 12 weeks. In conclusion, anti-platelet agents treatment may decrease arterial stiffness in people with type 2 diabetes. Cilostazol may play an important role in protecting arterial stiffness by decreasing PWV as well as aspirin in diabetes.

PCS-12-2

Levels of baPWV, ABI and TBI in Diabetic Patients and Related Risk Factors

Lei Zhang, Xiaoyun Dong, Yanhu Dong and Weiwei Qian

Department of Endocrinology and Metabolism, Qingdao Endocrine & Diabetes Hospital, China

AIMS: Ankle brachial index (ABI), toe brachial index (TBI) and brachial-ankle pulse wave velocity (baPWV) are straightforward and reproducible method for the detection of peripheral vascular disease. The aim of this study was to investigate the levels of ABI, TBI and baPWV in type 2 diabetic patients.

METHODS: We conducted a case-control study in 157 Chinese patients with type 2 diabetes and 150 healthy controls. Anthropometric indicators, plasma glucose, lipid profiles, HbA1c and serum uric acid were collected. ABI, TBI and baPWV were assessed using Omron VP-1000 vascular Profiler. Multi-variable adjusted regression analysis was used to assess independent associations between ABI, TBI or baPWV and risk factors such as age, sex, body mass index, systolic blood pressure, fasting glucose, 2-h glucose (2hPG), HbA1c, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol and uric acid.

RESULTS: Compared with the control group, baPWV was significantly increased (1695.34 ± 425.87 vs 1361.82 ± 209.45 cm/s, $P < 0.05$) while TBI reduced (0.84 ± 0.17 vs 0.90 ± 0.13 , $P < 0.05$) in the diabetic group. In the multivariate adjusted logistic regression model, age was independently associated with ABI (OR: 1.06, 95% CI: 1.03–1.10) and TBI (OR: 1.18, 95% CI: 1.10–1.26). SBP (OR: 1.10, 95% CI: 1.06–1.14), 2hPG (OR: 1.13, 95% CI: 1.01–1.27) and HbA1c (OR: 1.20, 95% CI: 1.08–1.35) were independently associated with baPWV, while HDL-C (OR: 0.67, 95% CI: 0.60–0.77) was protective for TBI.

CONCLUSION: Arterial elasticity can be evaluated by baPWV, ABI and TBI in diabetic patients. Intensive control of blood pressure and blood sugar may slow down the progress of atherosclerosis.

PCS-12-3

Evaluation of Systemic Arteriosclerosis is a Useful Tool for Predicting Coronary Artery Disease in Japanese Type 2 Diabetic Patients

Ayumu Hirata, Ken Kishida, Hideaki Nakatsuji, Aki Shimizu, Tohru Funahashi and Ichihiro Shimomura
Departments of Metabolic Medicine, Graduate School of Medicine, Osaka University, Japan

OBJECTIVES: To evaluate systemic arteriosclerosis non-invasively and to investigate an important determinant to coronary artery disease (CAD) in patients with type 2 diabetes mellitus (T2DM).

METHODS: In consecutive 102 outpatients with type 2 diabetes mellitus, we evaluated non-invasively atherosclerosis in carotid, renal artery, abdominal aorta and bifurcation of common iliac arteries with ultrasound scanning. We estimated visceral fat area by bioelectrical impedance analysis (BIA) method. Laboratory data including adipocytokines were collected. The determinant factor of coronary artery disease were evaluated statistically by multiple regression analysis.

RESULTS AND CONCLUSION: Over 80% of patients had carotid lesions. Among them, 75% had arteriosclerotic lesions in other multiple arteries. T2DM patients with metabolic syndrome (Mets) had significantly a higher prevalence of multiple arteriosclerotic lesions compared with those without Mets ($P < 0.001$). Multiple arteriosclerotic lesions correlated with carotid max intima-media thickness (IMT), duration of T2DM, microvascular complications of T2DM, ABI, and TBI in age-sex-adjusted simple logistic analysis. Multiple logistic regression analysis identified only the number of lesions as a significant determinant of CAD ($P < 0.001$). In addition, systemic arteriosclerosis was significantly determined only by Mets. These results suggested that evaluations of systemic arteriosclerosis should be a useful method to predict of coronary artery disease in T2DM, and patients with Mets could be remarkably high risk patients for systemic arteriosclerosis.

PCS-12-4

Serum YKL-40 Level is Related to Angiographic Severity and Extent of Coronary Artery Disease in Type 2 Diabetes Patients

Yun Kyung Jeon and Bo Hyun Kim
Department of Internal Medicine and Division of Endocrinology and Metabolism, Pusan National University Hospital, Korea

OBJECTIVE: YKL-40 has been established as an inflammatory marker in chronic inflammation. Chronic inflammation is important in the development of both coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM). The aim of this study was to evaluate the association of serum YKL-40 with angiographically significant CAD in T2DM patients and non-diabetic patients.

METHODS: Serum YKL-40 was measured in 78 patients (including 38 T2DM patients) with stenosis of more than 50% of luminal diameter in at least one of coronary artery in coronary angiography. The atherosclerotic burden was obtained by three independent angiographic scores: the severity, Gensini score (GS) and Extent score (ES).

RESULTS: There were significant differences in serum YKL-40 levels according to three subgroups with a different number of significant stenosed vessels ($P = 0.014$). Serum YKL-40 levels significantly correlated with GS ($P = 0.003$) and ES ($P = 0.001$), whereas C-reactive protein (CRP) did not with both GS and ES in univariate analysis. After adjusting for several confounding factors, serum YKL-40 was significant correlation with GS ($P = 0.040$) and ES ($P = 0.024$). The serum YKL-40 levels were significantly higher in the T2DM than in non-diabetic patients ($P = 0.018$). The significant

correlations between GS and ES with serum YKL-40 persisted in patients with T2DM, whereas lost in non-diabetic patients.

CONCLUSIONS: Serum YKL-40 as an inflammatory marker is associated with angiographic extent and severity of CAD. This finding is mainly observed in patients with T2DM.

PCS-12-5

Serum Zinc Level and Peripheral Arterial Disease Events in Patients with Type 2 Diabetes

Shih Chueh Chen¹, Kuo Ting Sun², Jin-Lian Lai¹ and Pei Chi Chen³

¹Department of Endocrinology, Cheng Ching hospital, Taiwan; ²Department of Dentistry, Chinese Medical Hospital, Taiwan; ³Department of Nutrition, Taichung Province University

OBJECTIVE: Low serum zinc level may predispose non-diabetic subjects to cardiovascular diseases. Our aim was to investigate whether serum zinc level predicts peripheral arterial disease (PAD) events in subjects with type 2 diabetes.

RESEARCH DESIGN AND METHODS: The original study population consisted of 747 patients with type 2 diabetes, aged from 34 to 85 years. Mean duration of diabetes was 8.3 years. Serum zinc values were available from 446 subjects.

RESULTS: During the follow-up, patients with serum zinc concentration ≤ 800 $\mu\text{g/L}$ at baseline had a higher risk for PAD than patients with serum zinc level > 800 $\mu\text{g/L}$ (25.4 and 15.3%, respectively; $P = 0.001$). In Cox regression analyses, low serum zinc concentration was significantly associated with PAD and received surgery (relative risk [RR] 2.63, $P = 0.002$) and all PAD events (RR 1.55, $P = 0.023$), even after adjustment for confounding variables.

CONCLUSIONS: In this cross sectional study of type 2 diabetic patients, low serum zinc level was an independent risk factor for PAD events.

PCS-12-6

Glycemic Target Associated with Better Outcomes in Patients with Acute Myocardial Infarction

Chi Pun Chan and Ip Tim Lau
Department of Medicine, Tseung Kwan O Hospital, Hospital Authority, Hong Kong

INTRODUCTION: There had been study showing intensive glucose control had poorer outcome in adults in the ICU setting. Moreover, there has been controversy on glycaemia targets in diabetes (DM) patients with acute myocardial infarction (AMI).

OBJECTIVES: To review the range of glucose levels after AMI that was associated with better outcomes.

METHODOLOGY: This is a retrospective study. DM patients who had AMI (non-ST or ST-elevation) were reviewed. Adverse events included hypoglycaemia, infection, unplanned readmission and mortality. Chi-square test and Logistic regression were used.

RESULTS: There were 397 patients. They were 35–97 years old. Two hundred and ninety-five (74.3%) were more than 65 years old. Two hundred and fifteen (54.2%) was male. Forty-two (10.6%) patients admitted for ST-elevation AMI. Sixteen out of 42 patients were given thrombolytic. Hypoglycaemia was associated with mean glucose during hospital stay 6–8 mmol/L (RR 1.978, 95% CI 1.105–3.541, $P < 0.05$). It was inversely associated with mean glucose > 8 mmol/L (RR 0.551, 95% CI 0.303–1.001, $P = 0.05$). Infection was inversely associated with mean glucose during hospital stay 6–8 mmol/L (RR 0.433, 95% CI 0.193–0.970, $P < 0.05$). It was associated with mean glucose during hospital stay > 8 mmol/L (RR 3.911, 95% CI 1.703–8.984, $P < 0.05$). LOS > 3 days was inversely associated with glucose 6–8 mmol/L (RR 0.545, 95% CI 0.338–0.881, $P < 0.05$). It was associated with mean glucose > 8 mmol/L (RR 2.134, 95% CI 1.3–3.503, $P < 0.05$). Readmission was not associated with any range of glucose levels. 28 days mortality was inversely associated with mean glucose 6–8 mmol/L (RR 0.389, 95% CI 0.153–0.988, $P < 0.05$). Six months mortality was not associated with any range of glucose levels.

CONCLUSIONS: From this retrospective review, mean glucose level < 8 mmol/L may be better in terms of infection, length of stay, and short term mortality but higher risk of hypoglycaemia. However, it was not associated with longer term mortality rate.

PCS-12-7

Combined Cardiac MRI in Detecting Coronary Artery Disease in Asymptomatic Type 2 Diabetes Mellitus

Kwang Joo Kim¹, Sang Hoon Shin², Hyuk Jae Chang², Hyun Min Kim³, Eun Seok Kang³, Bong Soo Cha³, Hyun Chul Lee³, Byung-Wan Lee³, Young Jin Kim⁴ and Jae Hyuk Lee⁵

¹Severance Executive Healthcare Clinic, Severance Hospital, Yonsei University Health System, Korea; ²Division of Cardiology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; ³Division of Endocrinology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; ⁴Department of Radiology, Yonsei University College of Medicine, Seoul, Korea; ⁵Division of Endocrinology, Department of Internal Medicine, Kwandong University College of Medicine, Goyang, Korea

OBJECTIVE: To evaluate the diagnostic power of stress perfusion cardiac MR (SP-CMR), CMR angiography (CMR-A) or combined cardiac MRI (c-CMR) in asymptomatic type 2 diabetic (T2DM) patients for detecting CAD or significant CAD (>50% narrowing) in comparison with invasive coronary angiography (ICA)

RESEARCH DESIGN AND METHODS: A total of 100 asymptomatic T2DM subjects (51 men and 49 women; mean age: 56.4 ± 7.6 years) were enrolled. Clinical and laboratory parameters, including HbA1c, glycoalbumin, lipid profile were evaluated and cardiovascular magnetic resonance (CMR) was performed. Abnormal findings of CMR were defined as any one of the followings: (1) Silent myocardial infarction (2) Inducible ischemia (3) Suspected CAD. Within 90 days after taking CMR, invasive coronary angiography (ICA) was performed in selective patients.

RESULTS: Among 100 patients, a total of 51 patients [silent myocardial infarction ($n = 3$), inducible ischemia ($n = 11$), suspected CAD ($n = 37$)] had at least one abnormal finding on CMR and ICA was recommended. Finally, 20 patients underwent ICA, and 13 subjects had significant CAD (A total of 60 coronary territories assess). Overall, in asymptomatic T2DM patients, the positive predictive value (PPV) of SP-CMR, CMR-A, c-CMR are 100%. However, the PPV of each MRI to detect significant stenosis are 73%, 57% and 54%, respectively.

CONCLUSIONS: In asymptomatic T2DM patients, stress perfusion CMR showed higher PPV than CMR-A.

PCS-12-8

Predicted 4-Year Risk of Major CVD of Diabetic Patients

Banzragch Bataa¹, Sainbileg Sonomtseren² and Suvd Junai²

¹Department of Endocrinology, Second General Hospital, Mongolia; ²Department of Endocrinology, School of Medicine, Health Sciences University of Mongolia

AIMS: Aims of this study were to evaluate Predicted 4-year risk of major CVD of DM patients.

METHODS: Cross-sectional study included 50 (24 male and 26 female) DM patients with mean age 65.04 ± 8.22 years old. Predicted 4-year risk of major CVD was calculated by using ADVANCE Risk Engine of the George Institute for Global Health, Australia. Ten parameters (age at diagnosed diabetes, duration of diabetes, sex, atrial fibrillation, retinopathy, HbA1c, pulse pressure, hypertension, albuminuria and Non HDL-cholesterol) were used for risk calculation.

RESULTS: Results of our study relieved mean age at diagnosed diabetes was 57.28 ± 8.71 years old and mean diabetes duration was 7.92 ± 5.52 years. DM patient with atrial fibrillation, retinopathy and hypertension were 0(0%), 12(24%) and 34(68%). Mean level of HbA1c was $7.72 \pm 1.4\%$. DM patients with good control (HbA1c < 6.5%), with moderate control (HbA1c 6.5–7.5%) and with bad control (HbA1c > 7.5%) were 9(18.0%), 19(36.0%) and 22(44.0%). Mean level of microalbuminuria was 25.33 ± 69.37 mg/L, pulse pressure was 47.6 ± 12.38 mm Hg and Non HDL cholesterol was 3.57 ± 0.86 mmol/L. Mean Predicted 4-year risk of major CVD was $5.2 \pm 5.56\%$ (Range 0.6–23.0%). DM patients with <10%, 11–20% and >20% Predicted 4-year risk of major CVD were 42(84.0%), 6(12.0%) and 2(4.0%).

CONCLUSIONS: 84.0% of DM patients have <10%, 12.0% have 11–20% and 4.0% have >20% Predicted 4-year risk of major CVD.

PCS-13-1

Current Status of Therapeutic Target Achievement According to Duration of Diabetes in Korean Type 2 Diabetic patients

Ji Hye Suk¹, Chang Won Lee², Sung Pyo Son³, Min Chul Kim⁴, Jun Hyeob Ahn⁵, Jeong Hyun Park⁶, In Joo Kim⁷ and Kwang Jae Lee⁸

¹Department of Internal Medicine, Maryknoll Medical Center, Korea; ²Department of Internal Medicine, Busan St. Mary's Medical Center; ³Department of Internal Medicine, Bongseng Memorial Hospital; ⁴Department of Internal Medicine, Ilsin Christian Hospital; ⁵Department of Internal Medicine, Good Moonhwa Hospital; ⁶Department of Internal Medicine, College of Medicine, Inje University; ⁷Department of Internal Medicine, Pusan National University School of Medicine Hospital; ⁸Department of Internal Medicine, Daedong Hospital

BACKGROUND AND AIMS: Substantial evidence has shown that good glycemic, blood pressure (BP) and lipid control reduces the risk of diabetic complications. However, data regarding the proportion of individuals with diabetes who have optimal control are limited in Asian populations. We performed this study to investigate the current status of therapeutic target achievement according to duration of diabetes in Korean type 2 diabetic patients.

SUBJECTS AND METHODS: This study was an analysis from participants of the REBOUND Study, which is a prospective multi-center cohort study in Korea. Two thousands and seventeen type 2 diabetic patients aged 30 years or more were analyzed, and patients with duration of diabetes <12 months were excluded. Glycemic, blood pressure, and lipid targets were defined as hemoglobin A1c <7%, BP <130/80 mm Hg, and LDL cholesterol <100 mg/dL, respectively.

RESULTS: Median age and duration of diabetes were 60 and 8 years, respectively. Median HbA1c was 7.1%. Prevalence of hypertension was 68.7%. Percentages reaching treatment goals of glycemic, lipid, and BP were 42.5%, 34.8%, and 38.8%, respectively. Percentage reaching treatment goals of glycemic control decreased gradually according to duration of diabetes. But, that kind of trend didn't appear in lipid and BP control.

CONCLUSION: In our study, glycemic control seems to worsen gradually according to duration of diabetes, in contrast with BP and lipid control. Strategies to improve awareness and implement evidence-based guidelines are needed to reduce the effect and burden of diabetic complications.

PCS-13-2

Comparisons of Intact Proinsulin/Insulin Ratio Between the Non-Elderly and Elderly Diabetic Patients

Hiroshi Yoshino¹, Koji Kuboki², Takehiko Watanabe¹ and Gen Yoshino¹

¹Department of Internal Medicine, Shin-suma Hospital, Japan; ²Division of Diabetes, Metabolism and Endocrinology, Department of Internal Medicine (Omori), Toho University School of Medicine

BACKGROUND AND AIM: Plasma intact proinsulin/insulin (PI/I) ratio in diabetic subjects can be an indicator for insulin secretory mechanism from the standpoint of insulin processing. The present study was conducted to examine whether insulin secretory mechanism of elderly diabetic patients differs from that of non-elderly diabetic patients.

METHODS: The study subjects consist of 85 patients. They were separated into 4 groups according to their age and an association of type 2 diabetes. Twenty-eight elderly diabetic (mean age 77.3 ± 7.0), 20 elderly non-diabetic (mean age 83.0 ± 7.7), 19 non-elderly diabetic (mean age 53.6 ± 8.4) 18 non-elderly non-diabetic (mean age 44.3 ± 9.4) subjects were enrolled. Age, PI/I ratio, HbA1c (NGSP) were investigated. Plasma insulin and Intact proinsulin were measured by immunoradiometric and by chemiluminescence assay (MLT Research Ltd., USA), respectively. To avoid breakdown of proinsulin during assay, incubation for reaction was done overnight at 4°C. ANOVA were employed for comparison of intact proinsulin, insulin, and PI/II ratio between the two groups.

RESULTS: PI/I ratio in the elderly diabetic group was higher than that of elderly non-diabetic group (0.23 ± 0.12 vs 0.11 ± 0.05 , $P < 0.05$). However, there was no significant difference in this ratio between elderly diabetic and non-elderly diabetic group (0.23 ± 0.13 vs 0.16 ± 0.13).

It is noteworthy that 2 non-elderly diabetic subjects showed abnormally high PI/II ratio (higher than 0.45).

DISCUSSION: It is concluded from the present data that insulin secretory mechanism is abnormal from the standpoint of insulin processing not only in the non-elderly diabetic but also in elderly diabetic patients but further deterioration was not observed with age.

PCS-13-3

Combined Assessment of Hemoglobin A1c and Glycated Albumin Improves the Efficacy of Diabetes Screening in Chinese Subjects

Qing Li, Weiping Jia, Yuqian Bao, Jieming Pan, Xiaojing Ma and Junling Tang
Department of Endocrinology and Metabolism, Shanghai Clinical Center for Diabetes, China

OBJECTIVE: To assess the validity of combined detecting with hemoglobin A1c (HbA1c) and glycated albumin (GA) in diabetes screening in Chinese subjects.

METHODS: A total of 1480 subjects in our out-patient department from March 2007 to December 2009, suspicious of diabetes or at high-risk of diabetes were enrolled in the present study. The study population included 677 males and 803 females, with mean age of 52.7 years. All the subjects were performed with oral glucose tolerance test (OGTT) after 10 h fasting. Glycated albumin (GA) and hemoglobin A1c (HbA1c) were measured with liquid enzyme method and high pressure liquid chromatography analysis, respectively.

RESULTS: (1) According to WHO diabetes diagnosis criteria, there were 562 subjects with normal glucose tolerance (NGT), 411 subjects with impaired glucose regulation (IGR) and 507 subjects with new diagnosed diabetes mellitus (DM). The level of HbA1c and GA had increasing tendency among NGT, IGR and DM groups ($P < 0.01$). (2) Pearson correlation analysis demonstrated that HbA1c had positive association with GA ($r = 0.75$, $P < 0.01$). (3) Using OGTT as golden standard of diabetes diagnosis, receiver operator characteristic (ROC) curve indicated that HbA1c and GA were high predictors of diabetes. The area under curve (AUC) is 0.882 and 0.881, respectively, with no significant difference ($P > 0.05$). (4) The sensitivity of combined using HbA1c and GA at optimal cut-off of 6.1% and 17.1% was significantly higher than that of single using HbA1c or GA in diabetes screening (94.7% vs 81.1%, 94.7 vs 88.4%, $P < 0.01$).

CONCLUSIONS: Combined detecting of HbA1c and GA could improve the efficacy of diabetes screening. The subject with HbA1c $\geq 6.1\%$ or GA $\geq 17\%$ was suggested to accept OGTT for confirming diabetes diagnosis.

PCS-13-4

Association Between Nutritional Status (Subjective Global Assessment and Albumin Plasma) with Hemoglobin A1c in Type 2 Diabetes Mellitus

Nanny Natalia Mulyani Soetedjo¹, Gaga Irawan², Hikmat Permana¹, Augusta Y. L. Arifin¹ and Sri Hartini K. S. Kariadi¹

¹Endocrinology and Metabolism Division, Internal Medicine Department, Hasan Sadikin General Hospital, Faculty of Medicine, Padjadjaran University, Indonesia; ²Clinical Nutrition Department, Faculty of Medicine, Padjadjaran University, Bandung, Indonesia

HbA1c became tool to diagnosis not only as target in type 2 diabetes mellitus (T2DM) management. Clinicians used to think that only glucose influence HbA1c, actually there are a lot of other factors such haemoglobin, pregnancy, triglyceride, liver-renal function and also method of HbA1c examination. These misinterpretation of HbA1c would result in inadequate management of T2DM. Nutritional status in T2DM sometimes not recognized but we thought that actually it has correlation with HbA1c levels. So the aim of this study to evaluate the correlation between nutritional status (Subjective Global Assessment (SGA) and plasma albumin) with HbA1c in T2DM.

This retrospective observational analytic study performed in January-May 2011. Subject were T2DM patients in Endocrine Outpatient Clinic Hasan Sadikin General Hospital which fulfill the inclusion and exclusion. Datas were analyzed using Spearman or Pearson Correlation test and multiple regression test to know correlation between HbA1c and others.

Sixty subjects consisted of 34 males (56.73%) and rest were women; mean aged 59.32 ± 8.35 years; median duration of diabetes was 3(1-19) years; median BMI 23.45 ($15.99-37.11$) kg/m^2 and 8.33% with BMI $< 19 \text{ kg/m}^2$; median HbA1c 7.8 ($5.7-13.1$)%; median plasma albumin 3.32 ($2.62-5.28$) g/dL . All subjects had A in SGA (good nutritional). It showed significant correlation between HbA1c with plasma albumin ($r = -0.91$, $P < 0.001$), fasting plasma glucose ($r = 0.46$, $P < 0.001$) and age ($r = -0.44$, $P < 0.001$).

Nutritional status in T2DM cannot be examined only by history taking and physical examination such SGA and BMI. Because of a significant correlation between plasma albumin level with HbA1c level in T2DM we recommended to exam plasma albumin in T2DM with high HbA1c.

PCS-13-5

Assessing Diabetes-Specific Health-Related Quality of Life of Hong Kong Chinese Patients with Type 2 Diabetes Mellitus

Colman S. C. Fung, Carlos K. H. Wong, William C. W. Wong, Daniel T. P. Lam and Cindy L. K. Lam

Department of Family Medicine and Primary Care, The University of Hong Kong, Hong Kong

OBJECTIVE: This study aims to investigate the health-related quality of life (HRQOL) of Hong Kong Chinese patients with type 2 diabetes mellitus (T2DM), its association with socio-demographic and diabetes-related characteristics.

METHODS: An interviewer-administered survey was conducted on a sample of 386 patients with T2DM under a government-funded general outpatient clinic in Hong Kong in 2010. The survey questionnaire included socio-demographic, diabetic-related clinical information, and the diabetes-specific quality of life instrument, Audit of Diabetes-Dependent Quality of Life (ADDQoL), which had 19 life domains and each domain score ranged from -9 (maximum negative impact) to +3 (maximum positive impact). Independent t-test and linear regression were used to find the significant factors associated with ADDQoL score.

RESULTS: Out of the 19 ADDQoL life domains, lack of freedom to eat and drink had the first and second greatest negative weighted impact scores respectively (-3.63 ± 1.99 ; -2.41 ± 1.93), while living condition had the lowest (-0.05 ± 0.42). Independent t-test showed lower ADDQoL average weighted impact score in patients with shorter duration of diabetes, obesity, and on oral hypoglycaemic drugs. Similarly, regression analysis found that shorter duration of diabetes, obesity and use of oral hyperglycemic drugs were more likely to have lower average weighted impact score of ADDQoL.

CONCLUSION: This study identified the key components of HRQOL being affected by the diabetes in patient's life. Obesity and oral hyperglycemic drugs therapy may have a negative impact on quality of life in T2DM patients, suggesting the importance of weight reduction and non-drug management in the overall management of Chinese diabetic patients.

PCS-13-6

The Relations Between Serum Magnesium Levels and Some Clinical Data in Male Outpatients with Glucose Intolerance

Noboru Saito¹, Mizuho Ban², Minako Yamana³, Hitomi Nishikawa⁴, Fusae Ohtsuji⁴ and Shoji Nishiyama⁵

¹Department of Internal Medicine, Kusatsu General Hospital, Japan; ²Faculty of management, Osaka Seikei University; ³Faculty of Nutrition, Seibi Junior College; ⁴Dietician; ⁵Faculty of Pharmacology, Osaka Ohtani University

OBJECTIVE: This study is aimed to clarify the relations among serum magnesium (Mg), some clinical data and blood pressure (BP), and also between urinary glucose and urinary Mg in male outpatients with glucose intolerance.

METHODS: In this study 109 male outpatients aged mean 65 years were recruited, involving 63 males without any drug. Fasting blood and urinary samples were obtained early in the morning. All participants were divided into 4 groups according to serum Mg levels (mg/dL): < 2.2 (group 1, G1), $2.2 \leq$, < 2.3 (G2), $2.3 \leq$, < 2.5 (G3) and $2.5 \leq$ G4).

RESULTS: FBS, HbA1c, HOMA- β , systolic BP (SBP), and diastolic BP (DBP) were higher significantly in G1 than in G2 to G4. There were furthermore significantly negative correlations between serum Mg and FBS ($r = -0.44$), HbA1c ($r = -0.49$), SBP ($r = -0.38$) or DBP ($r = -0.32$), while significantly positive one was $r = 0.26$ between serum Mg and HOMA- β . When urinary glucose/creatinine (Cr) became larger in over 170 mg/dL of FBS, urinary Mg/Cr tended to be higher, but not significant.

CONCLUSION: Low levels of serum Mg were accompanied with glucose intolerance and high BP in male outpatients.

PCS-13-7

The Serum Electrolyte Cation Levels in Normal, Impaired Glucose Regulation, and Diabetic Subjects

Shenqi Wang¹, Xuhong Hou¹, Yu Liu², Huijuan Lu² and Weiping Jia¹

¹Department of Endocrinology and Metabolism, Shanghai JiaoTong University Affiliated 6th People's Hospital, China; ²Shanghai Diabetes Institute, Shanghai Clinical Center for Diabetes China

OBJECTIVE: To compare serum electrolyte cation (Na^+ , K^+ , Ca^{2+} , Mg^{2+}) levels among the subjects with normal glucose regulation (NGR), impaired

glucose regulation (IGR) and diabetes mellitus (DM), and to assess their correlations with plasma glucose in DM subjects.

METHODS: A gender-, age-matched case-control study, involved 1170 subjects with NGR, 389 subjects with IGR and 374 subjects with DM. A 75 g oral glucose load was done for participants without a prior diagnosis of DM. Fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1C), serum electrolyte cation levels and other indicators were measured. The data collection included demographic information, medical history and physical examination.

RESULTS: Compared to the NGR or IGR group, serum Na^+ and Mg^{2+} levels of the DM group significantly decrease ($P < 0.01$), while serum Ca^{2+} level of the DM group significantly increases compared to the NGR group ($P < 0.01$). Multivariable linear regression shows that in the DM group, serum Na^+ and Mg^{2+} levels are negatively, while serum Ca^{2+} level is positively correlated with FPG and HbA1C ($P < 0.05$). The adjusted β values are -0.327 , -0.401 for Na^+ , -0.009 , -0.018 for Mg^{2+} and 0.005 , 0.011 for Ca^{2+} respectively.

CONCLUSION: Serum Na^+ , Mg^{2+} , and Ca^{2+} levels significantly change in normal, IGR and DM subjects; Significant associations of Na^+ , Mg^{2+} , and Ca^{2+} level with FPG and HbA1C exist in DM subjects.

PCS-14-1

Clinical Features of Slowly Progressive Insulin-Dependent Diabetes Mellitus (SPIDDM) in Our Hospital

Tomoko Asano, Hodaka Yamada, Atsushi Aoki, Aki Ikoma, Ikuyo Kusaka, Hideo Toyoshima, Masafumi Kakei and San-e Ishikawa

Department of Endocrinology, Jichi Medical University Saitama Medical Center, Saitama, Japan

OBJECTIVE: SPIDDM belongs to type 1 diabetes, which has Langerhans islet-specific antibodies. It's clinical characteristics resembles type 2 diabetes, however, it gradually proceeds to insulin-dependent condition. The present study was undertaken to determine clinical and laboratory features of SPIDDM.

METHODS: Thirty-nine patients with SPIDDM were enrolled in the present study. They had positive GAD antibody (1.5 U/mL) and their clinical features resembled type 2 diabetes.

RESULT: They were 18 males and 21 females with the ages of 59.7 ± 11.4 years. The duration of diabetes was 11.3 ± 8.7 years. When diagnosed 16 patients had symptoms of polydipsia and weight loss, but other 17 patients were diagnosed incidentally by regular medical check. It took 6.6 ± 8.0 years until they clarified positive GAD antibody and diagnosed as type 1 Diabetes. BMI was 22.8 ± 4.6 , with the maximal BMI of 27.0 ± 3.5 . HbA1c (NGSP) was $7.9 \pm 1.3\%$ at the examination, but they were extremely as high as $10.8 \pm 2.8\%$ at the diagnosis of Diabetes. GAD antibody titer was $290.3 \pm 889.2 \text{ U/mL}$, ranging from 1.6 to 4340 U/mL. Serum C-peptide was $1.2 \pm 1.2 \text{ ng/mL}$. Eleven patients had become insulin-dependent state. We divided 3 groups according to GAD antibody titer (<10 , $10\text{--}100$, $100\leq \text{U/mL}$). The high GAD group had significantly shorter duration of 2.1 ± 4.2 years until type 1 DM was diagnosed ($P = 0.036$). Also, the high GAD group had less duration of Diabetes and higher HbA1c as compared to other two groups.

CONCLUSION: These findings indicated that there is no particular clinical feature in SPIDDM. The measurement of GAD antibody is of value to early diagnose SPIDDM at the initial visit.

PCS-14-2

A Case Report of Fulminant Type 1 Diabetes Mellitus that Developed Following Type A Influenza Infection

Kazuo Tsuji and Hideya Fujiwara

Department of Internal Medicine, Nishi-Kobe Medical Center, Japan

PATIENT: A 43-year-old male chiefly complaining of dry mouth.

HISTORY AND CONDITION: Ten days before the patient's initial examination, his child had been infected with influenza; 5 days after that, the patient himself had a fever of approximately 38°C and began to take an influenza treatment drug. Two days before his initial examination, he felt dry mouth, and since then he had been taking 12 liters per day of an isotonic drink. He was 179 cm tall and weighed 103 kg.

EXAMINATION RESULTS: BS, 877 mg/dL; urine ketones, (+++); pH, 7.210; acetoacetic acid, 3820 $\mu\text{mol/L}$; 3-OH-butyric acid, 9780 $\mu\text{mol/L}$; HbA1c

(NGSP), 7.2%; AMY, 43 IU/L; elastase I, 1280 ng/dL; glucagon load (at 0 and 6 min), CPR 0.1/0.3 ng/mL; U-CPR, $< 4.4 \mu\text{g/day}$; anti-GAD antibody, (–); IA-2 antibody, (–); insulin antibody, (–); CF for type A influenza, 32; and CF for type B influenza, indeterminate.

PROGRESS: At first, 'soft drink' ketoacidosis was suspected, but his illness was ultimately diagnosed as fulminant type 1 diabetes mellitus because of impaired insulin secretion. We report this case because there are few reports of cases of fulminant type 1 diabetes mellitus that developed following type A influenza infection, although some such cases following type B influenza infection have been reported.

PCS-14-3

Autoimmune Type 1 Diabetes Mellitus Acutely Presented on Steroid Pulse Therapy Against Early Stage of Stevens-Johnson Syndrome in a Female with Graves' Disease

Ikuko Yamamori¹, Tatsuhiko Kitamura², Masako Yamauchi¹, Yasuko Watanabe³, Naoko Iwata¹, Ryo Horibe¹ and Miho Ushida¹

¹Department of Endocrinology and Metabolism, Japanese Red Cross Nagoya Daiichi Hospital, Japan; ²Department of Dermatology, Japanese Red Cross Nagoya Daiichi Hospital, Japan; ³Health Control Center, Japanese Red Cross Nagoya Daiichi Hospital, Japan

A 43 year-old Japanese female was referred to our department because marked hyperglycemia was observed on the second day of steroid pulse therapy against early stage of Stevens-Johnson syndrome caused by antibiotics. She had a 3-year history of Graves' disease and was euthyroid on oral methimazole at 5 mg 4 times weekly. She was 154 cm high and weighed 91.1 kg (body mass index 38.4 kg/m^2). She also had a history of non-alcoholic fatty liver disease. On presentation, evening premeal blood glucose was 20.7 mmol/L, and low dpse s.c. insulin was given. Laboratory data were as follows: HbA1c (NGSP) 6.0%, glycoalbumin 15.4%, fasting glucose 8.3 mmol/L, fasting serum C-peptide 2.4 ng/mL, anti-GAD 65 antibody 23.0 U/mL, anti-IA-2 antibody $<0.4 \text{ U/mL}$, urinary C-peptide 55.0 $\mu\text{g/day}$. She was negative for diabetic microvascular complications. Insulin therapy was introduced, and her glucose profile was improved with insulin lispro 50 mix preparation thrice daily (total 19 U/day). Pathophysiological aspect of her diabetes will be discussed.

PCS-14-4

Evaluation of Glycated Albumin as a Clinical Marker for Glycemic Variability in Type 1 Diabetes by Continuous Glucose Monitoring

Chiharu Tsutsumi¹, Akihisa Imagawa², Yuko Murase-Mishiba¹, Hiroyuki Sano¹, Mineki Onishi¹, Junjo Terasaki¹ and Toshiaki Hanafusa¹

¹Department of Internal Medicine (I), Osaka Medical College, Japan; ²Department of Metabolic Medicine, Graduate School of Medicine, Osaka University, Japan

OBJECTIVE: This study is conducted to evaluate the utility of HbA1c and/or GA as a clinical marker for glycemic variability in patients with type 1 diabetes by using a continuous glucose monitoring (CGM) system.

METHODS: Twenty-one outpatients with type 1 diabetes (age 47.2 ± 16.6 years with a duration of diabetes of 11.1 ± 7.0 years, 13 MDI and 8 CSII) underwent up to 72 h of CGM with the CGMS Gold (Medtronic). Treatment for diabetes did not change for at least the past 2 months. We analyzed the correlation between 10 measures (mean glucose, area under the curve (AUC) at 180/70 mg/dL, %High/Low, SD, J-index, %CV, HBGI/LBGI, M-value, MAGE and MODD) obtained from CGM and the levels of glycemic markers (HbA1c, GA and GA: HbA1c ratio), within the following 8 days monitored by CGM.

RESULTS: The average levels (%) of HbA1c, GA and GA: HbA1c ratio were 7.9 ± 0.9 , 25.6 ± 4.4 and 3.4 ± 0.5 , respectively. Pearson correlation analysis showed that both levels of HbA1c and GA were closely related to CGM-measured mean glucose, AUC-180, %High, HBGI and M-value. GA levels also positively correlated with SD ($R = 0.46$, $P = 0.035$), J-index ($R = 0.67$, $P = 3.5 \times 10^{-3}$) and MAGE ($R = 0.45$, $P = 0.042$), while HbA1c levels did not. In addition, GA: HbA1c ratio correlated significantly with only four measures of glycemic variability; SD ($R = 0.58$, $P = 5.7 \times 10^{-3}$), J-index ($R = 0.45$, $P = 0.039$), M-value ($R = 0.46$, $P = 0.035$) and MAGE ($R = 0.60$, $P = 4.3 \times 10^{-3}$).

CONCLUSION: Both GA and GA: HbA1c ratio could be a better clinical marker for blood glucose level itself and glycemic variability than HbA1c in type 1 diabetes.

PCS-15-1

Insulin Secretory Capacity and Insulin Sensitivity in Impaired Fasting Glucose in Japanese

Rie Mitsui¹, Mitsuo Fukushima², Ataru Taniguchi³, Yoshikatsu Nakai⁴, Sae Aoyama², Yoshitaka Takahashi⁵, Hideaki Tsuji⁵, Daisuke Yabe⁶, Koichiro Yasuda⁷, Takeshi Kurose⁶, Toshiko Kawakita⁸, Yutaka Seino⁶ and Nobuya Inagaki⁹

¹Center for Preventive Medicine, St Luke's International Hospital, Japan; ²Division of Clinical Nutrition and Internal Medicine, Okayama Prefectural University, Okayama, Japan; ³Department of Internal Medicine, Kyoto Preventive Medical Center, Kyoto, Japan; ⁴Karasumaoike Nakai Clinic, Kyoto, Japan; ⁵Faculty of Health and Welfare Science, Okayama Prefectural University, Okayama, Japan; ⁶Division of Diabetes and Clinical Nutrition, Kansai-Denryoku Hospital, Osaka, Japan; ⁷Department of Diabetes and Endocrinology, Saiseikai Noe Hospital, Osaka, Japan; ⁸Center for Preventive Medicine, St. Luke's International Hospital, Tokyo, Japan; ⁹Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Kyoto, Japan

OBJECTIVE: Impaired fasting glucose (IFG) increases risk of developing diabetes mellitus (DM). This study was conducted to characterize Japanese subjects having fasting glucose levels (FPG) between 100 and 109 mg/dL (IFG₁₀₀₋₁₀₉).

METHODS: Two thousand one hundred and seventy-nine Japanese subjects were examined by oral glucose tolerance test. We compared insulin secretory capacity (insulinogenic index) and insulin sensitivity (ISI composite) of IFG₁₀₀₋₁₀₉/NGT (100 < FPG < 110 mg/dL and 2-h postchallenge glucose level (2-hPG) < 140 mg/dL) with NGT (100 mg/dL < FPG and 2-hPG < 140 mg/dL) and IFG₁₁₀₋₁₂₅/NGT (110 < FPG < 126 mg/dL and 2-hPG < 140 mg/dL). In addition, IFG₁₀₀₋₁₀₉ subjects were analyzed in three subgroups according to glucose intolerance by 2-hPG.

RESULTS: Of the three categories of IFG₁₀₀₋₁₀₉, IFG₁₀₀₋₁₀₉/DM had the lowest insulinogenic index despite an ISI composite showing only a small decline from IFG₁₀₀₋₁₀₉/NGT via IFG₁₀₀₋₁₀₉/IGT (100 < FPG < 110 mg/dL and 140 < 2-hPG < 200 mg/dL) to IFG₁₀₀₋₁₀₉/DM (100 < FPG < 110 mg/dL and 200 mg/dL < 2-hPG). Both insulinogenic index and ISI composite were decreased significantly from NGT via IFG₁₀₀₋₁₀₉/NGT to IFG₁₁₀₋₁₂₅/NGT. In addition, almost 40% of IFG₁₀₀₋₁₀₉ were impaired glucose tolerance (IGT) or diabetes mellitus (DM) because of 2-hPG.

CONCLUSION: Although impaired early-phase insulin secretion plays the more important role in the elevation of postchallenge glucose in IFG₁₀₀₋₁₀₉ subjects, both impaired early-phase insulin secretion and decreased insulin sensitivity are involved in the deterioration of fasting plasma glucose in Japanese. In addition, insulin secretory defect and decreased insulin sensitivity already have begun in subjects with IFG₁₀₀₋₁₀₉.

PCS-15-2

Incretin Secretion in Japanese with Normal, Impaired and Diabetic Glucose Tolerance: Deterioration of Glucose Homeostasis without Impaired Incretin Secretion

Yui Sakuramachi¹, Daisuke Yabe¹, Akira Kurose¹, Koin Watanabe¹, Masahiro Hishizawa¹, Takanori Hyo¹, Takeshi Kurose¹, Akihiro Hamasaki², Norio Harada², Yoshiyuki Hamamoto³, Nobuya Inagaki², Souchou Lee⁴, Tsutomu Hirano⁴, Jens J. Holst⁵, Carolyn F. Deacon⁵ and Yutaka Seino¹

¹Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, Japan; ²Department of Diabetes and Clinical Nutrition, Kyoto University Graduate School of Medicine, Japan; ³Center for Diabetes and Endocrinology, Kitano Hospital, Japan; ⁴Department of Diabetes, Metabolism and Endocrinology, Showa University School of Medicine, Japan; ⁵Department of Biomedical Sciences, University of Copenhagen, Denmark

OBJECTIVES: Involvement of incretin in pathogenesis of Japanese type 2 diabetes has not been fully investigated. Here, we examined levels of GIP and GLP-1 in Japanese with normal, impaired and diabetic glucose tolerance in response to oral glucose-tolerance and meal-tolerance tests (OGTT and MTT).

METHODS: Japanese healthy controls (Control; $n = 35$; age 50 ± 2 ; BMI 22.0 ± 5.4), subjects with impaired glucose tolerance (IGT; $n = 27$; age 56 ± 2 ; BMI 23.1 ± 1.0) and untreated patients with type 2 diabetes (T2DM; $n = 51$; age 59 ± 1 ; BMI 24.5 ± 0.5 ; duration 4.0 ± 0.8 years) were subjected to 75 g OGTT and MTT on two separate days.

RESULTS: Insulin was significantly reduced in T2DM as early as at 10 min in OGTT and at 20 min in MTT. Fasting and postprandial glucagon were elevated throughout OGTT and MTT in T2DM. Fasting levels of total and intact GLP-1 and GIP were similar among the three groups of glucose tolerance. In OGTT, total and intact GLP-1 reached peak 20–30 min after glucose ingestions. Total and intact GIP reached peak as early as 10 min after

glucose ingestions. In MTT, total and intact GLP-1 showed no distinct peaks. Total and intact GIP reached peak 30 min after meal ingestions in the three groups.

CONCLUSION: The current study finds reduced early phase insulin secretion, enhanced glucagon secretion, and little enhancement of meal-induced GLP-1 secretion in Japanese T2DM patients, but no significant differences in incretin secretion among the different groups of glucose tolerance, indicating that deterioration of glucose homeostasis can develop in the absence of impaired GIP or GLP-1 secretion.

PCS-15-3

Changes of EPA/AA Ratio in Patients with Type 2 Diabetes

Mayumi Negishi¹, Takashi Shirakawa¹, Kouji Kikkawa¹, Ayako Watanabe¹, Nobuyoshi Ishiyama¹, Nobuo Nagano¹, Masako Akuzawa¹, Masaki Takahashi¹, Yohnosuke Shimomura¹ and Isao Kobayashi²

¹Diabetes and Metabolic Disease Research Center, Hidaka Hospital, Japan; ²Gunma Paz College, Japan

OBJECTIVE: To investigate the relation between eicosapentaenoic acid (EPA)/arachidonic acid (AA) ratio and factors of patients with type 2 diabetes mellitus for a year.

METHODS: Ninety-six patients with type 2 diabetes were enrolled into the study. Age, duration of diabetes, body mass index (BMI), and waist circumference were measured. Fasting blood samples were used to determine blood glucose, HbA1c, serum insulin, serum lipids and EPA/AA ratio. Dietary education was performed to all individuals. After 12 months, same measurements and blood sampling were repeated. Patients were divided into two groups according to their EPA/AA ratio or changes of EPA/AA ratio for 12 months.

RESULTS: Serum EPA/AA ratio was positively associated to age. The low EPA/AA group (EPA/AA ratio < 0.5) was significantly younger than the high EPA/AA group (EPA/AA ratio ≥ 0.5). Serum triglyceride level was negatively associated to EPA/AA ratio. While baseline EPA/AA ratio had no association to duration of diabetes, Changes of EPA/AA ratio for 12 months (Δ EPA/AA) was negatively associated with type 2 diabetes. The decreased EPA/AA (negative Δ EPA/AA) group had significantly longer duration of diabetes than the increased EPA/AA (positive Δ EPA/AA) group. Blood glucose, HbA1c, serum insulin, BMI and waist circumference had no significant association to EPA/AA ratio and Δ EPA/AA.

CONCLUSION: EPA/AA ratio was lower in younger patients with type 2 diabetes. It was difficult to increase EPA/AA ratio of patients who had long duration of type 2 diabetes mellitus.

PCS-15-4

Characterization of Proinsulin-to-Insulin Ratio and its Significance in Diabetic Patients

Takako Mitsumatsu¹, Masao Yano², Sumie Okahata¹, Kentaro Sakamoto¹ and Teruo Shiba¹

¹Division of Diabetes and Metabolism, Toho University Ohashi Medical Center, Japan; ²Central Clinical Laboratories, Mitsui Memorial Hospital, Japan

AIMS: The proinsulin-to-insulin ratio (P/I ratio) is attracting growing attention for its potential usefulness as a clinical index of the effects of incretin-related agents. We investigated the clinical implications of the P/I ratio in Japanese patients with type 2 diabetes.

METHODS: A series of 31 NGTs, 32 IGTs and 26 DMs (89 subjects; 64.3 ± 9.4 years) was recruited based on the results of 75 g oral glucose tolerance tests performed in a health screening. Insulin, proinsulin (PI), and adiponectin were also measured.

RESULTS: The fasting P/I ratio was significantly higher in DM than in NGT and IGT (NGT, $0.093 \pm 0.002^{**}$; IGT, $0.106 \pm 0.020^{**}$; DM, 152 ± 0.004). The 1- and 2 h-P/I ratios were also significantly higher in DM than in IGT. Fasting and 1 h-P/I ratios were positively correlated with the insulinogenic index (I.I.) and HbA1c. Group by group, however, the fasting P/I ratio and I.I. were significantly correlated only in IGT, and the P/I ratio and HbA1c showed no correlations at all. Fasting and 1 h-P/I ratios were significantly related to adiponectin in DM, but not in the subjects altogether.

CONCLUSION: The P/I ratio reportedly correlates with the Insulin secretory function. Yet our analyses in each category indicate this not to be the case in DM so far. The P/I ratio reflects insulin resistance and glucose control in diabetic subjects, probably due to uncompensated insulin secretory response.

This should be kept in mind when elucidating the mechanism by which incretin improves the P/I ratio (** $P < 0.01$ v.s. DM).

PCS-15-5

A 20-Year Trend of Patients with Type 2 Diabetes at First Diagnosis in Urban Japan

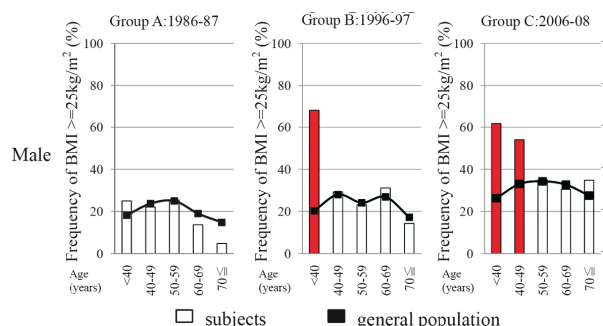
Akifumi Kushiyama, Yoko Yoshida, Tazu Tahara, Yukiko Onishi, Naoki Suzawa, Mayumi Yamamoto, Takako Kikuchi, Toshiko Takao and Shoji Kawazu
Division of Diabetes and Metabolism, The Institute for Adult Diseases, Asahi Life Foundation, Japan

We aimed to investigate trends of patients at first hospital visit for type 2 diabetes mellitus in the last 20 years.

Data from type 2 diabetic patients never treated until their first hospital visit were extracted for 1986–87 (group A), 1996–97 (group B) and 2006–08 (group C). Data on each patient's symptom, age, BMI, untreated duration and HbA1c were also collected.

As a result, obesity in younger patients increased with time in both males and females (Figure). Younger subjects in group C had worse glycemic control associated with obesity, while untreated duration was shorter because frequency of health check recommendation in visit motivation was getting larger. BMI >23 kg/m² was an independent risk factor for HbA1c $>8.4\%$ in group C, even after correction for gender, age, duration and symptom.

It is now revealed that glycemic control is getting worse at present in young, obese patients in urban Japan, although the untreated duration of type 2 diabetes has become shorter.



PCS-15-6

The Changes of Bone Mineral Density in Japanese Patients with Type 2 Diabetes

Toshihiro Nakamura¹, Kanta Fujimoto¹, Yoshiyuki Hamamoto¹, Sachiko Honjo¹, Yukiko Kawasaki¹, Atsuko Matsuoka¹, Kanako Mori¹, Hisato Tatsuoka¹, Yoshiharu Wada¹, Hiroki Ikeda¹, Jun Fujikawa² and Hiroyuki Koshiyama¹

¹Center for Diabetes & Endocrinology, Tazuke Kofukai Foundation Medical Research Institute Kitano Hospital, Osaka, Japan; ²Department of Clinical Laboratory, Tazuke Kofukai Foundation Medical Research Institute Kitano Hospital, Osaka, Japan

OBJECTIVE: There have been few studies about the long-term changes of the bone mineral density (BMD) in type 2 diabetes (T2DM). We have previously reported that BMD is positively associated with urinary C-peptide secretion or exogenous insulin dosage, and negatively with serum cholesterol level, and that BMD is higher in overt nephropathy, while not being influenced by statin use.

METHODS: To evaluate the changes of BMD in Japanese patients with T2DM, we examined the changes of lumbar 2nd–4th spines BMD of patients with T2DM between 2006 and 2011 in our institute. The observation period was 48 months (every 12 months follow-up). We also examined the BMD in healthy subjects.

RESULTS: The subjects included 481 patients with T2DM (mean age; 66 ± 10 years, mean HbA1c value; $6.82 \pm 1.10\%$, 252 men and 229 women,) and 1238 healthy subjects (58 ± 12 years, 645 men and 593 women). In the patients with T2DM, the baseline T-score was -0.32 ± 1.85 and Z-score was 1.15 ± 1.72 . T-score showed no significant changes from the baseline at all points. There was no correlation between the change of T-score and HbA1c value. In healthy subjects, baseline T-score was -0.24 ± 1.60 and Z-score was 0.81 ± 1.51 . T-score was significantly reduced from the baseline at 36 months (-0.45 ± 1.62 ; $P < 0.05$) and 48 months (-0.66 ± 1.77 ; $P = 0.001$).

CONCLUSION: The BMD shows no significant decrease during 48 months in Japanese subjects with T2DM, while the BMD in healthy subjects is decreased.

PCS-16-1

A Lower Rate of Nocturnal Hypoglycaemia in Elderly Patients with Insulin Degludec vs Insulin Glargine: A Meta-Analysis

Christopher Sorli¹, Mark Warren², Jacob Hyllested-Winge³, Thue Johansen⁴ and David Oyer⁵

¹Billings Clinic, Billings, MT, United States; ²Endocrine Research Physicians East PA, Greenville, PA, USA; ³Novo Nordisk PL, Tokyo, Japan; ⁴Novo Nordisk A/S, Soeborg, Denmark; ⁵Northwestern University, Feinberg School of Medicine, Chicago, IL, USA

OBJECTIVES: Insulin degludec (IDeg), a new basal insulin with an ultra-long and stable time-action profile, has demonstrated less hypoglycaemia than other current basal insulins. This analysis compared hypoglycaemia rates of IDeg vs insulin glargine (IGlar) in subjects aged ≥ 65 years.

METHODS: A pre-planned meta-analysis evaluating data from the IDeg 3a program using a negative binomial regression model was performed in a pooled population with type 1 (T1DM) or type 2 (T2DM) diabetes to compare hypoglycaemia rates with IDeg vs IGlar. Confirmed hypoglycaemia was defined as PG <56 mg/dL or requiring assistance; nocturnal hypoglycaemia occurred between 00:01 and 05:59. The analysis included patient level data from all open-label, randomized, treat-to-target, confirmatory 26- or 52-week trials with IDeg ($n = 2899$) vs IGlar ($n = 1431$) dosed once daily in T1DM (2 trials) and T2DM (5 trials). Here we present the pre-planned sub-analysis in subjects aged ≥ 65 years (IDeg, $n = 632$; IGlar, $n = 283$) using the same model.

RESULTS: Across trials, 21.1% of all subjects (6.4% of T1DM and 25.3% of T2DM) were aged ≥ 65 years. Confirmed hypoglycaemia rates were numerically lower in IDeg-treated elderly subjects (rate ratio (RR) IDeg/IGlar: 0.82 [95% CI: 0.66; 1.00]), approaching statistical significance. Nocturnal hypoglycaemia rates were significantly 35% lower with IDeg (RR: 0.65 [95% CI: 0.46; 0.93]).

CONCLUSION: Elderly subjects experienced a 35% lower rate of nocturnal hypoglycaemia with IDeg vs IGlar confirming what has been seen throughout the IDeg clinical program. The lower rate of hypoglycaemia associated with IDeg may be of particular benefit in the elderly population on insulin.

PCS-16-2

Pharmacodynamic Variability of Insulin Degludec is Consistently Lower Than Insulin Glargine Over 24 h at Steady State

Tim Heise¹, Lidia Hermanski¹, Leszek Nosek¹, Andre Feldmann¹, Soeren Rasmussen², Marcus Niemeier³ and Hanne Haahr²

¹Profil Institut fuer Stoffwechselforschung, Neuss, Germany; ²Novo Nordisk A/S, Soeborg, Denmark; ³Novo Nordisk A/S, Bagsvaerd, Denmark

OBJECTIVES: Insulin degludec (IDeg) has been shown to have a lower within-subject pharmacodynamic (PD) variability than insulin glargine (IGlar). Here we present a *post-hoc* analysis that aimed to investigate whether the lower within-subject variability of IDeg was consistent throughout 24 h.

METHODS: PD variability was investigated in 54 patients with type 1 diabetes who underwent a 24-h euglycemic glucose clamp on the 6th, 9th and 12th day of treatment with once-daily IDeg or IGlar (0.4 U/kg). The consistency of variability over time was analysed with successive log-transformed endpoints for the area under the glucose infusion rate curve (AUC_{GIR}) in 2-h intervals.

RESULTS: Overall, IDeg demonstrated lower within-subject variability for total AUC_{GIR,0-24 h} (CV 23 vs 72%, $P < 0.001$) for GIR_{max} (21 vs 53%, $P < 0.0001$) and for the fluctuation around the mean GIR value over 24 h (31 vs 62%, $P < 0.001$). The lower within-subject variability of IDeg was consistent over time (CVs of 33% for AUC_{GIR,0-2 h}, 33% for AUC_{GIR,10-12 h} and 33% for AUC_{GIR,22-24 h}) whereas the variability of IGlar was higher and increased substantially after 8-h post-dosing (CVs of 60% for AUC_{GIR,0-2 h}, 135% for AUC_{GIR,10-12 h} and 115% for AUC_{GIR,22-24 h}).

CONCLUSION: IDeg demonstrated consistently low day-to-day variability, which is due to the slow release of IDeg monomers from soluble multi-hexamers that form after sc injection. IDeg's consistently low day-to-day variability should facilitate insulin titration to lower fasting plasma glucose targets than achievable with IGlar, and contribute to the lower risk of hypoglycaemia observed with IDeg in clinical trials.

PCS-16-3

Insulin Degludec: Two-Fold Longer Half-Life and a More Consistent Pharmacokinetic Profile Than Insulin Glargine

Hanne Haahr¹, Ulrike Hoefelmann², Leszek Nosek², Susanne Gammelgaard Boettcher³, Charlotte Granhall¹, Marcus Niemeyer⁴ and Tim Heise²
¹Novo Nordisk A/S, Soeborg, Denmark; ²Profil Institut fuer Stoffwechselforschung, Neuss, Germany; ³Novo Nordisk A/S, Aalborg, Denmark; ⁴Novo Nordisk A/S, Bagsvaerd, Denmark

OBJECTIVE: We describe the pharmacokinetic properties of insulin degludec (IDeg), a new-generation basal insulin with an ultra-long, flat action profile, in comparison to those of insulin glargine (IGlar) at steady-state in patients with T1DM ($n = 66$).

METHODS: IDeg and IGlar were given once-daily for 8 days in a crossover trial, at 0.4, 0.6 or 0.8 U/kg with 7–21 days wash-out. Pharmacokinetic samples were taken throughout each treatment period and for 120 h after the last dose. A 42 h euglycaemic glucose clamp was performed on Day 8.

RESULTS: IDeg showed stable serum concentrations at steady-state with minimal fluctuations and increasing proportionally with increasing dose. Serum exposure to IDeg was equally distributed between the first and second 12-h post-dosing whereas IGlar showed a higher exposure during the first 12 h. The cumulated AUC below and above the average glucose infusion rate was considerably lower for all doses of IDeg than with IGlar. IDeg was detectable in serum for at least 120 h following the final dose, whereas, for most subjects, IGlar fell below the lower limit of quantification after 36–48 h post dosing. Mean terminal half-life of IDeg was twice that of IGlar (25.4 vs 12.5 h).

CONCLUSION: IDeg has a half-life of more than 25 h, twice as long as that for IGlar. Pharmacokinetic exposure is more consistent and evenly distributed across a 24-h dosing interval for IDeg than for IGlar. Consequently the glucose-lowering effect is more consistent and evenly distributed across a 24-h dosing interval for IDeg than for IGlar.

PCS-16-4

Safety Analysis and Clinical Effect of Glargine Combining Acarbose in Treating Aged Patients with Type 2 Diabetes Mellitus

Shuping Li
 Huazhong Hospital, China

OBJECTIVE: To research clinical effect and safety analysis of glargine combining acarbose treating aged patients with type 2 diabetes mellitus.

METHODS: Eighty-six aged patients of type 2 diabetes mellitus were selected randomly and divided into observation group and control group, each with 43 patients, all around 82–98 years hospitalized from 2010.1 to 2011.12. By way of diabetic diet and exercise therapy, the control group was treated with Novolin 30R, while observation group, using glargine plus acarbose, both groups' FPG, 2 hPBG, HbA1C plus adverse reactions were recorded, and maintained for 16 weeks' observation.

RESULTS: After treatment, both groups' FPG, or 2 hPBG decreased remarkably ($P < 0.05$); The rate of HbA1C targeting higher in observation group than in control group ($P < 0.05$); Observation group presented low rate of hypoglycemia against control group.

CONCLUSION: It provided better efficacy and safety by using glargine combining acarbose in treating aged patients with type 2 diabetes mellitus.

PCS-16-5

Comparison of Bolus First and Basal First Insulin Regimens: Multifaceted Effects on Patients with Type 2 Diabetes

Takehiro Kanamori, Yumie Takeshita, Yuki Kita, Kenichiro Kato, Hirofumi Misu, Shuichi Kaneko and Toshinari Takamura
 Department of Disease Control and Homeostasis, Kanazawa University Graduate School of Medical Sciences, Japan

OBJECTIVE: Glucose fluctuation is an important target for glycemic control because it may aggravate atherosclerosis through oxidative stress, sympatho-ovagal imbalance and endothelial dysfunction. Several trials reported that either prandial insulin initiation (Bolus First) or basal insulin initiation (Basal First) have equal HbA1c lowering efficacy, but it is not well known how each insulin regimens affect glucose fluctuation and the risks for atherosclerosis.

METHODS: A total of 38 type 2 diabetic patients with poor HbA1c levels ($>7.4\%$) were randomly assigned either to Bolus First (insulin aspart three

times daily) or Basal First (insulin detemir at bedtime) for 2 weeks. The primary outcome was the M value reflecting glucose fluctuation. Other cardiovascular risks were also studied.

RESULTS: M values were not significantly different between each group while mean glucose level was lower in Bolus First than in Basal First ($P = 0.020$). Daily insulin doses were higher in Bolus First ($P < 0.001$). The changes in oxidative stress level, urinary 8-hydroxydeoxyguanosine, were positively correlated to daily insulin doses ($r = 0.588$; $P = 0.010$). Body mass index was reduced in Basal First ($P < 0.001$). Basal metabolic rate didn't change in both groups. The low frequency/high frequency ratio indicating sympatho-vagal balance decreased at afternoon but not night and early morning in Bolus First.

CONCLUSIONS: Bolus First achieved better glycemic control than Basal First. On the other hand, Bolus First consequently required more doses of insulin, and insulin doses had a higher association with oxidative stress in patients with type 2 diabetes.

PCS-16-6

Similar Pharmacokinetic and Pharmacodynamic Properties of Insulin Degludec in Japanese and Caucasian Subjects with T1DM

Hanne Haahr¹, Ippei Ikushima², Koichi Hirao³, Fumiaki Kiyomi⁴ and Tim Heise⁵
¹Novo Nordisk A/S, Soeborg, Denmark; ²LTA Clinical Pharmacology Center, Sumida Hospital, Tokyo, Japan; ³Internal Medicine, H.E.C Science Clinic, Yokohama, Japan; ⁴Novo Nordisk PL, Tokyo, Japan; ⁵Profil Institut fuer Stoffwechselforschung, Neuss, Germany

OBJECTIVES: The pharmacokinetic and pharmacodynamic properties of insulin degludec (IDeg), a new generation, ultra-long-acting basal insulin, were compared between Japanese and Caucasian subjects with T1DM as investigated at steady-state in two separate randomised, single-centre, double-blind, multiple-dose trials.

METHODS: In the Japanese study, 21 subjects underwent a 26-h euglycaemic clamp after the sixth dose of 0.4 U/kg IDeg. In the Caucasian study, a 42-h euglycaemic clamp was performed after the eighth dose of 0.4, 0.6 or 0.8 U/kg IDeg in 21, 21 and 22 subjects, respectively.

RESULTS: The glucose-lowering effect of IDeg extended beyond 26 h for all Japanese subjects with T1DM and no increase from clamp target was observed in individual blood glucose for any of the Japanese subjects at 26 h. Total exposure was similar in Japanese and Caucasian subjects [$AUC_{IDeg, \tau}$, SS at 0.4 U/kg: geometric mean (CV) 81270 pmol $\cdot$ h/L (28%) and 82612 pmol $\cdot$ h/L (28%), respectively]. For both populations a similarly high serum IDeg concentration was demonstrated 42 h after administration with IDeg detectable in serum for at least 120 h. As a clear relationship between exposure and glucose-lowering effect has been demonstrated for IDeg, duration of exposure predicts also duration of action.

CONCLUSION: These results confirm that the ultra-long pharmacokinetic and pharmacodynamic properties of IDeg observed in Caucasian subjects are preserved in Japanese subjects. Therefore, duration of action of IDeg in Japanese subjects is expected to be within the same range as in Caucasian subjects with T1DM, where it was observed to be >42 h.

PCS-16-7

Rapid-Acting Insulin Analog Rather Than Short-Acting Insulin, can Decrease Wound Infection Risk with Controlling Blood Glucose Drifting in the Surgical Diabetic Patients

Hiroki Ueno¹, Anna Tamai¹, Yoko Yoshida¹, Yosuke Yakushiji¹, Yoshiko Otsuka¹, Yuki Inokuchi¹, Megumi Okada¹, Nagaaki Tanaka², Keiko Yamagami¹, Mariko Fukumoto¹, Isao Kawasaki¹, Yosikazu Hiura² and Masayuki Hosoi¹
¹Department of Metabolism and Endocrinology, Osaka City General Hospital, Japan; ²Department of Metabolism and Endocrinology Juso City Hospital

Hyperglycemia is a risk for infection after surgery. In this study, we randomized the surgical diabetic patients to the glucose control using rapid-acting insulin analog (rapid-group) or using short-acting insulin (short-group), and compared with glucose control and risk of wound infection.

METHOD: In the gastroentero-surgical ward, 246 diabetic patients underwent operation were enrolled consequently, and randomly assigned to the rapid-group ($n = 120$) or the short-group ($n = 123$). We designated to aim for glucose level 150–199 mg/dL. Estimation of glucose control was the average and standard deviation (SD) of blood glucose level and hypoglycemia rate. Glucose variability was expressed as the M value ($= [10 \times \text{LogBS}/100]^3$), a

quantitative index of diurnal glucose fluctuation. Infection control team investigated into occurrence of postoperative wound infection.

RESULTS: Mean HbA1c at the entry was $7.3 \pm 1.2\%$ and 53 patients suffered postoperative wound infection, and infections rate in using short-group was 32.1%, vs 15.1% for using rapid-group (hazard ratio with short-group, 2.73; 95% confidence interval (CI), 1.43–5.19; $P < 0.002$). HbA1c was no difference between short-group and rapid-group. However, average and SD for blood glucose level and hypoglycemic rate were significantly lower in rapid-group than short-group (181.3 ± 31.5 vs 194.9 ± 26.2 $P = 0.03$; 49.8 ± 19.3 vs 56.2 ± 22.5 $P = 0.05$; 0.82 ± 1.4 vs $1.64 \pm 2.6\%$, $P = 0.04$), and the M value showed low level in a rapid-group in postoperative days 3–5 while the diet quantity was unstable. Length of stay in hospital is shorter in rapid-group than short-group ($P < 0.001$).

CONCLUSION: In the perioperative glycemic control for the diabetic patients, rapid-acting insulin analog can control blood glucose drifting more than short-acting insulin, and decrease postoperative wound infection risk.

PCS-16-8

Initiation of Basal Insulin in Chinese Patients with T2DM Inadequately Controlled by OADs: FINE Asia Registry Analysis

Linong Ji¹, Karim Admane², Jay Lin³, Edward Wang⁴ and Jian Wang⁵

¹Department of Endocrinology and Metabolism, Peking University People's Hospital, China; ²Sanofi, Paris, France; ³Novos Health, Flemington, NJ, USA; ⁴Sanofi, Bridgewater, NJ, USA; ⁵Jinling Hospital, Nanjing, Jiangsu, China

OBJECTIVE: The First Basal Insulin Evaluation (FINE) Asia study evaluated basal insulin initiation in Asian patients with type 2 diabetes mellitus (T2DM) inadequately controlled by oral antidiabetic drugs (OADs). This *post-hoc* analysis evaluated overall efficacy and safety of basal insulin in Chinese patients. **METHODS:** Basal insulin was initiated with or without concomitant OADs. Efficacy and safety data were collected at inclusion, Month 3, and Month 6. Primary efficacy endpoint was change in HbA1c from baseline to Month 6. Secondary endpoints included change in fasting blood glucose (FBG), responses rates (HbA1c and FBG), insulin dose and hypoglycemic events.

RESULTS: There were 491 patients included (43.4% female). Mean (SD) age, weight, and body mass index (BMI) were 56.0 (12.0) years, 69.7 (12.3) kg, and $25.5 (5.4) \text{ kg/m}^2$, respectively. Duration of diabetes and OAD use was 6.3 (5.2) and 5.8 (5.2) years, respectively. All patients were on OADs. Overall, 61.9% of patients used glargine and 37.5% NPH insulin. At 6 months, HbA1c decreased from 9.4 (1.6) to 6.8 (0.9)% ($P < 0.001$) and FBG from 10.3 (2.6) to 6.3 (1.0) mmol/L ($P < 0.001$). The proportion of patients achieving HbA1c $< 7\%$ and FBG < 6.1 mmol/L was 71.5% and 49.9%, respectively. Insulin dose increased from 12.3 (5.8) to 13.7 (6.2) U. The prevalence of severe hypoglycemia was 0.4%.

CONCLUSIONS: Addition of basal insulin to OADs in Chinese patients with T2DM significantly improved glycemic control, with a low incidence of hypoglycemia. Basal insulin is a safe and effective option in these patients.

This study was supported by Sanofi.

PCS-17-1

Efficacy and Safety of Starting Insulin Aspart Premix Therapy from Different Oral Agents in Routine Clinical Practice

Pradana Soewondo¹, Zafir Ahmed Latif², Siddharth Shah³, Jihad Haddad⁴, Vinay Prusty⁵ and Yuxiu Li⁶

¹Department of Internal Medicine, University of Indonesia, Jakarta, Indonesia; ²BIRDEM, Dhaka, Bangladesh; ³Bhatia Hospital, Mumbai, India; ⁴Division of Endocrinology, Prince Hamazeh Hospital, Amman, Jordan; ⁵Novo Nordisk International Operations A/S, Zurich, Switzerland; ⁶Peking Union Medical College Hospital, Beijing, China

OBJECTIVE: To examine the effect of prior oral glucose-lowering drug (OGLD) therapy following 24 weeks of treatment with biphasic insulin aspart 30; subgroup analysis of data from insulin-naïve people with type 2 diabetes (T2DM) participating in the A1chieve study.

METHODS: A1chieve was non-interventional study evaluating the safety and clinical effectiveness of insulin analogues in people with T2DM ($n = 66\ 726$) in routine clinical care in 28 countries across four continents.

RESULTS: Insulin dose by 24 weeks did not differ consistently by prior OGLD group (Table). Marked improvement in glycaemic control (overall HbA1c -2.1%) was found with all prior OGLDs and combinations thereof. This was also true for FPG and PPPG. Change in reported severe hypoglycaemia was also similar between prior OGLDs, but change of overall hypoglycaemia erratic and inconsistent regionally, though with no change globally. There was

Table: Clinical outcome for seven OGLD sub-groups of insulin-naïve people 24 weeks of biphasic insulin aspart.

		Pre-study therapy						
Mean (SD)		OGLD only (n = 23 342)	Metformin only (n = 2880)	SU only (n = 1765)	Metformin + SU (n = 9733)	Metformin + TZD (n = 748)	Metformin + SU + TZD (n = 2332)	Metformin + SU + glucosidase inhibitor (n = 708)
Dose (U/kg/day)	24 weeks	0.47 (0.21)	0.43 (0.20)	0.46 (0.18)	0.46 (0.21)	0.45 (0.16)	0.55 (0.27)	0.48 (0.21)
HbA1c (%)	Change	2.1 (1.6)*	-2.1 (1.7)*	-1.8 (1.7)*	-2.0 (1.5)*	-2.4 (1.7)*	-2.0 (1.3)*	-2.0 (1.4)*
FPG (mmol/l)	Change	-4.0 (3.2)*	-3.4 (3.0)*	-4.0 (3.4)*	-4.0 (3.1)*	-4.8 (2.8)*	-4.1 (3.1)*	-4.3 (3.3)*
PPG (mmol/l) (breakfast)	Change	-5.8 (4.1)*	-4.8 (3.8)*	-5.4 (4.2)*	-6.0 (4.0)*	-7.2 (3.7)*	-6.5 (4.3)*	-7.0 (4.3)*
Weight (kg)	Change	0.1 (3.2)	0.1 (3.1)	0.6 (3.0)	0.1 (3.0)	-0.2 (2.6)	0.1 (3.2)	0.6 (3.1)
Hypoglycaemia (events/person-year)								
All	Baseline	1.00	0.74	0.74	0.93	1.09	0.79	1.06
	Final visit	1.01	0.57	1.01	0.99	0.52*	1.23**	1.76
Major hypoglycaemia (events/patient year)	Baseline	0.10	0.04	0.13	0.09	0.10	0.10	0.09
	Final visit	0.00*	0.00	0.01	0.00*	0.00	0.00*	0.00

* $p < 0.001$ ** $p < 0.005$

no clinically significant change in body weight when starting aspart premix in any group (Table).

CONCLUSIONS: Starting insulin therapy with biphasic insulin aspart can be clinically successful independent of prior OGLD.

PCS-17-2

Basal Replacement with Glargine in Insulin-Treated Patients with Type 2 Diabetes in a Real-Life Setting: ALOHA Study Subanalysis

Takashi Kadowaki¹, Tetsuya Ohtani² and Masato Odawara³

¹Department of Diabetes and Metabolic Diseases, Graduate School of Medicine, The University of Tokyo, Japan; ²Sanofi-aventis K.K., Japan; ³Department of Diabetology, Metabolism, and Endocrinology, Tokyo Medical University, Japan

OBJECTIVE: To demonstrate the effectiveness and safety regarding the replacement of basal component with glargine, we analyzed data from 439 poorly-controlled patients who treated by insulin other than glargine and oral antidiabetic agents, a subsample of the Add-on Lantus to Oral Hypoglycemic Agents (ALOHA) study that is a observational, non-interventional, 24-week follow-up study.

METHODS: Change in hemoglobin A1c (A1C), fasting plasma glucose (FPG) and weight were evaluated at 24 weeks or at glargine discontinuation. Information on dose and hypoglycemic episodes was obtained from medical records. In addition to overall analysis, a subgroup analysis was performed regarding pre-study basal components (Intermediate, Low-Mix, and Long-acting).

RESULTS: A1C and FPG improved at endpoint ($-0.76 \pm 1.21\%$ and $-36.3 \pm 77.1 \text{ mg/dL}$, respectively; $P < 0.001$ for both). A1C significantly decreased in patients replaced from three groups ($P < 0.001$ for all). FPG reductions in Intermediate and Long-acting groups were statistically significant ($P < 0.01$ for both), though FPG measurement was derived from about a one-third subsample. While, weight change was minimal ($0.5 \pm 2.4 \text{ kg}$; $P < 0.001$) and hypoglycemic cases and episodes were limited (4 non-severe episodes from 1 patient in Long-acting group). Mean daily dose decreased from $20.0 \pm 12.4 \text{ U/day}$ in pre-study to $17.6 \pm 11.1 \text{ U/day}$ at endpoint ($P < 0.001$). Proportion of patients with once-daily injection increased from 53.5% to 91.6%.

CONCLUSION: Our results suggest that the replacement of the basal component in insulin regimens with glargine in patients with HbA1c $> 7.9\%$ can attain a better glycemic control and a reduced time of injection without a substantial weight gain or an elevated hypoglycemic risk in poorly-controlled patients with type 2 diabetes.

PCS-17-3

Glycemic Control and Hypoglycemia Prevalence in Chinese T2DM Patients Treated with Insulin Glargine or NPH: FINE Asia

Jian Wang¹, Karim Admane², Edward Wang³, Jay Lin⁴ and Linong Ji⁵

¹Department of Endocrinology, Jinling Hospital, China; ²Sanofi, Paris, France; ³Sanofi, Bridgewater, NJ, USA; ⁴Novos Health, Flemington, NJ, USA; ⁵Peking University, Beijing, China

OBJECTIVE: This *post-hoc* analysis evaluated the safety and efficacy of glargine vs NPH in Chinese patients with type 2 diabetes mellitus (T2DM) from the First Basal Insulin Evaluation (FINE) Asia registry.

METHODS: Efficacy and safety data were collected at 3 and 6 months. The primary efficacy measure was change in HbA1c from baseline at Month 6. Fasting blood glucose (FBG) was also recorded. The primary safety endpoint was the incidence of severe hypoglycemia at 6 months.

RESULTS: There were 505 patients (44% female) included in the study; 304 patients treated with glargine and 201 with NPH. At 6 months, mean $\pm$ SD HbA_{1c} was significantly reduced with both glargine ($9.4 \pm 1.5\%$ to $6.7 \pm 0.9\%$) and NPH ($9.3 \pm 1.6\%$ to $7.0 \pm 1.0\%$); change in HbA_{1c} was $-2.7 \pm 1.5\%$ with glargine and $-2.3 \pm 1.7\%$ with NPH ($P < 0.01$). FBG was also reduced with both glargine (9.9 ± 2.5 – 6.2 ± 0.9 mmol/L) and NPH (10.9 ± 2.8 – 6.7 ± 1.5 mmol/L). More patients in the glargine group achieved HbA_{1c} $< 7\%$ (75.0% vs 64.2%; $P < 0.01$) or FBG < 6.1 mmol/L (57.2% vs 35.8%; $P < 0.01$) compared with the NPH group. The incidence of severe hypoglycemia was lower with glargine than NPH (0.33% vs 2.49%; $P < 0.03$).

CONCLUSION: In Chinese patients with T2DM, initiation of insulin glargine vs NPH was associated with a greater proportion of patients achieving HbA_{1c} and FBG targets, as well as with a lower incidence of severe hypoglycemia. Randomized controlled trials are warranted to confirm these findings.

This study was supported by Sanofi.

PCS-17-4

Glycemic Control and Hypoglycemia Prevalence by Age in Japanese Subjects with Type 2 Diabetes: ALOHA Study Subanalysis

Tetsuya Ohtani¹, Takashi Kadowaki², Karim Admane³, Jay Lin⁴, Edward Wang⁵ and Masato Odawara⁶

¹Sanofi-aventis K.K., Japan; ²Department of Diabetes & Metabolic Diseases, Graduate School of Medicine, University of Tokyo, Tokyo, Japan; ³Sanofi, Paris, France; ⁴NovoSys Health, Flemington, NJ, USA; ⁵Sanofi, Bridgewater, NJ, USA; ⁶Department of Diabetology, Metabolism & Endocrinology, Tokyo Medical University, Tokyo, Japan

OBJECTIVE: The ALOHA (Add-on Lantus to Oral Hypoglycemic Agents) study assessed the effect of insulin glargine plus oral antidiabetic drugs (OADs) in Japanese patients with type 2 diabetes (T2DM).

METHODS: Patients taking insulin glargine plus OADs were observed for 24 weeks in a real-life setting. Demographics, HbA_{1c}, fasting plasma glucose (FPG), postprandial plasma glucose (PPG), and hypoglycemia were analyzed according to age (< 65 , ≥ 65 years).

RESULTS: A total of 3946 patients (< 65 years, $n = 2133$; ≥ 65 years, $n = 1813$) comprised the study population. At baseline, HbA_{1c} was significantly lower in the ≥ 65 -years group; FPG and PPG were similar. After 24 weeks, mean HbA_{1c}, FPG, and PPG values were significantly reduced ($P < 0.001$) and change from baseline was similar in both groups. More elderly patients achieved HbA_{1c} $< 7\%$ vs the younger group (19.1% vs 14.3%, $P < 0.001$). Mean daily dose of insulin glargine was significantly lower in the ≥ 65 -years vs the < 65 -years group (8.8 vs 9.7 U; $P < 0.001$). Incidence of severe hypoglycemia was very low and similar between groups (0.2% vs 0.05%).

CONCLUSION: In Japanese patients with T2DM who initiated insulin glargine after failing to maintain glycemic control with OADs, significantly more elderly than younger patients achieved HbA_{1c} $< 7\%$. Given the suboptimal study-end FPG levels and low incidence of hypoglycemia, more aggressive insulin titration may enable more patients to safely reach target; this needs confirmation in future trials.

This study was supported by Sanofi.

PCS-17-5

Use of Insulin Detemir is Associated with Improved Glycaemic Control without Weight Gain – Findings from A₁chieve

Guillermo Gonzalez-Galvez¹, Sei Hyun Baik², Jihad Haddad³, Zafir Ahmed Latif⁴, Jian-Wen Chen⁵ and Alexey Zilov⁶

¹Instituto Jalisciense de Investigación en Diabetes y Obesidad SC, Guadalajara, Mexico; ²Department of Endocrinology & Metabolism, Korea University Guro Hospital, Seoul, Korea; ³Division of Endocrinology, Prince Hamazeh Hospital, Amman, Jordan; ⁴BIRDEM, Dhaka, Bangladesh; ⁵Novo Nordisk International Operations A/S, Zurich, Switzerland; ⁶Department of Endocrinology, First Moscow State Medical University, Moscow, Russian Federation

OBJECTIVES: Weight gain is a common problem with insulin therapy and can present a barrier for people with type 2 diabetes (T2DM) when starting insulin. We investigated weight gain when starting insulin detemir, in a large cohort ($n = 12\ 078$) of insulin-naïve people with T2DM.

METHODS: A₁chieve was a non-interventional study evaluating the safety and effectiveness of insulin analogues in people with T2DM ($n = 66\ 726$) in routine clinical care in 28 countries. This is a subgroup analysis.

RESULTS: Detemir insulin dose at 24 weeks was 26.7 (15.1) U/day. At baseline, HbA_{1c} was poor but improved markedly by week 24 (overall -2.1%),

as did both fasting plasma glucose (-4.2 mmol/L) and notably postprandial plasma glucose (-5.5 mmol/L; Table). Despite this, body weight did not show clinically significant change (-0.3 kg), nor did hypoglycaemia (Table).

Table. Glycaemic control and body weight following 24 weeks' treatment with insulin detemir by region

	All regions	China	South Asia	East Asia
n	12 078	88	2608	3195
HbA _{1c} (%)				
Baseline	9.5 (1.6)	8.5 (1.8)	9.4 (1.4)	9.6 (1.9)
Change	-2.1 (1.6)*	-1.6 (1.8)*	-2.1 (1.5)*	-1.8 (1.9)*
FPG (mmol/L)				
Baseline	11.2 (3.2)	9.5 (3.7)	11.1 (2.8)	11.5 (4.0)
Change	-4.2 (3.2)*	-3.1 (3.8)*	-3.9 (2.4)*	-4.4 (4.2)*
PPPG (breakfast) (mmol/L)				
Baseline	15.0 (4.2)	13.3 (2.8)	16.2 (3.4)	15.2 (5.0)
Change	-5.5 (4.2)*	-4.9 (3.2)*	-5.6 (3.6)*	-5.4 (5.5)*
Hypoglycaemia (overall), (events/person-year [% of individuals with event])				
Baseline	1.14 (4.1)	0.3 (1.1)	1.02 (6.4)	1.14 (3.7)
Week 24	1.33 (4.4)†	0.23 (1.8)†	0.10 (0.6)*	0.97 (3.7)†
Body weight (kg)				
Baseline	76.5 (16.3)	71.7 (11.1)	70.2 (10.9)	64.7 (12.3)
Change	-0.3 (4.0)*	-0.6 (4.1)†	-0.5 (3.5)*	0.5 (3.8)*

Mean (SD) or as stated; * $p < 0.001$; †NS; FPG, fasting plasma glucose; NS, not significant; OGLD, oral glucose-lowering drug; PPPG, postprandial plasma glucose

CONCLUSION: These results confirm the effectiveness and safety of starting insulin therapy with detemir and support findings from other studies of weight neutrality or weight loss among people using this insulin.

PCS-17-6

Starting Insulin Aspart is Associated with Improved Quality of Life Regardless of Age – Findings from the A₁chieve Study

Nabil K. El Naggar¹, Philip Home², Rachid Malek³, Zafir Ahmed Latif⁴, Ole Bech⁵ and Su-Yen Goh⁶

¹Internal Medicine, Hai Aljamea Hospital, Jeddah, Saudi Arabia; ²Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK; ³Internal Medicine, CHU Setif, Setif, Algeria; ⁴BIRDEM, Dhaka, Bangladesh; ⁵Novo Nordisk Pharmaceuticals, Beijing, China; ⁶Singapore General Hospital, Singapore

OBJECTIVES: Management of type 2 diabetes (T2DM) becomes more complex in older patients, due to increased comorbidities and risk of

Table. Glycemic control, body weight and HRQoL following 24 weeks' treatment with insulin aspart.

	≤ 65 years	> 65 years
n	2249	420
Insulin dose (U/kg/day)		
Week 0	0.42 (0.19)	0.42 (0.19)
Week 24	0.41 (0.19)	0.45 (0.23)
Health-related quality of life (VAS 0-100)		
Baseline	62.3 (17.7)	64.2 (16.6)
Change	16.7 (17.7)*	12.1 (16.7)*
HbA _{1c} (%)		
Baseline	9.6 (1.8)	9.5 (1.9)
Change	-2.4 (1.9)*	-2.0 (1.8)*
FPG (mmol/L) [mg/dl]		
Baseline	11.6 (4.0) [209 (71)]	10.5 (4.1) [190 (73)]
Change	-4.0 (3.3)* [-72 (60)]*	-3.0 (3.2)* [-53 (58)]*
PPPG (mmol/L) [mg/dl]		
Baseline	16.7 (4.8) [301 (87)]	15.2 (5.2) [273 (94)]
Change	-6.0 (4.2)* [-108 (76)]*	-4.8 (4.3)* [-87 (78)]*
Hypoglycemia (events/person-year [% of individuals with events])		
All events		
Baseline	1.54 (6.0)	1.95 (5.5)
Week 24	0.65 (2.5)*	2.11 (5.7)
Major		
Baseline	0.12 (0.8)	0.22 (1.2)
Week 24	0.0 (0.0)*	0.0 (0.0)†
Body weight (kg)		
Baseline	68.6 (11.9)	65.7 (11.4)
Change	0.2 (2.7)	0.3 (3.1)
(p = 0.018)		

Mean (SD) or as stated; * $p < 0.001$; †NS; FPG, fasting plasma glucose; PPPG, postprandial plasma glucose; VAS, visual analog scale

hypoglycaemia. Here we investigate the effectiveness of meal-time(s)-only insulin aspart (aspart), and its impact on quality of life (HRQoL) in insulin-naive younger (≤ 65 years) and older (> 65 years) adults.

METHODS: A₁chieve was a non-interventional study evaluating the safety and efficacy of insulin analogues in T2DM ($n = 66\ 726$) in routine clinical care in 28 countries.

RESULTS: Insulin dose at 24 weeks was similar by age group, while HbA_{1c} improved markedly, as did fasting and postprandial plasma glucose (Table). In both groups, HRQoL also improved to a clinically useful extent (Table). Hypoglycaemia rate was numerically higher in the older age group, but the overall rate remained very low (Table). Body weight was not changed to a clinically significant extent.

CONCLUSION: Introducing insulin aspart in older and younger adults with T2DM was effective and well-tolerated.

PCS-17-7

Recovery of Insulin Secretion After Short-Term Intensive Insulin Therapy

Takahiro Suzuki, Kenji Takahashi, Daisuke Fujiwara, Yuko Wada, Shiho Nakai, Masakazu Shii, Yukako Nakashima, Sato Takekawa, Atsushi Yoshida and Takashi Matsuoka

Department of Diabetic Medicine, Kurashiki Central Hospital, Japan

OBJECTIVE: To elucidate the change of insulin secretion after near-normalization with intensive insulin therapy (IIT), we analyzed serum C-peptide (CPR) concentrations before and after 2-week IIT for hyperglycemic non-obese patients with type 2 diabetes (T2DM) under standard meal during the hospital stay.

METHODS: From our diabetes database 2008–2010, of the 569 patients with T2DM, 291 whose BMI was under 25 were subjected to the study, in whom disease duration was 12.4 ± 10.1 years, HbA_{1c} was $10.3 \pm 1.9\%$ (mean $\pm$ SD). Patients were near-normalized with IIT over 2 weeks, and serum CPR was sampled before starting and after IIT. CPR indices provided for analyses were fasting CPR (FCPR), CPR 2-h after breakfast (CPR2h), CPI, and SUIT, and CPR increment by glucagon loading was added to the analysis.

RESULTS: According to the treatment protocol, patients were finally classified into 3 therapy groups: oral hypoglycemic agent (OHA) alone ($n = 103$), basal-supported oral therapy (BOT; $n = 56$), and multiple daily insulin injection (MDI; $n = 132$). In comparison of baseline CPR levels, many of the levels significantly lower in MDI group compared to that of OHA or BOT group ($P < 0.05$). In OHA group, each CPR level after IIT except FCPR was higher ($P < 0.01$), and in BOT, only SUIT was higher ($P < 0.01$) compared with the baseline, respectively. No elevation of any CPR indices after IIT was seen in MDI group.

CONCLUSIONS: In non-obese T2DM, recovery of insulin secretion after short-term IIT was dependent on baseline CPR levels and mode of the therapy of diabetes defined after IIT.

PCS-17-8

Glucose-Lowering Effect of Insulin Degludec is Independent of Subcutaneous Injection Region

Leszek Nosek¹, Hans-Veit Coester¹, Henrik Thomsen², Carsten Roepstorff³, Hanne Haahr³, Marcus Niemeyer⁴ and Tim Heise¹

¹Profil Institut fuer Stoffwechselforschung, Neuss, Germany; ²Novo Nordisk A/S, Aalborg, Denmark; ³Novo Nordisk A/S, Søborg, Denmark; ⁴Novo Nordisk A/S, Bagsvaerd, Denmark

OBJECTIVES: This randomized, open-label, cross-over trial evaluated the pharmacokinetic and pharmacodynamic properties of insulin degludec (IDeg), a new ultra-long-acting basal insulin, as a function of administration region.

METHODS: Twenty healthy subjects (17 males/3 females; mean age: 37 years, BMI: 24.1 kg/m^2) received single s.c. doses of IDeg (0.4 U/kg) in the thigh, the deltoid and the abdomen. Blood samples for pharmacokinetic assessment were taken up to 120 h after each injection, and the pharmacodynamic response was evaluated during a 24-h euglycemic glucose clamp (Biostat; target blood glucose: 81 mg/dL).

RESULTS: As observed with other insulin preparations, total exposure of IDeg ($\text{AUC}_{\text{IDeg},0-120\text{ h,SD}}$) was slightly greater (by 6–7%) after s.c. injection in the deltoid or the abdomen compared to the thigh (deltoid/thigh and abdomen/thigh mean ratios [95% confidence interval]: 1.06 [1.01; 1.10] and 1.07 [1.03; 1.11], respectively). There was no difference between the deltoid and abdomen

(abdomen/deltoid mean ratio [95% confidence interval]: 1.01 [0.96; 1.06]). The glucose infusion rate (GIR) profiles were similar for the three s.c. injection regions: mean $\text{AUC}_{\text{GIR},0-24\text{ h,SD}}$ (coefficient of variation %) was 2572 (38), 2960 (43), and 2833 (42) mg/kg for thigh, deltoid and abdomen, respectively; mean $\text{GIR}_{\text{max,SD}}$ was 2.7 (32), 3.0 (42), and 3.0 (37) mg/kg/min, respectively. The glucose-lowering effect extended beyond 24 h in all subjects for all three s.c. injection regions.

CONCLUSION: IDeg can be administered s.c. in the thigh, the deltoid or the abdomen with similar glucose-lowering effect from a clinical perspective.

PCS-18-1

Changing from a Glargine-Based Insulin Regimen to Biphasic Insulin Aspart 30 in People with Type 2 Diabetes

Zanariah Hussein¹, Mohammad Khamseh², Wenying Yang³, Siddharth Shah⁴, Jian-Wen Chen⁵ and Leon Litwak⁶

¹Medical Department, Hospital Putrajaya, Putrajaya, Malaysia; ²Institute of

Endocrinology and Metabolism, Tehran University of Medical Sciences, Tehran, Iran;

³China-Japan Friendship Hospital, Beijing, China; ⁴Bhatia Hospital, Mumbai, India;

⁵Novo Nordisk International Operations A/S, Zurich, Switzerland; ⁶Endocrinology and Nuclear Medicine, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

OBJECTIVE: A subgroup analysis from A₁chieve explored clinical outcomes in people with poorly controlled type 2 diabetes (T2DM) changing from insulin glargine $\pm$ oral glucose-lowering drugs (OGLDs) to biphasic insulin aspart 30 $\pm$ OGLDs during routine clinical care.

METHODS: A₁chieve was a 24-week, non-interventional study evaluating the safety and effectiveness of insulin analogues in people with T2DM ($n = 66\ 726$) in routine clinical care in 28 countries across four continents.

RESULTS: Insulin dose increased by 64% in the 1395 people studied. Mean HbA_{1c} at baseline was 9.7% (SD 1.7%) and reduced by 1.9% (1.7%) to 7.8% (1.3%) at 24 weeks. Other measures of glycaemic control improved similarly and 21.9% of patients achieved an HbA_{1c} $< 7.0\%$ compared to 3.3% at baseline, with reduced incidence of reported overall and major hypoglycaemia (Table).

Table. Demographic and outcome data at baseline and week 24 [mean (SD)] for patients changing to a biphasic insulin aspart 30 regimen ($n = 1395$).

Demographic data			
Age (yr)	56.2 (12.2)		
Duration of diabetes (yr)	10.3 (6.3)		
Duration of insulin therapy (yr)	2.5 (2.8)		
Outcome data			
	Baseline	24 weeks	Change
HbA _{1c} (%)	9.7 (1.7)	7.8 (1.3)	-1.9 (1.7)*
FPG (mmol/l)	10.4 (3.4)	7.5 (2.2)	-2.9 (3.7)*
Post-breakfast PG (mmol/l)	15.0 (4.2)	10.4 (3.5)	-4.6 (4.4)*
Overall hypoglycaemia (events/person-yr)	3.10	2.98	-0.12
Major hypoglycaemia (events/person-yr)	0.16	0.01	-0.15
Insulin dose (U/kg/day)	0.50 (0.21)	0.59 (0.26)	0.09 (NA)

* $p < 0.001$; *Pre-study insulin dose (insulin glargine) was 0.36 (0.19) U/kg/day; NA, not available; FBG, fasting plasma glucose; PG, plasma glucose

CONCLUSION: Changing from insulin glargine to biphasic insulin aspart 30 was associated with improvements in glycaemic control, with reduced incidence of hypoglycaemia and particularly notable improvements in postprandial glucose levels.

PCS-18-2

Insulin Therapies for Diabetes Mellitus on Patients with Liver or Renal Dysfunction

Hsun-I Lin, Ya-Hui Hu, Shi-Wen Kuo and Ming-Chin Wu

Department of Nursing, Buddhist Tzu Chi General Hospital, Taipei Branch, Taiwan

Hypoglycemia is a nightmare to patients who are in the therapy for Diabetes Mellitus. Early morning hypoglycemia occurs more frequently to patients with liver cirrhosis or with severe renal dysfunction than to those without liver and renal dysfunction. For patients with liver or renal dysfunction, it is safer to use basal bolus insulin therapy than to use pre-mixed insulin or sulfonylurea therapy. For patients with liver cirrhosis or severe renal dysfunction, the required basal insulin could be only a small portion in the daily required total insulin. Many of them do not even need to use basal insulin as bolus insulin being the great majority in use for their therapies.

PCS-18-3

Comparison of Glulisine with Other Rapid-Acting Insulin on Post-Prandial Plasma Glucose Level and Daily Glycemic Variability

Daisuke Tsuruya, Hiroshi Morita, Takuya Hashimoto, Tetsu Morioka, Shigekazu Sasaki and Yutaka Oki

2nd Department of Internal Medicine, Hamamatsu University School of Medicine, Japan

OBJECTIVE: Insulin Glulisine (Glu) is considered to have faster acting profile compared with other rapid-acting insulin analogues. In this study, we investigated the effect of Glu on post-prandial plasma glucose (PPG) and daily glycemic variability compared with Insulin Aspart (Asp) and Lispro (Lis).

METHODS: In 15 diabetic patients (age: 57.5 years; BMI: 22.9 kg/m²; HbA_{1c}: 9.76%) who were treated three times daily with Asp or Lis (dose: 22.2 U/day) in the hospitalization, the treatment was switched to that with Glu on Day 1. Daily glycemic variability was also observed by continuous glucose monitoring (CGM) in eight patients.

Day 1: Blood sampling was conducted 10 times (before and 30, 60, 120, 180 and 240 min after breakfast, after lunch, before and after dinner, 23:00) for measuring plasma glucose concentration and serum CPR. Day 2: Glu was switched back to the previous rapid-acting insulin, and the same sampling with Day 1 was performed.

RESULTS: Glu treatment decreased PPG and serum CPR levels at 30 and 60 min compared with either Asp or Lis treatment (151.7 ± 43.1 vs 172.3 ± 32.0 mg/dL, 2.69 ± 1.63 vs 2.98 ± 1.57 ng/mL, $P < 0.05$, at 30 min. 161.7 ± 49.9 vs 176.1 ± 34.6 mg/dL, 2.81 ± 2.00 vs 3.24 ± 1.89 ng/mL, n.s., at 60 min) and increased PPG at 240 min (137.3 ± 42.4 vs 125.8 ± 34.4 mg/dL, n.s.). Glu treatment significantly decreased mean blood glucose level with less its standard deviation evaluated by CGM.

CONCLUSION: Treatment with Glu suppresses endogenous insulin secretion by improving PPG at 30–60 min compared with that with Asp or Lis, which suggested that beta cell functions could be protected with less post-prandial hypoglycemia.

PCS-18-4

Insulin Related Knowledge Amongst Healthcare Professionals from a Tertiary Hospital

Timothy Peng Lim Quek¹, Melvin Kok Seng Lee², Zhenghong Liu² and Daniel Ek Kwang Chew¹

¹Department of Endocrinology, Tan Tock Seng Hospital, Singapore; ²Yong Loo Lin School of Medicine, National University of Singapore, Singapore

BACKGROUND: Approximately 30% of admissions to our tertiary hospital are diabetes-related. Insulin is required to manage both patients with diabetes and non-diabetic patients who develop inpatient hyperglycaemia. At the same time, insulin therapy has also become more complex with the introduction and increased use of insulin analogs. Although there are numerous other factors, knowledge gaps regarding insulin therapy among healthcare professionals caring for patients with hyperglycaemia contributes to insulin-use errors and adverse patient outcomes.

MATERIALS AND METHODS: A multiple-choice questionnaire assessing knowledge of insulin characteristics, prescription, preparation and administration was administered under supervision to 375 healthcare professionals from a tertiary hospital, including 138 medical physicians, 209 registered nurses and 28 pharmacists.

RESULTS: The number of questions answered correctly (out of a maximum score of 14) was low for physicians (median score 8, interquartile range 6–10) and nurses (median score 7, interquartile range 6–8). Physicians did better at questions related to insulin characteristics and prescription, while nurses did better at questions related to insulin preparation and administration. Pharmacists did well overall (median score 12, interquartile range 10.5–12) and in both question categories.

CONCLUSION: There are significant knowledge gaps regarding insulin therapy among healthcare professionals. Specific information about these gaps may help guide education on insulin therapy to different groups of healthcare professionals. A multidisciplinary approach to inpatient diabetes care with support from pharmacists could help address insulin-use errors, with the aim of improving patient safety and reducing adverse outcomes.

PCS-18-5

Glycemic Control and Hypoglycemia Prevalence by BMI in Japanese Patients with Type 2 Diabetes: ALOHA Study Sub-Analysis

Masato Odawara¹, Karim Admane², Jay Lin³, Edward Wang⁴, Tetsuya Ohtani⁵ and Takashi Kadowaki⁶

¹Department of Diabetology, Metabolism, and Endocrinology, Tokyo Medical University, Japan; ²Sanofi, Paris, France; ³NovoSys Health, Flemington, NJ, USA; ⁴Sanofi, Bridgewater, NJ, USA; ⁵Sanofi-aventis K.K., Tokyo, Japan; ⁶Department of Diabetes and Metabolic Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

OBJECTIVE: The reduction in HbA_{1c} and prevalence of hypoglycemia among Japanese people with type 2 diabetes (T2DM) receiving insulin glargine plus oral antidiabetic drugs (OADs) were analyzed according to BMI (<25 and ≥25 kg/m²).

METHODS: Patients with T2DM taking insulin glargine plus OADs were observed for 24 weeks in a real-life setting. Baseline and endpoint HbA_{1c}, fasting blood glucose (FPG), postprandial plasma glucose (PPG), body weight, and BMI were measured.

RESULTS: BMI was <25 kg/m² (mean [SD] 21.8 [2.2] kg/m²) in 2496 patients and ≥25 kg/m² (27.2 [1.4] kg/m²) in 1410 patients. After 24 weeks, patients with BMI <25 kg/m² had a greater reduction in HbA_{1c} levels kg/m² (–1.50 [1.22]% vs –1.27 [1.27]%; $P < 0.001$), a greater percentage achieved target HbA_{1c} <7% (18.3% vs 13.2%; $P < 0.001$), took a lower dose of insulin glargine (8.71 [5.27] vs 10.31 [7.03] U/day; $P < 0.001$), and had greater reductions in FPG and PPG than in patients with BMI ≥25 kg/m². Body weight increased in both groups. The incidence of severe hypoglycemia was low in both groups (0.07% vs 0.12%; $P = 0.64$).

CONCLUSIONS: The insulin glargine plus OADs regimen resulted in significant HbA_{1c} reductions with a low rate of severe hypoglycemia and weight gain in T2DM Japanese patients. Greater reduction in HbA_{1c} was seen in non-overweight compared with overweight patients. While insulin glargine dosing may have been suboptimal for all patients, it was more evident in overweight patients.

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PCS-18-6

Ultra-Long Pharmacokinetic Properties of Insulin Degludec in Younger Adults Preserved in Geriatric Subjects with T1DM

Stefan Korsatko¹, Sigrid Deller¹, Julia Mader¹, Katharina Glettler¹, Gerd Koehler¹, Gerlies Bock¹, Martina Urschitz¹, Michael Wolf¹, Hanne Hastrup-Nielsen², Flemming Soendergaard³, Hanne Haahr², Marcus Niemeyer⁴ and Thomas Pieber¹

¹Medical University Graz, Graz, Austria; ²Novo Nordisk A/S, Soeborg, Denmark; ³Novo Nordisk A/S, Aalborg, Denmark; ⁴Novo Nordisk A/S, Bagsvaerd, Denmark

OBJECTIVES: This study investigated the pharmacokinetic and pharmacodynamic properties of insulin degludec (IDeg), an ultra-long acting basal insulin with a flat, stable action profile, in geriatric (≥65 years) vs younger adult (18–35 years) subjects with T1DM.

METHODS: This was a randomised, double-blind, two-period cross-over, multiple-dose study with 6 days of once-daily administration of 0.4 U/kg IDeg or 0.4 U/kg insulin glargine. Data are shown for IDeg only. Fourteen geriatric (mean age: 67.8 years; baseline HbA_{1c}: 7.7%; BMI: 26.2 kg/m²) and 13 younger adult (mean age: 27.1 years; baseline HbA_{1c}: 7.8%; BMI: 24.4 kg/m²) subjects participated.

RESULTS: The mean IDeg concentration-time profile at steady-state was similar in geriatric and younger adult subjects. There was no statistically significant difference in total exposure (area under the curve [AUC_{IDeg,τ,SS}]; least square mean 85 673 pmol·h/L in geriatric and 82 727 pmol·h/L in younger adults or maximum concentration (C_{max,IDeg,SS}) of IDeg, mean ratio geriatric/younger adults [95% CI] AUC_{IDeg,τ,SS}: 1.04 [0.73; 1.47], C_{max,IDeg,SS}: 1.02 [0.74; 1.39]. The ultra-long properties of IDeg were preserved in geriatric subjects; the estimated harmonic mean terminal half-life was 25 h. There was no statistically significant difference in total glucose-lowering effect of IDeg (AUC_{GIR,τ,SS}) between geriatric (least square mean 1923 mg/kg) and younger adults (least square mean 2457 mg/kg), mean ratio geriatric/younger adults [95%CI] 0.78 [0.47; 1.31].

CONCLUSION: The ultra-long pharmacokinetic properties of IDeg in younger adults were preserved in geriatric subjects. Total exposure was similar and there were no differences in the glucose-lowering effect of IDeg between geriatric and younger adult subjects.

PCS-18-7

Hypoglycemia in Patients with Type 2 Diabetes Treated by Insulin Glargine with Oral Agents in Real-Life: ALOHA Study Subanalysis

Masato Odawara¹, Tetsuya Ohtani² and Takashi Kadowaki³

¹Department of Diabetology, Metabolism, and Endocrinology, Tokyo Medical University, Japan; ²sanofi-aventis K.K., Japan; ³Department of Diabetes and Metabolic Diseases, Graduate School of Medicine, The University of Tokyo, Japan

OBJECTIVES: To investigate the extent of hypoglycemic risk regarding basal supported oral therapy (BOT) using insulin glargine and oral antidiabetic drugs, we analyzed data from 4219 patients in the Add-on Lantus to Oral Hypoglycemic Agents (ALOHA) study that is a observational, non-interventional, 24-week follow-up study.

METHODS: All adverse events were collected as reported by physicians notified by patient's symptoms during the follow-up as well as glycemic controls and weight change. Of those, we focused on glargine-related hypoglycemic episodes to analyze the rate and the risk factors about patient backgrounds.

RESULTS: Of 4219 patients, 44 (1.0%) experienced hypoglycemic episodes [41 of 3732 (1.1%) in insulin naive patients; and 3 of 487 (0.6%) in insulin-treated patients]. Of all patients with hypoglycemia, 37 (84%) had just one episode during 24 weeks. Increasing trend of hypoglycemia continued until 14 weeks in cumulative incidence curve analysis. A significant difference among patient backgrounds about age [$P < 0.05$, number needed to harm (NNH) = 108 for ≥ 65], diabetic complications ($P < 0.05$, NNH = n.s.), and eGFR ($P < 0.01$, NNH = 57 for < 60) was showed, though a very low rate in any background groups.

CONCLUSION: Our results suggest that glargine-BOT is an option of insulin therapy of a low risk of hypoglycemia in patients with type 2 diabetes, though some patient groups, aged and those with a low renal function, should be carefully watched by physicians and family members at an early phase after insulin initiation.

PCS-18-8

Transferring from Biphasic Human Insulin to Biphasic Insulin Aspart: Improved Glycemic Control and Reduced Hypoglycemia

Minxiang Lei¹, Yuxiu Li², Chengjiang Li³, Bing Chen⁴, Guijun Qin⁵, Yongquan Shi⁶, Liming Chen⁷ and Wenying Yang⁸

¹Department of Endocrinology, The First Xiangya Hospital of Central South University, China; ²Department of Endocrinology, Peking Union Medical College Hospital, China; ³Department of Endocrinology, The First Affiliated Hospital of College of Medicine, Zhejiang University, China; ⁴Department of Endocrinology, Southwest Hospital of Third Military Medical University, China; ⁵Department of Endocrinology, The First Affiliated Hospital of Zhengzhou University, China; ⁶Department of Endocrinology, Shanghai Changzheng Hospital, China; ⁷Department of Endocrinology, Tianjin Medical University Metabolic Diseases Hospital, China; ⁸Department of Endocrinology, China-Japan Friendship Hospital, China

OBJECTIVE: To study clinical safety and effectiveness of biphasic insulin aspart 30 (BIAsp 30) in Chinese patients with type 2 diabetes (T2D).

METHODS: A₁chieve was a prospective, open-label, non-interventional study in patients with T2D initiating insulin analogues in 28 countries across Asia, Africa, Europe, and Latin America. Data were collected at baseline and week 24 (end of study).

RESULTS: In China, 1191 patients whom were previously treated with biphasic human insulin 30 (BHI 30) $\pm$ OADs started BIAsp 30 $\pm$ OADs as new therapy (55.0% males, mean $\pm$ SD age 57.5 $\pm$ 15.5 year, BMI 25.0 $\pm$ 3.2 kg/m², duration of T2D 10.6 $\pm$ 6.6 year). Glycemic control was significantly improved after 24 weeks as measured by HbA_{1c} (from 8.7 $\pm$ 2.1% to 7.0 $\pm$ 1.1%, change -1.6 $\pm$ 1.9%) fasting plasma glucose (FPG, from 9.1 $\pm$ 3.2 to 6.9 $\pm$ 1.5 mmol/L, change -2.2 $\pm$ 3.2 mmol/L) and postprandial plasma glucose (PPPG, from 12.9 $\pm$ 4.2 to 9.1 $\pm$ 2.0 mmol/L, change -3.8 $\pm$ 4.3 mmol/L; all $P < 0.001$). The proportion of patients achieving HbA_{1c} target $< 7.0\%$ increased from 18.7% to 55.3%. The rates of total, major, and nocturnal hypoglycemia (events/patient/year) were 7.20, 0.51, and 2.15 for the 4 weeks before baseline and 2.37, 0.00, and 0.43 for the 4 weeks before Week 24 (all $P < 0.0001$).

CONCLUSION: In the A₁chieve study, transferring from BHI 30 to BIAsp 30 significantly improved glycemic control and reduced the incidence of hypoglycemia in Chinese patients with T2D.

PCS-19-1

DPP4 Inhibitor Might be the Drug for Less Glucose Excursion

Sun Ok Song, Kwang Joon Kim, Byung-Wan Lee, Seok Kang Eun, Bong Soo Cha and Hyun Chul Lee

Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine, Korea

Glycated albumin (GA) is known to be a more useful glycation index than hemoglobin A1c (A1c) for monitoring fluctuating glucose level in type 2 diabetic patients. The aim of this study was to investigate which drug results in the greatest glycemic excursion as assessed by GA/A1c ratio.

We retrospectively reviewed medical records of patients who were treated with oral hypoglycemic agents (OHA). We checked fasting glucose and postprandial glucose, glycated A1c and GA at baseline and 3 month later. We calculated the change (delta) based on the difference between the baseline values and values after 3 months across all variables and GA/HbA1c ratio.

Patients were divided into three groups according to the OHAs classes - metformin only (M), metformin with DPP4 inhibitor (D), metformin with sulfonylurea (SU) group). There were no differences in GA or GA/A1c among the three groups at baseline. However, GA (13.40% in M, 12.25% in D, 17.736% in SU, $P = 0.001$) after 3 months of SU were significantly higher than those of other groups. And, Δ GA and GA/A1c ratio in D after 3 months were significantly lower than those of SU ($P = 0.45$, $P = 0.29$, respectively), but not than M.

Based on the concept that GA and GA/A1c are indicators that can monitor glycemic excursion, DPP-4 inhibitor might results in the greatest reduction in glycemic excursion.

PCS-19-2

Different Beneficial Effects of Pioglitazone and Alogliptin in a Patient with Type B Insulin Resistance Syndrome and Hypoglycemia

Yuki Onishi¹, Taro Yasuma¹, Yutaka Yano¹, Mei Uemura¹, Masako Sakamoto¹, Toshinari Suzuki¹, Ryoma Sasaki¹, Kazutaka Matsumoto¹, Esteban Gabazza², Yasutaka Sumida³ and Yoshiyuki Takei⁴

¹Department of Diabetes, Metabolism and Endocrinology, Mie University Graduate School of Medicine, Japan; ²Department of Immunology, Mie University Graduate School of Medicine, Tsu, Mie, Japan; ³Center for Physical and Mental Health, Mie University, Tsu, Mie, Japan; ⁴Department of Gastroenterology and Hepatology, Mie University Graduate School of Medicine, Tsu, Mie, Japan

BACKGROUND: Type B insulin resistance syndrome with severe hypoglycemia is sometimes induced by the insulin-mimic action of anti-insulin-receptor antibodies. To date, there is no report showing that hypoglycemia is improved by a combination of pioglitazone and alogliptin.

CASE REPORT: We report a case of type B insulin resistance syndrome with severe hypoglycemia treated with a combination of pioglitazone and alogliptin. A 73-year old Japanese man with hyperglycemia was treated with insulin. He frequently had severe hypoglycemia in the early morning during treatment and even after insulin withdrawal. Type B insulin resistance syndrome was diagnosed because he had hyperglycemia, hyperinsulinemia and positivity for anti-insulin-receptor antibodies. We treated the patient with a combination of pioglitazone and alogliptin. Hypoglycemia in early morning improved after treatment with pioglitazone (30 mg) or alogliptin (6.25 mg). Moreover, the combination of pioglitazone (30 mg) and alogliptin (12.5 mg) improved hyperglycemia as shown by the mean blood glucose level (212.5 $\pm$ 43.0 $\rightarrow$ 135.0 $\pm$ 34.0 mg/dL), and the mean amplitude of glycemic excursion (174.0 $\rightarrow$ 74.0 mg/dL). Plasma total adiponectin (16.4 $\rightarrow$ 47.3 μ g/mL), high molecular weight adiponectin (5.4 $\rightarrow$ 18.1 μ g/mL) levels and glucose infusion rate (0.87 $\rightarrow$ 2.45 mg/kg/min) measured by glucose clamp technique was increased after pioglitazone treatment.

CONCLUSIONS: We report for the first time a beneficial effect of the combination therapy of pioglitazone and alogliptin in a case of type B insulin resistance syndrome with hypoglycemia.

PCS-19-3

Serious Adverse Effects of Oral Antidiabetic Drugs - Metformin Associated Lactic Acidosis (MALA)

Pei-Tzu Lin¹ and Kuan-Yi Lin²

¹Department of pharmacy, Chiayi Chang Gung Medical Memorial Hospital of the C.G.M.F, Taiwan; ²Changhua Christian Hospital Lukang Branch, Taiwan

OBJECTIVES: Lactic acidosis induced by metformin is a rare but critical event with high mortality rate. There are some contraindications and precautions

about metformin, but health-care related professions usually ignore them. To analyze the cases of MALA from regional teaching hospital in southern Taiwan.

METHODS: The data was claimed from Reporting System of Adverse Drug Reaction of a regional teaching hospital from Jan 2002 to Feb 2012. Numbers of adverse drug reactions associated metformin were extracted by material code (metformin, PME018M; Glucomet, PME070M; Avadamet, PME064M; Janumet, PME099M; Amaryl M, PME090M).

RESULTS: Six cases with mean age of 69.80 ± 7.05 years old about MALA had been reported. One third was females. Two of them suffered from acute renal failure episode due to upper gastrointestinal bleeding and four of cases had renal insufficiency history, including two with regular hemodialysis, one man with creatinine concentration of 2.4 mg/dL and one female with creatinine concentration of 1.93 mg/dL. Besides nephritic disease, one cases was liver cirrhosis with child B and another one is heart failure with function class two. They were acidosis with pH < 7.2 and serum lactate above 130 mmol/L. All of them were alive after intensive hemodialysis.

LIMITATION: The reporting system is passive to collate data.

CONCLUSIONS: Acute or chronic renal dysfunction may the major causes of MALA here. MALA were exceedingly rare but we should pay more attention on metformin utility to avoid prescribe in the inadequate patients and keep closely monitor after taking to prevent serious side effects.

PCS-19-4

Evaluation of α -Glucosidase Inhibitors for Body Weight Reduction and Blood Glucose Control in Japanese Obese Type 2 Diabetes

Mototsugu Nagao¹, Hitoshi Sugihara¹, Masanobu Kawakami² and Shinichi Oikawa¹

¹Division of Endocrinology and Metabolism, Department of Medicine, Nippon Medical School, Japan; ²Department of Medicine, Saitama Medical Center, Jichi Medical University, Japan

AIMS/INTRODUCTION: α -Glucosidase inhibitors (α GIs) have been globally used in the primary treatment of type 2 diabetes. We compared the clinical effects of three drugs (miglitol, acarbose, and voglibose) in Japanese type 2 diabetes with obesity.

MATERIALS AND METHODS: The Japanese patients ($n = 81$) with type 2 diabetes and obese (BMI > 25 kg/m²) were enrolled in this multicenter, open-labeled study. They were randomized into the miglitol ($n = 18$), acarbose ($n = 22$), voglibose ($n = 19$), or control group ($n = 22$). Blood glucose control (fasting blood glucose, HbA1c and 1,5-AG), body weight, leptin, adiponectin, and lipids (LDL-C, TG, HDL-C) were evaluated every 4 weeks for 12 weeks under the treatment.

RESULTS: In miglitol group, diabetic control was significantly improved from the baseline as shown by HbA1c decrease and 1,5-AG increase in all points. In voglibose group, significant improvements in HbA1c and 1,5-AG were observed in some points. Body weight was significantly decreased only in miglitol group throughout the study. There were significant changes of HbA1c and 1,5-AG in miglitol group as compared with those in control group at 12 weeks. In addition, a significant correlation between the changes of HbA1c and body weight was observed in miglitol group at 12 weeks ($R = 0.75$, $P < 0.01$). Serum leptin, adiponectin, and lipid levels were not altered in any groups.

CONCLUSIONS: α GIs, especially miglitol, has a potency to achieve better body weight and blood glucose control in Japanese type 2 diabetes with obesity. This study was registered with UMIN (no. UMIN000006465).

PCS-19-5

Nateglinide has Comparable Effectiveness with Acarbose in Reducing Postprandial Glycemic excursions in Chinese Anti-Hyperglycemic Agent Naive Subjects with Type 2 Diabetes

Jian Zhou¹, Hong Li², Xiuzhen Zhang³, Yongde Peng⁴, YuQian Bao¹ and Weiping Jia¹

¹Department of Endocrinology and Metabolism, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, China; ²Department of Endocrinology and Metabolism, Sir Run Run Shaw Hospital, School of medicine, Zhejiang University, China; ³Department of Endocrinology and Metabolism, Tong Ji Hospital Affiliated to Tong Ji University, China; ⁴Department of Endocrinology and Metabolism, Shanghai Jiao Tong University Affiliated First People's Hospital, China

OBJECTIVE: Recent data have shown that postprandial glycemic excursions were risk factors for diabetic complications. This multi-center, open-label,

randomized, active-control, parallel-group study compared the effects of nateglinide paralleled with those of acarbose on postprandial glycemic excursions in Chinese subjects with type 2 diabetes by continuous glucose monitoring system (CGMS).

METHODS: A total of 103 anti-hyperglycemic agent naive subjects with type 2 diabetes whose HbA1c levels ranged from 6.5% to 9.0% from four hospitals in China were randomized (1:1) to nateglinide or acarbose groups.

RESULTS: After 14 days treatment, compared with baseline, both nateglinide and acarbose reduced the incremental areas above preprandial glucose values (AUCpp) significantly ($P < 0.001$). Whereas no significant differences were found between two groups ($P = 0.691$). The mean blood glucose (MBG), mean amplitude glycemic excursions (MAGE) and the standardized deviation of daily blood glucose excursion (SD) decreased significantly in both groups (all $P < 0.001$). No significant differences were found between two groups in reductions of MBG, MAGE, and SDBG after treatment. Both the two agents had comparable effects on reducing serum glycated albumin ($P = 0.098$). The rates of adverse events (AE) and AE related to trial products were higher in acarbose group than nateglinide group ($P < 0.05$). No serious AE was noted. The rates of hypoglycemic episodes were comparable in two groups. There was no severe hypoglycemic episode being noted in either group.

CONCLUSIONS: Nateglinide had comparable effectiveness in reducing postprandial glycemic excursions when compared with acarbose in anti-hyperglycemic agent naive Chinese adult with type 2 diabetes mellitus.

PCS-19-6

Clinical Evidence for the Effectiveness of Bangladeshi Medicinal Plants Action for Different Types of Diabetes Mellitus

Md. Ariful Haque Mollik

Department of Biological Sciences, Peoples Integrated Alliance, Bangladesh

Medicinal plants are very much important for public health as well as for plant and animal protection. The studies were undertaken to assess the hypoglycemic effect of alcoholic extracts of *Curcuma amada* Roxb., *Grewia asiatica* L., *Leonurus sibiricus* L., *Oldenlandia corymbosa* L., and *Xanthium italicum* Moretti were studied in streptozotocin induced diabetes mellitus. Wistar rats were made diabetes mellitus by intraperitoneal injection of streptozotocin (30 mg/kg) in citrate buffer. On confirmation of diabetes mellitus after 48 h of injection, alcoholic extract of medicinal plant (250 or 500 mg/kg) or glibenclamide (300 μ g/kg) administered orally to Wistar rats for 30 days. These medicinal plants produced dose and duration dependent hypoglycemia very similar to that of glibenclamide. At the end of 1 month, serum glucose levels of streptozotocin diabetes mellitus Wistar rats with daily doses of 500 mg/kg of any one of the alcoholic extract were (more or less) comparable to that of normal Wistar rats. The anti-diabetes mellitus effect of these medicinal plants might be due to enhanced insulin secretion from the viable β -cells of islets of Langerhans as evidenced by presence of more viable β -cells and less necrotic changes in the pancreas of diabetes mellitus Wistar rats as compared to that of control diabetes mellitus Wistar rats. In consequence, these medicinal plants appear to be better alternative for the diabetes mellitus patients who are prone to develop side effects with the regular use of synthetic hypoglycemic drugs as these are also medicinal plants devoid of any untoward or toxic effects.

PCS-20-1

Efficacy and Safety of Liraglutide in Patients with Type 2 Diabetes: The SEDIK Study

Takehiro Kawata¹, Akira Kanamori², Akira Kubota², Hajime Maeda², Kiyokazu Matoba², Shogo Ito², Hikaru Amamiya², Masahiko Takai², Hideaki Kaneshige², Nobuaki Minami², Fuyuki Minagawa², Koutarou Iemitsu², Masashi Ishikawa², Kazuhiko Hoshino², Masaaki Miyakawa², Yoshikazu Naka², Masao Toyoda³, Yasuo Terauchi⁴, Daisuke Suzuki³, Yasushi Tanaka¹ and Ikuro Matsuba²

¹The Study Group of Diabetes Committee, Kanagawa Physicians Association/St. Marianna University School of Medicine, Japan; ²The Study Group of Diabetes Committee, Kanagawa Physicians Association, Japan; ³Department of Internal Medicine, Division of Nephrology and Metabolism, Tokai University School of Medicine, Japan; ⁴Department of Endocrinology and Diabetes, Yokohama City University, Japan

There have been few reports from Japan on the results of treatment with liraglutide, a GLP-1 receptor agonist, in patients with type 2 diabetes. Therefore, in the present study, the effects of liraglutide on glucose and lipid

metabolism, blood pressure, and body weight were evaluated in Japanese patients with type 2 diabetes. In total, 202 patients with type 2 diabetes were treated with liraglutide (113 men, 89 women; age, 57.3 ± 12.8 years). The patients were divided into the following two groups: a liraglutide monotherapy group (147 patients) and a liraglutide-sulfonylurea combination therapy group (55 patients). Clinical parameters were measured before and after liraglutide administration, and their changes were evaluated. In both groups, HbA_{1c} (NGSP; %) decreased significantly after 12 and 24 weeks of treatment ($P < 0.0005$). Furthermore, body weight also decreased significantly after 12 and 24 weeks ($P < 0.05$) in both groups. Adverse events after starting liraglutide occurred in 45 patients (22.3%), and 23 patients (11.4%) discontinued treatment. Since HbA_{1c} improved significantly and body weight decreased significantly in both groups, liraglutide has two advantages for the treatment of patients with diabetes: it improves glycemic control, and it significantly decreases body weight. Consequently, liraglutide is indicated in obese patients with non-insulin-dependent type 2 diabetes.

PCS-20-2

Comparison of Liraglutide and Exenatide with Continuous Glucose Monitoring (CGM) Among Different Types of Diabetes

Kanako Mori¹, Yoshiyuki Hamamoto², Sachiko Honjo², Yukiko Ohgita², Hisato Tatsuoka², Kanta Fujimoto², Atsuko Matsuoka², Hiroki Ikeda², Yoshiharu Wada², Nobuya Inagaki¹ and Hiroyuki Koshiyama²

¹Department of Diabetes and Clinical Nutrition, Kyoto University, Japan; ²Center for Diabetes & Endocrinology, The Tazuke Kofukai Foundation Medical Research Institute Kitano Hospital, Japan

OBJECTIVE: Liraglutide (Lira) and exenatide (Ex) have a definite structural difference. We compared the effects of Lira and Ex on diurnal glycemic properties evaluated by Continuous glucose monitoring (CGM) among patients with type 2 diabetes (T2D), diabetes associated with cirrhosis (LC; $n = 7$), and steroid-induced diabetes (ST; $n = 2$).

METHODS: Fourteen patients were hospitalized and given insulin therapy. After glycemic control had been achieved, Lira 0.6 mg daily or Ex 5 µg twice daily were randomly administered for two consecutive days per each in cross-over manner, and blood glucose levels (BG) were monitored by CGM. A day was divided into four equal time periods started from 6 a.m., and each period, postprandial period (2 h after meals) and a whole day were compared by calculating area-under-the-curve (AUC).

RESULTS: Lira administration brought three peaks of BG, but only two peaks were observed in Ex by CGM analyses. The 2-h AUC of BG after breakfast and dinner were higher in Lira, whereas that of after lunch and the AUC of midnight were higher in Ex. The AUC of WD with Lira administration was significantly lower only in LC. The mean BG was lower in Lira, but the duration of hypoglycemia was longer in Ex.

CONCLUSION: Our results showed that (1) Lira had a higher efficacy to control midnight glycemia than Ex, (2) Ex had a higher efficacy to control postprandial glycemia after breakfast and dinner, and that (3) Lira is more suitable for patients with LC than Ex.

PCS-20-3

Lixisenatide in Asian Patients with Type 2 Diabetes (T2DM) Uncontrolled on Metformin ± Sulfonylurea (SU): GetGoal-M Asia

Chang Yu Pan¹, Q. Zhao² and Elizabeth Niemoeller³

¹Department of Endocrinology, Chinese People's Liberation Army General Hospital, China; ²Sanofi, Shanghai, China; ³Sanofi, Frankfurt, Germany

OBJECTIVE: To evaluate once-daily (QD) lixisenatide in Asian patients with T2DM insufficiently controlled on metformin ± SU.

METHODS: This 24-week, multicenter, double-blind study, conducted in China, Malaysia, Thailand, and Hong Kong, randomized patients to lixisenatide 20 µg QD ($N = 196$) or placebo ($N = 195$), with a 1-step dose increase regimen (NCT01169779). The primary endpoint was absolute HbA_{1c} change from baseline to Week 24.

RESULTS: Mean ± SD age was 54.8 ± 10.4 years; diabetes duration 6.6 ± 4.7 years; BMI 26.9 ± 3.8 kg/m²; HbA_{1c} $8.0 \pm 0.7\%$; 44.6% were

Efficacy parameters to Week 24 (mITT population; LOCF)			
		Lixisenatide n=195	Placebo n=193
HbA _{1c}	Mean (SD) baseline	7.95 (0.81)	7.83 (0.70)
	LS mean change	-0.83%	-0.47%
	LS mean difference (95% CI) vs placebo	-0.36% (-0.55, -0.16); $p=0.0004$	
Proportion of patients achieving target HbA _{1c} $\leq 6.5\%$; p vs placebo		32.4%; $p=0.0010$	18.1%
		53.0%; $p=0.0030$	38.8%
2-hour PPG, mmol/L	Mean (SD) baseline	16.27 (3.82)	17.34 (4.16)
	LS mean change	-5.61	-1.33
	LS mean difference (95% CI) vs placebo	-4.28 (-5.36, -3.20); $p<0.0001$	
FPG, mmol/L	Mean (SD) baseline	8.83 (2.12)	8.75 (1.84)
	LS mean change	-0.69	-0.21
	LS mean difference (95% CI) vs placebo	-0.48 (-0.85, -0.11); $p=0.0109$	
Body weight, kg	Mean (SD) baseline	73.57 (14.03)	72.94 (13.61)
	LS mean change	-1.50	-1.24
	LS mean difference (95% CI) vs placebo	-0.27 (-0.78, 0.24); $p=0.2960$	
Safety to Week 24 (safety population)			
		Lixisenatide n=196	Placebo n=194
Patients with any TEAE, n (%)		126 (64.3)	92 (47.4)
Patients with any serious TEAE, n (%)		3 (1.5)	4 (2.1)
Patients with any gastrointestinal TEAEs, n (%)		57 (29.1)	18 (9.3)
Nausea		32 (16.3)	5 (2.6)
	Vomiting	15 (7.7)	2 (1.0)
	Diarrhea	7 (3.6)	2 (1.0)
Patients with symptomatic hypoglycemia ^a , n (%)		11 (5.6)	5 (2.6)
Patients with severe symptomatic hypoglycemia, n (%)		0	0

^aEvent with clinical symptoms with either plasma glucose <3.3 mmol/L or prompt recovery after oral carbohydrate, intravenous glucose or glucagon administration if no plasma glucose measurement was available; SD=standard deviation; mITT=modified intent to treat (patients with baseline and at least one post-baseline measurement); LOCF=last observation carried forward; HbA_{1c}=glycated hemoglobin; SD=standard deviation; CI=confidence interval; PPG=postprandial glucose; FPG=fasting plasma glucose; TEAE=treatment emergent adverse event

receiving SU. At Week 24, improvements from baseline in HbA_{1c}, 2-h PPG and FPG were all significantly greater with lixisenatide vs placebo (Table). The study was completed by 91.3% of lixisenatide- and 94.4% of placebo-treated patients. Lixisenatide was well tolerated, with gastrointestinal events being the most frequent treatment-emergent adverse events.

CONCLUSIONS: Over 24 weeks, lixisenatide significantly improved HbA_{1c} from low baseline levels, with a particularly pronounced effect on PPG, and was well-tolerated in Asian patients with T2DM uncontrolled on metformin ± SU.

Supported by Sanofi.

PCS-20-4

Liraglutide Added to Insulin Therapy in Poorly-Controlled Japanese Type 2 Diabetes

Tsukasa Morii, Mihoko Hosoba, Hiroki Fujita, Katsushi Tsukiyama, Takuma Narita and Yuichiro Yamada

Department of Endocrinology, Diabetes and Geriatric Medicine, Akita University Graduate School of Medicine, Japan

BACKGROUND AND AIMS: We investigated the effects of 12 months treatment with liraglutide added to insulin on glycemic control, insulin dose and body weight reduction in poorly-controlled insulin-treated Japanese type 2 diabetic patients. This study is currently in process, so we report preliminary data in this abstract.

MATERIALS AND METHODS: Twelve poorly controlled Japanese type 2 diabetic patients (seven men, mean age 57.8 ± 13.4 years, BMI 28.4 ± 4.1 kg/m², diabetes duration 18.9 ± 9.7 years) with insulin therapy were studied. They were initiated liraglutide at 0.3 mg/day, reducing to half dose of their insulin administration. Maximal dose of liraglutide is 0.9 mg/day in Japan.

RESULTS: After 3 months, glycemic control was improved (HbA1c 8.9 ± 0.9 – $7.9 \pm 1.2\%$, $P < 0.05$) and marked reduction of insulin dose (42.2 ± 21.2 – 16.6 ± 14.2 U/day, $P < 0.001$) and body weight (77.0 ± 15.5 – 73.9 ± 15.1 kg, $P < 0.05$). Changes of these parameters were sustained up to 6 months. After 6 months, serum C-peptide and SUIT index were increased (C-peptide: 1.17 ± 0.29 – 1.49 ± 0.44 ng/mL, $P < 0.05$, SUIT index: 17.7 ± 7.5 – 28.4 ± 15.4 , $P < 0.05$). Only two patients complained nausea and vomiting at first period and all patients have continued the study until now. No episodes of major hypoglycemia and acute pancreatitis were reported during the study. Nine patients have finished the study at present.

CONCLUSION: For poorly-controlled Japanese type 2 diabetic patients with insulin treatment, liraglutide combination therapy with insulin provided improved glycemic control and sustained weight loss for up to 6 months. Their β -cell function was improved and insulin dose was markedly reduced.

PCS-20-5

Clinical Use of GLP-1 Analogue (Exenatide) in Obese Type 2 DM Taiwanese

Kuo-Yang Lee, Ching-Chu Chen and Ching-Chung Chang

Department of Internal Medicine, China Medical University Hospital, Taiwan

OBJECTIVE: The prevalence of obesity rises in T2DM and high BMI (Body Mass Index) is harmful for health and life quality. We apply the novel T2DM medication GLP-1 analogue (exenatide) to patients with poor HbA1C (over 8%) under original therapy and with BMI over 27 kg/m².

METHODS: Patients received exenatide 5 μ g twice daily for 1 month and then 10 μ g twice daily for 2 months combined with titrating OAD (oral antidiabetic drug).

RESULTS: Fifteen patients were enrolled. Female is predominant (13, 86.7%). The average age is 45.2 years old. The average T2DM duration is 6.3 years. BMI before exenatide is 32.4. Baseline HbA1C is 9.1%. The average OAD (oral antidiabetic drug) for those without insulin therapy is 2.8 kinds. After exenatide 5 μ g for 1 month, HbA1C decreases to 8.9% and body weight reduction is 1.2 kg. And after two more months of exenatide 10 μ g, HbA1C decreases to 8.5% and body weight reduction is 2.4 kg from baseline. Ten patients (66.7%) achieved both HbA1C improvement with body weight reduction. Side effects were reported in 66.7% cases. The most common side effect is nausea (40%). But most side effects were tolerable and decreased over time. Only one case (6.7%) withdrew due to severe dizziness to 10 μ g dose.

CONCLUSION: Exenatide offered both HbA1C improvement as well as body weight reduction in obese T2DM Taiwanese.

PCS-20-6

Withdrawn

PCS-21-1

Linagliptin Therapy Shows Similar Long-Term Safety and Efficacy to Metformin in Japanese Patients with Type 2 Diabetes

Nobuya Inagaki¹, Hirotsuka Watada², Masako Murai³, Tatsuo Kagimura³, Yan Gong⁴, Sanjay Patel⁵ and Hans-Juergen Woerle⁴

¹Department of Diabetes and Clinical Nutrition, Kyoto University Graduate School of Medicine, Japan; ²Department of Metabolism and Endocrinology, Juntendo University Graduate School of Medicine, Japan; ³Nippon Boehringer Ingelheim, Japan; ⁴Boehringer Ingelheim, Ingelheim, Germany; ⁵Boehringer Ingelheim, Bracknell, UK

OBJECTIVES: To evaluate safety and efficacy of oral linagliptin vs metformin, in Japanese patients with type 2 diabetes (T2DM) and insufficient glycemic control despite background oral antidiabetic drug (OAD) monotherapy.

METHODS: Five hundred and seventy-four patients, HbA1c $\geq 7\%$ to $\leq 10\%$, entered this 52-week, open-label, multicenter, parallel-group trial. Patients on sulfonylurea (SU) or α -glucosidase inhibitor (A-GI) were randomized to add-on linagliptin (once daily, 5mg) or metformin (bid/tid, maximum 2250 mg/day). Additionally, patients on biguanide, glinide, or glitazone received add-on linagliptin.

RESULTS: At week 52, add-on linagliptin and metformin (mean dose, mg/day: 709.02 [A-GI group], 653.23 [SU]) significantly reduced mean HbA1c levels (vs baseline: from 7.9% through 8.1%), in all groups. Add-on linagliptin was as effective as metformin after 52 weeks: adjusted mean change from baseline HbA1c: -0.66% (95% confidence interval, CI, -0.81 , -0.51) for linagliptin + SU ($n = 123$) vs -0.84% (CI, -1.02 to -0.65) for metformin + SU ($n = 62$), non-significant treatment difference, 0.18% (CI, -0.03 to 0.39); corresponding results were -0.92% (CI, -1.10 to -0.73) for linagliptin + A-GI ($n = 61$) vs -1.00% (CI, -1.17 to -0.83) for metformin + A-GI ($n = 61$), non-significant treatment difference, 0.09% (CI, -0.13 to 0.30). Adverse events: mostly mild/moderate, similar rates across all groups. Hypoglycemic event rates: similar for linagliptin and metformin (A-GI groups: 2% vs 3%; SU groups: 14% vs 16%, respectively).

CONCLUSION: Once-daily linagliptin provides well-tolerated, effective therapy with significant HbA1c reductions, similar to metformin, over 52 weeks in Japanese patients with inadequately controlled T2DM despite OAD monotherapy.

PCS-21-2

Vildagliptin is Effective Even with 50 mg per Day for Japanese Type 2 Diabetic Patients

Naotaka Fujita, Hirohito Kuwata, Satoru Tsujii, Yuko Hataji, Yusuke Arai, Satoshi Matsunaga, Shintaro Okamura, Tadao Iburu, Kaori Nishiura, Tsuyoshi Mashitani, Miyuki Furuya, Masako Kitatani, Yasuaki Hayashino and Hitoshi Ishii

Department of Endocrinology, Tenri Hospital, Japan

OBJECTIVE: To reveal the effectiveness of vildagliptin on Japanese type 2 diabetic patients.

METHODS: Eligibles were type 2 diabetic patients who started their therapy with vildagliptin in our hospital and who continued it more than 26 weeks. Usage of vildagliptin was classified depending on the following situations: (1) add-on to diet therapy, (2) add-on to other oral anti-diabetic drugs (OAD), (3) add-on plus discontinuation of some OADs, (4) add-on plus discontinuation of all other OADs, and (5) switch from insulin therapy.

RESULTS: Analyzed were 142 patients. Their mean age, diabetic duration, HbA1c, and BMI were 67.9 ± 10.8 years old, 12.0 ± 10.5 years, $7.4 \pm 1.2\%$, and 22.5 ± 5.5 kg/m². Data are mean $\pm$ SD HbA1c changed from baseline to week 26, 7.6 ± 1.6 – 6.5 ± 0.6 , 8.5 ± 0.7 – 7.5 ± 1.2 , 7.7 ± 0.8 – 7.6 ± 1.1 , 6.9 ± 0.8 – 6.8 ± 0.7 , and 7.0 ± 1.3 – 7.2 ± 1.7 in situation (1), (2), (3), (4), and (5), respectively. In situation (1) and (2), HbA1c was reduced by 1.0%. And there was no significant change in situation (3), (4), and (5). Vildagliptin in 50 mg per day was administered to 90 of 142 (63.4%) patients. There was no significant change in HbA1c reduction ($P = 0.51$) between the 50 mg dose group (Δ 0.7%, $n = 41$) and the 100 mg dose group (Δ 1.0%, $n = 18$) in situation (1) and (2). And no significant change was either observed in HbA1c reduction ($P = 0.39$) between the 50 mg dose group (Δ -0.1% , $n = 49$) and the 100 mg dose group (Δ 0.1%, $n = 34$) in situation (3), (4), and (5).

CONCLUSION: Vildagliptin was effective even with 50 mg per day for Japanese type 2 diabetic patients in clinical practice.

PCS-21-3

The Conversion Trial from Glinide to DPP4 Inhibitor on Japanese Type 2 Diabetes

Yoshiji Ogawa¹, Takanori Kudo², Nobuhiko Kasai², Noriyuki Hasegawa³, Yuki Matsuhashi³, Yasuaki Tazawa¹, Shouko Kawashima¹, Akihito Kon¹ and Ken Tomotsune⁴

¹Diabetes Center, Aomori Prefectural Chuo Hospital, Japan; ²Department of Endocrinology and Diabetes/Hachinohe City Hospital, Japan; ³Internal Medicine/Itayanagi Chuo Hospital, Japan; ⁴Internal Medicine/Saiseikai Utsunomiya Hospital, Japan

INTRODUCTION: DPP4 inhibitor has now become one of the most popular agents for type 2 diabetes, and often administrated to the patients with HbA1c (JDS) levels between 7.0% and 8.0% as a first line. Therefore, it would commonly compete with Glinide, mild stimulator on pancreatic beta cells.

OBJECTIVE: We tried to compare the effects of either Sitagliptin (S) or Glinide (G) on Japanese type 2 diabetes by conversion from G to S.

METHODS: Fifty-one Japanese type 2 diabetic patients treated with G were recruited. After getting their consensus, G was changed to S and the course of HbA1c, C-peptide index (CPI), HOMA-R, serum lipids, serum cystatin C (CysC), and proinsulin/insulin (PI/I) ratio were measured before and 3 months after the conversion.

RESULTS: HbA1c, serum lipids, HOMA-R and PI/I ratio were not significantly changed by the conversion. However, either insulin-secretion assessed by CPI or CysC were significantly lower (CPI: $1.20 \pm 0.44 \rightarrow 1.00 \pm 0.45$, CysC: $0.94 \pm 0.20 \rightarrow 0.88 \pm 0.20$; mean $\pm$ SD) after the treatment with S. The data were also analyzed among the subgroup treated together with other hypoglycemic agents such as pioglitazone (P), metformin (M), or α -GI (A). Consequently, HbA1c levels tended to become better by mono-therapy of S or multi-therapy with M.

CONCLUSION: The Effects of S concerning HbA1c reduction was almost equal with G, simultaneously less insulin secretion was required. The decrease of CysC levels by S might correspond to vascular protection. Subgroup-analysis suggested that we should consider the compatibility among many oral hypoglycemic agents, and DPP4 inhibitor would be well-suited with metformin.

PCS-21-4

Effect of Sitagliptin on Glycemic Control Depends on the Postprandial Glucagon Suppression in Type 2 Diabetic Patients

Tomonobu Nakamura¹, Akizuki Morikawa¹, Yuko Morikawa¹, Masahiro Nomura¹, Jun Watanabe¹ and Masakazu Haneda²

¹Department of Internal Medicine, Asahikawa Red Cross Hospital, Japan; ²Department of Medicine, Asahikawa Medical University, Asahikawa, Japan

OBJECTIVE: To determine whether the degree of stimulation in insulin secretion and suppression in glucagon secretion in postprandial state correlate with the effect of sitagliptin (dipeptidyl peptidase-4 inhibitor) on the reduction of HbA1c in Japanese patients with type 2 diabetes.

METHODS: Twenty eight type 2 diabetic patients, inadequately treated with diet alone or hypoglycemic agents, received sitagliptin (50 mg/day) for 12 weeks without alteration of the previous treatment. After an overnight fast, patients consumed test meal (450 Kcal; carbohydrates 51.4%, fats 33.3%, proteins 15.3%) at the start of study and week 12. Fasting and postprandial (30 min after test meal consumption) glucose, insulin and glucagon concentrations were measured.

RESULTS: After 12 weeks of sitagliptin treatment, mean HbA1c significantly decreased from baseline (7.4 ± 1.0 vs 7.9 ± 1.1 , $P = 0.007$). Whereas no significant changes were observed in fasting and postprandial insulin and glucagon levels, insulinogenic index, HOMA-IR and HOMA-beta between baseline and week 12. Significant positive correlation was observed between changes in HbA1c and changes in postprandial glucagon secretion (Δ glucagon at week 12- Δ glucagon at baseline; $P = 0.038$). However no significant correlation was observed between parameters of insulin secretion and changes in HbA1c.

CONCLUSION: In Japanese type 2 diabetic patients, Effect of sitagliptin on glycemic control mainly depends on the suppression of postprandial glucagon secretion.

PCS-21-5

Add-On Effect of Sitagliptin in an Obese Type 2 Diabetic Patient with Glimepiride and Metformin on Blood Glucose Control and Incretin Response

Hiroyuki Konya¹, Taku Tsunoda¹, Mai Kamitani¹, Hayato Fukuoka¹, Tomoyuki Katsumo², Tomoya Hamaguchi³, Jun-ichiro Miyagawa², Mitsuyoshi Namba² and Yoshio Kanayama¹

¹Department of Internal Medicine, Ashiya Municipal Hospital, Japan; ²Divisions of Diabetes and Metabolism, Department of Internal Medicine, Hyogo College of Medicine, Japan; ³Divisions of Innovative Diabetes Treatment, Department of Internal Medicine, Hyogo College of Medicine, Japan

BACKGROUND AND METHODS: To determine whether sitagliptin administration improves glycemic control and reduces insulin resistance in an obese type 2 diabetes mellitus (T2DM) man (age 58, BMI 28.6, HOMA-R 5.26) treated with glimepiride and metformin, we analyzed the add-on effect of sitagliptin 50 mg on blood glucose control, incretin response during meal tolerance test (MTT). A 460 kcal MTT was performed at baseline and after 6 months, and the levels of plasma glucose and immunoreactive insulin, active GLP-1, total GIP and glucagon were measured. Various parameters of glucose metabolism and lipid metabolism and urinary albumin were also determined.

RESULTS: Sitagliptin showed a stimulatory effect on insulin, active GLP-1 secretion and reduced the levels of plasma glucose, glucagon, total GIP during MTT. In addition to HbA1c, sitagliptin also lowered HOMA-R and urinary albumin after 6 months.

CONCLUSIONS: Sitagliptin may improve glycemic control via increasing the plasma level of active GLP-1, decreasing glucagon and total GIP. Sitagliptin could also reduce hepatic insulin resistance in the patient, since it has been reported that GLP-1-(7-36)-amide would show a potent inhibitory effect on glucagon secretion from the alpha cells of endocrine pancreas, and also reported that GLP-1 might have a direct effect on hepatocytes, by activating genes involved in fatty acid β -oxidation and insulin sensitivity. These data indicate that sitagliptin may have the beneficial effects not only on glycemic control and incretin response, but also on the prevention of the vascular complications of diabetes.

PCS-21-6

The DPP-4 Inhibitors Improves BNP in Type 2 Diabetes Patients of Japan

Nobuyasu Noritake, Eri Yoshida, Yoshitaka Ogawa, Hiroya Sakuma and Hiroshi Murase

Department of Endocrinology, Daiyukai General Hospital, Japan

The evidence of the cardiovascular system with the DPP4 inhibitor is still few it. We pay attention to BNP which is surrogate marker for the cardiovascular system this time.

The object is 240 type 2 diabetes patients. It is 122 patients receiving Sitagliptin for blood sugar control insufficiency (Sitagliptin group).

With 118 patients considered to be it that blood sugar control is enough (non- Sitagliptin group)

I measured HbA1c, BP, BW, BNP 24 weeks later if before the dosage.

There is no change in blood pressure and the weight with both groups.

In the Sitagliptin group HbA1c is $6.9 \pm 0.5\%$ from $8.2 \pm 0.9\%$, 99% (121/122 patients) improved the ratio that HbA1c improved.

BNP is improved 36.8 ± 39.1 - 19.0 ± 22.2 , 96% (117/122 patients) improved the ratio that BNP improved. In the non- Sitagliptin group HbA1c is $6.8 \pm 0.6\%$ from $6.9 \pm 0.6\%$. BNP is 30.0 ± 31.8 rose to 34.5 ± 36.0 . The ratio that BNP improved is 32% (38/118 patients).

We accepted significant improvement of BNP by the Sitagliptin this time.

Is that the effect is the thing by the blood sugar improvement effect the thing by the incretin effect? I do not become clear.

Because the improvement of BNP confirms the improvement of HbA1c in the case more than 95%, too.

It was thought that the DPP4 inhibitor could improve BNP even if I made whichever.

The evidence that is connected directly with life convalescence is expected, but therefore long-term observation will be necessary in future. Rather it was thought that the significance to measure BNP which is surrogate marker for the cardiovascular system was very important.

PCS-21-7

Is Sitagliptin Replaceable for Sulfonylurea (SU) in Type 2 Diabetic Patients Treated with SU + Metformin or Pioglitazone?

Atsushi Nakagawa¹, Makoto Nishizawa¹, Shinichi Tsuda¹, Sumie Fujii², Takashi Seta², Hiroyuki Takata³, Yoshio Hiraiwa³, Hajime Nakabayashi⁴ and Daisuke Koya¹

¹Department of Diabetology and Endocrinology, Kanazawa Medical University, Japan;

²Department of Diabetology and Endocrinology, Ishikawa Prefectural Central Hospital, Japan; ³Department of Internal Medicine, Toyama Red Cross Hospital, Japan;

⁴Department of Internal Medicine, Kanazawa Munehiro Hospital, Japan

OBJECTIVE: DPP-4 inhibitors are categorized into antidiabetic drugs possessing insulinotropic action. Since sulfonylurea (SU)s also stimulate insulin secretion, we examined whether sitagliptin was replaceable for SU in patients with type 2 diabetes (T2D) on SU + metformin or pioglitazone treatment to achieve proper glycemic control.

METHODS: Subjects were 46 outpatients with T2D who had been treated with fixed doses and directions of SU + metformin or pioglitazone for >8 weeks, and remained in HbA1c levels of 6.9–9.4% with fluctuations of 0.5% or less for 4–8 weeks. SUs were changed to once-daily sitagliptin of 50 mg, but further up to 100 mg when HbA1c increased from the baseline by >0.5%. The primary outcome was changes of HbA1c between the baseline and 12 weeks after switching to sitagliptin.

RESULTS: Two patients dropped out because of marked glycemic aggravation. HbA1c significantly increased from $7.8 \pm 0.7\%$ to $8.1 \pm 1.1\%$. Noteworthy, HbA1c improved and worsened by $>|\pm 0.5\%|$ in 9% and 27% of the subjects, respectively, suggesting that there exist marked responders and/or extreme non-responders. Using multiple regression analyses, the following factors correlated significantly with HbA1c changes during 12 weeks of sitagliptin treatment: changes of fasting plasma glucose among changing factors indicating glycemic control and insulin secretion, and doses of SUs among the above-mentioned factors and clinical characteristics at the baseline.

CONCLUSION: In seeking better glycemic control in patients treated with SU + metformin or pioglitazone, switching from SUs to sitagliptin must be done with caution. Further studies are needed to clarify characters of responders and non-responders of sitagliptin.

PCS-21-8

Chronic Effect of Sitagliptin on the Metabolic and Incretin Responses During Cookie Meal Tests in Type 2 Diabetes

Aya Maeda¹, Masami Nakazawa², Masaaki Suzuki³, Motoyoshi Ikebuchi⁴, Aki Harano² and Yutaka Harano⁵

¹Niseikai Center for Lifestyle-Related Diseases, Japan, Department of Internal Medicine, Saiseikai Senri Hospital, Japan, Japan; ²Niseikai Center for Lifestyle-Related Diseases, Japan; ³Department of Internal Medicine, Saiseikai Senri Hospital, Japan; ⁴Ikebuchi-clinic, Japan; ⁵Niseikai Center for Lifestyle-Related Diseases, Japan/Department of Internal Medicine, Saiseikai Senri Hospital, Japan/Nutrition Research Institute, Nichidan Inc., Japan

Chronic effect of sitagliptin (SG, 50–100 mg, 2–10 mol/L) was evaluated using cookie meal tests (CMT) in type 2 diabetes with average duration of DM, 10 years, who required better glycemic control on the oral agents. CM (SARAYA. Co) consisted of 75 g carbohydrate, 29 g butter fat and 7 g protein for a total of 580 kcal. BMI unchanged with 24.2 kg/m^2 , HbA1c decreased from 8.0% to 6.3% (NGSP). Plasma glucose improved at 0, 1 and 2 h during CMT by 20–25%. No significant increase of plasma insulin was noted after SG. All insulin levels doubled with hyperinsulinemia in 1, in the other 3, only 21–36 pmol/L elevation at 1, 2 h after SG. Insulin resistance factor (IRF, $\text{AUC}_{\text{insulin}} \times \text{AUC}_{\text{glucose}}$) showed the improvement in 2, while in the 3, aggravated. In the other four cases insulin levels decreased with IRF alleviated. IRF diminished in six out of nine after SG. Plasma GLP-1 responded 3.5, 7.6, 6.3 pmol/mL to the meal, which increased 2–2.5 folds after SG. Initial GIP responses were 45.8, 616.9, 443.1 pg/mL, which significantly increased at 1, 2 h by 1.5–2 folds after SG. The initial fasting IRG levels was 120 pg/mL, which did not change following meal, nor after SG. δTG and $\delta\text{apoB-48}$ following meal significantly reduced after SG, indicating possible suppressive effect of GLP-1 on intestinal chylomicron formation. SG was effective in glycemic control as well as suppressive effect on intestinal chylomicron production. In 70% of the cases, insulin resistance factor diminished, suggesting possible GLP-1 action to stimulate insulin action.

PCS-22-1

Palmitic Acid Promotes Dysfunction of Human Umbilical Vein Endothelial Cells

Jing Liu¹, Wenting Tie², Qi Ma² and Ruilan Niu²

¹Department of endocrinology in Gan Su Province Hospital, Department of Endocrinology in Gan Su Province Hospital, Lan Zhou, Gan SU, China; ²First Clinical Medicine College in Lan Zhou University, Lan Zhou, Gan Su, China

OBJECTIVE: In this study, we attempt to evaluate the effect of palmitic on human umbilical vein endothelial cells.

METHODS: HUVECs were isolated from freshly collected umbilical cords, stimulated with palmitic acids. HUVECs survival rate was calculated by MTT assay, the levels of NO and nitric oxide synthase (NOS) were detected by colorimetric analysis, contents of endothelin-1 (ET-1) were detected by ELISA. Real-time PCR measure the mRNA expression of eNOS and ET-1.

RESULTS: Palmitic acids significantly induced decrease in expression of NO and NOS, and EMs can antagonize the damage. In addition, the palmitic acids induced increase in the production of ET-1 and the expression of ET-1 mRNA; decrease the expression of eNOSmRNA.

CONCLUSIONS: We propose that palmitic acid promotes the dysfunction of human umbilical vein endothelial cells.

PCS-22-2

Human Adipose Tissue-Derived Stem Cells Improves Diabetes in Streptozotocin-Induced Diabetes Rats

Pei-Yi Tsai¹, Pei-Wen Chou², Mei-Ling Hou¹, Tsung-Yen Ho², Ting-Yu Lin², Julia Yi-Ru Chen² and Jia-Ming Chang¹

¹Department of Animal Pharmacology, Development Center for Biotechnology, Taiwan;

²Guang Li BioMedicine, Inc.; Bionin Nanobiomedicine, Inc., New Taipei City, Taiwan

OBJECTIVE: Type 1 Diabetes Mellitus is caused by the dysfunction of insulin-producing beta cells in the pancreas, leading to insufficient insulin to lower the blood glucose. Stem cells offers great hope for a cure and better treatments for diabetes. In the present study, we examined whether human adipose-derived stem cells (ADSCs) and stromal vascular fraction (SVF) are able to increase the insulin via differentiation of stem cells to β -cells or stimulation of endogenous host β -cells in streptozotocin (STZ)-induced type 1 diabetic rats.

METHODS: Diabetic rats were induced by a single intraperitoneal injection of STZ (60 mg/kg) in Sprague-Dawley rats, which blood glucose levels determined $>250 \text{ mg/dL}$ were accepted as diabetes. The diabetic rats were administered with ADSCs and SVF via intravenous injection, respectively, which diabetic rats were administered with normal saline as vehicle controls and diabetic rats were implanted with insulin capsule as positive controls. Blood glucose, insulin, C-peptide, and HbA1c were monitored to evaluate the efficacy of ADSCs and SVF in diabetic rats.

RESULTS: The administration of SVF could decrease blood glucose in the diabetic rats from day 8 to day 22, compared to diseased control. Another blood glucose decrease was observed in ADSC treated groups on day 22. Both administration of ADSCs or SVF could increase serum insulin levels. The serum C-peptide levels were solely increased in SVF treated diabetic rats.

CONCLUSION: These results suggest that ADSCs and SVF increased insulin levels through different routes, and both are potential used as therapeutic strategy for diabetic disease.

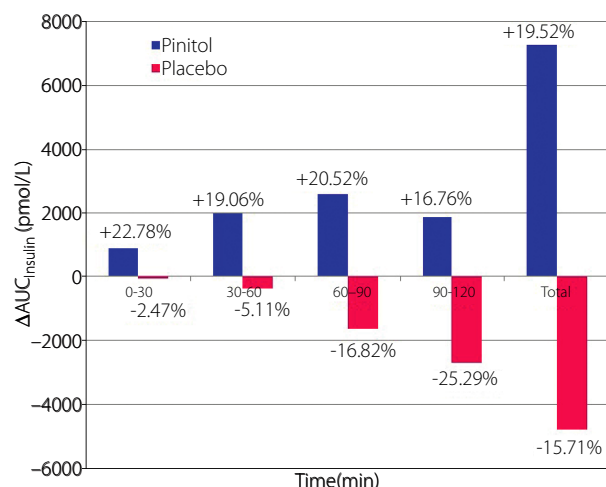
PCS-22-3

The Effects of Pinitol on Insulin Secretion During Oral Glucose Tolerance Test in Korean Prediabetes

Dong Pil Kim, Kang Seo Park, Hea Min Yu, Jae Min Lee and Seong Gyu Lee

Department of internal medicine, Eulji University School of Medicine, Korea

Pinitol is a methyl derivatives of D-chiro-inositol and phospholipid mediating intracellular insulin signaling pathway. In previous clinical study, Administration of pinitol improved glucose metabolism in type II diabetes mellitus patient. However, there was no clinical study about the effect of pinitol on prediabetes. We performed a randomized, double-blind, placebo-controlled, parallel designed study in 22 prediabetes who did not take the medication influencing glucose metabolism. Twelve subjects were assigned to pinitol group and 10 subjects were assigned to placebo group. There were no differences in basal clinical and laboratory parameters between the pinitol and placebo groups except body weight and BMI. After 12 weeks study, pinitol group increased insulin concentration and area under the curve (AUC) during



oral glucose tolerance test, but placebo group decreased in comparison to baseline. Especially insulin concentration during first 30 min and AUC from 30 to 60 min was statistically significant. Administration of pinitol to prediabetes improved decline of early phase insulin secretion that first sign of impaired glucose metabolism.

PCS-22-4

Association of the-250G/A Promoter Polymorphism of the Hepatic Lipase Gene with the Risk of Type 2 Diabetic in Chinese Han

Jing Liu¹, Jun-ling Zhang², Ju-xiang Liu² and Rui-Lan Niu³

¹Department of Endocrinology in Gan Su Province Hospital, Department of Endocrinology in Gan Su Province Hospital, Lan Zhou, Gan SU, China; ²Department of Endocrinology in Gan Su Province Hospital, Lan Zhou, Gan SU, China; ³First Clinical Medicine College in Lan Zhou University, Lan Zhou, Gan Su, China

OBJECTIVES: In population-based studies, dyslipidemia related to insulin resistance (high triglyceride level and low high-density lipoprotein cholesterol level) is a risk factor for type 2 diabetes. Therefore, variants in genes regulating lipid and lipoprotein metabolism are potential candidate genes for diabetes. We investigated whether the G-250A polymorphism of the hepatic lipase gene (LIPC) is associated with the type 2 diabetes in Chinese Han.

METHODS: For this study, a normal control group of 133 healthy subjects and an experimental group of 130 patients with T2DM were examined. polymorphisms in the promoter of the LIPC gene were studied by PCR amplification, DraI enzyme digestion. A logistic regression analysis was performed to determine the association between the rare allele and Type 2 diabetes mellitus.

RESULTS: The frequency of the-250A allele was 0.297 in the T2DM group and 0.388 in the control group ($P < 0.05$), with the difference remaining significant.

CONCLUSIONS: Patients who are carriers of the rare-250A allele in the promoter of the hepatic Lipase Gene are susceptible to Type 2 diabetes mellitus in China.

PCS-22-5

Effects of Physician Specialty on Glycaemic Control in Diabetic Outpatients: A 4-Year Observational Study in a Medical Center

Chia-Lin Lee, Jun-Sing Wang, I-Te Lee, Li-Nien Tseng, Yuh-Min Song, Shih-Yi Lin and Wayne Huey-Herng Sheu

Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Veterans General hospital, Taiwan

BACKGROUND: Previous studies revealed that physician specialty imposed certain influences on process measures and outcomes in diabetes care. However, long-term glycaemic control by physician specialty remained unclear.

METHODS: Diabetic outpatients were enrolled from July 2006 to December 2006, dividing into two groups (endocrinology = EN, non-endocrinology = non-EN). Medication for glycaemic control were recorded. Glycated hemoglobin (A1C) were recorded from 2007 to 2010. Student t-test was used for comparison of difference of mean baseline A1C between EN and non-EN groups. Mixed model repeated measures (MMRM) was used to estimate the annually improvement of A1C between EN and non-EN groups.

RESULTS: A total of 1522 outpatients were enrolled (1061 in EN group and 461 in non-EN group) and 1288 (84.6%) of them (877 in EN group and 411 in non-EN group) completed follow up. Mean A1C at baseline was significantly higher in EN group than in non-EN group ($8.3 \pm 1.9\%$ vs $7.6 \pm 1.5\%$, $P < 0.001$). At the end of study, mean A1C were $7.8 \pm 1.6\%$ ($P < 0.001$ compared with baseline) and $7.5 \pm 1.6\%$ ($P = 0.262$ compared with baseline) in EN and non-EN group, respectively. The adjusted annual change of A1C was $-0.13\%/year$ ($P < 0.001$) and $-0.03\%/year$ ($P = 0.165$) in EN and non-EN group, respectively. The rate of A1C reduction between groups reached statistical significance (P for interaction = 0.002).

CONCLUSION: Patients in EN group had higher baseline A1C than those in non-EN group. However, rate of A1C reduction was significantly better in EN group than in non-EN group. Our results indicate that endocrinologists may provide better glycaemic control than non-endocrinologists in outpatients diabetes care.

PCS-22-6

The Curative Effect of Stilamin on Diabetes Mellitus Ketoacidosis

Nan Zhang, Dahai Xu, Bailin Yan, Jing Wang, Xiuxian Zang, Shaokun Wang, Dan Shi and Yang Wu

Emergency Department, The First Hospital of Jilin University, China

OBJECTIVE: To investigate the curative effect of Stilamin on Diabetes mellitus ketoacidosis (DKA).

METHOD: Seventy-two female patients of DKA were randomly divided into two groups: the treatment group (40 patients) and the observing group (32 patients). The observing group accepted comprehensive treatment; the treatment group accepted Stilamin on the basis of comprehensive treatment. Recorded and analysed the glucose level, the rate of patients with urine acetone body positive before treatment, 4, 12 and 24 h after treatment between the two groups above.

RESULTS: On glucose level and rate of urine acetone positive: (1) The two groups had no significant differences before treatment. (2) Four hours after treatment: treatment group respectively (14.51 ± 3.61) mmol/L, 95.00%; observing group respectively (19.51 ± 5.73) mmol/L, 96.88%. And the two groups had significant differences on glucose level ($P < 0.05$), but no significant differences on rate of urine acetone positive. (3) Twelve hours after treatment: treatment group respectively (10.73 ± 3.23) mmol/L, 75.00%; observing group respectively (14.65 ± 3.45) mmol/L, 87.50%. And the two groups had significant differences on glucose level ($P < 0.05$), but no significant differences on rate of urine acetone positive. (4) Twenty-four hours after treatment: treatment group respectively (8.69 ± 2.51) mmol/L, 27.50%; observing group respectively (9.27 ± 2.16) mmol/L, 46.88%. And the two groups had significant differences on rate of urine acetone positive ($P < 0.05$), but no significant differences on glucose level.

CONCLUSION: Stilamin has curative effect on decreasing the level of glucose and urine acetone, and can be considered as an auxiliary treatment on DKA.

PCS-22-7

Effect of Hypoglycemic Formula on Chronic Inflammation and Thrombotic Risk Factors in Type 2 Diabetic Patients

Chueh Chen Shih¹, Ting Sun Kuo², Lian Lai Chin¹, Kung-Chi Chan³ and Pei Chi Chen³

¹Department of Internal medicine, section of endocrinology, Cheng Ching Hospital, Taiwan; ²Department of Dental Medicine, Chinese Medical University Hospital, Taiwan; ³Department of Food and Nutrition, Providence University, Taichung, Taiwan

Hyperglycemia-induced oxidative damage plays an important role in the development of chronic complications in type 2 diabetic patients.

Therefore, the purpose of this study was to investigate the effectiveness of market-sold hypoglycemic formula (HF) on chronic inflammation and thrombotic risk in type 2 diabetic patients.

Ninety type 2 DM patients were randomly assigned into four experimental groups in this double-blinded study. Treatment groups were placebo, low HF group (LG), medium HF group (MG), high HF group (HG). Before and after supplementation for 8 weeks, concentration of fasting plasma glucose, HbA1c, Insulin resistance (HOMA), MDA, inflammatory markers (hs-CRP and IL-6), von Willebrand factor (vWF), activity of coagulation factor VII (FVII), plasminogen activator inhibitor-1 (PAI-1) and anticoagulation factors (anti-thrombin III, AT-III and protein C, PC) were measured.

The results of this study showed that concentration of fasting glucose was decreased in HF groups, HbA1c was decreased and insulin level was increased in HG group. MDA was decreased in HF groups. Activity of PC was elevated

by supplementing HG. Concentration of hs-CRP, vWF and PAI-1 all tended to be decreased by HF supplementation.

In conclusion, supplementing high dosage hypoglycemic formula may provide beneficial effects to decrease fasting glucose and oxidative stress, to ameliorate chronic inflammation, abnormal blood coagulation, and hence decrease thrombotic risk in type 2 diabetic patients.

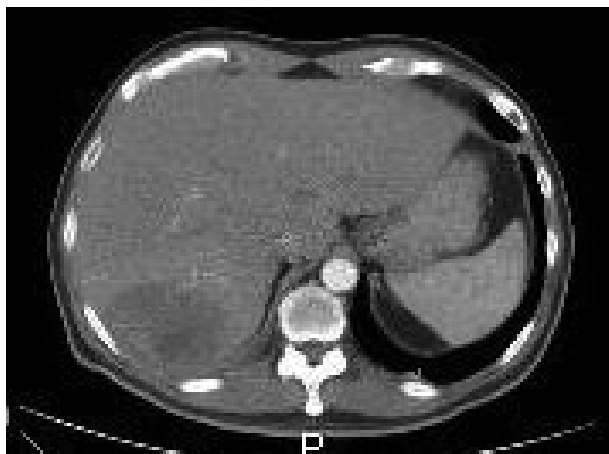
PCS-23-1

Pyogenic Liver Abscess in a Case of Diabetes Mellitus with Glycemic Poorly Controlled

Ju Ying Jiang¹ and Chien Chu Lin²

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Far Eastern Memorial Hospital, Taiwan; ²Division of Gastroenterology, Department of Internal Medicine, Far Eastern Memorial Hospital, Taiwan

Pyogenic liver abscess is a life-threatening disease. We report a case of 55-year-old man who presented to our Emergency Department complaining of fever and chilliness for about 5 days. His blood sugar 280 mg/dL, serum ketone 40 mg/dL without metabolic acidosis. His white blood cell count was $11.06 \times 10^3/\mu\text{L}$. His glycosylated hemoglobin (HbA1c) was 12.5%. Persisted spiking fever under antibiotics use whereas blood culture yielded *Klebsiella pneumoniae*. Then, abdominal computed tomography demonstrated a liver abscess approaching 8 cm in size on the posterior segments of the liver. Percutaneous drainage was done. Pus culture yielded *Klebsiella pneumoniae*. Eyeground examination showed no evidence of endophthalmitis. Blood sugar was controlled aggressively with insulin for about 2 months then follow up HbA1c improved to 6.7%. Later, glycemic controlled was shifted from insulin to oral hypoglycemia agents. In conclusion, *Klebsiella pneumoniae* liver abscess is an important and well known infection complication in diabetic patients in Taiwan, early diagnosis and treatment with good glycemic controlled improved outcome.



PCS-23-2

Effect of Metabolic Syndrome and Hypoadiponectinemia on Gastroesophageal Reflux Disease Symptom in Type 2 Diabetics

Kana Inoue¹, Ayumu Hirata¹, Ken Kishida¹, Hideaki Nakatsuji¹, Aki Shimizu¹, Tohru Funahashi² and Ichi Shimomura¹

¹Department of Metabolic Medicine, Osaka University Graduate School of Medicine, Japan; ²Department of Metabolism and Atherosclerosis, Osaka University Graduate School of Medicine, Japan

OBJECTIVE: To investigate the relation between gastroesophageal reflux disease (GERD) symptom and metabolic syndrome, adiponectin in the patients with type 2 diabetes mellitus (T2DM).

METHODS: In consecutive 66 T2DM patients, we evaluated GERD symptom by using Frequency Scale for the Symptoms of GERD (FSSG) score. We regarded patients with more than eight points of FSSG score positive in GERD. We estimated visceral fat area (VFA) by bioelectrical impedance analysis (BIA) method. Laboratory data including metabolic parameter and adipocytokine, were also measured.

RESULTS AND CONCLUSION: Twenty-three percentages of the subjects had more than eight in FSSG. The prevalence of FSSG score >7 and average FSSG score in T2DM subjects with metabolic syndrome were significantly higher compared to those without metabolic syndrome. Next, the subjects were divided into two groups, those with low and high circulating levels of adiponectin (cutoff value 6.31 $\mu\text{g/mL}$ for men, 8.62 $\mu\text{g/mL}$ for women, median value, respectively). The prevalence of FSSG score >7 and average FSSG score in T2DM subjects with low levels of serum adiponectin were significantly higher compared to those with high levels of serum adiponectin. Multiple regression analysis (adopted factors; age, sex, Mets, adiponectin, Mets x adiponectin) identified interaction term (Mets x adiponectin) as a significant determinant of GERD symptom score ($P = 0.047$). These data suggested that metabolic syndrome and hypoadiponectinemia both related to GERD symptom, and the combination of Mets and hypoadiponectinemia had a multiplicative effect on GERD symptom score.

PCS-23-3

Comparisons of Subcutaneous and Visceral Fat in Relation to Carotid Atherosclerosis and Cardiovascular Risk Factors in Patients with T2DM

Chan-Hee Jung, Bo-Yeon Kim, Chul-Hee Kim, Sung-Koo Kang and Ji-Oh Mok

Department of Internal Medicine, Soonchunhyang University School of Medicine, Korea

OBJECTIVE: Whereas visceral adipose tissue (VAT) is known to be associated with cardiometabolic risk, there has been much debate regarding the role of subcutaneous adipose tissue (SAT). The aim of this study was to investigate and compare the relation of SAT and VAT with carotid atherosclerosis and cardiovascular risk factors in T2DM.

METHODS: A total of 234 patients (mean age: 53 years) were enrolled. Carotid atherosclerosis and abdominal subcutaneous and visceral fat thickness were assessed by the use of high-resolution B-mode ultrasonography. Insulin resistance status was assessed by HOMA-IR index. Subjects were divided into three groups by the tertiles of subcutaneous fat thickness, visceral fat thickness and mean carotid intima-media thickness (CIMT).

RESULTS: The visceral fat thickness showed significant positive correlations with HOMA-IR, blood pressure, TG and hsCRP and negative correlation with HDL-C after adjustment for age. The subcutaneous fat thickness showed significant negative correlations with mean CIMT, number of carotid plaques, duration of diabetes and positive correlations with hsCRP, TC, TG and LDL-C. With the increasing the levels of mean subcutaneous fat thickness, the mean CIMT were decreased significantly. With the increasing the levels of visceral fat thickness, the mean levels of HOMA-IR were increased. However, there were no statistically significant differences on levels of CIMT and plaques between the groups of tertiles of visceral fat thickness.

CONCLUSION: We found that abdominal SAT was associated inversely with carotid atherosclerosis. Whereas, VAT was associated positively with insulin resistance and components of metabolic syndrome. Further research into the different role of two adipose tissue is warranted.

PCS-23-4

Huge Psoas Muscle Abscess in Diabetes Mellitus

Ju Ying Jiang¹, Pei Hwei Chen² and Wing Keung Cheung³

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Far Eastern Memorial Hospital, Taiwan; ²Department of Urology, Far Eastern Memorial Hospital, Taiwan; ³Division of Medical Imaging, Department of radiology, Far Eastern Memorial Hospital, Taiwan

Psoas muscle abscess is a rare and life-threatening infection which might cause mortality if delayed diagnosed. Here, a 58-year-old woman with diabetes mellitus about 2 years under regular oral hypoglycemic agents treatment, rheumatoid arthritis under steroid use. She presented to our Emergency Department due to urinary frequency and dysuria. Her blood sugar was 278 mg/dL without metabolic acidosis nor ketones. White blood cell count $16.90 \times 10^3/\mu\text{L}$ and neutrophil count 87.2%. Urinalysis showed pyuria. Intensive glycemic control with insulin use and empirical antibiotics for urinary tract infection. Her HbA1c was 8.2%. Fever and pyuria persisted despite antibiotics treatment. Urine and blood culture yielded *Escherichia coli*. Abdominal sonography showed right hydronephrosis and computed tomography showed a huge right psoas abscess. Then, percutaneous drainage was performed and she recovered well. Clinician should be aware that abscess



formation is a critical complication of diabetes mellitus as they are immune compromised. Early aggressive glycemic controlled combined with percutaneous drainage and antibiotics use often offer good outcome.

PCS-23-5

A Case of Parkinson's Disease Associated with Hypoglycemia Induced by Selegiline

Akira Kuroe and Hideki Yano

Department of Internal Medicine, Hikone Municipal Hospital, Japan

CASE: A 87-year-old woman was admitted to our hospital because of hypoglycemic coma. Plasma glucose level was 21 mg/dL. After admission, hypoglycemia still occurred frequently before meal and in the midnight. She had been followed up with Parkinson's disease and hypertension. She had never been treated with any antidiabetic medications. Laboratory tests showed no disorder of hepatic and renal functions. Her GH, cortisol and thyroid hormone levels were normal. Fasting plasma insulin level was 4 μ U/mL. Radiographic studies showed no apparent insulinoma. Then, we had checked her all antiparkinson agents and stopped selegiline administration. After 22 days, no hypoglycemia was observed. Selegiline, a MAO-B (monoamine oxidase type B) inhibitor, is reported to induce hypoglycemia in a few studies. Decrease in renal gluconeogenesis is hypothesized, but the precise mechanism remains still unclear. Other antiparkinson medicine such as levodopa-carbidopa was reported to induce hyperglycemia. We also experienced such a case.

CONCLUSION: Anti Parkinson agents may affect blood glucose levels in some cases. A MAO-B inhibitor is likely to induce hypoglycemia in this case. We should take the antiparkinson drugs into consideration when hypoglycemia is observed without antidiabetic medications.

PCS-23-6

Malignant Solitary Fibrous Tumor with Hypoglycemia (Doege-Potter Syndrome): A Case Report

Chwen Yi Yang, C. W. Chou, K. Z. Tien and F. J. Yen

Division of Endocrinology & Metabolism, Department of Internal medicine, Chi-Mei Medical Center, Taiwan

Doege-Potter syndrome (DPS) is a paraneoplastic syndrome in which hypoglycemia is associated with the presence of one or more non-islet fibrous tumors in the pleural cavity. The hypoglycemia is the result of the tumors producing insulin-like growth factor 2. DPS is rare with a malignancy rate of 12–15%. Tumors causing DPS tend to be quite large. In X-rays, they appear as a single mass with visible, defined borders, appearing at the edges of the lungs or a fissure dividing the lobes of the lungs. Similar hypoglycemic effects have been related to mesenchymal tumors. Here, we reported a case of DPS.

A victim of 77 y/o male was admitted due to consciousness disturbance. Intractable hypoglycemia was noted even though dextrose water infusion. Chest X-ray and CT scan revealed right lower lung huge mass lesion (15 cm). Low serum insulin and C-peptide and IGF-I level were noted. Chest surgeon was consulted and performed total excision. Pathology report showed malignant solitary fibrous tumor (T2b). After operation, patient's

blood sugar became normalized without episode of hypoglycemia. Postoperative serum level of insulin, C-peptide, IGF-I were elevated after 1 month follow up.

PCS-23-7

Endogenous Insulin Secretory Function and Glycemic Control in Japanese Type 2 Diabetic Patients on Hemodialysis Treatment

Asako Gondo, Tomonari Okada, Hiroshi Matsumoto, Yume Nagaoka, Toshikazu Wada and Toshiyuki Nakao

Department of Nephrology, Tokyo Medical University, Japan

BACKGROUND AND AIMS: The number of diabetic dialysis patients has increased recently, and evaluation of endogenous insulin secretory function (EISF) is important to determine glycemic control in those. We evaluated EISF in type 2 Japanese diabetic hemodialysis (HD) patients, and studied the relationship between EISF and glucose metabolism by an intravenous glucose tolerance test performed during HD.

MATERIALS AND METHODS: The subjects were 80 diabetic HD patients, studied within 3 months of the initiation of maintenance HD. They were given 10 g/min of glucose intravenously during HD, before lunch or dinner, using an external circulation circuit. Blood glucose (GLU) and serum insulin (IRI) levels were measured before and 5 min after the glucose load. We evaluated EISF according to the difference in δ IRI level before and after the glucose load.

RESULTS: In all diabetic patients, the mean δ IRI level was 7.7 ± 8.5 μ U/mL, and there were statistically significant correlations between the mean levels of δ IRI and GLU, HbA1c and glycated albumin ($r = -0.48$, $P = 0.0001$; $r = -0.27$, $P = 0.017$; $r = -0.26$, $P = 0.022$). Among those patients who were dependent on insulin therapy, the mean δ IRI level was lower than that of the patients who did not need insulin therapy ($P = 0.004$).

CONCLUSION: EISF was lower in the patients who were dependent on insulin therapy, and there were statistically significant correlations between the levels of δ IRI and indicators of glucose metabolism.

PCS-23-8

Clinical Study for Diagnostic Efficacy of Diabetic Angiopathy Using Hemorheological Measurement System

Eunjin Kwon¹, Youngmi Lee¹, Hyunjeong Lee¹, Minkyung Kim¹, Jiyeon Ha¹, Chanhee Kyung¹, Sohee Kim¹, Jiwoon Kim¹, Taewoong Noh¹, Chulwoo Ahn¹, Kyungrae Kim¹, Sehyun Shin² and Byungkwon Lee¹

¹Department of Internal Medicine, Yonsei University School of Medicine, Korea;

²Department of Mechanical Engineering, Korea University, Seoul, Korea

Several key hemorheological parameters, such as erythrocyte deformability, erythrocyte aggregation are altered in patients with diabetes mellitus. These changes of erythrocyte in turn make whole blood more viscous and may play an important role on the pathogenesis of vascular complications of diabetes mellitus. So in this study, we intended to examine erythrocyte deformability and aggregation in patients with type 2 diabetes, and assess the differences of these parameters compared with healthy controls.

Forty-five subjects were enrolled and their blood and urine samples were obtained. The erythrocyte deformability was measured in terms of elongation index (EI) with microfluidic ektacytometer, RheoScan, which was very sensitive to detect changes in EI of erythrocytes due to hyperglycemic process. The aggregation index (AI) was measured with RheoScan, too. All subjects were divided by four groups according to their past history and test results as follows: Healthy control ($n = 11$), prediabetes (pre-DM, $n = 6$), diabetes without vascular complications (DM-no Cx, $n = 10$), diabetes with vascular complications (DM-Cx, $n = 18$).

A significant reduction of erythrocyte deformability was observed in DM-Cx group compared with healthy control (0.325 vs 0.347 , $P < 0.05$). Also, EI was significantly decreased in the group of higher HbA1c level ($a1c > 9\%$) compared with in the group of lower HbA1c level ($a1c < 7\%$, 0.324 vs 0.341 , $P < 0.05$).

EI is a sensitive parameter to detect impairment of erythrocyte in diabetic process. The results in this study suggest that significant reduction in the EI may have correlation with diabetic vascular complications, and furthermore could be one of the indicators of these complications.

PCS-23-9

Type 2 Diabetes Mellitus and Osteoporosis

Nanang Soebijanto Sajoei and Giri Aji

Departement of Internal Medicine, Fatmawati Hospital, Indonesia

BACKGROUND: Osteoporosis is an under appreciated complication of diabetes mellitus (DM). Unclear pathophysiology and contrary data from previous study may contribute to this, meanwhile there is a growing number of new diabetes case. Diabetes mellitus itself is associated with the increase of risk of fracture, but whether or not it increases the risk of osteoporosis, is still a question. Leptin from adipose tissue increases the understanding between osteoporosis and diabetes mellitus.

METHOD: A case control study with 114 subject, 56 type 2 DM patients and 58 non DM patients undergoes DXA Bone Mineral Densitometry for osteoporosis evaluation. The analysis of data was conducted with univariate and bivariate using Chi square method and Odds ratio.

RESULTS: Osteoporosis prevalence's in case population (type 2 DM) is 17.9%, while on non DM is 24.1%. There is no correlation between BMD result and type 2 DM. However, there is a correlation between BMD and age (OR 2.654, 95% CI: 1.154–11.564, $P = 0.031$) and between BMD and Body Mass Index (OR 0.227, 95% CI: 0.085–0.606, $P = 0.003$).

CONCLUSION: We found no correlation between type 2 DM and osteoporosis. We however found correlation between age and Body Mass Index with osteoporosis.

KEYWORDS: Type 2 diabetes mellitus, osteoporosis, bone mineral densitometry.

PCS-24-1

Surrogate Markers of Subclinical Atherosclerosis in Egyptian Children with Type1 Diabetes

Hoda Atwa¹, Hassan Shora² and Amal Elsayed³

¹Pediatrics, Faculty of Medicine, Suez Canal University, Egypt; ²Medicine, Ministry of Health, Ismailia, Egypt; ³Clinical Pathology, Faculty of Medicine, Suez Canal University, Egypt

BACKGROUND: Endothelial dysfunction may be a critical early target for preventing atherosclerosis and cardiovascular disease. Leptin/adiponectin ratio can serve as a clinical marker of endothelial dysfunction in children with type 1 diabetes.

AIM: We investigated the relationship between leptin/adiponectin ratio with carotid intima-media thickness cIMT and endothelial dysfunction.

SUBJECTS AND METHODS: Sixty eight type 1 diabetic children their mean age were ranged 8–14 years compared to 70 healthy control subjects matched for age sex and body mass index. Serum level of leptin was measured via radioimmunoassay and adiponectin level was measured using an enzyme linked immunosorbent assay. Flow Mediated Dilatation was assessed.

RESULTS: Flow Mediated Dilatation was significantly correlated with leptin 9.906 ± 1.688 ng/dL and adiponectin $r = -0.327$ $P = 0.055$ and leptin/adiponectin L/A $r = -0.301$, $P = 0.079$ but not correlated with adiponectin. Statistically significant correlation was found between carotid intima media thickness and L/A ratio, leptin and adiponectin $r = -0.274$ $P = 0.026$, $r = -0.302$ $P = 0.012$, $r = -0.301$ $P = 0.079$ respectively. BMI was correlated with cIMT.

CONCLUSION: FMD, L/A ratio and cIMT may be useful surrogate markers of subclinical atherosclerosis that make early preventive interventional strategies feasible in type 1 diabetic children.

PCS-24-2

Type 1 Diabetes with Serial Thyroid Function Pursued Until Graves' Disease Complicated

Hirokazu Ohfusa

Division of Health Assessment and Promotion, Nagano Red Cross Hospital, Japan

BACKGROUND: Many case reports of type1 diabetes (T1D) accompanied by Graves' disease (GD) are accumulated, but such a case has been scarcely reported that in preceding T1D, serial thyroid function could be pursued until GD complicated with T1D.

CASE PRESENTATION: Case1: A 44-year-old female having familial history of type 2 diabetes and past history of obesity admitted was found in laboratory data to have anti-glutamic acid decarboxylase antibody (GADA) of 6130 U/mL, HbA1c of 14.1% (NSGP), urinary CPR of 52 µg/day, FT4 of 1.47 ng/dL,

TSH of 1.36 µIU/mL, negative TSH receptor antibody (TRAb). She was diagnosed as slowly progressive insulin-dependent diabetes mellitus (SPIDDM). Every May, thyroid functions measured were all within normal range. At 48-year-old, she complained of hyper-sweating and palpitation. HbA1c of 6.8% (NSGP), FT4 of 2.95 ng/dL, TSH of <0.01 µIU/mL, anti-thyroid peroxidase antibody (anti-TPO) of 15.0 IU/mL, TRAb of 70.4% were determined.

Case 2: 32-year-old female with T1D referred to our hospital was found in laboratory data to have postprandial CPR of 0.30 ng/mL, FT4 of 1.02 ng/dL, TSH of 0.78 µIU/mL, TRAb of 8.3%. Annually thyroid functions were estimated. At 37-year-old, she complained of palpitation. HbA1c of 6.8% (NSGP), FT4 of 15.37 ng/dL, TSH of <0.01 µIU/mL, anti-TPO of 37.2 IU/mL, TRAb of 71.3% were determined.

They were considered as autoimmune polyglandular syndrome type 3 (APS3).

CONCLUSION: While in Japanese, GD mostly precedes T1D (in woman, high GADA, SPIDDM) was reported (Osaki et al, 2009), I could observe the changes in parameters of GD until it complicated with T1D. Though GD did not affect T1D apparently, observing T1D course whether to be complicated with GD or not is interesting to investigate APS3.

PCS-24-3

Newly Diagnosed Fulminant Type 1 Diabetes in a Patient Taking Imatinib Mesylate

Kyung Ae Lee, Jae Moon Kim, Sunhee Kim, Heung Yong Jin, Hong Sun Baek and Tae Sun Park

Division of Endocrinology and Metabolism, Department of Internal Medicine, Chonbuk National University Hospital, Korea

Imatinib mesylate is a potent inhibitor of the BCR-ABL tyrosine kinase associated with chronic myeloid leukemia. Recently, in addition to its direct effect on malignant cells, it has been suggested that imatinib treatment can have immunomodulatory activity. Furthermore, treatment with imatinib might favorably act at steps controlling physiological functions responsible for maintaining glucose homeostasis. Herein, we report an unusual case that fulminant type 1 diabetes mellitus occurred abruptly in a chronic myeloid leukemia patient who's taking imatinib mesylate for 6 months.

A 60-year old man was brought to the emergency department presenting with acute abdominal pain, nausea and vomiting. He was diagnosed with chronic myeloid leukemia, chronic phase about 6 months ago, and was taken an imatinib mesylate 400 mg per day since that time. On arrival, laboratory result are: capillary glucose high, ABGA pH 7.22, HCO₃ 8.1 mmol/L, TCO₂ 8.7 mmol/L, ketonuria, HbA1C 5.3%, serum glucose 1031 mg/dL, amylase 68 IU/L, lipase 52 U/L, c-peptide 0.11 ng/mL, insulin 4.25 Uµ/mL, Islet cell autoantibody (IA2 antibody, GAD antibody, insulin antibody) are negative results. The clinical characteristics of the patient were remarkably abrupt onset diabetes, very short duration of diabetic symptoms, acidosis at the time of diagnosis, negative findings for islet-related autoantibodies and no c-peptide secretion. His diagnosis was compatible with fulminant type 1 diabetes.

Unlikely our expectation, there is no protective effect of imatinib mesylate on fulminant type 1 diabetes occurrence. Fulminant type 1 diabetes is a distinct subtype within diabetes and multiple factors seem to play a crucial role in the pathogenesis of diabetes.

PCS-24-4

Fatty Liver and its Association in Children with Type1 Diabetes

Hoda Atwa¹, Badr Mesbah², Khaled Abdelhamed³ and Shreim Salem⁴

¹Pediatrics, Faculty of Medicine, Suez Canal University, Egypt; ²Pediatrics; ³Radiology; ⁴Pediatrics

BACKGROUND: Non-alcoholic fatty liver disease is associated with an increased prevalence of cardiovascular disease (CVD) in both non-diabetic and Type 2 diabetic individuals.

AIM: To study the relationship between NAFLD and subclinical atherosclerosis in children with Type 1 diabetes.

SUBJECTS AND METHODS: Cross-sectional. Fifty five children with T1DM and 55 healthy children matched for age and BMI were included group. Aorta intima media thickness was assessed. Liver size and echogenicity were measured.

RESULTS: The mean duration of T1DM children was (4.6 ± 2.8 year), their HbA1c was (8.6 ± 2.2) There was no significant difference between the two group as regard waist circumference. Mean aMT was significantly higher in children with T1DM (0.8 ± 0.2) than control group (5.2 ± 0.6) $P = 0.000$. Liver

size was larger in children with T1DM than control $p < 0.001$. Echogmetric was 21.8% in T1DM children and 0% in control group. There was significant correlation between liver size and aIMT.

CONCLUSION: Fatty liver may be associated with subclinical atherosclerosis.

PCS-24-5

Soluble Receptor for Advanced Glycation End-Products in Chinese Type 1 Diabetic Patients

Joanne King Yun Lam¹, Yiqun Wang², Sammy W. M. Shiu², Ying Wong² and Kathryn C. B. Tan²

¹Department of Medicine, Queen Mary Hospital, Hong Kong; ²Department of Medicine, University of Hong Kong, Hong Kong

OBJECTIVES: The receptor for advanced glycation end-products (RAGE) plays an important role in the pathogenesis of diabetic complications. Interfering with the activation of RAGE by using a soluble form of the receptor (sRAGE) ameliorates the vascular complications of diabetes in animal models. sRAGE in the human circulation is partly derived from ectodomain shedding of the membrane-associated receptor. We have investigated the effect of insulin on the generation of sRAGE *in vitro* and evaluated serum levels of sRAGE in a group of Chinese type 1 diabetic subjects.

METHODS: THP-1 cells were incubated with insulin *in vitro* and sRAGE in the medium measured by Western immunoblot. Cell-surface biotinylation and immunoprecipitation was performed to investigate ectodomain shedding. Serum level of sRAGE in diabetic patients was measured by ELISA.

RESULTS: Insulin increased sRAGE in cell conditioned-media in a time- and dose-dependent manner. Pretreatment of THP-1 cells with GM6001, a general metalloproteinase inhibitor which blocked cellular shedding events, significantly reduced the production of sRAGE. This would suggest that the increase in sRAGE upon incubation with insulin was partly due to the shedding of sRAGE by cleavage of full-length cell surface RAGE. In type 1 diabetic patients ($n = 120$), serum sRAGE was higher compared to a group of age-matched non-diabetic healthy subjects (1021.6 pg/mL [724.8–1212.4.0] vs 812.9 pg/mL [548.0–1202.2.5] respectively, $P = 0.004$).

CONCLUSIONS: Chinese type 1 diabetic patients have higher serum levels of sRAGE and we have shown that insulin can stimulate the ectodomain shedding of cell surface RAGE.

PCS-24-6

A Broad Repertoire of GAD65-Specific T Cells in Type 1 Diabetics with Graft Dysfunction After Islet Transplantation

Daisuke Chujo¹, Emile Foucat², Masayuki Shimoda¹, Kunimasa Yagi³, Marlon Levy⁴, Hideki Ueno² and Shinichi Matsumoto¹

¹Diabetes Research Center, National Center for Global Health and Medicine, Japan; ²Baylor Institute for Immunology Research, USA; ³Division of Cardiovascular Medicine, Kanazawa University, Japan; ⁴Baylor University Medical Center, USA

Islet transplantation is one of the most promising therapies for type 1 diabetes (T1D). A major issue in islet transplantation is the loss of graft function at late phase. Several studies suggested the involvement of islet-specific T cells in such islet graft dysfunction. In this study, we investigated the breadth and type of GAD65-specific T cells in T1D patients after allogeneic islet transplantation. Peripheral blood mononuclear cells were obtained from islet-transplanted T1D patients during insulin independent period, and cultured for 7 days with pools of GAD65 overlapping peptides in the presence of IL-2. Cytokine secretion profiles of peptide-reactive T cells were analyzed after a short-term re-stimulation with the same peptides, by a multiplex bead-based cytokine assay and by an intracytoplasmic cytokine detection assay. Robust GAD65-specific CD4+ and CD8+ T cell responses were detected in patients who eventually developed chronic graft dysfunction. Multiple GAD65 peptides were found to induce specific T cell responses in these patients, indicating that the repertoire of GAD65-specific T cells was broad. Furthermore, GAD65-specific CD4+ T cells were composed of heterogeneous populations which differentially expressed cytokines including IFN- γ and Type 2 cytokines, but not IL-10. In contrast, patients who showed only marginal GAD65-specific T cell responses maintained substantially longer graft survival and insulin independence. In conclusion, our study suggests that the emergence of islet-specific T cells precedes the development of chronic graft dysfunction in islet-transplanted patients. Thus, our observations support the hypothesis that these islet-specific T cells contribute to the development of chronic islet graft dysfunction.

PCS-25-1

A Randomized Controlled Trial to Investigate the Impact of a Low Glycemic Index (GI) Diet on Body Mass Index in Chinese Adolescents

Alice Pik Shan Kong¹, Kai Chow Choi², Ruth Chan¹, Andrea Lok¹, Risa Ozaki¹, Ronald Ma¹, Francis Chow¹, Jean Woo¹ and Juliana Chan¹

¹Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong; ²Nethersole School of Nursing, The Chinese University of Hong Kong, Shatin, Hong Kong

BACKGROUND: The role of low glycemic index (GI) diet in management of adolescence obesity is controversial.

OBJECTIVE: To study the changes in body mass index (BMI) and other obesity indices in obese adolescents randomized to a 6-month low GI diet vs a conventional Chinese diet.

METHODS: Obese adolescents aged 15–18 years were identified from population-recruited, territory-wide surveys. Obesity was defined as BMI ≥ 95 th percentile of Hong Kong local reference. Eligible subjects were randomized to either a 6-month intervention with low GI diet (45–50% carbohydrate and 30–35% fat with the remainder from protein) or conventional Chinese diet as control (55–60% carbohydrate and 25–30% fat with the remainder from protein). We used random intercept mixed effects model to compare the differential changes across the time point at baseline and month 6 between the two groups.

RESULTS: One hundred and four obese adolescents were recruited (52 in low GI group and 52 in control group; 43.3% boys). Mean age was 16.7 ± 1.0 years and 16.8 ± 1.0 years in low GI and control group respectively. 58.7% subjects completed 6 month study (65.4% in low GI group and 51.9% in control group). After adjustment for age and sex, subjects in low GI group had significant reduction in obesity indices including BMI, body weight and waist circumference compared to subjects in the control group (all $P < 0.05$).

CONCLUSION: A low GI diet appears to be a promising alternative to conventional diet in obese adolescents.

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PCS-25-2

Testosterone Treatment Improves Insulin Resistance in Male Metabolic Syndrome

Hajime Ueshiba

Department of Internal Medicine, Toho University School of Medicine, Japan

The metabolic syndrome involves a cluster of clinical features including visceral obesity, insulin resistance, hypertension, glucose intolerance, and dyslipidemia. Recent studies have shown that low testosterone levels are significantly associated with metabolic syndrome and type 2 diabetes.

We examined the change in insulin resistance after testosterone treatment in five Japanese men with metabolic syndrome and low free testosterone levels (age: 50.2 ± 8.7 years, BMI: 30.5 ± 5.0 , waist: 97 ± 7 cm; Mean $\pm$ SD). Testosterone supplements were administered by intramuscular injection (250 mg every 2 weeks) for 3–6 months.

Fasting plasma glucose (FPG), fasting serum insulin (F-IRI), HbA_{1c}, total cholesterol (TCHO), triglyceride (TG), HDL-cholesterol (HDL-C), free testosterone, BMI and waist circumference were measured. We used insulin resistance index as assessed by homeostasis model assessment (HOMA-R) and investigated the change in insulin resistance after testosterone treatment.

Average results before treatment were as follows: BMI 30.5 ± 5.0 , waist 97 ± 7 cm, FPG 112 ± 6 mg/dL, F-IRI 25.1 ± 8.5 μ IU/mL, HOMA-R 7.0 ± 2.7 , HbA_{1c} $5.8 \pm 0.3\%$, TCHO 227 ± 31 mg/dL, TG 185 ± 64 mg/dL, HDL-C 43 ± 9 mg/dL, free testosterone 5.9 ± 1.0 pg/mL. After treatment, F-IRI, HOMA-R and TCHO were significantly decreased to 12.9 ± 3.6 μ IU/mL, 3.3 ± 1.1 and 199 ± 29 mg/dL, respectively. Free testosterone was significantly increased to 8.5 ± 0.6 pg/mL.

In conclusion, these results suggest that testosterone treatment improves insulin resistance in Japanese men with metabolic syndrome and low free testosterone levels.

PCS-25-3

The Clinical Features of Visceral Obesity According to Gender Differences in Patients with Type 2 Diabetes

Eon Ju Jeon and Ji Hyun Lee

Department of Internal Medicine, School of Medicine, Catholic University of Daegu, Korea

The aim of this study was to investigate the clinical features of visceral fat accumulation in diabetic patients by gender and to assess factors affecting visceral fat amount and to estimate cut-off value for visceral fat area (VFA) to predict central obesity in type 2 diabetic patients.

Total 363 subjects with type 2 diabetes (191 men, 172 women) were enrolled in this study. VFA was measured by single slice abdominal computed tomography scanning. Laboratory parameters such as fasting blood glucose, HbA1c, insulin resistance (HOMA-IR), and lipid profile were included. Central obesity was defined as a waist circumference in men >90 cm and in women >85 cm and BMI > 23 kg/m² in both men and women.

Women compared with men had increased total fat (29322.7 ± 9773.4 vs 23439.8 ± 8361.8, $P < 0.005$), subcutaneous fat (18333.0 ± 6823.3 vs 12107.3 ± 4806.4, $P < 0.001$), but visceral fat (10989.7 ± 4400.2 vs 11332.5 ± 4717.5, $P = 0.05$) was no significant difference. The area under the ROC curve (AUC) value for VFA to predict the obesity according to waist circumference and BMI were analyzed (respectively, 0.820 and 0.806 for men, 0.826 and 0.836 for women). The optimal cut-off points for VFA to predicting central obesity according to waist circumference were 104.93 cm² for men and 96.46 cm² for women and according to BMI were 86.97 cm² for men and 95.88 cm² for women.

Men diabetic patients were relatively visceral obesity compared to women diabetes. Visceral fat amount in both men and women showed a significant correlate with cardiovascular risk factors such as age, insulin resistance and lipid metabolism.

PCS-25-4

Is Uric Acid an Indicator of Metabolic Syndrome in the First-Degree Relatives of Patients with Type 2 Diabetes?

Rezvaneh Salehidoost, Ashraf Aminoroaya, Maryam Zare and Massoud Amini

Isfahan Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

BACKGROUND: To determine whether uric acid levels are associated with the components of metabolic syndrome and whether uric acid is a significant factor for development of metabolic syndrome in the first-degree relatives of type 2 diabetic patients as high risk group.

METHODS: A total of 694 (182 male and 512 female, aged 30–69 years) first-degree relatives of type 2 diabetic patients during 2007–2011 were enrolled. The height, weight, waist and blood pressure were measured. Fasting plasma glucose, lipid profile and uric acid concentration were assayed. Metabolic syndrome was defined by NCEP-ATP III.

RESULTS: Uric acid was associated with waist circumference, blood pressure, triglyceride level and HDL-cholesterol in both sexes. The prevalence of metabolic syndrome in the fourth quartile of uric acid was significantly more than those in the first and second quartiles in both sexes. The mean of uric acid in people with metabolic syndrome was significantly higher than in those without ($P = 0.0001$). The age adjusted odds ratios (95% confidence interval) of uric acid for metabolic syndrome in univariate analysis were 1.60 (1.23–2.07) for men and 1.61 (1.34–1.92) for women but the effect of uric acid in multivariate logistic regression was not significant.

CONCLUSIONS: Uric acid is associated with majority of the metabolic syndrome components. People with metabolic syndrome have higher uric acid levels. However, uric acid probably is not an independent factor to predict the metabolic syndrome.

PCS-25-5

Enhanced Waist Circumference in Male Subjects with Normal Body Mass Index and Glucose Tolerance is Associated with Insulin Resistance

Ryoma Sasaki

Department of Diabetes, Metabolism and Endocrinology, Mie University Graduate School of Medicine, Japan

BACKGROUND: We previously reported the presence of insulin resistance in metabolically obese but normal weight (MONW) with excess visceral fat

accumulation by computed tomography. There are no reports on the profile of glucose tolerance test in MONW as evaluated by the waist circumference, and with normal glucose tolerance (NGT).

OBJECTIVE: We investigated the association of glucose and insulin levels during glucose tolerance test in male subjects with ≥85 cm of waist circumference with normal BMI and NGT.

DESIGN: We categorized 168 subjects in three groups as follows: Group A; BMI < 25 kg/m² and waist ≥85 cm ($n = 33$), Group B; 22.5 ≤ BMI < 25 kg/m² and waist < 85 cm ($n = 59$), Group C; BMI < 22.5 kg/m² and waist < 85 cm ($n = 76$). We measured the plasma glucose and serum insulin levels before glucose loading and after 30 and 120 min and serum high molecular weight (HMW) adiponectin levels.

RESULTS: The plasma glucose levels were significantly increased in Group A as compared to Group C ($P < 0.05$) before loading and after 120 min. The serum insulin levels were significantly increased in Group A as compared to Group B ($P < 0.05$) or Group C ($P < 0.0001$) before loading and compared to Group B ($P < 0.05$) or Group C ($P < 0.001$) after 120 min. Subjects from Group A showed significantly increased HOMA-IR compared with Group B ($P < 0.01$) or Group C ($P < 0.0001$). Serum HMW adiponectin levels significantly and inversely correlated with the waist circumference ($r = -0.19$, $P < 0.02$).

CONCLUSION: These data suggests that enhanced waist circumference in male subjects with normal BMI and NGT is associated with insulin resistance.

PCS-25-6

Non-Alcoholic Fatty Pancreatic Disease (NAFPD) Could be an Early and Strong Predictor for Metabolic Syndrome

Wan-Chen Wu and Chih-Yuan Wang

Department of Internal Medicine, National Taiwan University Hospital, Hsin-Chu Branch, Taiwan

AIMS: Fatty liver is associated with insulin resistance, dyslipidemia, and obesity and is therefore considered a phenotype of metabolic syndrome. However, less is known regarding the metabolic abnormalities associated with non-alcoholic fatty pancreatic disease (NAFPD; fatty pancreas). The present study was performed to ascertain whether fatty pancreas is associated with specific metabolic risk factors and with metabolic syndrome as defined by the Adult Treatment Panel III.

METHODS: Five-hundred-fifty-seven healthy and consecutive subjects without known hypertension or diabetes and who received a health investigation at the National Taiwan University Hospital Health Management Center were enrolled in this retrospective study. Fatty pancreas was diagnosed via trans-abdominal ultrasonographic findings.

RESULTS: Seventy-two (12.9%) subjects diagnosed with fatty pancreas comprised the fatty pancreas group, and remaining subjects comprised the normal pancreas group. The presence of various demographic and metabolic risk factors was recorded for all subjects, and the two groups were examined for statistically significant differences in these factors. As compared to the absence of fatty pancreas, the presence of the disease was associated with older age and with higher values for each of the following: BMI, abdominal girth/height, abdominal girth (both genders), fasting and postprandial blood glucose, HbA1c, total cholesterol, triglycerides, LDL-cholesterol, systolic blood pressure, and platelet count. In contrast to previously reported findings, serum amylase values were lower in the fatty pancreas as compared to the control group.

CONCLUSION: The presence of fatty pancreas serves as an early and strong predictor of metabolic syndrome and could represent a meaningful manifestation of metabolic syndrome.

PCS-25-7

Association Between hs-CRP and HbA1c in Overweight Type 2 Diabetic Female

Veerasak Sarinnapakorn and Warangkana Wanichagool

Internal Medicine, Rajavithi Hospital, Rangsit University, Thailand

BACKGROUND AND OBJECTIVE: The previous studies showed that hs-CRP is associated with insulin resistance and type 2 diabetes. Because of the type 2 diabetic patients are often overweight women. This study investigated the relationship between hs-CRP and HbA1c levels in such patients.

MATERIALS AND METHODS: This study design was retrospective study of the type 2 diabetic patients in Rajavithi hospital from January 2009 until June

2011 and all of them were female aged 40 years or more who had body mass index more than 25 kilogram per metre². The patients had been examined and collected blood for hs-CRP and HbA1c level.

RESULTS: Data from 75 cases, classified patients into two groups according to level of hs-CRP divided by risk of coronary artery disease. Thirty-five from 75 patients had hs-CRP levels <1 mg/L. The remaining 40 patients had hs-CRP levels between 1 mg/L or more. Representing 46.67% and 53.33% respectively, and found that the value of hs-CRP correlated with HbA1c level. The hs-CRP <1 mg/L had median HbA1c $7.36 \pm 1.23\%$. The hs-CRP between 1 mg/dL or more had median HbA1c $8.77 \pm 1.78\%$, with statistical significance at P -value <0.001.

CONCLUSIONS: In this study, patients with type 2 diabetes showed that the hs-CRP levels have correlated with HbA1c levels. Median HbA1c levels were significantly higher in patients who have hs-CRP levels 1 mg/L or more (P -value < 0.001). Other factors correlated, but not statistically significant.

KEYWORDS: hs-CRP, HbA1c.

PCS-26-1

Relation Between Adiponectin and Oxidative Stress Evaluated with d-ROMs as Reactive Oxygen Species and with BAP as Anti-Oxidative Capacity

Shohei Kawaguchi, Kayoko Ryomoto, Rieko Okano, Emiko Teramoto, Yukako Sakaguchi, Toshihiko Uematsu, Yoshimoto Kiyohara, Yoji Hazama, Masashi Kubota, Makoto Ohashi and Makoto Nomura

Center for Diabetes Mellitus, Osaka Rosai Hospital, Japan

OBJECTIVE: Adiponectin have been the specific hormone to originate from fat tissue consistently associated with obesity, insulin resistance, type 2 diabetes, and coronary artery disease. Recent data have revealed that adiponectin possesses a vascular protective role by preserving endothelial cell function and suppresses development of arteriosclerosis with the metabolic syndrome. It was reported that one of the protective roles was antioxidative properties of adiponectin. Oxidative stress is one of the mechanisms with arteriosclerosis and is generated by an excess of reactive oxygen species (ROS) to the antioxidant capacity. The assay of oxidative stress is difficult in the general medical examination institution, but FRAS4 systems enabled easily measuring ROS and antioxidant capacity. We investigated the relation between adiponectin and oxidative stress by FRAS4 systems.

METHOD: The subjects were 24 males and 18 females who underwent a checkup examination. ROS was evaluated as d-ROMs and antioxidant capacity was evaluated as BAP measuring by FRAS4 systems. We investigated the relation between metabolic factors, BAP, d-ROMs and adiponectin using correlation coefficients of Pearson or Spearman.

RESULT: Adiponectin significantly correlated with BAP ($r = 0.42$), HDL-C ($r = 0.67$), and negatively with BMI ($r = -0.34$), waist circumference ($r = -0.42$), TG ($r = -0.49$), FBS ($r = -0.40$) and CRP ($r = -0.58$). BAP significantly correlated with HDL-C ($r = 0.61$), and negatively with BMI ($r = -0.42$), waist circumference ($r = -0.47$), and TG ($r = -0.57$). There was no relation between adiponectin and d-ROMs.

CONCLUSION: BAP as the anti-oxidant capacity significantly correlated with adiponectin. The pathogenesis of reduced BAP may be similar as metabolic disorders induced by decrease of adiponectin. These results suggest that BAP could reflect the role of adiponectin as anti-oxidative properties.

PCS-26-2

Difference in Adipokine Levels Among Non-Diabetic Population Stratified by Age and Sex

Jin Sae Yoo, Eun Soo Lee, Eun Joo Jo, Yeon Shik Choi, Choon Hee Chung and Hong Min Kim

Department of Endocrinology, Yonsei University Wonju College of Medicine, Korea

PURPOSE: Despite the growing evidence of importance of adipokines in diabetes, few studies investigated the adipokine levels of healthy adults, especially in Korean population. Therefore, the adipokine levels of healthy Korean adults were analyzed. Additionally, various biochemical measurements were obtained, and their relationship to adipokine level was observed.

METHODS: Fifty-nine Korean adults who visited Yonsei University Wonju Christian Hospital were included in the study. Venous blood was obtained and centrifuged for biochemical and adipokine analysis. Adipokine concentration were measured using enzyme-linked immunosorbent assay kit.

RESULTS: The mean age of the subjects was 49.40 ± 11.01 years. The mean leptin, adiponectin, angiopoietin-related growth factor (AGF), and retinol-binding protein 4 (RBP4) was 6.0 ± 6.1 ng/mL, 7.6 ± 3.7 µg/mL, 78.8 ± 25.3 ng/mL, and 73.6 ± 47.3 µg/mL, respectively. Leptin was higher in women ($P = 0.000$), while borderline significant, RBP4 was higher in men ($P = 0.065$). Adiponectin and AGF were not significantly different between men and women ($P = 0.238$, $P = 0.640$, respectively). When divided into age quartiles, RBP4 significantly decreased with increasing age quartile in men ($P = 0.045$), while AGF showed tendency to increase ($P = 0.018$). In women, there was no significant pattern of adipokine change related to age. Biochemical analysis revealed leptin to be strongly associated with homeostasis model assessment of insulin resistance (HOMA-IR) ($P = 0.006$).

CONCLUSION: In non-diabetic Korean men, RBP4 and AGF levels changed in relation to age, while it does not in women. Women showed higher leptin level, which was found to be related to insulin resistance.

PCS-26-3

Improvement in the Fasting, but not the Postprandial, Glucose Level is Strongly Associated with Oxidative Stress Reduction in Type 2 Diabetes Patients

Makoto Ohara, Kentaro Watanabe, Kazunari Suzuki, Motoshi Ouchi, Tatsuya Suzuki, Hiroshi Nakano and Kenzo Oba

Divisions of Cardiology, Hepatology, Geriatrics, and Integrated Med, Department of Internal Medicine, Nippon Medical School, Japan

AIMS: This study aimed to evaluate the relationship between improvement of glucose metabolism and oxidative stress in type 2 diabetes patients.

MATERIALS AND METHODS: The study subjects were 47 type 2 diabetes patients (mean age: 64.5 ± 12.1 years). As the first daily profile, the levels of plasma glucose and diacron-reactive oxygen metabolites (d-ROMs) were determined on admission. Then, for the second daily profile, plasma glucose and d-ROM levels were evaluated after treatment was administered to improve glucose metabolism. The areas under the curves (AUC) of the daily profiles of all plasma glucose (AUCDP), the nocturnal fasting state (AUCNF), the postprandial state (AUCPP), all plasma d-ROMs (AUCd-ROMs), and the coefficient of variation (CV) of plasma glucose (CVPG) were calculated for each profile. Finally, the relationship between glucose metabolism and oxidative stress in type 2 diabetes was evaluated using the above variables.

RESULTS: The second determinations of AUCDP, AUCPP, and AUCNF were significantly less than the first, but no significant difference was observed in CVPG. AUCd-ROMs also showed a significant decrease. Linear regression analysis demonstrated significant associations between the changes in AUCd-ROMs and in both AUCDP and AUCNF, while no significant association between the change of AUCd-ROMs and that of either AUCPP or CVPG was observed.

CONCLUSION: This study demonstrated that oxidative stress is reduced by improvement of glucose metabolism in type 2 diabetes patients. Furthermore, improvement of the fasting glucose level, but not of the postprandial glucose level, is strongly associated with reduction of oxidative stress in type 2 diabetes patients.

PCS-26-4

α-Lipoic Acid can Improve Endothelial Dysfunction in Subjects with Impaired Fasting Glucose

Ling Yue

Huazhong Hospital, China

The crucial mechanism of the endothelial dysfunction with impaired fasting glucose (IFG) remains unclear. We hypothesized that oxidative stress may be partially responsible for the impairment in EDAD in subjects with IFG. Thus, the present study was designed to assess whether the antioxidant α-lipoic acid can improve endothelial dysfunction in subjects with IFG. Eighty subjects with newly diagnosed IFG < 40 healthy individuals with normal glucose tolerance were enrolled. Subjects were randomized into two groups: untreated experimental group ($n = 40$) < α-lipoic acid treatment group ($n = 40$, α-lipoic acid 600 mg via intravenous infusion once a day for 3 weeks). We measured EDAD at baseline < after 4 weeks of intervention. At baseline, EDADs in untreated experimental group < α-lipoic acid treatment group were 4.13% and 4.34%, respectively, which were significantly lower than that in controls (5.72%) ($P < 0.001$). After 4 weeks of intervention, there was a remarkable increase in EDAD (reaching 5.80%; ΔEDAD, 25.6%) ($P < 0.01$). Endothelium-dependent arterial dilation remained unchanged before and

after intervention in the untreated experimental group. Our data showed that IFG subjects have impaired endothelial function < that antioxidant α -lipoic acid can improve endothelial function.

PCS-26-5

Association Between Serum Fibroblast Growth Factor 21 and Coronary Artery Disease in Patients with Type 2 Diabetes

Wonjin Kim, In Joo Kim, Bo Hyun Kim, Sang Soo Kim, Yun Kyung Jeon, Min Jung Bae and Yang Seon Yi

Department of Internal Medicine, Pusan National University Hospital, Korea

OBJECTIVE: Fibroblast growth factor 21 (FGF-21) is an important metabolic regulator with multiple beneficial effects on glucose and lipid metabolism. The aim of this study was to evaluate the association of serum FGF-21 with angiographically significant coronary artery disease (CAD) in patients with type 2 diabetes mellitus (T2DM) and non-diabetic patients.

METHODS: Serum FGF-21 was measured in 120 patients undergoing coronary angiography from Pusan National University Hospital between Jun 2009 and May 2011. Patients were divided into four groups based on the presence/absence of T2DM and of significant CAD. The atherosclerotic burden was obtained by three independent angiographic scores: the severity, Gensini score (GS) and Extent score (ES).

RESULTS: Serum FGF-21 levels were significantly higher in T2DM than in non-diabetic patients ($P = 0.014$). A significant difference existed among non-diabetic patients, according to the presence or absence of significant CAD ($P = 0.001$). However, there was no significant difference between CAD groups among T2DM ($P = 0.069$). After adjusting for several confounding factors, both GS and ES were significantly associated with serum FGF-21 in all patients ($\gamma = 0.271$, $P = 0.014$; $\gamma = 0.217$, $P = 0.041$, respectively). In non-diabetic patients, serum FGF-21 levels significantly correlated with only GS in final model ($\gamma = 0.262$, $P = 0.043$). However, serum FGF-21 lost significant correlation with both GS and ES with T2DM in the final model.

CONCLUSIONS: The patients with T2DM and CAD feature elevated serum FGF-21 levels. Serum FGF-21 levels are associated with angiographic severity and extent of CAD.

PCS-26-6

Relation Between Oxidative Stress and Postprandial Metabolic Disorders with Cookie Test in Fasting Normal Subjects

Yukako Sakaguchi, Kayoko Ryomoto, Rieko Okano, Emiko Teramoto, Shohei Kawaguchi, Yoshimoto Kiyohara, Youji Hazama, Masashi Kubota, Makoto Ohashi and Makoto Nomura

Center for Diabetes Mellitus, Osaka Rosai Hospital, Japan

OBJECTIVE: Oxidative stress causes inflammation on the vessel wall associated with the arteriosclerosis. Oxidative stress is generated by an excess of reactive oxygen species (ROS) to the anti-oxidative capacity. FRAS4 system enabled the convenient measurement of ROS as d-ROMs and anti-oxidant capacity as BAP. We investigated the relation between postprandial metabolic disorders and oxidative stress by measuring d-ROMs and BAP with Cookie test.

METHOD: We analyzed seven male and 13 female who were non-diabetic and fasting normolipidemia. The blood samples were obtained at 0, 60 and 120 min after the intake of the cookie consisting of 75 g carbohydrate and 25 g fat. We examined the relation between glucose, triglyceride, d-ROMs and BAP by FRAS4 using correlation coefficients of Pearson.

RESULTS: There were three subjects with impaired glucose tolerance and five subjects with postprandial dyslipidemia defined by exceeding 66 mg/dL of triglyceride at 60 or 120 min above basal. BAP negatively correlated with the level of triglyceride at 120 min ($r = -0.46$) and the increase of triglyceride at 120 min above basal ($r = -0.65$). D-ROMs significantly correlated with the level of glucose at 60 min ($r = 0.45$) and the increase of glucose at 60 min above basal ($r = 0.45$).

CONCLUSION: In non-diabetic and fasting normolipidemia subjects, the increase of triglyceride correlated with decreased anti-oxidant capacity and the increase of glucose correlated with ROS after the cookie test. The detection of postprandial hyperglycemia and hyperlipidemia by the cookie test would be useful early to prevent metabolic disorders and arteriosclerosis.

PCS-26-7

Association of Serum Free Fatty Acid Level with Coronary Artery Disease

Yaping Hao¹, Xiaojing Ma¹, Mi Zhou¹, Meifang Gao², Zhigang Lu², Jingyu Hang², Yuqian Bao¹ and Weiping Jia¹

¹Department of Endocrinology and Metabolism, Shanghai Jiaotong University Affiliated Sixth People Hospital, China; ²Department of Cardiology, Shanghai Jiaotong University Affiliated Sixth People Hospital, China

OBJECTIVE: Recently some studies have shown that free fatty acid (FFA) is related with obesity, diabetes and atherosclerosis. In this study, we use coronary angiography as the diagnostic criteria of coronary artery disease (CAD) and to analyze the relationship between serum FFA level and CAD.

METHODS: A total of 169 individuals (male 105, female 64) who underwent coronary angiography were collected. Severity of coronary artery disease was assessed by the coronary stenosis index (CSI). Metabolic syndrome was diagnosed according to the Guideline on Prevention and Treatment of Blood Lipid Abnormality in Chinese Adults.

RESULTS: (1) Coronary angiography revealed that 115 (men 80) had CAD. The level of fasting FFA and 2 h postprandial FFA (2 hFFA) showed no difference between men and women ($P > 0.05$). (2) The level of fasting FFA ([641(478–894)] μ Eq/L vs [532(407–698)] μ Eq/L, $P < 0.05$) and CSI ([10(6–15)] vs [0(0–1)], $P < 0.01$) in CAD were higher than non-CAD. However the level of HDL-c was decreased ([1.00(0.82–1.20)] mmol/L vs [1.10(0.93–1.33)] mmol/L, $P < 0.05$). (3) The fasting FFA level was higher in subjects with 1-vessel ([673(442–919)] μ Eq/L vs [532(407–698)] μ Eq/L, $P < 0.05$) and multi-vessel lesions ([636(487–843)] μ Eq/L vs [532(407–698)] μ Eq/L, $P < 0.05$) than non-CAD patients. But there was no difference in the level of 2 hFFA ($P > 0.05$). (4) Logistic regression demonstrated that fasting FFA was independently correlated with CAD after adjustment of other traditional factors.

CONCLUSION: Serum fasting free fatty acid level was associated with coronary artery lesion.

PCS-26-8

Relationship Between Carbohydrate Content of Diet and Attenuation of Postprandial Vascular Endothelial Function

Kazunari Suzuki, Kentaro Watanabe, Masao Hashimoto, Makoto Ohara, Tatsuya Suzuki, Hiroshi Nakano and Kenzo Oba

Nippon Medical School, Japan

AIMS: The relationship between different degrees of postprandial attenuation of brachial artery flow-mediated dilation (FMD) and differences in the carbohydrate content of the diet was evaluated in healthy individuals.

MATERIALS AND METHODS: Thirty-seven healthy individuals with no family history of diabetes were divided into three groups: the 75-g oral glucose loading (OG) group ($n = 14$), the test meal (TM) (400 kcal, carbohydrate content 40.7 g) group ($n = 12$), and the control group ($n = 11$). FMD was measured at pre-load (FMD0), and 60 (FMD60) and 120 (FMD120) minutes after loading. Plasma glucose (PG) and immunoreactive insulin (IRI) levels were determined at pre-load (PG0, IRI0), 30 (PG30, IRI30), 60 (PG60, IRI60), and 120 (PG120, IRI120) minutes after loading. We evaluated the relationships of glucose metabolism variables and FMD among the three groups.

RESULTS: Percentage changes from FMD0 to FMD60 in the TM and OG groups were significantly decreased significantly more than in the control group. The percentage change from FMD0 to FMD120 in the OG group decreased significantly more than those in the control and TM groups. FMD60 was significantly correlated with HOMA-IR ($r = -0.389$; $P < 0.05$). FMD120 was significantly correlated with IRI60 ($r = -0.462$; $P < 0.05$), and AUC of IRI ($r = -0.468$; $P < 0.05$). Furthermore, the percentage change from FMD0 to FMD120 was significantly correlated with the CV of PG ($r = 0.404$; $P < 0.05$), IRI60 ($r = 0.401$; $P = 0.042$; $P < 0.05$), and the AUC of IRI ($r = 0.427$; $P < 0.05$).

CONCLUSION: Differences in the attenuation of postprandial vascular endothelial function induced by different carbohydrate contents may occur a long time postprandially, but not shortly after the meal.

PCS-26-9

HbA1c is Associated with Dyslipidemia in an Apparently Healthy Older Nondiabetic Adults

Sangyong Kim, Jinhwa Kim, Hakyeon Bae and Jiin Kang

Department of Internal Medicine, Chosun University School of Medicine, Korea

OBJECTIVE: Elevated HbA1c levels are associated with a higher incidence of microvascular & macrovascular complications in diabetes. Data from the National Health and Nutrition Examination Survey & the Framingham Offspring Study suggest that HbA1c levels increase with age even after adjustments for demographic & glycemic variables among nondiabetic subjects. The aim of this study is to estimate the association of HbA1c with cardiovascular disease risk factors in an apparently healthy older nondiabetic adults.

METHODS: We retrospectively studied asymptomatic Korean adults of 60 years old or older who underwent voluntary regular health check-ups at the Health Promotion Center of Chosun University Hospital (Gwangju, Republic of Korea) from January 2009 to September 2011. Individuals previously diagnosed with diabetes, hypertension, or dyslipidemia & those treated with hypoglycemic agents, antihypertensive agents, & lipid lowering agents were excluded. After these exclusions, 421 individuals were included in this study.

RESULTS: HbA1c revealed a significant correlation with age, waist circumference, fasting plasma glucose, triglyceride, LDL cholesterol, & HDL cholesterol. Multiple regression analysis showed that HbA1c had a association with fasting plasma glucose ($\beta \pm SE$, 0.009 ± 0.002), LDL cholesterol (0.001 ± 0.001), & HDL cholesterol (-0.003 ± 0.001).

CONCLUSION: The HbA1c level is independently correlated with dyslipidemia other than fasting glucose level in older nondiabetic Korean adults.

PCS-27-1

Ectopic Fat Accumulation and Distant Organ-Specific Insulin Resistance in People with Nonalcoholic Fatty Liver Disease

Kenichiro Kato¹, Yumie Takeshita¹, Hirofumi Mitsu¹, Tsuguhito Ota¹, Kumpei Tokuyama², Shoichiro Nagasaka³, Munehisa Matsuhisa⁴, Shuichi Kaneko¹ and Toshinari Takamura¹

¹Department of Disease Control and Homeostasis, Kanazawa University Graduate School of Medical Sciences, Japan; ²Graduate School of Comprehensive Human Science, University of Tsukuba, Japan; ³Department of Medicine, Division of Endocrinology and Metabolism, Jichi Medical University, Japan; ⁴Clinical Research Center for Diabetes, Tokushima University, Japan

OBJECTIVE: The aim of this study was to examine the association between ectopic fat and organ-specific insulin resistance (IR) in insulin-target organs in patients with nonalcoholic fatty liver disease (NAFLD).

METHODS: IR of liver (hepatic glucose production $\times$ fasting plasma insulin), muscle (insulin-stimulated glucose disposal), and adipose tissue (suppression of FFA by insulin) were measured in 29 patients clinically diagnosed with NAFLD (age 48 ± 15 years, BMI 31.9 ± 9.0 kg/m²) using an euglycemic hyperinsulinemic clamp with tracer infusion ([6,6-2H₂]glucose). Liver fat, intramyocellular lipid (IMCL), and body composition were measured by liver biopsy, proton magnetic resonance spectroscopy, and the bioelectrical impedance analysis, respectively.

RESULTS: IR of liver, muscle and adipose tissue was associated with each other. Unexpectedly, indices of fat accumulation in the liver, muscle and adipose tissue were not associated with their own organ-specific IR. Both liver steatosis score and intrahepatic lipid were positively associated with muscle IR ($r = -0.66$, $P < 0.001$; $r = -0.58$, $P < 0.01$, respectively), but not with liver IR. IMCL was not associated with muscle IR. Body fat and its percentage were associated with liver IR ($r = 0.65$, $P < 0.001$; $r = 0.64$, $P < 0.001$, respectively) and muscle IR ($r = -0.63$, $P < 0.01$; $r = -0.56$, $P < 0.01$, respectively), but not with adipose IR.

CONCLUSIONS: Present study revealed dissociation between ectopic fat and local organ-specific insulin resistance. Instead, liver fat is associated with muscle insulin resistance, suggesting a network between liver and muscle to maintain homeostasis of whole body energy metabolism.

PCS-27-2

Correlation of Insulin Sensitivity and Cytokines with Adiponectin Receptor Expression in Children with Prader-Willi Syndrome and in Obese Children

Sung Yoon Cho¹, Su Jin Kim², Young Bae Sohn³, Se Hyun Maeng¹ and Dong-Kyu Jin¹

¹Department of Pediatrics, Samsung Medical Center, Korea; ²Department of Pediatrics, Kwandong University College of Medicine, Myongji Hospital, Goyang, Korea; ³Department of Medical Genetics, Ajou University Hospital, Suwon, Korea

OBJECTIVE: Prader-Willi syndrome (PWS), a genetic disorder characterized by childhood-onset obesity, is reported to have elevated levels of adiponectin. The actions of adiponectin are mediated by adiponectin receptors (ADIPORs) which include ADIPOR1 and ADIPOR2. Several cytokines such as adiponectin, TNF- α , and IL-6, have been known to be involved in insulin sensitivity.

METHODS: We compared the 30 PWS children (median age 7.1 year, 18 boys, 12 girls) who were being receiving GH therapy and 32 obese children not receiving GH therapy (median age 9.1 year, 15 boys, 17 girls). The relative expression of adiponectin, ADIPORs, several proinflammatory cytokines including TNF- α , and IL-6 measured in peripheral blood mononuclear cells (PBMCs) using real-time PCR. Their correlation was analyzed by homeostasis model assessment insulin resistance index (HOMA-IR).

RESULTS: The PWS children showed increased expression of ADIPOR2 ($P = 0.02$) and decreased expression of IL-6 ($P = 0.03$) compared to the obese children. There was a significant positive correlation between the ADIPORs and TNF- α (ADIPOR1 vs TNF- α : $r = 0.66$, $P < 0.001$ in PWS, $r = 0.80$, $P < 0.001$ in control group; ADIPOR2 vs TNF- α : $r = 0.69$, $P < 0.001$ in obese group). The ADIPORs in the obese group showed significant negative correlation with HOMA-IR (ADIPOR1 vs HOMA-IR: $\rho = 0.41$, $P = 0.02$, ADIPOR2 vs HOMA-IR: $\rho = 0.46$, $P < 0.01$).

CONCLUSION: Inflammatory cytokine expression was closely associated with the expression of the ADIPORs in the PBMCs of both the children with PWS and the obese group. In addition, ADIPOR2 expression was highly expressed in the PBMCs of the children with PWS.

PCS-27-3

Acromegaly and Pheochromocytoma as Clinical Models of Effect of IGF-1 and Catecholamine on Insulin Resistance

Eriko Yamaguchi, Yukiko Kawasaki, Sachiko Honjo, Yoshiyuki Hamamoto, Kanta Fujimoto, Hisato Tatsuoka, Kanako Mori, Atsuko Matsuoka, Yoshihiro Iwasaki, Hiroki Ikeda, Yoshiharu Wada, Kazuhiro Nomura and Hiroyuki Koshiyama
Center for Diabetes & Endocrinology, Medical Research Institute Kitano Hospital, Japan

OBJECTIVE: Acromegaly and pheochromocytoma are frequently accompanied with impaired glucose tolerance, and they can be viewed as clinical models of effects of growth hormone (GH)/insulin-like growth factor-1 (IGF-1) or catecholamine on insulin resistance, respectively.

METHODS: Subjects included a total of 14 patients with acromegaly (A group) and five patients with pheochromocytoma (P group), who received operation from 2006 to 2009. All patients received 75 g OGTT (oral glucose tolerance test) before and after surgery. Homeostasis model assessment of insulin resistance (HOMA-R) and insulinogenic index (IG) were calculated.

RESULTS: In A group, eight patients had impaired glucose tolerance (IGT) and one patient had diabetes mellitus (DM) patterns; their fasting plasma glucose (FPG) level was 99.0 ± 2.8 mg/dL and HOMA-R was 2.07 ± 0.31 . Postoperatively, both FPG and HOMA-R decreased significantly (92.9 ± 3.5 mg/dL, 1.49 ± 0.28 , respectively), whereas IG showed no significant change. HOMA-R showed a significantly positive correlation with serum IGF-1 levels both before and after surgery, but not with serum GH levels. The differences in HOMA-R between before and after surgery also showed a significantly positive correlation with those in IGF-1 concentrations. In P group, they showed DM pattern in two cases and NGT in three cases preoperatively. IG and HOMA-R showed an increase and a decrease after the surgery, respectively.

CONCLUSION: Insulin resistance is correlated with serum IGF-1 levels, not with GH levels, in acromegaly, and it is associated with catecholamines in pheochromocytoma.

PCS-27-4

Association Between Gastric *Helicobacter pylori* Colonization and Oral Glucose Tolerance

Hideo Kanehara, Keiko Aoki, Kazuhide Ishikura, Azusa Hisada, Yukihiro Bando, Daisyu Toya and Nobuyoshi Tanaka

Department of Internal Medicine, Fukui-ken Saiseikai Hospital, Japan

BACKGROUND: The relationship between *H. pylori* colonization and diabetes is inconsistent. Few studies have evaluated the potential influence of *H. pylori* on postprandial glucose level.

METHODS: We conducted cross-sectional analyses using data from 525 male participants in the medical examination. We evaluated BMI, HOMA-IR, HOMA beta, glucose tolerance test, gastroscopy and abdominal ultrasonography. We classified BMI from Q1 to Q4 and examined the frequency of impaired glucose intolerance.

RESULTS: There was not significant association between *H. pylori* colonization and impaired glucose tolerance. Average HOMA-IR was 1.15 ± 0.67 in *H. pylori* seropositive subjects, 1.26 ± 0.76 in seronegative subjects ($P = 0.05$). Average HOMA-beta was 65.5 ± 44.3 in *H. pylori* seropositive subjects, 58.9 ± 36.9 in seronegative subjects ($P = 0.0035$). The subjects with *H. pylori* seropositive had significant incidence of chronic gastritis ($P < 0.0001$). Two hour glucose level was no significant difference in both groups. *H. pylori* seronegative Q4 subjects were more likely to develop impaired glucose tolerance than those who were seronegative Q1 subjects [OR 2.4 (95% CI 1.04–5.66)]. However, *H. pylori* seropositive Q4 subjects were not likely to develop impaired glucose tolerance [OR 1.66 (95% CI 0.75–3.68)].

CONCLUSIONS: We found that serological evidence of *H. pylori* infection was not associated with an increased rate of impaired glucose tolerance.

PCS-27-5

The Impact of Overweight on β -cell Function and Insulin Resistance in Subjects with Impaired Fasting Glucose: A Cross-Sectional Study in Korea

Hannah Seok, Hyun Min Kim, Sun-Ok Song, Ji Hye Huh, Byung-Wan Lee, Eun Seok Kang, Hyun Chul Lee and Bong Soo Cha

Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine, Korea

OBJECTIVE: The aim of this study was to evaluate the effect of overweight on insulin secretion and insulin resistance in subjects with impaired fasting glucose (IFG).

METHODS: This was a large-scale, community-based, and cross sectional study conducted from January 2010 to December 2010. A total of 4025 subjects without any history of diabetes were enrolled. Laboratory tests, physical examinations and questionnaires were obtained from all participants. Subjects were classified as normal-weight, overweight, and obese according to Asian-specific WHO definition (BMI < 23 , 23 – 25 , and > 25 kg/m², respectively). Multiple linear regressions and logistic regressions were used for statistical analysis.

RESULTS: A total of 685 (17.0%) subjects were diagnosed with IFG. After adjustment for covariables, HOMA- β (homeostasis model assessment for β -cell function) and HOMA-IR (homeostasis model assessment for insulin resistance) were significantly increased and QUICKI (quantitative insulin sensitivity check index) was decreased in both overweight and obese subjects. BMI was strongly correlated with HOMA- β , HOMA-IR and QUICKI (regression coefficient: 0.384, 0.430 and -0.424 , respectively, all $P < 0.001$). Compared with normal-weight subjects, overweight and obese subjects had increased risk of IFG with odds ratios of 1.80 (95% CI: 1.42–2.29) and 2.88 (95% CI: 2.33–3.57), respectively.

CONCLUSION: In this study, BMI was independent predictors of IFG. Not only obesity, but also overweight was significantly correlated with hyperinsulinemia, increased insulin resistance, and subsequently increased risk of IFG. Overweight should be taken more attention for prevention of IFG.

PCS-27-6

Association of Serum Glycine Levels with Obesity and Glucose Metabolism in Non-Diabetic Japanese Adults

Chisa Takashina, Taku Watanabe, Shinji Sakaue, Daisuke Ikeda, Takahiro Sato, Asuka Yamada, Hiroshi Ohira, Yoshinori Ohtsuka, Ichizo Tsujino and Masaharu Nishimura

First Department of Medicine, Hokkaido University School of Medicine, Japan

OBJECTIVE: The role of glycine in obesity and/or glucose regulation has not been clearly established. We investigated the relationship between serum glycine levels and indices of obesity and glucose metabolism in non-diabetic Japanese adults.

METHODS: Ninety-three non-diabetic Japanese men and women participated in this study. Serum glycine was measured by high-performance liquid chromatography. The participants underwent 75-g oral glucose tolerance tests, and homeostasis model assessment for insulin resistance (HOMA-IR) and oral glucose insulin sensitivity (OGIS) index were determined. Visceral fat area (VFA) at the umbilical level was determined by magnetic resonance imaging.

RESULTS: The demographics of study participants were as follows: male/female 72/21; mean age ($\pm$ standard deviation), 34.5 ± 6.1 ; mean body mass index (BMI), 22.8 ± 2.8 ; mean waist circumference (WC), 79.6 ± 7.9 cm; and mean VFA, 73.3 ± 4.3 cm². The mean serum glycine level was 216.9 ± 36.5 nmol/mL. Univariate regression analysis showed an inverse association of serum glycine levels with body weight ($r = -0.34$, $P < 0.05$), BMI ($r = -0.42$, $P < 0.05$), WC ($r = -0.45$, $P < 0.05$) and VFA ($r = -0.48$, $P < 0.05$), fasting ($r = -0.27$, $P < 0.05$), and 2-h glucose levels ($r = -0.42$, $P < 0.05$), HOMA-IR ($r = -0.32$, $P < 0.05$) and OGIS ($r = 0.41$, $P < 0.05$).

CONCLUSION: Elevated serum glycine levels were associated with low BMI and VFA, lower serum glucose levels and increased insulin sensitivity in non-diabetic Japanese adults. A putative role for glycine in obesity and glucose regulation warrants further study.

PCS-28-1

Insulin Response in Korean Patients with Glucose Intolerance

Junghwan Park, Sangmo Hong, Changbum Lee, Yongssoo Park, Woonghwan Choi, Youhern Ahn and Dongsun Kim

Division of Endocrinology and Metabolism, Department of Internal Medicine, Hanyang University School of Medicine, Korea

OBJECTIVES: Diabetes develops as a bihormonal disease. This study investigated the changes of serum insulin and glucagon levels in Korean patients with carbohydrate metabolism abnormalities.

METHODS: A total of 110 subjects who had suspicious carbohydrate metabolism abnormality in health check-up were examined: normal subjects (CONTROL), impaired fasting glucose (IFG), impaired glucose tolerance (IGT), IFG/IGT, and type 2 diabetes of isolated fasting hyperglycemia (IFH), isolated postprandial hyperglycemia (IPH), and fasting and postprandial hyperglycemia. Plasma levels of glucose, insulin and glucagon were measured in the fasting state (GTT0), and at 30 (GTT30) and 120 (GTT120) minutes after glucose loading.

RESULTS: Patterns of insulin response showed the delayed hyperinsulinemia except IFG and IFH which were similar to CONTROL. Insulinogenic index decreased in diabetic patients except IFH. In patients of diabetes with increased glycated hemoglobin of more than 7.5%, even though they were newly diagnosed, insulin secretion was markedly decreased. In CONTROL, there was no change of glucagon levels before and after glucose loading. In all patients, fasting glucagon levels were higher than CONTROL. In all patients, a rise of glucagon levels was observed at GTT30. There was impairment of glucagon suppression at GTT120 except IFG and IGT.

CONCLUSION: According to our data, insulinogenic index preserved in early glucose intolerance, especially IFH and glucagon imbalance starts before diabetes is diagnosed. There were differences in pattern of insulin or glucagon response according to phenotypes of glucose intolerance. Further studies about different mechanisms in various types of glucose intolerance are needed.

PCS-28-2

Identification of *INS* and *KCNJ11* Gene Mutations in Type 1B Diabetes in Japanese Children with Onset Before 5 years of Age

Maki Moritani¹, Ichiro Yokota¹, Kohji Tsubouchi², Ryuzo Takaya³, Koji Takemoto⁴, Kanshi Minamitani⁵, Mitsuo Itakura⁶, Tsutomu Ogata⁷, Shigetaka Sugihara⁸ and Shin Amemiya⁹

¹Laboratory for Pediatrics Genome Medicine, Department of Clinical Research, Kagawa National Children's Hospital, Japan; ²Department of Pediatrics, Chuno Kosei Hospital, Japan; ³Department of Pediatrics, Osaka Medical College Hospital, Japan; ⁴Department of Pediatrics, Ehime University School of Medicine, Japan; ⁵Department of Pediatrics, Teikyo University Chiba Medical Center, Japan; ⁶The University of Tokushima, Japan; ⁷Department of Pediatrics, Hamamatsu University School of Medicine, University Hospital, Japan; ⁸Department of Pediatrics, Tokyo Women's Medical University Medical Center East, Japan; ⁹Department of Pediatrics, Saitama Medical University Faculty of Medicine, Japan

OBJECTIVE: The etiology of type 1 diabetes (T1D) is heterogeneous and is according to presence or absence of pancreatic autoantibodies divided into

two subtypes: type 1A (autoimmune-mediated) and type 1B (non-autoimmune-mediated). Although several genes have been linked to type 1A diabetes, the genetic cause of type 1B diabetes in Japanese individuals is far from understood.

The aim of this study was to test for monogenic forms of diabetes in autoantibody-negative Japanese children with T1D.

METHODS: Thirty four (19 males and 15 female) unrelated Japanese children with glutamate decarboxylase (GAD) 65 antibodies and/or IA-2A –negative T1D and diabetes diagnosed at <5 years of age were recruited from 17 unrelated hospitals participating in the Japanese Study Group of Insulin Therapy for children and adolescent diabetes (JSGIT). We screened the genes of insulin (INS) and KCNJ11 gene, which encode the ATP-sensitive K⁺ channel by direct sequencing in 34 Japanese children with T1D.

RESULTS: We identified three novel (C31Y, C96R and C109F) mutations and one previously reported mutation (R89C) in the INS gene in five children, in addition to one mutation in the KCNJ11 gene (H46R) in one child. These mutations are most likely pathogenic and therefore the cause of diabetes in carriers.

CONCLUSION: Our results suggest that monogenic forms of diabetes, particularly INS gene mutations, can be detected in Japanese patients classified with type 1B. Mutation screening, at least of the INS gene, is recommended for Japanese patients diagnosed as autoantibody negative at <5 years of age.

PCS-28-3

Association Between Variation in SRR and Type 2 Diabetes in Chinese Population

Simin Zhang, Xueyao Han, Yong Tang, Xianghai Zhou and Linong Ji
Department of Endocrinology, Peking University People's Hospital, China

OBJECTIVE: A recent genome-wide association study in Han Chinese have identified several novel genetic loci in SRR and PTPRD for type 2 diabetes (T2DM) in Taiwan. Our purpose was to determine whether variants in SRR can be replicated among Chinese population.

METHODS: Two single-nucleotide polymorphisms (SNPs) in SRR (rs391300 and rs4523957) were genotyped in 9827 unrelated Chinese Han individuals from China National Diabetes and Metabolic Disorders Study, including 2355 subjects with established T2DM, 2811 newly diagnosed T2DM subjects without treatment (NDM) and 4661 subjects with normal glucose tolerance. The associations of SNPs with T2D and phenotypes were analyzed by Multiple linear regression, logistic regression and ANOVA association analysis.

RESULTS: In normal glucose tolerance population and newly/established T2DM, no associations were observed between rs391300, rs4523157 and T2DM in the additive model after adjusted for sex, age and BMI ($P = 0.74$ and $P = 0.92$, respectively). Moreover, in normal glucose tolerance subjects, we observed that the risk allele rs391300-A and rs4523957-G were associated with higher blood glucose at 30 min of OGTT after adjusted for sex, age, BMI with β s follows: 0.086 ($P = 0.038$) and 0.096 ($P = 0.022$) for additive model. However in newly diagnosed T2DM population rs391300 and rs4523957 were negatively associated with fasting and postprandial blood glucose. Established T2DM population with medical treatment were not analyzed between genotypes and phenotypes.

CONCLUSIONS: In our study, SRR was not observed to be associated with T2DM in Chinese Han population. SRR-rs391300 and rs4523957 most likely have impact on 30 min blood glucose.

PCS-28-4

Association of the DDAH2 Gene Polymorphism with Type 2 Diabetes and Hypertension

Kwi-Hyun Bae¹, Hyun-Ae Seo¹, Su-Won Kim¹, Ji-Yun Jeong¹, Jong Ho Kim¹, Mi-Kyung Kim², Jung-Eun Lee³, Jung-Guk Kim¹, In-Kyu Lee¹ and Keun-Gyu Park¹

¹Department of Internal Medicine, Kyungpook National University Hospital, Korea;

²Department of Internal Medicine, Keimyung University Hospital, Korea; ³Division of Endocrinology, Department of Internal Medicine, CHA Gumi Medical Center, CHA University, Korea

AIMS: The aim of this study was to investigate whether the polymorphism of DDAH2 is associated with type 2 diabetes and hypertension in Korean population.

METHODS: Total 605 subjects were included in this study: 403 patients with type 2 diabetes and 202 nondiabetic control subjects. The SNP rs805304 and SNP rs2272592 in DDAH2 were analyzed. We examined the association of

SNP rs805304 and rs2272592 in DDAH2 with type 2 diabetes and hypertension.

RESULTS: SNP rs2272592 was significantly associated with type 2 diabetes ($P < 0.001$) while SNP rs805304 was not ($P = 0.716$). We observed that the prevalence of the AG + GG genotypes were significantly greater than AA homozygotes in type 2 diabetes (AA vs AG + GG; OR 20.74, 95% CI 6.48–66.35, $P < 0.001$). Significance was maintained after adjusting for age, sex, BMI, DBP and BUN (OR 21.03, 95% CI 2.83–151.14, $P = 0.003$). Both SNP rs805304 and rs2272592 in DDAH2 were not significantly associated with hypertension.

CONCLUSIONS: In the present study, we found that SNP rs2272592 in DDAH2 is associated with type 2 diabetes but SNP rs805304 in DDAH2 is not. DDAH2 SNP rs2272592 AG + GG genotypes are associated with genetic susceptibility to type 2 diabetes in Korean population.

KEYWORDS: DDAH2, polymorphism, Type 2 diabetes, hypertension

PCS-28-5

Survey of MODY1~6 in Japanese Patients with Early-Onset Diabetes

Mayumi Enya, Yukio Horikawa and Jun Takeda

Department of Diabetes and Endocrinology, Gifu University Hospital, Japan

OBJECTIVE: To provide data on the prevalence of MODY (Maturity onset diabetes of the young) 1–6 patients in Japanese for comparison to Caucasian.

METHOD: We examined 319 (male 140, female 179) early-onset diabetic patients suspected of MODY from our and other facilities. We performed genetic testing of the six known MODY genes: HNF4A, GCK, HNF1A, IPF1, HNF1B, NEUROD1. The criteria for suspected MODY were age of diagnosis or onset of <35 years of age, autoimmune antibody negativity, and no severe obesity. Family history was not included because sporadic cases occur often. The genetic test involved direct sequencing of all exons and flanking regions of MODY1–6 genes. For MODY5, large genomic rearrangements also were examined by quantitative multiplex PCR. When a candidate missense mutation was detected, whether or not it was rare polymorphism was determined by direct sequencing of 567 normal subjects (mean HbA1c $5.4 \pm .36\%$) and protein functionality prediction program.

RESULT: The mutations were found in 55 patients: 26 in HNF1A, 16 in GCK, six in HNF1B, three in HNF4A, two in IPF1, and two in NEUROD1. The two missense mutations of IPF1 were identified as rare polymorphisms by protein functionality prediction program.

CONCLUSION: MODY2 is more frequent in Japanese than expected and MODY1, 4 and 6 are extremely rare, as in Caucasian. Causal genes for more than 80% of MODY remain to be elucidated in Japanese.

PCS-28-6

Interleukin-6 Receptor Gene 48892 A/C Polymorphism is Associated with Metabolic Syndrome in Young Female Adolescents

Hsieh Chang Hsun¹, Yi Jen Hung¹ and Nain Feng Chu²

¹Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taiwan; ²Departments of Public Health and Community Medicine, Tri-

Service General Hospital, National Defense Medical Center, Taiwan

The study evaluated the relationship between the IL-6 receptor (IL-6R) 48892 A/C single nucleotide polymorphism (SNP) (rs8192284) and metabolic syndrome (MetS) among young adolescents. We enrolled 925 adolescents. Subjects had three or more of the following abnormalities that occur in MetS: high blood pressure (BP), high fasting glucose, high triglyceride (TG), low high-density lipoprotein cholesterol (HDL-C), and obesity. The characteristics of the MetS components associated with different alleles and genotypes of the rs8192284 were compared. The frequencies of alleles and genotypes of the rs8192284 were similar in both sexes. Females with C-alleles had higher waist circumference (WC) (68.0 ± 7.9 vs 67.0 ± 7.7 cm) and lower HDL-C levels (50.7 ± 11.1 vs 52.2 ± 11.7 mg/dL) than A-allele carriers ($P = 0.05$). The odds ratios for high WC, low HDL-C levels, and MetS for female C-allele carriers were 1.54 (95% CI: 1.01–2.34), 1.49 (95% CI: 1.01–2.18), and 2.19 (95% CI: 1.15–4.18), respectively comparing with A-allele carriers. In brief, the rs8192284 is associated with high TG and WC, and low HDL-C levels. Additionally, a gender difference in the incidence of MetS indicated a possible gene-gender interaction of the rs8192284 in MetS among Taiwanese adolescents.

PCS-28-7

Variants of the Adiponectin Gene and Diabetic Microvascular Complications in Patients with Type 2 Diabetes

Eun Yeong Choe, Hannah Seok, Hyun Min Kim, Sun Ok Song, Eun Seok Kang, Byung-Wan Lee, Bong Soo Cha and Hyun Chul Lee

Department of Internal Medicine, Yonsei University College of Medicine, Korea

OBJECTIVE: The aim of this study was to examine the association between common polymorphisms of the adiponectin gene (ADIPOQ) and microvascular complications in patients with type 2 diabetes mellitus.

RESEARCH DESIGN AND METHODS: Rs2241766 and rs1501299 of ADIPOQ were genotyped by single primer extension in 708 patients with type 2 diabetes mellitus (T2DM). Fundus photography, nerve conducting velocity, and urine analysis were performed to check for the presence of microvascular complications as diabetic nephropathy, retinopathy and neuropathy.

RESULTS: The prevalence of diabetic nephropathy defined as urine albumin creatinine ratio (UACR) 30 mg/g or more was 48.1% in patients with the GG genotype, 31% with the TG genotype, and 36.5% with the TT genotype of rs2241766 ($P = 0.057$). The GG genotype of rs2241766 was associated with increased nephropathy risk after adjustment for age, sex, body mass index, duration of diabetes, HDL-cholesterol, smoking status, and blood pressure (odds ratio = 1.98; 95% confidence interval = 1.01–3.87). Also, +G haplotype was correlated with UACR increase ($P = 0.087$). There was no significant association between the rs1501299 genotype of ADIPOQ and the prevalence of all of diabetic microvascular complications.

CONCLUSION: These data suggest that the GG genotype at rs2241766 might be associated with the presence of microalbuminuria as UACR more than 30 mg/day and may contribute to diabetic nephropathy in patients with T2DM.

PCS-28-8

The Relationship Between Diabetic Complications and Rage Polymorphisms in Japanese type 2 Diabetic Patients

Atsuko Watarai¹, Eitaro Nakashima², Takayoshi Tsukahara³, Rui Imamine², Yu Kouchi², Minoru Kusama², Akio Kanai², Takahiko Kawamura², Takahisa Sano², Yutaka Oiso⁴, Jiro Nakamura⁵ and Nigishi Hotta²

¹Department of Diabetes and Endocrinology, Chubu Rosai Hospital/Aichi Medical University, Japan; ²Department of Diabetes and Endocrinology, Chubu Rosai Hospital, Japan; ³School of Nutritional Sciences, Nagoya University of Arts and Sciences, Japan; ⁴Department of Diabetes and Endocrinology, Nagoya University, Japan; ⁵Division of Diabetes, Aichi Medical University, Japan

OBJECTIVE: Receptor for advanced glycation endproducts (RAGE) plays an important role in the development of chronic diabetic complications. We investigated the potential association among the RAGE genetic variances, clinical anthropometric variables, and the prevalence of diabetic micro- and macro- angiopathy.

METHODS: A total of 528 type 2 diabetic outpatients were enrolled in this study. Genotyping of polymorphisms in RAGE [+557G>A, -374T>A, -492T>C, and 63-bp deletion (-407 to -345)] were performed by polymerase chain reaction restriction fragment length polymorphism method. The prevalence of diabetic micro- and macro- angiopathy and clinical anthropometric variables were collected. Statistical analyses were performed using the program SPSS.

RESULTS: There were no significant differences in genotypic or allelic distribution of RAGE single nucleotide polymorphisms (SNPs) and mutation (+557G>A, -492T>C, and 63-bp deletion) among patients with or without diabetic angiopathy. But the A allele group (TA + AA; 190 patients) at -374T>A polymorphism showed lower prevalence of arteriosclerotic obliterans (ASO) than that of TT group (338 patients) significantly ($P = 0.038$). After adjustment for age, sex, body mass index, duration of diabetes, systolic blood pressure, smoking, and levels of HbA1c, albumin-creatinine ratio, LDL-cholesterol, and HDL-cholesterol in multivariate logistic-regression analysis, patients with TA + AA genotype were significantly more likely not to have ASO than patients with the TT genotype (Odds ratio 0.169, 95% Confidence Interval 0.03–0.91, $P = 0.039$).

CONCLUSION: In this study we found that RAGE SNP at -374T>A may relate the prevalence of ASO in Japanese type 2 diabetic patients. Further studies are needed to verify these results.

PCS-28-9

Effect of Calpain-10 and Adiponectin Gene Polymorphism on Insulin Secretion and Insulin Resistance of Type 2 Diabetes Mellitus

Youngmi Lee, S. H. Kim, C. H. Kyung, M. K. Kim, J. Y. Ha, E. J. Kwon, H. J. Lee, J. W. Kim, T. W. Noh, S. A. Kang, J. S. Park, C. W. Ahn and K. R. Kim

Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University School of Medicine, Korea

BACKGROUND: It is thought that genetic variations in the Calpain-10 and adiponectin gene effect insulin secretion in the patients with type 2 diabetes mellitus. Recently, several single nucleotide polymorphisms (SNPs) in the adiponectin and Calpain-10 gene have been reported to be associated with type 2 diabetes and components of the insulin resistance and secretion.

The aim of this study was to determine whether there is an association between specific CAPN10, adiponectin gene and T2DM in the Korean population. Furthermore evaluate association of genetic variations in the Calpain-10, adiponectin gene and metabolic syndrome.

METHODS: Overall, 249 Korean patients with T2DM and 131 non-diabetic controls with no family history of diabetes were enrolled in this study.

G276T and T45G frequencies of the adiponectin gene was examined in 249 unrelated type 2 diabetic and 131 non-diabetic control Korean subjects. All the subjects were genotyped according to CAPN10 SNP-43 and -63. The clinical characteristics and genetic levels of the subjects were compared within these genotypes.

RESULTS: Among 249 to and 131 control evaluated genetic polymorphism. Variation in calpain 10, SNP-63 T/T showed higher association in type 2 diabetes. The results of this study suggest that single SNP-63 increases the susceptibility to type 2 diabetes. But calpain 10, SNP -43, adiponectin T45G and intron G276T genetic frequency is not associated.

CONCLUSIONS: Variation in calpain 10, SNP-63 plays a role in the susceptibility to type 2 diabetes individually. SNP-43 and Adiponectin SNP-45, -276 are not associated with glucose tolerance

PCS-29-1

Exercise Therapy Improves Flow-Mediated Dilatation in the Brachial Artery of Patients with Type 2 Diabetes

Makoto Igaki¹, Motoyoshi Sakaue², Katsushige Taniguchi¹, Hiroto Honda¹ and Motoaki Komatsu³

¹Department of Rehabilitation, Toyooka Public Hospital Association Hidaka Medical Center, Japan; ²Graduate School of Human Science and Environment, University of Hyogo, Japan; ³Department of Internal Medicine, Toyooka Public Hospital Association Hidaka Medical Center, Japan

OBJECTIVE: Flow-mediated dilation in the brachial artery (FMD) was reported to be impaired in patients with type 2 diabetes (T2DM). Aim of this study was to examine whether the effect of exercise therapy on FMD differed between patients with T2DM and those with other lifestyle-related diseases.

SUBJECTS AND METHODS: Sixteen patients with lifestyle-related diseases participated in this study. The diabetic (age 62.5 ± 7.1 years) consisted of eight diabetics, while patients in the non-diabetic ($n = 8$, age 58.0 ± 6.8 years) had hypertension and/or dyslipidemia. Aerobic exercises were performed at least twice a week for 30–40 min per session. FMD, cardio-ankle vascular index (CAVI), body mass index (BMI), waist circumference, and HbA1c were measured at the beginning and after 6 months of the exercise therapy.

RESULTS: The percent of FMD in the diabetic was significantly improved by the exercise therapy ($3.1 \pm 1.2\%$ to $4.9 \pm 1.7\%$), whereas the non-diabetic did not show significant increase. Significant change was not observed in CAVI value of each group. The diabetic did not show any significant reductions in the waist circumference, BMI, or HbA1c level, while the waist circumference and BMI in the non-diabetic were significantly reduced during the exercise therapy.

CONCLUSION: Our results demonstrated that the endothelial dysfunction in T2DM was improved by the exercise therapy, in weight-loss or glycemic control independent manner. It was also suggested that FMD would be more sensitive indicator to evaluate of vascular endothelial dysfunction than CAVI.

PCS-29-2

Endurance Training Increases Serum Uncarboxylated Osteocalcin Level and Decreases HOMA-IR via Reduction of Serum Leptin in Obese Young Patients

Hyun Jeong Lee¹, S. H. Kim¹, C. H. Kyung¹, M. K. Kim¹, J. Y. Ha¹, E. J. Kwon¹, Y. M. Lee¹, J. W. Kim¹, Y. S. Kim², T. W. Noh¹, S. A. Kang¹, J. S. Park¹, C. W. Ahn¹ and K. R. Kim¹
¹Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Korea; ²Department of Medical Science, Yonsei University College of Medicine, Korea

Recently, serum osteocalcin (OC) secreted from osteoblast has been reported to enhance glycemic control. Between two forms of OC [uncarboxylated OC (unOC) and carboxylated OC (cOC)], unOC is the predominant form in the circulation. Leptin is known to increase the expression of osteostetular protein tyrosine phosphatase, which in turn decreases OC secretion by inducing OC carboxylation. This suggests that reduction of leptin may result in increased osteoblastic activity, OC production/secretion, and consequently, enhanced glycemic control. This study investigated whether endurance training may regulate levels of ucOC and parameters of glycemic control via leptin reduction. Thirty-nine class I obese, normoglycemic young males were randomly assigned to control (C, $n = 10$) or exercise group (Ex, $n = 29$). The subjects in Ex group underwent 8 week-supervised-endurance exercise training (2400 Kcal/week). Weight, BMI, waist circumference, % body fat, leptin, fasting plasma insulin, and HOMA-IR decreased significantly. Whereas ucOC and total OC increased in Ex without significant change of cOC. There was negative correlation between the change in leptin and ucOC. Total adiponectin decreased but the ratio of high molecular weight adiponectin to total adiponectin increased by 6.6 fold. Fasting plasma glucose and AUC from oral glucose tolerance test showed no significant change. Bone alkaline phosphatase and bone mineral density were unaffected by the exercise training. These results suggest endurance training may contribute to increased circulating OC and decreased HOMA-IR without significant change in bone metabolism. Considering that this study was limited to the normoglycemic obese individuals, further study in the prediabetic and diabetic individuals may be warranted.

PCS-29-3

Combination of the Anti-Obesity Herbal Medicine Bofutsushosan and Physical Exercise Improves Insulin Sensitivity in Otsuka Long-Evans Tokushima Fatty (OLETF) Rats

Ryohei Kobayashi, Daizo Saito, Masaru Nagasaki, Tomoko Uno, Toshihiko Osawa and Yuzo Sato

Program of Health Sciences, Graduate School of Psychological and Physical Science, Aichi Gakuin University, Japan

BACKGROUND AND AIMS: Obesity is a key factor in the development of the metabolic syndrome, and is the most important risk factor for the development of insulin resistance. Previous studies have shown that the herbal medicine bofutsushosan (BTS) has an anti-obesity effect. In the current study, we investigated the effects of bofutsushosan, physical exercise, and their combination on insulin sensitivity (IS) in OLETF rats.

MATERIALS AND METHODS: Male OLETF rats aged 16 weeks were divided into four groups: control (C), BTS treatment (BTS), physical exercise (EX), and combination of BTS and exercise (BTS + EX). The EX rats were individually placed in voluntary exercise wheel cages. After 7 weeks of intervention, euglycemic hyperinsulinemic clamps at an insulin infusion rate of 3 mU/kg/min were performed in awaked rats was evaluated.

RESULTS: At 23 weeks of age, C, BTS, EX and BTS + EX rats weighed averages of 656 ± 20 , 582 ± 10 , 459 ± 5 and 417 ± 9 g and had epididymal fat weights of 2.99 ± 0.05 , 2.36 ± 0.17 , 1.09 ± 0.12 and 0.66 ± 0.02 g/100 g BW, respectively. The glucose infusion rate (GIR) during the euglycemic clamp, an index of IS, was significantly higher in BTS + EX rats than in C, BTS and EX rats.

CONCLUSION: These results suggest that BTS + EX improves insulin action in OLETF rats more than BTS or exercise alone. Therefore, combination of BTS and EX can be considered beneficial for the prevention of obesity-induced type 2 diabetes mellitus.

PCS-29-4

Walking and Diabetes

Telmen Boldbaatar, Sarnai Otgonbayar and Sainbileg Sonomtseren
 School of Medicine, Health Sciences University of Mongolia, Mongolia

AIMS: Aims of this study were to evaluate walking effect on blood glucose level of diabetic patients.

METHODS: This study included 61 DM patients. We measured and compared blood glucose level of DM patients before and after 30 min walking.

RESULTS: We studied 34 (55.4%) male and 27 (44.3%) female DM patients with mean age 53.29 ± 11.43 years old (Range is 24–76 years old). Before walking mean blood glucose level of DM patients was 13.13 ± 4.44 mmol/L (Range is 4.6–23.0 mmol/L). But, after 30 min of walking mean blood glucose level of DM patients was 12.26 ± 4.46 mmol/L (Range is 4.7–21.9 mmol/L). After walking, mean blood glucose level of DM patients was significantly lowered (13.13 ± 4.44 mmol/L vs 12.26 ± 4.46 mmol/L; $P < 0.0001$ by Paired Sample Test).

CONCLUSIONS: Walking is effective for diabetes.

PCS-29-5

Aggravated Diabetic Nephropathy in Patients Performing 'Severe Carbohydrate Restriction Diet'

Hiroyuki Koshiyama, Hisato Tatsuoka, Yoshiyuki Hamamoto, Sachiko Honjo, Yukiko Kawasaki, Kanta Fujimoto, Atsuko Tatsuoka, Yoshiharu Wada and Hiroki Ikeda
 Center for Diabetes & Endocrinology, The Tazuke Kofukai Medical Research Institute, Japan

BACKGROUND: Diet therapy is still the cornerstone in management of diabetes mellitus. Recently in Japan, 'severe carbohydrate restriction diet (SCRD)' is getting popularity through among some lay people and patients with diabetes, and even in some physicians. It is possible that, on the contrary, 'SCRD' may hamper or even aggravate the clinical outcome.

SUBJECTS AND METHODS: We conducted a study including those who performed 'SCRD' of themselves. The study included seven cases, who had performed 'SCRD' by history taking or nutritional counseling.

RESULTS: All cases were male of age from 51 to 71 years. Glycemic control were poor or terrible in all of them (HbA1c 7.0–11.0%). Three of them showed a marked aggravation of diabetic nephropathy with an increase of urinary albumin excretion or serum creatinine. Two cases stopped the medication therapy, and one of them was admitted because of sepsis. One case developed pancreatic cancer.

DISCUSSION: The Japan Diabetes Society guideline recommends that patients should take carbohydrate corresponding to 55–65% of total calorie. 'SCRD' is based upon individual experiences only. Although there have been controversies whether lipid restriction or 'moderate' carbohydrate restriction is better for patients with diabetes or obesity, there has been no evidence indicating the merit of 'SCRD'. It should not be confused with moderate carbohydrate restriction, whose benefit is of debate.

CONCLUSION: The 'SCRD' should not be recommended to Japanese subjects with diabetes mellitus, especially those with overt nephropathy, since it has the risk of worsening diabetic nephropathy and of suspension of conventional medical therapy.

PCS-29-6

Effect of Exercise on Glucose Tolerance and Total White Blood Cell Count in Japanese Male Workers

Junko Oya¹, Tomoko Nakagami¹, Yoshihiko Naito², Yayoi Yamamoto¹, Yasuhiro Endo³ and Yasuko Uchigata¹

¹Diabetes Center, Tokyo Women's Medical University, Japan; ²School of Human Environmental Science, Mukogawa Women's Medical University, Japan; ³Department of Health and Community Medicine, Saitama-ken Saiseikai Kurihashi Hospital, Japan

The aim of this study was to investigate the cross-sectional relationship between exercise and total white blood cell (WBC) count in Japanese male workers with different glucose tolerance levels. Subjects were 926 middle-aged male workers who participated in the general health check-up at S.S.K Hospital. The participants completed a questionnaire regarding their usual pattern of physical activities in the previous month. Glucose tolerance levels were categorized into three groups depending on the HbA1c level (G1: <5.6%, G2: 5.6–5.9%, and G3: 6.0–6.4%). The WBC counts were compared between persons with different glucose tolerance levels, who

performed and did not perform exercise (Ex+, Ex-). Multiple linear regression analysis was performed to examine the effect of exercise and each glucose tolerance level on the elevated WBC count. The WBC counts increased with an increase in the HbA1c levels ($P = 0.002$). Among all glucose tolerance levels, the WBC counts in Ex+ subjects were lower than those in the Ex- subjects. Compared with the G1 subjects (Ex- and Ex+), Ex- subjects in G2 and G3 had significantly higher WBC counts, but the WBC counts did not significantly differ between Ex+ subjects in G2 and G3. The multivariate logistic regression model showed that Ex- subjects in G3 had a 3.42-fold higher risk of having elevated WBC counts than those in G1. Similar results were observed when the fasting plasma glucose levels were categorized into three groups and analyzed in the same manner. Low-grade systemic inflammation, leading to glucose intolerance, might be suppressed by exercise.

PCS-29-7

Insulin Degludec Results in Lower Rates of Nocturnal Hypoglycemia Despite Lower FPG Levels Compared to Insulin Glargine

David Russell-Jones¹, Stefano Del Prato², Jacob Hyllested-Winge³, Nathan Lassota⁴ and Michaela Diamant⁵
¹Royal Surrey County Hospital & University of Surrey, Guildford, UK; ²University of Pisa, Pisa, Italy; ³Novo Nordisk PL, Tokyo, Japan; ⁴Novo Nordisk A/S, Soeborg, Denmark; ⁵VU University Medical Center (VUMC), Amsterdam, The Netherlands

OBJECTIVE: We investigated the relationship between FPG and nocturnal confirmed hypoglycemia in patients with diabetes treated with once-daily insulin degludec (IDeg) or insulin glargine (IGlar).

METHODS: This analysis includes all open-labeled, phase 3a, randomized, treat-to-target (FPG < 90 mg/dL; < 5 mmol) trials of once-daily IDeg vs IGlar [T1DM: 2 trials ($n = 957$); T2DM: 5 trials ($n = 3360$)]. Confirmed hypoglycemia was defined as PG < 56 mg/dL (3.1 mmol/L) or severe episodes requiring assistance, and nocturnal hypoglycemia occurring between 00:01 and 05:59.

RESULTS: For all trials (seven of seven), mean end-of-trial FPG levels were consistently lower for IDeg than IGlar, reaching statistical significance in three trials (Table). Similarly, IDeg was associated with a 23–40% lower rate of nocturnal confirmed hypoglycemia relative to IGlar, which was statistically significant in four of seven trials, regardless of type of diabetes or background therapy.

Table 1. Fasting plasma glucose and nocturnal hypoglycemia

Trial ID	Patients	Number Randomized (n)		Mean EOT FPG (mg/dL)		Nocturnal Hypoglycemia	
		IDeg	IGlar	IDeg	IGlar	Rate ratio (IDeg/IGlar)	95% CI
3579	T2DM (BOT)	773	257	106.2	114.7*	0.64*	[0.42; 0.98]
3672	T2DM (BOT)	228	229	105.7	113.1*	0.64	[0.30; 1.37]
3586	T2DM (BOT)	289	146	99.9	101.8	0.62	[0.38; 1.04]
3668	T2DM (BOT)	229*	230	105.3	112.1*	0.77	[0.44; 1.35]
3582	T2DM (BB)	744	248	121.7	127.3	0.75*	[0.58; 0.99]
3583	T1DM (BB)	472	157	141.1	149.0	0.75*	[0.59; 0.96]
3770	T1DM (BB)	164*	164	149.4	151.3	0.60*	[0.44; 0.82]

Given once-daily in a compulsory, rotating morning and evening dosing schedule, creating 8–40 h intervals between doses; *Significant (95% CI excluding 1); BOT, basal-oral therapy; BB, basal-bolus therapy; EOT, end-of-trial.

CONCLUSION: While once-daily IDeg treatment achieves consistently lower FPG levels compared to IGlar it is also associated with reduced rates of nocturnal hypoglycemia in individuals with T1DM and T2DM.

PCS-30-1

In T2D Patients with Baseline A1c <8.0%, Liraglutide Achieves A1c Targets More Often than Sitagliptin or Exenatide

Allen B. King¹, Eduard Montanya², Richard Pratley³, Lawrence Blonde⁴, Claus Svendsen⁵ and Morten Donsmark⁵
¹Diabetes Care Center, USA; ²IDIBELL-Hospital Universitari Bellvitge, Barcelona, Spain; ³Florida Hospital, Orlando, FL, USA; ⁴Ochsner Medical Center, New Orleans, LA, USA; ⁵Novo Nordisk A/S, Soeborg, Denmark

OBJECTIVE: Limited data are available on the efficacy of incretin therapies in type 2 diabetes (T2D) patients who are near but not at glycemic target.

METHODS: Our *post-hoc* analysis compared the efficacy of liraglutide 1.8 mg once-daily (OD) to exenatide 10 µg twice daily (BD) (LEAD-6) and to

sitagliptin 100 mg OD (LIRA-DPP-4) after 26 weeks' treatment; only patients treated as add-on to only metformin with a baseline A1c <8% were included.

RESULTS: In LEAD-6 and LIRA-DPP-4, liraglutide treatment resulted in a significantly higher proportion of patients achieving both glycemic targets compared to exenatide and sitagliptin, respectively (Table). Weight loss with liraglutide was greater vs exenatide but did not reach statistical significance, whereas the difference was significant vs sitagliptin. Few patients (8–10%) experienced minor hypoglycemia with all therapies.

Table. Efficacy of incretin therapies in patients already close to target

	LEAD-6			LIRA-DPP-4		
	Liraglutide 1.8 mg OD (n = 44)	Exenatide 10 µg BID (n = 41)	ETD [95% CI]	Liraglutide 1.8 mg OD (n = 72)	Sitagliptin 100 mg OD (n = 61)	ETD [95% CI]
Change in A1c, % (SE)	-0.87 (0.09)	-0.60 (0.09)	-0.27 [-0.55; 0.00]*	-1.01 (0.08)	-0.48 (0.08)	-0.53 [-0.76; -0.30]***
Patients to target, %			OR [95% CI]			OR [95% CI]
6.5%	64.5	35.1	3.4 [1.3; 8.6]*	52.8	18.9	4.8 [2.1; 10.9]**
<7.0%	84.0	61.5	3.3 [1.2 to 9.5]*	77.6	36.7	6.0 [2.7; 13.1]***
Change in weight, kg (SE)	-3.68 (0.48)	-2.62 (0.51)	-1.06 [-2.54; 0.42]	-3.46 (0.41)	-0.50 (0.44)	-2.96 [-4.19; -1.73]***

Data are least squares (LS) mean from intention to treat (ITT), last observation carried forward (LOCF). Analysis of covariance on ITT, LOCF for estimated treatment differences (ETD). Logistic regression on ITT, LOCF for Odds ratio (OR). * $p < 0.05$, ** $p < 0.05$, *** $p < 0.0001$.

CONCLUSIONS: In patients already close to target, liraglutide 1.8 mg brings significantly more patients to target than exenatide or sitagliptin. This should be considered by clinicians when adding to metformin therapy in patients close to target.

PCS-30-2

The Efficacy of Liraglutide in the Treatment of Japanese Type 2 Diabetes Mellitus

Ihoko Nakashotani, Ryoko Nishii, Yozo Kanamaru, Takashi Katsura, Takahiro Okusu, Kazutomi Yoshiuchi, Kenya Sakamoto and Keisuke Kosugi
 Department of Internal Medicine, Osaka Police Hospital, Japan

OBJECTIVE: To elucidate the efficacy and the clinical predictive factors for improvement glycemic control by Liraglutide (Lira) in Japanese type 2 diabetes mellitus (T2DM).

METHODS: Fifty-eight Japanese T2DM patients who had received Lira for 36 weeks were divided into two groups according to achieving target HbA_{1c} levels [group 1 ($n = 28$) <6.9%, group 2 ($n = 30$) ≥6.9%] to compare the clinical characteristics between both groups.

RESULTS: There was no significant difference between baseline HbA_{1c} in both groups. Group 1 had a higher body weight (80.0 ± 18.7 vs 68.8 ± 14.1 kg, $P < 0.05$) and higher fasting serum C-peptide (CPR) (1.5 ± 0.7 vs 1.0 ± 0.5 ng/mL, $P < 0.01$) and urinary CPR (65.7 ± 42.8 vs 41.3 ± 33.5 µg/day, $P < 0.01$). Group 1 achieved HbA_{1c} target of <6.9% after 8 weeks, furthermore, showed the significant reductions compared with group 2 in HbA_{1c} (-2.6 vs -0.7% , $P < 0.05$) after treatment for 36 weeks. The rate of change in body weight after 36 weeks was significantly higher with group 1 (-3.7 vs -0.5% , $P < 0.05$). 75 g OGTT were performed a week after the administration of Lira in 10 patients (five from group 1 and five from group 2), blood glucose at 180 min was significantly lower with group 1 compared with group 2 (BG < 140 vs ≥140 mg/dL, $P < 0.05$).

CONCLUSIONS: The clinical factors affecting the well response of Lira treatment in Japanese T2DM were baseline BMI, duration of diabetes and serum and urinary CPR. The blood glucose at 180 min of OGTT also could be a marker of responsive cases to Lira.

PCS-30-3

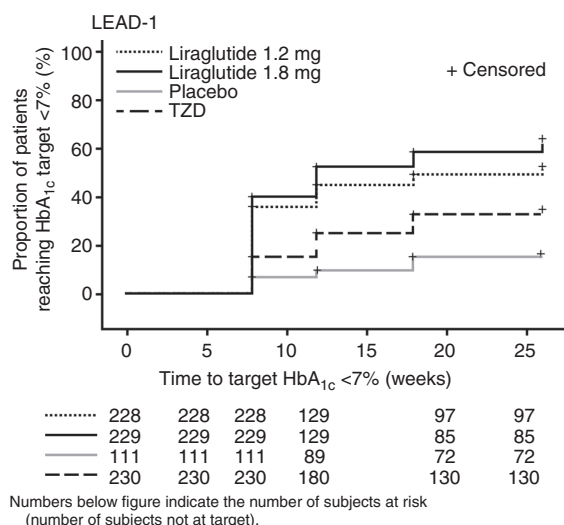
Patients are More Likely to Reach A1C Target When Liraglutide is Added to an SU than Adding Rosiglitazone or Placebo

Michael Braendle¹, Stephen Colagiuri², Claus Svendsen³, Sabina Furber³ and Michel Marre⁴
¹Department of Internal Medicine, Kantonsspital St Gallen, Switzerland; ²The Boden Institute of Obesity, Nutrition, Exercise and Eating Disorders, The University of Sydney, Sydney, Australia; ³Novo Nordisk A/S, Soeborg, Denmark; ⁴Department of Endocrinology, Diabetology and Nutrition, Bichat Hospital, Paris, France

OBJECTIVE: To determine the proportions of patients reaching target A1C < 7.0% in a phase 3a trial: liraglutide vs rosiglitazone or placebo, all as add-on to SU (LEAD-1).

METHODS: The incidence of subjects reaching target at 8, 12, 18 and 26 weeks was visualised by a Kaplan-Meier plot. 'Time to A1C target' was analysed by a Cox hazards model, with current and previous treatment as fixed effects and baseline A1C as covariate.

RESULTS: The proportion of subjects reaching target was greater with liraglutide vs rosiglitazone and placebo (Figure). With liraglutide 1.8 mg, the estimated hazard ratio (HR) was 2.94 [95%CI: 2.21; 3.92], representing an estimated chance of reaching target at any given time during treatment almost two times higher for liraglutide 1.8 mg than rosiglitazone ($P < 0.0001$). With liraglutide 1.2 mg, the HR was 2.08 [95%CI: 1.54; 2.79], representing an estimated chance of reaching target 108% higher for liraglutide 1.2 mg than rosiglitazone ($P < 0.0001$).



CONCLUSION: We demonstrate liraglutide is significantly more likely than rosiglitazone to help patients achieve target A1C quickly.

PCS-30-4

Efficacy of the GLP-1 Receptor Agonist Exenatide: Indicator of Therapeutic Potential of this Drug in Type 2 Diabetes

Kenjiro Imai, Tetsuro Tsujimoto, Ritsuko Yamamoto-Honda, Hiroshi Noto, Miyako Kishimoto, Hiroshi Kajio and Mitsuhiro Noda
Division of Diabetes, Endocrinology and Metabolism, Departments of Internal Medicine, Diabetes and Metabolic Medicine, National Center for Global Health and Medicine, Japan

OBJECTIVE: To evaluate the efficacy of exenatide, a GLP-1 receptor agonist, in patients with type 2 diabetes and to investigate the clinical characteristics of patients who exhibited a better response to exenatide and who thus are more likely to benefit from the treatment (responders) than other patients (non-responders).

METHODS: A physical examination including body mass index (BMI), measurements of markers for glucose metabolism including HbA_{1c}, 24-h urinary C-peptide (U-CPR), and a glucagon stimulation test were conducted for the patients in whom exenatide was newly prescribed during their admission. After 3 months, HbA_{1c} was measured (HbA_{1c}_3M) and the changes from the baseline (Δ HbA_{1c}) were used as a marker for identification of responders and non-responders. Statistical analysis was performed with the Mann-Whitney method.

RESULTS: In all patients (11 men and eight women), the average age, HbA_{1c} levels, and BMI were 64 ± 13 years, $9.7 \pm 1.7\%$, and 27.5 ± 5.3 kg/m², respectively. Compared to the patients with low U-CPR level (≤ 50 μ g/day), the patients with high U-CPR level (> 50 μ g/day) showed significantly lower HbA_{1c}_3M levels ($8.2 \pm 0.6\%$ vs $7.3 \pm 1.1\%$, $P = 0.03$) and also showed significantly greater Δ HbA_{1c} values ($-0.7 \pm 1.0\%$ vs $-3.3 \pm 2.1\%$, $P = 0.005$). There was no statistically significant correlation between the levels of HbA_{1c}_3M or Δ HbA_{1c} and the levels of serum CPR levels during the glucagon stimulation test.

CONCLUSION AND DISCUSSION: Exenatide can be considered to be an efficacious drug for those who were guaranteed a certain level of endogenous insulin secretion. Further investigation will be necessary to find out definite criteria for the introduction of incretin related drugs such as exenatide.

PCS-30-5

Long-Term Safety of Once-Daily (QD) Lixisenatide in Japanese Patients with Type 2 Diabetes (T2DM): GetGoal-Mono Japan

Yutaka Seino¹, T. Akane², Elizabeth Niemoeller³ and T. Sakaki²

¹Kansai Electric Power Hospital, Japan; ²Sanofi, Tokyo, Japan; ³Sanofi, Frankfurt, Germany

OBJECTIVE: To assess long-term safety and efficacy of lixisenatide monotherapy in Japanese patients with T2DM.

METHODS: This 76-week, open-label, parallel-group, multicenter study randomized patients with T2DM ($N = 69$) not treated with antidiabetic agents to lixisenatide using a 1- or 2-step dose increase regimen (10 μ g QD for 2 weeks, 20 μ g QD thereafter; or 10 μ g QD and 15 μ g QD for 1 week each, then 20 μ g QD) (NCT00905255). Primary objective: safety at Week 24 with both regimens; secondary objective: overall safety and efficacy.

RESULTS: Baseline characteristics (mean $\pm$ SD) were: 84.1% males; age, 58.7 ± 8.7 years; diabetes duration, 8.6 ± 7.2 years; HbA_{1c}, $8.2 \pm 7.6\%$; body weight, 68.7 ± 15.5 kg. At Week 24, safety was comparable between groups (Table). Sustained efficacy of lixisenatide monotherapy was observed regardless of dose increase regimen.

Safety (safety population)			
Time period	Week 24		Week 76
Population	Two-step dose increase N = 33	One-step dose increase N = 36	Pooled N = 69
Patients with any TEAE, n (%)	27 (81.8)	32 (88.9)	63 (91.3)
Patients with any serious TEAE, n (%)	2 (6.1)	0	3 (4.3)
Patients with any TEAE leading to death, n (%)	0	0	0
Patients with any TEAE leading to permanent treatment discontinuation, n (%)	3 (9.1)	4 (11.1)	10 (14.5)
Patients with any gastrointestinal TEAEs, n (%)	21 (63.6)	28 (77.8)	51 (73.9)
Nausea	12 (36.4)	18 (50.0)	30 (43.5)
Abdominal discomfort	4 (12.1)	6 (16.7)	11 (15.9)
Vomiting	4 (12.1)	1 (2.8)	5 (7.2)
Dyspepsia	4 (12.1)	1 (2.8)	5 (7.2)
Constipation	2 (6.1)	2 (5.6)	5 (7.2)
Diarrhea	1 (3.0)	3 (8.3)	4 (5.8)
Patients with symptomatic hypoglycemia, * n (%)	2 (6.1)	1 (2.8)	5 (7.2)
Efficacy (modified intent-to-treat population)			
Time point	Week 24		Week 76
Population	Two-step dose increase N = 33	One-step dose increase N = 36	Pooled N = 33
Mean, SD (95% CI) change from baseline in HbA _{1c} , % ^{a,b}	-0.99, 1.07 (-1.45 to -0.52)	-0.74, 0.79 (-1.02 to -0.46)	-0.72, 1.20 (-1.15 to -0.30)
Mean (SD) change from baseline in FPG, mmol/L ^b	-1.16 (1.20)	-0.56 (1.54)	-0.46 (2.08)
Mean (SD) change from baseline in body weight, kg ^b	-0.43 (2.08)	-1.08 (1.66)	-1.58 (2.15)

*Event with clinical symptoms with either plasma glucose < 3.3 mmol/L or prompt recovery after oral carbohydrate, intravenous glucose or glucagon administration if no plasma glucose measurement was available; ^aas-observed data; CI = confidence interval; FPG = fasting plasma glucose; HbA_{1c} = glycated hemoglobin; SD = standard deviation; TEAE = treatment-emergent adverse event

CONCLUSION: Lixisenatide 20 μ g QD monotherapy was well tolerated using a 1- or 2-step dose increase regimen in Japanese patients with T2DM, with no new safety signals observed. Additionally, lixisenatide was associated with sustained efficacy over 76 weeks.

Supported by Sanofi.

PCS-31-1

Efficacy and Safety of Sitagliptin in Japanese Patients with Type 2 Diabetes – Sitagliptin Registration Type 2 Diabetes-Juntendo Collaborating Project (SPIRITS-J) –

Tomoya Mita¹, Hirotaka Watada¹, Hirotoshi Ohmura², Yoshinobu Taneda³, Masahiro Sugawara⁴, Hideaki Funayama⁵ and Hiroyuki Daida²

¹Department of Medicine, Metabolism and Endocrinology, Juntendo University Graduate School of Medicine, Japan; ²Department of Cardiovascular Medicine, Juntendo University Graduate School of Medicine, Japan; ³Taneda Clinic, Japan; ⁴Sugawara Medical Clinic, Japan; ⁵Funayama Clinic, Japan

OBJECTIVES: The aim of this study was to investigate clinical efficacy and safety of sitagliptin in Japanese patients with type 2 diabetes.

METHODS: Three thousand two hundred and twenty-seven patients who received sitagliptin for at least 6 month in addition to diet therapy and any other diabetic medicine were recruited in this study. Standard laboratory data and blood pressure were evaluated at baseline, and 1, 3 and 6 month after starting sitagliptin. To search for clinical factors affecting blood glucose lowering effect of sitagliptin, we performed simple regression analysis between the changes in HbA1c and anthropometric data of study subjects.

RESULTS: Here, we analyzed the data of 2346 subjects (970 women, 1376 man) who had already finished 6 month observation period. Clinical parameters at baseline were as follows; age was 65.4 ± 11.5 years (Mean $\pm$ SD), BMI was 25.0 ± 6.0 kg/m² and HbA1c (NGSP) $7.86 \pm 1.20\%$. The mean initial and final dosages of sitagliptin were 48.8 mg/day and 48.9 mg/day. The treatment of sitagliptin significantly reduced mean HbA1c ($7.49 \pm 1.02\%$ at 1 month $P < 0.0001$, $7.16 \pm 0.91\%$ at 3 month $P < 0.0001$, $7.12 \pm 0.97\%$ at 6 month $P < 0.0001$). Random blood glucose level, LDL cholesterol, triglyceride, systolic blood pressure and diastolic blood pressure were also significantly reduced after sitagliptin treatment. The change of HbA1c associated with the treatment was negatively associated with basal HbA1c. Forty cases of hypoglycemia including a severe hypoglycemia and 39 cases of mild gastrointestinal symptom (diarrhea, abdominal distension and constipation) were observed during the observation period.

CONCLUSIONS: Sitagliptin is effective for diabetic management and generally well tolerated in Japanese type 2 diabetic patients.

PCS-31-2

Factors Influencing Glycemic Control Response of Sitagliptin

Gun Woo Kim¹, Jae Hyun Kim¹, Mi Young Lee¹, Jang Yel Shin¹, Young Goo Shin¹, Eunho Ha² and Choon Hee Chung¹

¹Department of Endocrinology, Yonsei University Wonju College of Medicine, Wonju, Korea; ²Department of Information & Statistics, Yonsei University College of Science of Technology, Wonju, Korea

BACKGROUND: Dipeptidyl peptidase 4 (DPP-4) inhibitors are proposed to reduce blood glucose in type 2 diabetes by prolonging the activity of circulating incretins. But the factors that affect the efficacy of sitagliptin have not been proved yet. Therefore, we studied these factors in Korean population.

METHODS: We performed a retrospective analysis in the patients taking sitagliptin in Wonju Christian Hospital. One hundred-fifty patients whose serum HbA1c ranged from 6.5% to 11% participated in this study. These patients were divided into two groups: responder and non-responder. Responder group consisted of subjects with glucose lowering >5% of baseline HbA1c. All others were classified as non-responder group. We analyzed anthropometric data and biochemical markers in all groups, then compared responder group and non-responder group by *t*-test.

RESULTS: The change in HbA1c level across all group was from $8.25 \pm 0.82\%$ to $7.64 \pm 1.03\%$ (P -value = 0.000). There were 93 and 57 patients in responder and non-responder group, respectively. The responder group had lower BMI, body fat (kg), and body fat (%) than non-responder group (P -value = 0.036, P -value = 0.009, P -value = 0.002, respectively), and HbA1c lowering effect of sitagliptin was greater in male than female (P -value = 0.000).

CONCLUSION: In this study, HbA1c was effectively lowered in 62% of the patients. The factors that affect the efficacy of sitagliptin were BMI, body fat (kg) body fat (%), sex. With these results, we suppose that sitagliptin has better glucose lowering effect in non-obese, male patients.

PCS-31-3

Comparison of Glycaemia Variability in Patients with Type 2 Diabetes given Mitiglinide or Sitagliptin, Using Continuous Glucose Monitoring

Kiyotaka Ando, Rimei Nishimura, Daisuke Tsujino, Chiaki Seo, Aya Morimoto, Masaya Sakamoto and Kazunori Utsunomiya

Department of Internal Medicine, Jikei University School of Medicine, Japan

OBJECTIVE: This study aimed to compare glucose variability given Mitiglinide (M) or Sitagliptin (S), using CGM.

METHODS: This study included 11 patients with type 2 diabetes. The patients were randomly assigned to receive either M 30 mg/day or S 50 mg/day. After 2 months of treatment with M or S, they were hospitalised for 4 days, for evaluation by CGM. When the patients were discharged from the hospital, the drugs they received were switched. Again, after 2 months of treatment, they were hospitalised for evaluation by CGM. Variables that were compared by using *t*-test included (1) the mean glucose levels, (2) the range of glucose

increase from pre-prandial to post-prandial peak glucose levels, (3) the time from pre-prandial to post-prandial peak glucose levels, and (4) the area under the curve (AUC) that measured over 140 mg/dL three hours after each meal.

RESULTS: The patients were 58 ± 12 (mean $\pm$ SD) years old, had HbA1c value $7.3 \pm 1.2\%$. The AUC after breakfast (4812 ± 4219 and 7807 ± 6391 , $P = 0.042$) and lunch (5658 ± 5856 and 8492 ± 7161 , $P = 0.050$) were significantly smaller with M than with S but, there was no significant difference after dinner.

CONCLUSIONS: This study showed that the AUC above 140 mg/dL 3 hours after breakfast and lunch were significantly smaller with M than with S, but as for the other results, M was equivalent to S.

PCS-31-4

Evaluation of Alogliptin's Efficacy and Safety Based on Renal Function in Type 2 Diabetic Patients. eGFR Study

Takanori Hyo¹, Takeshi Kurose¹, Minoru Matsumoto¹, Ryota Usui¹, Hitoshi Kuwata¹, Shuichi Fujiwara¹, Koin Watanabe¹, Akihiro Yasuhara², Daisuke Yabe¹ and Yutaka Seino¹

¹Division of Diabetes, Clinical Nutrition and Endocrinology, Department of Internal medicine, Kansai Electric Power Hospital, Japan; ²Division of Nephrology, Department of Internal medicine, Kansai Electric Power Hospital, Japan

Today we can use few medications with efficacy and safety in type 2 diabetic patients (T2DM) with renal dysfunction, though they account for almost half of Japanese T2DM. In Japan, alogliptin is only DPP-4 inhibitor titrated with renal function level.

In order to evaluate the efficacy and safety of alogliptin based on renal function in T2DM, we designed prospective observational study (eGFR study), and we have evaluated the dosage of alogliptin, the glycemic control, eGFR, body weight and adverse events in T2DM registered with this study from August 2011 to April 2012.

Study participants were all Japanese and 237 male and 148 female. Mean age was 64 ± 12 years, HbA1c (NGSP) was $7.6 \pm 1.0\%$, fasting plasma glucose was 144.0 ± 36.7 mg/dL, eGFR was 75.7 ± 22.5 mL/min/1.73 m², body weight was 64.29 ± 14.39 kg, the dosage of alogliptin was 22.64 ± 5.26 mg.

After 24 weeks follow up HbA1c (NGSP) was $7.1 \pm 0.9\%$ ($P < 0.05$), fasting plasma glucose was 128.5 ± 33.2 mg/dL (ns). Body weight and eGFR were not changed. There was only one report of hypoglycemia in the case with sulfonylurea, but there were no severe adverse events.

Treatment with alogliptin in Japanese T2DM is effective and safety at least in 24 weeks follow up.

We need to accumulate more cases, especially with moderate and severe renal dysfunction, and keep following up for more years, in order to evaluate the long-term efficacy and safety of alogliptin based on renal function in T2DM.

PCS-31-5

Sitagliptin Add-on to Low Dosage Sulfonylureas: Efficacy and Safety of Combination Therapy on Glycemic Control and Insulin Secretion Capacity in Type 2 Diabetes

Shin-ichi Harashima, Masahito Ogura, Daisuke Tanaka, Toru Fukushima, Tomoaki Osugi, Yu Wang and Nobuya Inagaki

Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

AIMS: To assess the efficacy and safety of combination therapy with sitagliptin and low dosage sulfonylureas on glycemic control and insulin secretion capacity in Japanese type 2 diabetes.

METHODS: Eighty-two subjects were sequentially recruited for the 52-week, prospective, single arm study. Sitagliptin was added on to sulfonylureas (glimepiride or gliclazide) with or without metformin. The primary endpoint was change in HbA1c in 52-week. The secondary endpoints were changes in BMI, insulin secretion capacity, blood pressure, and urinary albumin excretion, unresponsive rate, and hypoglycemia. Insulin secretion capacity was evaluated by glucagon loading test.

RESULTS: Change in HbA1c was -0.80% (95%CI -0.90 to -0.68) ($P < 0.001$). Change in BMI, systemic and diastolic blood pressure, and urinary albumin excretion were -0.38 kg/m² ($P < 0.05$), $-6.7/-3.6$ mmHg ($P < 0.001$), and -43.2 mg/gCr ($P < 0.001$), respectively. Mild hypoglycemia was observed in three cases. The unresponsive rate was 6.1%. Glucagon loading test showed that 0-min and 6-min CPR at baseline and 52-week were not significantly changed: 0-min CPR, $1.58-1.71$ ng/mL; 6-min CPR, $3.48-3.58$ ng/mL. Insulin secretion capacity, CPI, and SUIT index at baseline did not predict the efficacy of the combination therapy. The final dosages of

glimepiride and gliclazide were 1.44 and 34.5 mg, respectively. The dosage of sitagliptin was increased from 50–69.0 mg in 52-week. Conclusions: The combination therapy with sitagliptin and low dosage sulfonylureas was safe and effective for glycemic control. Glucagon loading test indicated that 1 year administration of sitagliptin and sulfonylureas preserved insulin secretion capacity.

PCS-31-6

Sitagliptin Provides Similar Glycemic Improvement with Less Hypoglycemia in the Elderly with Type 2 Diabetes (T2DM) Compared to Sulfonylurea

Michael J. Davies, Ravi Shankar, Samuel S. Engel, Lei Xu, Gregory T. Golm, Keith D. Kaufman and Barry J. Goldstein
Merck Sharp & Dohme Corp., USA

OBJECTIVE: To compare the efficacy and safety of sitagliptin vs sulfonylurea in elderly patients with T2DM.

METHODS: Data of patients ≥ 65 years were pooled from three double-blind studies to compare the effects of sitagliptin (100 mg/day) or sulfonylurea on change from baseline in HbA_{1c}, fasting plasma glucose (FPG), and body weight (BW) and incidence of symptomatic hypoglycemia. Patients were randomized to sitagliptin or a sulfonylurea. The analyses included 373 elderly patients who completed trials through 30 weeks.

RESULTS: HbA_{1c} and FPG decreased with sitagliptin and sulfonylurea, with no statistical difference between treatments. The proportion of patients with an HbA_{1c} $< 6.5\%$ was similar. Significantly lower incidence of symptomatic hypoglycemia was observed with sitagliptin. BW decreased significantly from baseline with sitagliptin. More patients on sitagliptin achieved the composite endpoint of $> 0.5\%$ HbA_{1c} reduction with no hypoglycemia or BW gain at 30 weeks.

	Sitagliptin N = 178	Sulfonylureas N = 195
Baseline HbA _{1c} , %	7.5 $\pm$ 0.7	7.5 $\pm$ 0.8
Δ HbA _{1c} , %	-0.73 (-0.84, -0.61)	-0.78 (-0.89, -0.67)
HbA _{1c} $< 6.5\%$, n (%)	63 (35.4)	73 (37.4)
Baseline FPG, mg/dL	150.9 $\pm$ 32.8	157.4 $\pm$ 38.4
Δ FPG, mg/dL	-21.3 (-26.5, -16.1)	-23.4 (-28.4, -18.3)
Patients with AE of hypoglycemia, n (%)	11 (6.2)	55 (28.2)*
Baseline BW, kg	84.6 $\pm$ 14.6	83.6 $\pm$ 15.1
Δ BW, kg	-1.7 (-2.3, -1.2)	0.4 (-0.1, 1.0)*
Composite ¹ , n (%)	78 (44.1)	31 (15.9)*

AE = adverse event; Data are mean $\pm$ SD, LS mean change (Δ) from baseline (95% CI), or counts (proportion of patients). * $p < 0.001$ for difference between sitagliptin and sulfonylurea. ¹Composite = patient experienced an HbA_{1c} decrease $> 0.5\%$ with no symptomatic hypoglycemia and no body weight gain.

CONCLUSION: Sitagliptin treatment is associated with weight loss and significantly less hypoglycemia, while providing similar glycemic efficacy compared to sulfonylurea in elderly patients with T2DM.

PCS-31-7

Effect of Sitagliptin on Intact Proinsulin/Insulin Molar Ratio in Elderly Type 2 Diabetic Subjects

Gen Yoshino¹, Naoki Hiroi², Takehiko Watanabe³, Shuki Usui², Koji Kuboki², Miki Koga⁴, Hiroshi Yoshino¹ and Takahisa Hirose²

¹Department of Internal Medicine, Shinsuma General Hospital, Japan; ²Division of Diabetes, Metabolism and Endocrinology, Department of Internal Medicine, Toho University School of Medicine, Japan; ³Department of Internal Medicine, Mariners Koseikai Hospital, Japan; ⁴Department of Immunology, Mitsubishi BML Co Ltd., Japan

OBJECTIVE: The present study was conducted to examine the effect of sitagliptin, one of the DPP-VI inhibitors, on intact proinsulin/insulin molar ratio in elderly type 2 diabetic subjects.

METHODS: Sixty (23 male) type 2 diabetic patients were enrolled after informed consent was given. Their mean age and BMI were 64.5 years and 24.6, respectively. Before and 3 months after 50 mg daily of sitagliptin treatment blood was withdrawn after overnight fast with EDTA2Na. Blood glucose and HbA_{1c} (NGSP) were measured. Plasma insulin and intact proinsulin were measured by immunoradiometric and by chemiluminescence assay (MLT Research Ltd. USA), respectively. To avoid breakdown of proinsulin during assay system, incubation for reaction was done overnight and at 4°C. Five patients were treated with sitagliptin alone and 55 were on combination therapy.

RESULTS: Average fasting blood glucose levels of all patients decreased from 180 ± 45 to 141 ± 24 mg/dL, and HbA_{1c} also decreased from 8.7 ± 0.8

to $7.3 \pm 0.5\%$, significantly ($P < 0.05$ and < 0.001). Fasting plasma insulin did not change significantly. Intact proinsulin/insulin ratio in all patients decreased from 0.14 ± 0.08 to 0.11 ± 0.06 , significantly ($P < 0.01$). The decrease in this ratio of non-elderly subjects ($n = 33$, below 65 years of age) was also significant. Furthermore, that of elderly patients was slight but significant.

CONCLUSION: Sitagliptin improved both glucose metabolism and insulin secretory mechanism in type 2 diabetic subjects. Since decrease in proinsulin/insulin molar ratio after treatment was significant in not only non-elderly but also elderly patients, sitagliptin treatment can be recommended to start at any age from the stand point of insulin secretory mechanism.

PCS-31-8

The Beneficial Effects of Add-On Therapy with Acarbose in Japanese Type 2 Diabetes Mellitus Treated with Alogliptin

Yoshiki Kusunoki¹, Tomoyuki Katsuno¹, Makiko Abe¹, Kana Miyakoshi¹, Takashi Ikawa¹, Toshihiro Matsuo¹, Humihiro Ochi¹, Masaru Tokuda¹, Kazuki Murai¹, Masayuki Miuchi¹, Tomoya Hamaguchi², Jun-ichiro Miyagawa¹ and Mitsuyoshi Namba¹

¹Division of Diabetes & Metabolism, Internal Medicine, Hyogo College of Medicine, Japan; ²Division of Innovative Diabetes Treatment, Hyogo College of Medicine, Japan

AIM: To analyze the beneficial effects of add-on therapy with acarbose, α -glucosidase inhibitor (α -GI) in alogliptin, dipeptidyl peptidase-4 inhibitor (DPP-4I) treated Japanese type 2 diabetes mellitus (T2DM).

METHODS: Acarbose (100 mg x3/day) was added on 10 T2DM patients fairly to poorly controlled with alogliptin treatment with or without other oral hypoglycemic agents. Daily profiles of blood glucose levels were compared with continuous glucose monitoring (CGM) and plasma levels of glucose (PG), insulin (IRI), C-peptide immunoreactivity (CPR), glucagon (IRG), total glucose dependent insulinotropic peptide (total-GIP) and active glucagon-like peptide-1 (active-GLP-1) were analyzed with test meal ingestion before and after add-on therapy with acarbose.

RESULTS: Postprandial glucose levels were significantly decreased and SD of daily profiles of blood glucose levels was significantly improved. PG, IRI and CPR were also decreased significantly after the add-on therapy. The levels of total-GIP were decreased significantly after the add-on therapy and active-GLP-1 levels tended to be increased.

CONCLUSION: The blood glucose control, especially postprandial hyperglycemia in T2DM treated fairly to poorly with alogliptin was significantly improved by add-on therapy with acarbose possibly via the reciprocal change of the plasma levels of both potent incretins, GIP/GLP-1. In the treatment of T2DM, the combined therapy with α -GI and DPP-4I could exhibit the beneficial effects on not only the blood glucose control *per se*, but also the progression of macroangiopathy via the suppression of postprandial hyperglycemia/insulinemia.

PCS-32-1

Sitagliptin Reduces Microalbuminuria in Type 2 Diabetes Mellitus Patients

Hiroko Mori, Yosuke Okada and Yoshiya Tanaka

The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan

OBJECTIVE: The aim of this study was the effect of sitagliptin on microalbuminuria patients with in type 2 diabetes mellitus (T2DM).

METHOD: Eighty five patients with T2DM (HbA_{1c} $< 8.4\%$) were randomized to patients taking sitagliptin 50 mg or other anti-diabetic drugs. We evaluated at baseline and after 3 and 6 months following parameters: body weight, blood pressure, HbA_{1c}, FPG, FPI, LDL-C, HDL-C, TG, eGFR and the urinary albumin-to-creatinine ratio (ACR). The primary outcome of the study was changes in ACR at 6 months.

RESULT: (1) Sitagliptin significantly reduced ACR within 6 months, whose changes were marked in patients with higher amount of ACR (multivariate analysis). (2) Twenty six patients with normoalbuminuria had a reduction in ACR, suggesting a preventive effect of sitagliptin on the occurrence of microalbuminuria. Nine patients with microalbuminuria had a reduction in ACR, suggesting the beneficial effect of sitagliptin in the early stage of diabetic nephropathy. (3) There was no significant correlation between decrease of ACR and improvement of glucose metabolism, lipid metabolism and blood pressure. (4) A significant decrease of HbA_{1c} and FPG were obtained in both groups without any significant differences between the two groups. (5)

Sitagliptin significantly reduced LDL-C. (6) Body weight and blood pressure was not changed in both groups.

CONCLUSION: These results suggest that sitagliptin improved not only glucose and lipid metabolism but also microalbuminuria. The mechanism of reduced microalbuminuria might be direct effects as well as yet undetermined factors caused by an increase in active glucagon-like peptide-1, despite the blood pressure, body weight, glucose metabolism.

PCS-32-2

Efficacy and Safety of Sitagliptin (SITA) in Real Clinical Settings: Comparison of SITA, SITA/SU, and SITA/MET

Naoki Kuramoto¹, Hitoshi Kuwata¹, Minoru Matsumoto¹, Ryota Usui¹, Shuichi Fujiwara¹, Koin Watanabe¹, Takanori Hyo¹, Akihiro Yasuhara², Daisuke Yabe¹, Takeshi Kurose¹ and Yutaka Seino¹

¹Division of Diabetes and Clinical Nutrition, Kansai Electric Power Hospital, Japan;

²Division of Nephrology, Kansai Electric Power Hospital, Japan

OBJECTIVES: Potential interactions between DPP-4 inhibitor sitagliptin (SITA) and other oral anti-diabetic drugs, sulfonylurea (SU) or metformin (MET), in Japanese patients with type 2 diabetes (T2DM) in real clinical settings were investigated.

METHODS: Japanese T2DM ($n = 636$) who had started SITA as monotherapy or add-on therapy to SU or MET from December 2009 to April 2011 in Kansai Electric Power Hospital were registered. Patients on either SITA, SITA/SU, or SITA/MET for 56 weeks, who had been on appropriate diet and/or exercise before initiation of SITA, were analyzed for changes in HbA1c, body weight, other clinical parameters and adverse events. Patients receiving anti-diabetic agents other than SU or MET before initiation of SITA were excluded.

RESULTS: After 56 weeks, HbA1c reduction was 0.75% in SITA group [$n = 36$; age 61.9 ± 2.1 ; BMI 24.8 ± 0.6 ; HbA1c (NGSP, %) 7.4 ± 0.1]. In SITA/SU group [$n = 31$; age 64.8 ± 2.1 ; BMI 23.9 ± 0.9 ; HbA1c (NGSP, %) 7.8 ± 0.1] and SITA/MET group [$n = 7$; age 53.6 ± 4.6 ; BMI 27.7 ± 3.0 ; HbA1c (NGSP, %) 7.8 ± 0.3], HbA1c reduction was 0.72% and 0.84%, respectively. HbA1c reduction was correlated with reduction of body weight in all groups (linear regression; SITA group: $R^2 = 0.24$, $P < 0.01$; SITA/SU group: $R^2 = 0.23$, $P < 0.01$, SITA/Met group: $R^2 = 0.97$, $P < 0.01$). In SITA group, there were no significant changes in body weight, GOT, GPT, T-bil, Cre, TG, LDL-cho and HDL-cho from baseline.

CONCLUSIONS: In Japanese T2DM, SITA improved glycemic control and lost weight, with or without SU and MET. Our comparison in real clinical settings showed no significant difference in HbA1c reduction between groups.

PCS-32-3

Pleiotropic Effects of Sitagliptin vs. Voglibose as a First/Second-Line Therapy in Patients with Type 2 Diabetes: ERA-DM Study Chapter 1

Yukiko Matsushima, Yumie Takeshita, Kenichiro Kato, Hirofumi Misu, Tsuguhito Ota, Shuichi Kaneko, Toshinari Takamura and ERA-DM Study Group
Department of Disease Control and Homeostasis, Kanazawa University Graduate School of Medical Science, Japan

OBJECTIVE: The aim of this study is to evaluate the pleiotropic effects on metabolic and cardiovascular parameters of sitagliptin (S) vs voglibose (V) in Japanese patients with type 2 diabetes who did not achieve adequate glycemic control with diet therapy or/and a single oral hypoglycemic agent.

METHODS: In a multi-center, randomized, open, parallel-group trial, 254 patients who did not achieve adequate glycemic control with diet therapy or/and sulfonylurea, metformin, or pioglitazone ($>6.9\%$ NGSP) were randomized 1:1 to 12-week treatment with S 50 mg once daily or V 0.2 mg thrice daily before meals. The primary outcome is lowering HbA1c. We present the results from 182 patients (S, $N = 89$; V, $N = 93$) who have completed 12-week observation period.

RESULTS: After 12 weeks, both S and V significantly ($P < 0.001$) reduced HbA1c from baseline (7.47 ± 1.00 – $6.71 \pm 0.77\%$, 7.53 ± 0.80 – $7.18 \pm 1.03\%$). S was superior to V in lowering HbA1c [between-group difference (95% confidence intervals (CI))] = -0.4% (-0.5 to -0.3), $P = 0.024$] in any combination therapy. In cardiovascular parameters, both S and V significantly increased serum levels of adiponectin (3.08 ± 2.17 – 3.49 ± 2.59 $\mu\text{g/mL}$, $P < 0.001$, 3.39 ± 2.84 – 3.64 ± 2.66 $\mu\text{g/mL}$, $P = 0.004$). Only S significantly decreased FPG (152.4 ± 28.3 – 134.7 ± 23.3 mg/dL, $P < 0.001$), TG (131.3 ± 72.8 – 121.8 ± 72.7 mg/dL, $P = 0.036$) and sLDL (36.3 ± 13.7 – 34.2 ± 13.8 mg/dL, $P = 0.028$).

CONCLUSIONS: This study suggests S as a first/second-line therapy improves glycemic control and could reduce arteriosclerosis risk in Japanese patients with type 2 diabetes.

PCS-32-4

Sitagliptin Add-On to Glimepiride: Efficacy of Combination Therapy on Glycaemic Control and Renal Function in Type 2 Diabetes

Tsugiyasu Kanda¹, Hisanari Atsumi², Tomohiko Itoh² and Daisuke Isuda¹

¹Department of General Medicine, Kanazawa Medical University Himi Municipal Hospital, Japan; ²Department of Endocrinology and Metabolism, Kanazawa medical University Himi Municipal Hospital, Japan

We assessed the efficacy and safety of combination therapy with sitagliptin (S), the dipeptidyl peptidase-4 inhibitor on sulphonylurea, glimepiride (G) in Japanese type 2 diabetes.

One hundred diabetic subjects were recruited for the 24-weeks. S (50 mg/day) was added on to sulphonylurea, G (0.5–3 mg/day) in 63 patients, S with the removing of metformin (M) or thiazolidinediones (T) was added on to G in 20 patients (male 15, female 5). The other 17 patients were administered with S on G and no removal of anti-diabetic agents.

Reduction in average hemoglobin A1c (HbA1c) levels of approximately 0.6% compared with baseline after 24 weeks in S on G ($7.6 \pm 1.6\%$ vs $7.0 \pm 1.4\%$, $P < 0.01$). In patients with S on G removing of M or T, HbA1c was also reduced in comparison with the baseline ($7.6 \pm 1.7\%$ vs $7.1 \pm 1.2\%$, $P < 0.001$) after 24 weeks. S on G and no remove did not reducing of HbA1c compared with the baseline ($7.8 \pm 0.8\%$ vs $7.4 \pm 1.2\%$, $P > 0.05$). The circulating level of creatinine was significantly elevated after S on G for 24 weeks (0.86 ± 0.27 vs 0.82 ± 0.26 , $P < 0.001$) compared with the baseline.

The combination therapy with S add-on G was effective for glycaemic control, even if the removing of M or T after 24 weeks. The renal function may be worsened after S administration on G. The more clinical data should be needed in the effectiveness and safety of S on G.

PCS-32-5

Effect of Sitagliptin on Diurnal Variation of Plasma Glucose with Type 2 Diabetes Mellitus Treated with Sulfonylurea

Yoshiko Kanazaki, Yu Miyai, Sayo Ueda, Kayoko Nakauchi, Hiroki Inoue, Yo Nakai, Naotsugu Murakami, Eiji Yamamoto, Sunao Shimada and Yasumi Shintani
Division of Metabolism and Endocrinology, Tokushima Red Cross Hospital, Japan

OBJECTIVE: We evaluated the short-term effect of combined administration of sitagliptin on diurnal variation of plasma glucose in patients with type 2 diabetes treated with sulfonylureas (SU).

METHODS: Thirty-three patients (20 men, 13 women), inadequately controlled on oral hypoglycemic agents including SU, were enrolled in the study. They were 65 $\pm$ 11 years (mean $\pm$ SD) in age, 26.2 ± 4.0 kg/m² in BMI and $9.1 \pm 1.7\%$ in HbA1c (NGSP). The specific SUs being administered to the patients before combined therapy were glimepiride in 25, gliclazide in five and glibenclamide in three patients. α -glucosidase inhibitors ($n = 21$) and insulin-sensitizers ($n = 10$) were also administered. Sitagliptin (50 mg/day) was started with reduced dose of SU, and circadian variations of plasma glucose were evaluated before and after sitagliptin treatment.

RESULTS: Variation of plasma glucose before the administration of sitagliptin was 155 ± 51 at 7:00, 253 ± 57 at 11:00, 227 ± 69 at 14:00, 170 ± 54 at 17:00, 227 ± 50 mg/dL at 21:00, showing a marked postprandial hyperglycemia. Two to 5 days after the addition of sitagliptin, plasma glucose levels were significantly lowered despite the reduced SU: 134 ± 29 at 7:00, 172 ± 51 at 11:00, 170 ± 44 at 14:00, 137 ± 35 at 17:00, 196 ± 35 mg/dL at 21:00, showing a greater improvement especially around lunch time (-77 ± 54 at 11:00 and -54 ± 66 mg/dL at 14:00).

CONCLUSIONS: The effects of sitagliptin with SU develop early, and this combination therapy is beneficial for the reduction in diurnal variation of plasma glucose. This may be mainly attributable to the suppressive effect of GLP-1 on glucagon secretion.

PCS-32-6

Efficacy of Sitagliptin and its Predictive Factors: Investigation of Monotherapy, Switching, and Combination Therapy

Masae Toyonaga, Chisa Matsumoto, Ayumi Yamauchi, Hirofumi Imoto, Tetsuya Mizokami, Yuichi Sato and Kiyohide Nunoi
Division of Diabetes, St. Mary's Hospital, Japan

OBJECTIVE: To examine the effect of sitagliptin (S) on HbA1c and its predictive factors in Japanese type 2 diabetes.

SUBJECTS: Patients on S monotherapy ($n = 17$), patients switching to S from other oral hypoglycemic agents ($n = 49$), and patients added S on previous oral drugs ($n = 85$).

METHODS: Multiple regression analysis of the relationship between the change of HbA1c after 3 months and patient background factors. Data are shown in average.

RESULTS: HbA1c improved 1.2% on S monotherapy, 0.5% in those switching from α -glucosidase inhibitors and from pioglitazone. Interestingly, S showed marked improvement of HbA1c in 1/3 of those switching from sulfonylurea (SU). Among patients added S on previous SU or metformin, HbA1c improved 1.0% and 0.8% in glucose dependent manner. When S was added to the combination of SU plus metformin etc, HbA1c improved 0.9% or 0.7% in patients whose SU dose was sustained or reduced, HbA1c markedly improved in 1/4 of cases whose SU dose was reduced or not. Multiple regression analysis revealed that the improvement of HbA1c over 3 months correlated significantly with initial 1-month HbA1c change and baseline HbA1c values, but not significantly with BMI, insulin secretion capacity.

CONCLUSIONS: S was considered to be effective as first-line therapy for patients with HbA1c of 6–8%, according to its power and the correlation analysis. Addition of S is also useful, but we have to pay attention to the synergistic and independent effects with SU. The initial 1-month HbA1c change is useful for predicting the contribution of incretin system for hyperglycemia.

PCS-32-7

Sitagliptin Add-On Therapy to Insulin Improves Glycemic Control in Japanese Subjects with Type 2 Diabetes

Yoshiharu Wada¹, Yoshiyuki Hamamoto¹, Sachiko Honjo¹, Yukiko Kawasaki¹, Hisato Tatsuoaka¹, Kanta Fujimoto¹, Atsuko Matsuoka¹, Hiroki Ikeda² and Hiroyuki Koshiyama¹

¹Center for Diabetes and Endocrinology, Kitano Hospital, Japan; ²Ikeda Hospital, Japan

BACKGROUND: Recently, dipeptidyl peptide-4 inhibitors have been applied in various treatment regimens. In the present study, we investigated the efficacy of sitagliptin add-on therapy to insulin in Japanese subjects with type 2 diabetes.

SUBJECTS AND METHODS: This study included a total of 23 subjects (male 17, female 6; mean age: 62.7 ± 2.5 SE years) with type 2 diabetes, who had been administered with insulin (34.0 ± 4.5 units per day) and received 50 mg of sitagliptin add-on to insulin. Their A1C levels and body mass index were measured before (0 m) and after 2 and 4 months (2 and 4 m respectively) of sitagliptin administration.

RESULTS: The A1C levels were significantly decreased (7.9 ± 0.3 at 0 m, 7.1 ± 0.2 at 2 m; $P < 0.05$, 7.0 ± 0.2 at 4 m; $P < 0.05$) without significant change in body mass index (25.5 ± 0.7 at 0 m, 25.0 ± 0.7 at 2 m and 25.4 ± 0.9 at 4 m). Biguanides, sulfonylureas and α -glucosidase inhibitors were used in 48% ($n = 11$), 35% ($n = 8$) and 26% ($n = 6$) of the subjects, respectively. Hypoglycemic symptoms were reported by 30% ($n = 7$) of the subjects.

CONCLUSION: Sitagliptin adding on insulin therapy may be a good therapeutic option in Japanese subjects.

PCS-32-8

Fasting Serum C-Peptide (CPR) Level Before Starting Alogliptin as a Predictive Index in Controlling Blood Sugar of Diabetic Patients on Hemodialysis

Tung-Huei Chang¹, Tasuku Kikumura¹, Kiyomitsu Nagayama¹, Kouhei Shimizu¹, Morikuni Nishihira¹, Tomoo Murayama¹, Masako Kouchi¹, Tomoki Yonaha¹, Katsura Aragaki², Toyohumi Majikina², Hiroyuki Yogi³, Takeshi Toma², Moritake Higa² and Yoshiaki Shiohira¹

¹Department of Nephrology, Tomishiro Central Hospital, Japan; ²Department of Diabetology and Endocrinology, Tomishiro Central Hospital, Japan; ³Department of Diabetology and Endocrinology, Nanbu Hospital Okinawa, Japan

INTRODUCTION: Some diabetic CKD patients lose their glycemic control after induction of hemodialysis (HD) even though they once had been stopped hypoglycemic drug or insulin before the induction. Hypoglycemic drugs like dipeptidyl-peptidase IV inhibitors (DPP-IV: e.g. alogliptin) are preferred. But for diabetic HD patients with low insulin secretion capacity, DPP-IV may cause hyperglycemia. For such a kind of patients, insulin therapy was safer and more effective than oral hypoglycemic medication in low capacity.

Serum fasting CPR has been reported as an indicator for insulin secretion capacity in HD patients. We assumed fasting serum CPR as an index to predict efficacy of alogliptin and report the observational study.

METHOD: Patients of our group hospitals were observed retrospectively. They were all checked fasting serum CPR and HbA1c (JDS) were also checked before prescription and 3 months later in HbA1c. Cases were excluded if they had cancer, endocrine disease, or sulfonylurea and have been admitted during this period. Alogliptin had been stopped in case of no glycemic change in bad control for a week.

RESULT: Nine patients were eligible for evaluation. Patients lower than 9–10 ng/mL had not changed in HbA1c.

CONCLUSION: To choose better treatment for diabetic HD patients, serum fasting CPR may be some help. But accumulation of further cases and further discussion will be needed.

PCS-33-1

Canagliflozin Improves Glycemic Control and Beta-cell Function in Japanese Subjects with Type 2 Diabetes Mellitus

Nobuya Inagaki¹, Kazuoki Kondo², Toru Yoshinari³, Nobuko Maruyama³, Hiroaki Nakazawa³, Yutaka Susuta⁴ and Hideki Kuki⁵

¹Department of Diabetes and Clinical Nutrition, Kyoto University Graduate School of Medicine, Japan; ²Mitsubishi Tanabe Pharma Corporation, Japan; ³Clinical Research Planning and Coordination Department, Mitsubishi Tanabe Pharma Corporation, Japan; ⁴Data Science Department, Mitsubishi Tanabe Pharma Corporation, Japan; ⁵Global Project Management Department, Mitsubishi Tanabe Pharma Corporation, Japan

OBJECTIVE & METHODS: In a multi-center, randomized, double-blind, placebo-controlled study, efficacy and safety of a novel Sodium Glucose Co-Transporter 2 (SGLT2) inhibitor, Canagliflozin (CANA, TA-7284/JNJ-28431754) as monotherapy were investigated in Japanese subjects with T2DM. After a 4-week run-in period, 383 subjects (age 57 years, HbA1c 8.09%, FPG 165.6 mg/dL, body weight 69.37 kg at baseline) were randomized to receive CANA 50, 100, 200, 300 mg or matching placebo (PBO) once daily for 12 weeks. Postprandial glucose (PPG) was measured over 2 h by a meal tolerance test.

RESULTS: At Week 12, HbA1c was significantly decreased in all CANA treatment groups vs PBO. With CANA treatments, FPG and 2-h PPG were significantly reduced with lower endogenous insulin levels.

Adverse events (AEs) were reported in 35–49% of patients and the incidence did not differ among the treatment groups. All AEs were mild to moderate in intensity.

Change from Baseline at Week 12 (LOCF), LS Mean (SE)	50 mg (n=82)	100 mg (n=74)	200 mg (n=75)	300 mg (n=75)	PBO (n=75)
HbA1c (%)	-0.61 (0.06)	-0.80 (0.06)	-0.79 (0.06)	-0.88 (0.06)	+0.11 (0.06)
FPG (mg/dL)	-24.7 (2.1)	-33.1 (2.2)	-36.1 (2.2)	-38.3 (2.2)	-3.0 (2.2)
HOMA- β (%)	+2.97 (1.84)	+6.98 (1.94)	+4.80 (1.92)	+2.81 (1.92)	-1.61 (1.92)
Meal Tolerance Test	n=79	n=69	n=74	n=72	n=65
2h-PPG (mg/dL)	-42.6 (3.7)	-47.0 (3.9)	-48.6 (3.8)	-49.3 (3.8)	-11.0 (4.0)
2h-Insulin (μ U/mL)	-12.56 (1.992)	-12.07 (2.129)	-15.54 (2.070) ¹⁾	-14.27 (2.100) ²⁾	-1.662 (2.198)

1) $n=73$, 2) $n=71$

CONCLUSION: CANA was generally well tolerated and effective in improving glycemic control and beta-cell function in Japanese T2DM patients.

PCS-33-2

The Sodium Glucose Cotransporter-2 (SGLT-2) Inhibitor Empagliflozin Lowers Blood Pressure Independent of Weight or HbA1c Changes

Thomas Hach¹, Hiddo J. Lambers Heerspink², Egon Pfarr¹, Soren Lund¹, Ludwin Ley¹, Uli C. Broedl¹ and Hans J. Woerle¹

¹Boehringer Ingelheim Pharma GmbH & Co. KG, Germany; ²University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

OBJECTIVE: To evaluate effects of empagliflozin on systolic and diastolic blood pressure (SBP and DBP) and correlations between changes in weight or HbA1c from a pooled analysis of data from two randomized controlled 12-week phase 2b trials.

METHODS: Data were pooled from patients on empagliflozin 10 mg ($N = 152$), empagliflozin 25 mg ($N = 152$) and placebo ($N = 153$). Changes

from baseline in HbA1c, weight, BP were assessed and Pearson correlation coefficients calculated.

RESULTS: Baseline mean (SD) SBP and DBP (mmHg) ranged from 131.3 (13.8)–134.3 (15.9) and 79.1 (9.1)–80.9 (9.2), respectively. Mean [SE] changes from baseline in SBP (mmHg) in patients receiving empagliflozin 10, 25 mg and placebo were –3.8 [1.0], –4.5 [1.0], and –1.2 [1.0], respectively ($P < 0.05$ vs placebo for each dose) and appeared larger in patients with baseline SBP > 140 mmHg (–17.0 [2.6], –13.4 [2.3], –10.4 [2.4], respectively). Mean changes from baseline in DBP with empagliflozin 10, 25 mg and placebo were –2.3 [0.6], –2.7 [0.6], and –1.8 [0.6], respectively ($P = \text{NS}$ for each dose). Correlation coefficients between change in weight and change in SBP with empagliflozin 10, 25 mg and placebo were 0.10, 0.04 and 0.12 and between change in HbA1c and change in SBP were –0.09, –0.02 and 0.11, respectively ($P > 0.14$ for each). The number of patients with AEs was comparable among treatment groups [34.2% (empagliflozin 10 mg), 31.6% (empagliflozin 25 mg) and 34.6% (placebo)].

CONCLUSION: Empagliflozin provided statistically significant, clinically meaningful reductions in SBP, which seemed more pronounced when baseline SBP > 140 mmHg. BP changes were not correlated with changes in weight or HbA1c. Empagliflozin was generally well tolerated. These data were presented at EASD 2012. Funded by Boehringer Ingelheim.

PCS-33-3

Efficacy and Safety of Empagliflozin, a Sodium Glucose Cotransporter-2 Inhibitor, in Asian Patients with Type 2 Diabetes Mellitus: Sub-analysis of a 12-week, Randomized, Placebo-Controlled Study

Kun-Ho Yoon¹, Lee-Ming Chuang², Egon Pfarr³, Thomas Hach³, Yan Gong³ and Uli C. Broedl³

¹Seoul St. Mary's Hospital, The Catholic University of Medicine, Korea; ²Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; ³Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany

OBJECTIVE: To investigate the efficacy and safety of empagliflozin in Asian patients with T2DM.

METHODS: This was a *post-hoc* sub-analysis of Asian patients in a 12-week, Phase II, randomized study. Patients received empagliflozin 5 mg ($N = 29$), 10 mg ($N = 28$), 25 mg ($N = 27$) qd or placebo ($N = 28$).

RESULTS: After 12 weeks, empagliflozin led to significant reductions from baseline in HbA1c (primary endpoint), FPG and body weight vs placebo (Table). Adverse events (AEs) were reported by 27.6%, 25.0%, 22.2% and 35.7% of patients on empagliflozin 5, 10, 25 mg and placebo, respectively; most were mild or moderate. Serious AEs were reported for two patients on empagliflozin (myocardial infarction [5 mg], intestinal functional disorder [25 mg]; neither considered drug-related by investigator) and none on placebo. Two patients on empagliflozin (10, 25 mg) reported genital infections (resolved by study end). No urinary tract infection or hypoglycemia was reported with empagliflozin or placebo.

CONCLUSION: In Asian patients with T2DM, empagliflozin significantly reduced HbA1c, FPG and body weight vs placebo and was generally well tolerated. Funded by Boehringer Ingelheim.

PCS-33-4

The Effect of Hepatic Impairment on the Pharmacokinetics, Safety and Tolerability of Empagliflozin, a Potent Sodium Glucose Cotransporter-2 Inhibitor

Sreeraj Macha¹, Peter Rose², Michaela Mattheus³, Rodica Cinca⁴, Sabine Pinnetti², Uli C. Broedl³ and Hans J. Woerle³

¹Boehringer Ingelheim Pharmaceuticals, Inc., USA; ²Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; ³Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany; ⁴Pierrel Research HP-RO SRL, Timisoara, Romania

OBJECTIVE: Empagliflozin is a potent and selective sodium glucose cotransporter-2 inhibitor in development for the treatment of type 2 diabetes mellitus. This open-label, parallel-group study investigated the effect of various degrees of hepatic impairment on the pharmacokinetics, safety, and tolerability of empagliflozin.

METHODS: Thirty-six subjects (eight each with mild, moderate or severe hepatic impairment according to Child-Pugh classification, and 12 matched controls with normal hepatic function) received a single 50 mg dose of empagliflozin.

RESULTS: Mean (range) age was 53.9 (33–71) years and 17 subjects were male. Empagliflozin was rapidly absorbed and, after reaching peak levels,

plasma drug concentrations declined in a biphasic fashion. Compared with subjects with normal hepatic function, geometric mean ratios (90% CI) of $\text{AUC}_{0-\infty}$ and C_{max} were 123.15% (98.89–153.36) and 103.81% (82.29–130.95), respectively, in patients with mild hepatic impairment, 146.97% (118.02–183.02) and 123.31% (97.74–155.55), respectively, in patients with moderate hepatic impairment, and 174.70% (140.29–217.55) and 148.41% (117.65–187.23), respectively, in patients with severe hepatic impairment. Adverse events (AEs) were reported in 0, 3 and 2 subjects with mild, moderate and severe hepatic impairment, respectively, and six subjects with normal hepatic function. All AEs were mild or moderate in intensity.

	Placebo (N=28)	Empagliflozin 5 mg qd (N=29)	Empagliflozin 10 mg qd (N=28)	Empagliflozin 25 mg qd (N=27)
HbA_{1c} (%)				
Mean baseline	7.79	7.96	8.26	7.82
Mean (SE) change from baseline at week 12	-0.09 (0.15)	-0.64 (0.14)	-0.64 (0.15)	-0.76 (0.16)
Mean (95% CI) difference to placebo		-0.55** (-0.94, -0.16)	-0.55** (-0.95, -0.15)	-0.67** (-1.07, -0.27)
FPG (mg/dL)				
Mean baseline	152.64	168.00	177.39	173.19
Mean (SE) change from baseline at week 12	-8.00 (5.15)	-30.04 (5.11)	-34.67 (5.21)	-42.04 (5.36)
Mean (95% CI) difference to placebo		-22.04*** (-33.21, -10.87)	-26.66*** (-38.11, -15.21)	-34.03*** (-45.60, -22.46)
Body weight (kg)				
Mean baseline	71.91	69.38	67.36	67.20
Mean (SE) change from baseline at week 12	-0.63 (0.32)	-1.57 (0.31)	-2.28 (0.32)	-1.90 (0.33)
Mean (95% CI) difference to placebo		-0.94* (-1.79, -0.09)	-1.65*** (-2.51, -0.79)	-1.27** (-2.14, -0.40)
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$ versus placebo.				

CONCLUSIONS: Empagliflozin was well tolerated in subjects with hepatic impairment. The increase in empagliflozin exposure was < 2 -fold in patients with impaired liver function, therefore no dose adjustment of empagliflozin is required in these patients. These data were presented at ADA 2012. Funded by Boehringer Ingelheim.

PCS-33-5

Lack of QT Prolongation Effects of Single Dose of Luseogliflozin; a Thorough QT/QTc Study in Healthy Japanese Subjects

Yuji Kumagai¹, Tomoko Hasunuma², Yoshishige Samukawa³, Soichi Sakai³ and Takashi Watanabe³

¹Kitasato Clinical Research Center, Kitasato University East Hospital, Japan; ²Division of Rheumatology, Department of Internal Medicine, School of Medicine, Toho University, Japan; ³Taisho Pharmaceutical Co., Ltd., Japan

OBJECTIVE: Luseogliflozin (TS-071; LUSEO) is a selective SGLT2 inhibitor. To evaluate cardiac safety of LUSEO, a thorough QT/QTc study was conducted in healthy Japanese subjects. This is the first placebo controlled thorough QT/QTc study using positive control with oral hypoglycemic agent performed in Japan. The effects of moxifloxacin (MFLX) on QT prolongation were also evaluated to establish assay sensitivity.

METHODS: In this double-blind, placebo- and open label positive-controlled, four-way cross over study, 28 male and 28 female subjects received a single dose of LUSEO 5 mg, LUSEO 20 mg, placebo and MFLX 400 mg. Serial triplicate digital 12-lead electrocardiograms (ECGs) were recorded at pre- and post-dose, and results analyzed using the Fridericia correction (QTcF) method. Serial blood sampling was performed for pharmacokinetic analyses of

LUSEO and MFLX for the analysis of the relationship between QTcF interval and plasma concentration.

RESULTS: In MFLX group, the lower limits of the one-sided 95% confidence intervals (CIs) for baseline and placebo adjusted QTcF intervals (double-delta QTcF) was more than 0 ms at all time points. There was obvious relationship between plasma MFLX concentrations and changes in double-delta QTcF.

The upper limits of the one-sided 95% CIs for double-delta QTcF in the 5 and 20 mg LUSEO groups were <10 ms at all time points. LUSEO was well tolerated at both dose levels. LUSEO was well tolerated at both dose levels.

CONCLUSION: No arrhythmogenic effect of therapeutic (5 mg) and supra-therapeutic (20 mg) dose of LUSEO was shown in healthy Japanese subjects.

PCS-33-6

Lack of Interaction Between the Sodium Glucose Cotransporter-2 Inhibitor Empagliflozin and Hydrochlorothiazide or Torasemide in Patients with T2DM

Tim Heise¹, Sreeraj Macha², Michaela Mattheus³, Hans J. Woerle³ and Uli C. Broedl³
¹Profil Institut für Stoffwechselforschung GmbH, Germany; ²Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; ³Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany

OBJECTIVE: To investigate drug–drug interaction between empagliflozin and hydrochlorothiazide (HCT) or torasemide (TOR).

METHODS: Patients with T2DM ($N = 22$ treated) were randomized to receive empagliflozin 25 mg qd for 5 days and either HCT 25 mg qd for 4 days followed by HCT with empagliflozin for 5 days or TOR 5 mg qd for 4 days followed by TOR with empagliflozin for 5 days.

RESULTS: Based on standard criteria, co-administration of empagliflozin with HCT or TOR had no effect on $AUC_{\tau,ss}$ or $C_{max,ss}$ of empagliflozin, HCT or TOR (Table). Terminal elimination half-life and renal clearance of empagliflozin, HCT or TOR were similar when empagliflozin was co-administered with HCT or TOR (Table). Empagliflozin was well tolerated; no serious adverse events were reported.

Geometric mean ratio % (90% CI) of combination treatment vs monotherapy				
	Empagliflozin		HCT	TOR
	Empagliflozin alone	Empagliflozin + HCT / + TOR	HCT alone	TOR alone
$AUC_{\tau,ss}$	107.1 (97.1, 118.1)	107.8 (100.1, 116.1)	96.3 (89.1, 104.0)	101.4 (99.1, 103.9)
$C_{max,ss}$	102.8 (88.6, 119.3)	107.5 (97.9, 118.0)	101.8 (88.6, 116.9)	104.4 (93.8, 116.3)
Pharmacokinetic parameters, mean (% CV)				
	Empagliflozin		HCT	TOR
	Empagliflozin alone	Empagliflozin + HCT / + TOR	HCT alone	TOR alone
$t_{1/2,ss}$ (h)	15.3 (47.4)	14.8 (18.1)	10.6 (27.0)	4.8 (17.1)
$CL_{R,ss}$ (mL/min)	36.7 (31.4)	30.2 (36.0)	291 (24.7)	14.2 (25.7)

CONCLUSION: Based on pharmacokinetic assessment, no drug–drug interaction was observed between empagliflozin and HCT or TOR indicating that no dose adjustments are necessary for co-administration of empagliflozin with HCT or TOR. These data were accepted for publication by ADA 2012. Funded by Boehringer Ingelheim.

PCS-33-7

Lack of Pharmacokinetic Interaction Between the Sodium Glucose Cotransporter-2 (SGLT-2) Inhibitor Empagliflozin and Simvastatin in Healthy Volunteers

Sreeraj Macha¹, Benjamin Lang², Sabine Pinnett², Hans J. Woerle³ and Uli C. Broedl³
¹Boehringer Ingelheim Pharmaceuticals, Inc., USA; ²Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; ³Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany

OBJECTIVE: Investigate drug–drug interactions between empagliflozin and simvastatin following co-administration.

METHODS: Eighteen healthy volunteers [median (range) age 36.5 (20–50) years] received three single-dose treatments in a randomized order, with at least 7 days washout period between treatments: 25 mg empagliflozin, 40 mg simvastatin, and 25 mg empagliflozin with 40 mg simvastatin.

RESULTS: Relative bioavailability results are shown (Table). Based on standard criteria, co-administration of empagliflozin with simvastatin had no effect on exposure of empagliflozin or simvastatin acid (active metabolite of simvastatin). Minor deviations in simvastatin exposure were not considered clinically relevant. Six subjects (33.3%) reported AEs with empagliflozin, 4 (23.5%) with simvastatin, and 5 (27.8%) with combined treatment. Mild headache was the most frequent AE, reported by four subjects on empagliflozin, two on simvastatin, and two on combined treatment. No serious AEs or investigator-defined drug-related AEs occurred.

Parameter	Adjusted geometric mean ratio (%)	90% confidence interval
Empagliflozin + simvastatin / empagliflozin		
Empagliflozin		
$AUC_{0-\infty}$	102.05	(98.90, 105.29)
C_{max}	109.49	(96.91, 123.69)
Simvastatin + empagliflozin / Simvastatin		
Simvastatin		
$AUC_{0-\infty}$	101.26	(80.06, 128.07)
C_{max}	97.18	(76.30, 123.77)
Simvastatin acid (active metabolite)		
$AUC_{0-\infty}$	104.87	(90.09, 122.07)
C_{max}	97.27	(84.90, 111.44)

CONCLUSIONS: No clinically relevant drug–drug interaction was observed between empagliflozin and simvastatin. No dose adjustments for either drug are necessary when co-administered. Data were presented at ACCP 2012. Funded by Boehringer Ingelheim.

PCS-33-8

Drug-drug Interactions of Luseogliflozin (TS-071) with Other Oral Hypoglycemic Agents in Healthy Japanese Subjects

Takashi Sasaki¹, Yutaka Seino², Yoshishige Samukawa³, Soichi Sakai³ and Takashi Watanabe³

¹Diabetes and Endocrinology, Jikei University School of Medicine, Japan; ²Kansai Electric Power Hospital, Osaka, Japan; ³Taisho Pharmaceutical Co., Ltd., Tokyo, Japan

OBJECTIVE: Luseogliflozin (LUSEO) is a selective SGLT2 inhibitor. The aim of these studies was to assess the safety, pharmacokinetic (PK), and pharmacodynamic (PD) interactions between LUSEO and Glimepiride, Metformin, Sitagliptin, Pioglitazone, Voglibose in healthy subjects.

METHODS: Five studies were conducted using 12 each healthy hospitalized Japanese adults. Plasma concentration of LUSEO and other oral hypoglycemic agents (OHAs) except for Voglibose and the amount of urinary glucose excretion was measured to evaluate the effect of co-administration. Safety assessments included recording of adverse events, vital signs, ECG and clinical laboratory tests. Assessment of PK interaction was defined as the ratio of geometric means and 90% confidence interval (CI) for combination/monotherapy.

RESULTS: Except for Pioglitazone, PK of OHAs and LUSEO were unaffected by co-administration. After co-administration with Pioglitazone, the C_{max} of LUSEO was slightly higher than the upper statistical bound of the 90% CI, however the AUC of LUSEO was unaffected, indicating no clinically-significant effects of Pioglitazone on the PK of LUSEO. It is unlikely that administration of LUSEO with Pioglitazone would have a clinically-significant effect on the PK of Pioglitazone. LUSEO-induced urinary glucose excretion was unaffected by combination dosing up to 24 h after dosing. Combination dosing was safe and well-tolerated in the short-term studies. An additional study to assess interactions between LUSEO and Miglitol is ongoing.

CONCLUSION: Co-administration of LUSEO and Glimepiride, Metformin, Sitagliptin, Pioglitazone or Voglibose was well tolerated and combination treatments can be administered without need for dosage adjustments.

PC-33-9

Pharmacokinetics, Pharmacodynamics and Safety of Empagliflozin in Japanese Patients with Type 2 Diabetes Mellitus: Results from a 4-week Phase II Study

Akiko Sarashina¹, Shigeto Kanada², Kazuki Koiwai³, Atsushi Taniguchi³, Leo Seman⁴ and Hans J. Woerle⁵

¹Nippon Boehringer Ingelheim Co., Ltd., Japan; ²Heishinkai Medical Group Incorporated, OCRM Clinic, Osaka, Japan; ³Nippon Boehringer Ingelheim Co., Ltd., Tokyo, Japan; ⁴Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; ⁵Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany

OBJECTIVES: To evaluate pharmacokinetics, pharmacodynamics and safety of the sodium glucose cotransporter-2 inhibitor empagliflozin in Japanese patients with type 2 diabetes mellitus (T2DM).

METHODS: Patients (N = 100) were randomized to empagliflozin 1, 5, 10, 25 mg or placebo (once daily for 28 days). Pharmacokinetic (day 1 and 28) and pharmacodynamic parameters (urinary glucose excretion [UGE], fasting plasma glucose [FPG], 8-point glucose profile) were investigated.

RESULTS: Pharmacokinetic and pharmacodynamic data are presented (Table). Area under plasma concentration-time curve from time 0 to τ at steady state ($AUC_{\tau,ss}$) and maximum plasma concentration at steady state ($C_{max,ss}$) increased dose-proportionally. UGE increased, and FPG and 8-point glucose profiles decreased with increasing empagliflozin dose. Adverse events (all mild or moderate) were reported for 23/79 patients on empagliflozin and 2/21 on placebo; frequency was not dose-related.

	Placebo (n = 20)	Empagliflozin			
		1 mg (n = 19)	5 mg (n = 20)	10 mg (n = 18)	25 mg (n = 17)
Pharmacokinetic parameter, mean (% CV) (day 28)					
$AUC_{\tau,ss}$, nmol-h/L	–	281 (16.4)	1280 (14.6)	2610 (16.2)	6460 (21.1)
$C_{max,ss}$, nmol/L	–	43.3 (28.1)	190 (27.3)	407 (25.8)	869 (30.2)
$t_{max,ss}$, h [†]	–	1.50 (0.967–2.50)	1.50 (0.750–3.00)	1.50 (0.967–4.00)	1.50 (0.967–6.00)
$t_{1/2,ss}$, h	–	13.3 (41.1)	13.2 (45.3)	14.3 (38.3)	18.0 (40.7)
Pharmacodynamic parameter, adjusted mean (SE) change from baseline					
UGE, g (day 27) [§]	–2.10 (4.59)	40.8 (4.92)**	77.1 (4.60)**	80.9 (5.03)**	93.0 (5.14)**
FPG, mg/dL (day 28)	–15.4 (2.86)	–28.1 (2.97)*	–35.4 (2.87)**	–41.6 (3.01)**	–42.7 (3.09)**
8-point glucose profile, mg/dL (day 27)	–17.4 (3.93)	–35.3 (4.12)*	–39.9 (3.90)**	–43.6 (4.11)**	–45.7 (4.19)**

[†]median (range); [§]n = 18, 17 and 16 for empagliflozin 1 mg, 10 mg and 25 mg, respectively. *p < 0.01, **p < 0.0001 versus placebo

CONCLUSIONS: In Japanese patients with T2DM, empagliflozin at doses up to 25 mg once daily for 4 weeks resulted in a dose-proportional increase in empagliflozin exposure, improved glycemic control, and was well tolerated. Funded by Boehringer Ingelheim.

PC-34-1

Analysis on Hypotensive Drugs for Senior Hypertension Complicated with Type 2 Diabetes Mellitus

Shuping Li

Huazhong Hospital, China

OBJECTIVE: To analyze types of antihypertensives and its treatment methods, commonly used for aged patients of essential hypertension with type 2 diabetes mellitus, so as to provide the basis for effective treatment.

METHODS: The use of antihypertensive drugs and its statistic analysis were contrasted under two groups –diabetic group (59 patients caused by EH with type 2 diabetes mellitus) and control group (60 patients by EH only), all the patients were over 80 years old, hospitalised from January 1 to March 3 of 2012.

RESULTS: In diabetic group, the users of calcium channel-blocker (CCB) including 39 patients, accounting to 66.1%, in turn, users of angiotensin II receptor antagonist (ARB): 28/47.46%, users of β –receptor blocker and diuretics: 24/40.68%, users of angiotensin converting enzyme inhibitor

(ACEI):15/25.42%, and users of α -receptor blocker: 3/5.08%. Above cases provided statistically with no significant difference when comparing to the control group. 79.66% of the patients in diabetic group were treated with two kinds of antihypertensives, principally by using CCB + ARB. 45.76% of the patients received three-drug-combined treatment, of which percentage is much higher than in control group. Two-drug-combined treatment was relying mainly on CCB + ARB. Three-drug-combined treatment was relying mainly on CCB + ARB + β -receptor blocker (or diuretics).

CONCLUSIONS: For aged patients of essential hypertension with diabetes mellitus, most of them needed treating with combined antihypertensives, as CCB + ARB the major choice. More types of the said drugs were applied in observation group than in control group.

PC-34-2

Low Variability of Home Blood Pressure in Type 2 Diabetic Patients Treated with Calcium Channel Blockers

Emi Ushigome, Michiaki Fukui, Takafumi Senmaru, Naoko Nakanishi, Yusuke Mineoka, Hiroshi Okada, Shinobu Matsumoto, Hiroya Iwase, Kanae Kobayashi, Takuya Fukuda, Kazuteru Mitsuhashi, Saori Majima, Mai Asano, Masahiro Yamazaki, Goji Hasegawa and Naoto Nakamura

Department of Endocrinology and Metabolism, Kyoto Prefectural University of Medicine, Graduate School of Medical Science, Japan

OBJECTIVE: Recent studies have revealed the association between blood pressure variability and cardiovascular events. Furthermore, recent several meta-analyses of randomized controlled trials of antihypertensive drugs have shown that there are drug-class differences on blood pressure variability. This study was designed to investigate the relationship between antihypertensive-drug class and home blood pressure variability in patients with type 2 diabetes.

METHODS: We compared home blood pressure variability among patients treated with calcium channel blockers (n = 44), with angiotensin II receptor blockers and/or angiotensin-converting enzyme inhibitors (n = 159), and with calcium channel blockers combined with angiotensin II receptor blockers and/or angiotensin-converting enzyme inhibitors (n = 183). Next, we analyzed the effect of calcium channel blockers on home blood pressure variability in the morning using multiple linear regression analysis.

RESULTS: Coefficient variation of morning systolic blood pressure in patients treated with calcium channel blockers was significantly lower than that in patients treated with angiotensin II receptor blockers and/or angiotensin-converting enzyme inhibitors (P = 0.036). Multivariate linear regression analyses indicated that treatment with calcium channel blockers was significantly correlated with coefficient variation of morning systolic blood pressure after adjusting for other potential co-factors (β = –0.264, P = 0.001).

CONCLUSION: This study implies a possibility for validity on selecting calcium channel blockers in hypertensive patients with type 2 diabetes to reduce home blood pressure variability.

PC-34-3

High Sodium Intake is Associated with Masked Hypertension in Japanese Patients with Type 2 Diabetes and Treated Hypertension

Keiko Nakao, Takashi Uzu, Shin-ichi Araki, Satoshi Ugi, Hiromichi Kawai, Keiji Isshiki and Hiroshi Maegawa

Department of Medicine, Shiga University of Medical Science, Japan

BACKGROUND: Knowledge regarding the association between dietary sodium intake and the incidence of masked hypertension is limited.

METHODS: A total of 193 Japanese type 2 diabetic outpatients who had been treated with antihypertensive agents and with office blood pressures <140/90 mmHg were recruited. Masked hypertension was defined as having office blood pressure <140/90 mmHg and 24-h mean ambulatory blood pressure >130/80 mmHg. The dietary sodium intake was estimated by measuring the 24-h urinary sodium excretion.

RESULTS: Masked hypertension was found in 128 (66.3%) patients. An age and sex adjusted univariate logistic regression analysis showed that urinary albumin excretion, renin-angiotensin system inhibitor use, office systolic blood pressure, and amount of dietary sodium intake were significantly associated with masked hypertension. A multivariate logistic regression analysis also identified an older age, renin-angiotensin system inhibitor use, an office elevated SBP, and high dietary sodium intake to be independently associated with masked hypertension. Compared with those who consumed a low salt diet (sodium < 120 mEq/day), the odds ratio for the risk of exhibiting

masked hypertension in patients who consumed a medium salt diet (sodium 120 to <200 mEq/day) or a high salt diet (sodium > 200 mEq/day) were 5.3 ($P < 0.001$) and 12.6 ($P < 0.001$), respectively.

CONCLUSIONS: Masked hypertension is a common feature in type 2 diabetic patients being treated hypertension. The observed association with sodium intake raised the hypothesis that excessive sodium intake may play a part in the genesis of masked hypertension in these patients.

PCS-34-4

The Long-Term Effect of Statin on Glycemic Control in Patients with Type 2 Diabetes

Shih-Ting Tseng¹ and Su-Tze Chou²

¹Department of Food and Nutrition/Department of Endocrinology and Metabolism, Providence University/Kuang Tien General Hospital, Taiwan; ²Department of Food and Nutrition, Providence University, Taiwan

OBJECTIVE: In recent years, there have been evidences revealed that statin may be related to new onset of diabetes. However, there were very few studies focused on the effect of statin on glycemic control in patients with type 2 diabetes. This study aimed to clarify the issue.

METHOD: A retrospective study was designed. The patients must receive stable dose of antidiabetes agents for at least 3 months before the statin was prescribed. Total 39 type 2 diabetes patients (mean age = 58 ± 12.01 years; female = 26, male = 13) who received statin therapy at the outpatient department for 6 months–2 years (mean 381.62 ± 61.33 days) were collected. The doses of oral antidiabetes agents or insulin were reviewed by chart record. The biochemical profiles before and after the statin use were also assessed.

RESULTS: The fasting plasma glucose (170 ± 57.57 vs 168 ± 62.07 mg/dL, $P = 0.839$) and HbA1c (8.45 ± 1.64 vs $8.14 \pm 1.55\%$, $P = 0.198$) did not change after statin use although the cholesterol (217.86 ± 27.51 vs 166.19 ± 29.79 mg/dL, $P < 0.0001$) and LDL (low-density lipoprotein, 143.86 ± 23.18 vs 93.60 ± 23.85 mg/dL, $P < 0.0001$) levels decreased significantly. Neither insulin nor oral antidiabetic agents had difference between the doses before and after the statin use. Furthermore, in the group treated with atorvastatin ($N = 30$), the results were identical to the analysis of whole statin group.

CONCLUSION: The statin use in type 2 diabetes did not alter the glycemic control.

PCS-34-5

High Prevalence of Primary Aldosteronism Among Type 2 Diabetes

Kana Miyake, Yoko Matsuzawa, Eriko Nara, Ai Hayasaka, Yuichi Takashi, Mayu Kyohara, Takumi Kitamoto, Junya Takemoto, Jun Saito, Masao Omura and Tetsuo Nishikawa

Endocrinology and Diabetes Center, Yokohama Rosai Hospital, Japan

OBJECTIVE: Primary aldosteronism (PA) is caused by the autonomous secretion of aldosterone, easily inducing hypertension and cardiovascular events. Moreover, prevalence of PA was reported to be 14% among type2 diabetes with resistant hypertension. Then, we tried to screen diabetic inpatients for detecting probable PA by cutoff value of aldosterone-renin ratio (ARR > 200) which was recommended by Japan Endocrine Society's guideline of PA.

METHODS: We enrolled 231 type 2 diabetic patients who had been admitted to our hospital without ketoacidosis nor renal failure (Cr < 1.5). We obtained blood samples at the 2nd day after admission after 30 min-resting on recumbent position for determining plasma aldosterone concentration (A:PAC) and plasma renin activity (R:PRA). We could diagnose probable PA after screening by ARR > 200.

RESULTS: Hypertension (>140/90) was observed in 140 cases (61%). The cases showing ARR > 200 were observed in 12.5% and 13.2% of the patients with and without hypertension, respectively. K level was significantly different between ARR > 200 and ARR < 200 groups, while there were no differences in age, BMI, HbA1c, blood pressure, serum Cr level and urinary albumin excretion.

CONCLUSION: The present data clearly showed high prevalence of positive screening test of ARR > 200 among diabetic patients.

Diabetic cardiovascular complications including CVD, stroke and CKD are significantly related to LDL-cholesterol, triglycerides, blood pressure and HbA1c. In addition, it is recently suggested that aldosterone plays a crucial role on developing cardiovascular disorders with and without hypertension. Thus, we should precisely screen and definitely diagnose PA among diabetic patients because of high incidences of positive ARR among diabetic patients.

PCS-34-6

Analysis of Association Between the -759C/T Polymorphism of the 5-HT2C Receptor Gene and Type 2 Diabetes and Obesity in Chinese Male and Female Population

Jing Liu¹, Hong-xia Gao², Ju-xiang Liu³ and Rui-lan Niu²

¹Department of Endocrinology in Gan Su Province Hospital, Department of endocrinology in Gan Su Province Hospital, China; ²The First Clinical College of Lanzhou University, China; ³Department of Endocrinology, Gansu Provincial People's Hospital, China

OBJECTIVES: Serotonin (5-hydroxytryptamine, 5-HT) was one of the most important neurotransmitters that regulate energy. Both pharmacological and genetic evidence implicate the serotonin 2C (5-HT2C) receptor as a critical receptor mediator of serotonin's effects on feeding behavior and glucose homeostasis. The aim of this study was determine the possible association of the -759C/T polymorphism of the 5-HT2C receptor gene with type 2 diabetes and obesity in Chinese population. Methods We genotyped -759C/T polymorphism in a case-control study from Chinese, including 719 patients with T2DM and 780 control subjects, using polymerase chain reaction-ligase detection reaction (PCR-LDR) assay.

RESULTS: The frequency of genotypes and alleles of -759C/T polymorphism showed no significant difference between T2DM patients and control subjects ($P = 0.807$ and $P = 0.813$). Further analysis in male and female also showed no significant difference in genotype and allele frequencies between two groups ($P > 0.05$). In consistent, the frequency of genotypes and alleles of -759C/T polymorphism were similar in obesity and control subjects.

CONCLUSIONS: Our data indicated that the -759C/T polymorphism of the 5-HT2C receptor gene was not associated with type 2 diabetes and obesity in Chinese population. Moreover, we also found that the -759C/T polymorphism was not related to insulin resistance and blood lipid in a Chinese people.

KEYWORDS: Type 2 diabetes, 5-HT2C receptor, Serotonin, Polymorphism, Obesity

PCS-34-7

Serum EPA/AA Ratio is Related to Insulin Resistance through the Influence of Systemic Inflammation: Findings from the Hawaii-Los Angels-Hiroshima Study

Mitsunobu Kubota, Yuko Monzen, Maiko Mouri, Yasuyuki Mitama, Mami Shiwa, Tsuguka Shiwa, Masatoshi Hirano, Shusaku Maeda, Masayasu Yoneda, Tomokazu Awaya and Shuhei Nakanishi

Department of Molecular and Internal Medicine, Graduate School of Biomedical Sciences, Hiroshima University, Japan

OBJECTIVES: Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), abundantly included in fish oil and categorized as ω -3 polyunsaturated fatty acids (PUFAs), are known to have anti-inflammatory effect. In the present study, we hypothesize that serum EPA/AA of Japanese-Americans is lower than that of native Japanese and this aggravates insulin resistance and obesity by initiating systemic inflammation. Consequently, this may influence the onset of diabetes or metabolic syndrome.

METHODS: 659 Japanese-Americans (284 men, 375 women, mean age 61.9 ± 15.4) living in Hawaii and Los-Angeles were enrolled. The participants were determined their glucose tolerance status by 75 g OGTT. Serum fatty acids were measured by gas liquid chromatography.

RESULTS: Serum EPA/AA ratio was 0.18 (0.11–0.30) in the NGT group, 0.19 (0.12–0.35) in the IGT group and 0.19 (0.11–0.37) in the DM group respectively. We found no significant difference among the three groups ($P = 0.829$). In addition, any significant relationships between serum EPA/AA and serum glucose levels were not identified. In contrast, we found significant inverse relationships between serum EPA/AA ratio and HOMA-R ($\beta = -0.081$, $P = 0.033$), BMI ($\beta = -0.081$, $P = 0.037$), waist circumference ($\beta = -0.136$, $P = 0.001$) and hsCRP ($\beta = -0.125$, $P = 0.001$) respectively. The relationship between serum EPA/AA ratio and HOMA-R became nonsignificant after adjusting for hsCRP. On the other hand, the relationship between serum EPA/AA ratio and hsCRP remained significant even after adjusting for HOMA-R ($\beta = -0.110$, $P = 0.008$).

CONCLUSION: These results suggest that Japanese-Americans consume smaller amount of fish compared with native Japanese. Serum EPA/AA ratio may be related to insulin resistance through the influence of systemic inflammation.

PCS-34-8

Lipid-Lowering and Anti-inflammatory Effects of Individualizing Starting Doses of Atorvastatin according to Baseline LDL-Cholesterol Levels in Korean Patients with Type 2 Diabetes

Sung Rae Kim¹, Jong Hwa Kim², Ji Oh Mok³, Chang Beom Lee⁴ and Seung Joon Oh⁵

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Bucheon St Mary Hospital, The Catholic University of Korea, Korea; ²Division of Endocrinology and Metabolism, Sejong General Hospital, Korea; ³Division of Endocrinology and Metabolism, Soonchunhyang University Bucheon Hospital, Korea; ⁴Division of Endocrinology and Metabolism, Hanyang University Guri Hospital, Korea; ⁵Division of Endocrinology and Metabolism, Kyunghee University Medical Center, Korea

OBJECTIVE: To examine the effect of individualized starting doses of atorvastatin on achieving target low-density lipoprotein (LDL) cholesterol, atherogenic lipid profiles and surrogate markers of chronic inflammation in patients with type 2 diabetes.

DESIGNS: This was an 8-week, multicenter, prospective, open-label, single-step titration trial that enrolled 440 patients with type 2 diabetes to assess the safety and efficacy of patient-tailored atorvastatin therapies (10, 20 and 40 mg) based on a patient's baseline LDL cholesterol levels.

RESULTS: Overall, 91% of the patients achieved their LDL cholesterol target (100 mg/dL) at week 8 (94%, 93% and 81% in for doses of 10, 20 and 40 mg, respectively). Among those patients who achieved their target goal, over 92% achieved their LDL cholesterol target with the initial dose. There were significant reductions in total cholesterol (TC), triglycerides, non-high-density lipoprotein (HDL) cholesterol, the TC to HDL cholesterol ratio and small, dense LDL cholesterol compared to the baseline at week 8 for all of the doses. In addition, high-sensitivity CRP (hsCRP) levels were significantly decreased in those patients with baseline hsCRP levels over 3 mg/L, whereas adiponectin levels tended to increase after 4 weeks for all of the doses. Atorvastatin was well tolerated at all of the doses throughout the study period.

CONCLUSIONS: The administration of individualized starting doses of atorvastatin according to baseline LDL cholesterol levels was effective achieving target LDL cholesterol levels and in ameliorating atherogenic lipid profiles and low-grade inflammation in patients with type 2 diabetes.

PCS-35-1

Interaction of Advanced Maternal Age and High Body Mass Index on Risk of Gestational Diabetes Mellitus in Taiwanese Women

Mei-Chun Lu¹, Yuan-Hong Yan², Cheng-Wei Yu³ and Panchalli Wang¹

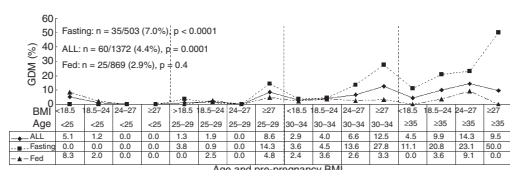
¹Department of Obstetrics and Gynecology, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chia-Yi City, Taiwan; ²Department of Medical Research, Chia-Yi Christian Hospital, Chia-Yi City, Taiwan; ³Department of Nutrition, Chia-Yi Christian Hospital, Chia-Yi City, Taiwan

In our previous study recommended that before receiving glucose challenge test (GCT) fasting at least 2 h would lead the GDM screening test more accurate. We further determine if GDM were associated with the interaction of age and BMI in Taiwanese women.

A 8-month prospective study was performed on 1372 pregnancies at one teaching hospital. Subjects followed the two-step approach for screening of GDM by NDDG criteria. The cut-off point of GCT was 140 mg/dL. Subjects were stratified into two groups by the time of last food ingestion: <2 and >2 h while receiving GCT, presented as fed and fasting groups.

There were significant associations between the screening results and the interaction of age and BMI in all subjects ($P = 0.0001$) and in fasting group ($P < 0.0001$), but not in fed group ($P = 0.4$).

The results suggest that advanced maternal age and maternal weight excess were associated with GDM. However, the trend of GDM in fed group was not similar with fasting group. It deserves further study.



PCS-35-2

Insulin Resistance in Thai Gestational Diabetes Mellitus

Chadsuphar Sirirachta, Veerasak Sarinnapakorn, Sathit Niramitmahapanya, Navaporn Napativamnuay, Thongkum Suthornthepavarakul and Chaicharn Deerochanawong
Department of Endocrinology & Metabolism, Rajavithi Hospital, Medical College of Rangsit University, Thailand

OBJECTIVE: This study was conducted to determine the insulin resistance in Thai gestational diabetes (GDM) compared to non-GDM.

METHODS: Cross-sectional study in women who attended antenatal care unit of Rajavithi hospital in Bangkok. 75 g OGTT was done for diagnosis GDM by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. Calculated HOMA-IR and HOMA- β used for insulin index.

RESULTS: 155 pregnant women, 49 patients (31.6%) with GDM and 106 patients (68.4%) of non-GDM. In GDM group; pre-pregnancy body weight, pre-pregnancy body mass index (BMI), systolic blood pressure and triglyceride are higher than non-GDM group ($P = 0.011$, 0.006, 0.029 and 0.002 respectively) but HDL-cholesterol is lower in GDM group ($P = 0.036$). When insulin index (HOMA-IR and HOMA- β) was compare highest quintile of BMI (Q4) with lower quintile of BMI (Q1,Q2 and Q3), we found more pre-pregnancy BMI had more HOMA-IR status across the quintiles by statistic significant ($P = 0.017$). However, did not seen statistic significant in HOMA- β status. ROC curve analysis was found the best cut of point of HOMA-IR is 1.22 ($P = 0.045$, sensitivity = 70.0%, specificity = 49.6%, AUC = 0.600, 95%CI = 0.509, 0.691).

CONCLUSIONS: In Thai GDM patients have more phenotype of metabolic syndrome prior pregnancy than non-GDM. Higher pre-pregnancy BMI had more insulin resistance status (HOMA-IR) in Thai GDM.

PCS-35-3

Fasting 2 h for 50-g Glucose Challenge Test Improve the Accuracy of the Screening of Gestational Diabetes Mellitus

Panchalli Wang¹, Yuan-Hong Yan², Cheng-Wei Yu³ and Mei-Chun Lu¹

¹Department of Obstetrics and Gynecology, Chia-Yi Christian Hospital, Taiwan; ²Department of Medical Research, Chia-Yi Christian Hospital, Taiwan; ³Department of Nutrition, Chia-Yi Christian Hospital, Taiwan

OBJECTIVE: To investigate the influence of prior food ingestion on the accuracy of 50-g glucose challenge test (GCT) result at 24–28 weeks of gestation.

METHODS: A 8-month prospective study of 1374 pregnant women who were enrolled at one teaching hospital in Taiwan. All subjects followed the two-step approach for screening of gestational diabetes mellitus (GDM); GCT was positive if the 1-h plasma glucose level was >140 mg/dL. GDM was diagnosed by a 100-g glucose tolerance test using the National Diabetes Data Group (NDDG) criteria. We designed a questionnaire to investigate the characteristics and the diet situation including the time and the contents of prior food ingestion while receiving GCT at 24–28 weeks of gestation. A dietitian calculated the total calories of the food. Study subjects were stratified into three groups: fasting interval <1, 1–2, and >2 h.

RESULTS: The characteristics of study subjects among the fasting interval groups had no significant difference. There were significant association between the fasting interval and the accuracy of the two-step approach ($P = 0.01$). We found 2.6%, 3.1%, and 6.9% of GDM in subjects with fasting interval <1, 1–2, and >2 h. IGT did not show similar trend. Furthermore, in the GCT positive subjects, predictive positive rate (PPR) showed significantly increased in subjects whose fasting interval <1 and 1–2 h (12.8% and 14.9%) compared to >2 h (27.1%) ($P = 0.02$).

CONCLUSIONS: Fasting at least 2 h before undergoing 50-g GCT showed high PPR. Thus, modifying the two-step approach would lead to the screening test more accurate for GDM.

PCS-35-4

Vitamin D Insufficiency Among Women with Former Gestational Diabetes

Toh Peng Yeow¹ and Shueh Lin Lim²

¹Department of Internal Medicine, Penang Medical College, Malaysia; ²Department of Endocrinology, Penang General Hospital, Penang, Malaysia

BACKGROUND: Gestational Diabetes Mellitus (GDM) is related to insulin resistance and beta-cell dysfunction. Vitamin D insufficiency has also been

shown to disturb glucose metabolism. Women with former GDM (fGDM) who has vitamin D (VitD) insufficiency may be at further heightened risk.

METHOD: Forty-two women with fGDM underwent 75 g Oral-glucose-tolerance-test and measurement of serum 25(OH) VitaminD as part of an RCT evaluating VitD replacement in improving glucose metabolism in fGDM (NMRR-10-679-6202).

RESULTS: The women were assessed on average of 689 days post-partum. The overall mean VitD is 39.9 ± 2.54 (Mean $\pm$ SEM in nmol/L). 4/42 (9.5%) has Vit D < 20 nmol/L (Mean $\pm$ SEM 15.4 ± 2.0). 32/42 (76%) has vitamin D < 50 nmol/L (Mean $\pm$ SEM 33.08 ± 10.75). 13/42 (31%) women have developed glucose intolerance by time of screening (IFG = 1, IGT = 6, DM = 6). There is no significant difference between VitD level in group with normal OGTT vs group with IFG/IGT/DM (41.4 ± 5.04 vs 39.2 ± 2.94). There is no significance difference between HbA1c, fasting and 2 h glucose during OGTT in the VitD sufficient vs insufficient group : mean HbA1c (%) 5.8 ± 0.28 vs 5.7 ± 0.18 ; mean fasting glucose (mmol/L) 4.22 ± 0.387 vs 4.32 ± 0.234 ; mean 2 h glucose 7.22 ± 0.978 vs 7.56 ± 0.636 ; ($P > 0.05$ in all).

CONCLUSION: Vitamin D insufficiency is prevalent among women with fGDM even in a tropical country like Malaysia. One third of these women has developed IGT or DM in <2 years after GDM delivery. Result of our RCT to evaluate effect of VitD replacement in slowing down this progression is keenly awaited.

PCS-35-5

Pap Smear Results in Postpartum Women with Gestational Diabetes Mellitus: A Pilot Study in Taiwan

Hsiao Ching Lin and Chao-po Lin

Obstetrics and Gynecology, Ditmanson Medical Foundation, Chia-Yi Christian Hospital, Taiwan

OBJECTIVE: Pap test is always done in postpartum surveillance in Taiwan. We tried to assess it in women with gestational diabetes (GDM) and diabetes mellitus (DM) within postpartum 2 months.

MATERIALS: Pap test data were collected from 2008 to 2010. Three groups were analyzed: GDM, DM, and normal.

METHODS: The individual rate of every group was calculated as 'positive', 'inflammation', 'normal', 'difficult to read', and 'others'. The 'positive' smear result consists of ASC-H, AGC-FN, LSIL, HSIL, AIS, and CANCER.

RESULTS: The total number of Pap test was 3405. Percentages of GDM, DM, and normal group were 2.9%, 0.5%, and 96.7%, respectively. The Pap result calculation in individual group was listed as Table 1 & 2. No significant difference in every group was noted.

Table1 : The first Pap smear results within postpartum two months.

Cytodiagnosis	Group			Total	p
	GDM	DM	Normal		
Total	97	16	3292	3405	
Positive	0 (0%)	0 (0%)	19 (0.61%)	19	1.00
Inflammation	16 (16.49%)	3 (18.75%)	420 (12.76%)	439	0.31
Normal	71 (80.7%)	13 (81.3%)	2650 (9.52%)	2734	0.42
Others	1 (1.1%)	0 (0%)	32 (1%)	33	0.66
Difficult to read	9 (9.3%)	0 (0%)	171 (5.2%)	180	0.17

※Other=ASC-US+Atypical glandular cells

Positive pap=ASC-H+AGC-FN+LSIL+HSIL+AIS+CANCER

GDM=Gestational Diabetes Mellitus

DM=Gestational Diabetes

Table2 : The bacterial infection situation of Pap smear inflammation within postpartum two months.

Cytodiagnosis	Group			Total	p
	GDM	DM	Normal		
Yes	0 (0%)	0 (0%)	40 (9.52%)	40	0.54
No	16 (100%)	3 (100%)	380 (90.48%)	399	

CONCLUSIONS: This is the first study of Pap test in postpartum women with GDM and DM. Diabetic women are inclined to get vaginitis, which may influence Pap test. However, we did not find any significant difference among these women.

PCS-35-6

Characteristics of Women with Gestational Diabetes Who Need Insulin Therapy

Kaori Tachibana, Kenichi Sakurai, Hidetaka Yokoh, Kou Ishikawa and Koutarou Yokote
Department of Diabetes Metabolism and Endocrinology, Chiba University Hospital, Japan

OBJECTIVE: The prevalence of gestational diabetes (GDM) is increasing after use of the new International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. Management of GDM is an important subject, especially in women who require insulin therapy. The aim of this study is to assess characteristics that are associated with necessity of insulin therapy in women with GDM.

METHODS: A retrospective review of clinical characteristics of women with GDM who attended Chiba University Hospital from July 2010 was conducted. We documented each woman's age, BMI, family history of diabetes, OGTT result, HbA1c and gestational week when their GDM was diagnosed. The outcomes of the woman's pregnancy were also reported.

RESULTS: Of the 57 women included in this study, 73.3% required insulin therapy. Age, BMI, HbA1c, and gestational week of GDM diagnosis were not significantly different between nutritional therapy group and insulin therapy group. In insulin therapy group, 13 cases (31.0%) were one-point-positive according to the new IADPSG criteria. The mean 1-h glucose level on OGTT in the insulin therapy group was significantly higher than that in the nutritional therapy group, but there were no differences in the fasting and 2-h glucose levels. Neonatal birth weight, morbidity and Apgar scores did not differ significantly between two groups. Insulin therapy group included two cases of hypertension in pregnancy and four cases that needed emergent caesarean delivery.

CONCLUSION: One hour glucose result on OGTT is associated with the need for subsequent insulin therapy in women with GDM.

PCS-35-7

Advanced Cervical Cancer in a Sexually Inexperienced Diabetic Woman – A Case Report

Chao-po Lin

Chia-Yi Christian Hospital, Taiwan

BACKGROUND: Cervical cancer is largely considered to be a sexually transmitted disease because human papillomavirus (HPV) infection appears to be a necessary factor in the development of almost all cases (>90%). Therefore, cervical cancer in sexually inexperienced woman was reported sporadically and it may be spread via nonsexual means. Nevertheless, no case was reported as disastrous as we reported here.

CASE: This 34 year-old woman has poor controlled type 2 diabetes mellitus for 4 years. She declared no sexual experience. She complained lower abdominal pain and one 5 cm adnexal cyst was noted. Two weeks later, dyspnea happened to her. Metastatic lung cancer was found. The CT scan showed enlarged uterus to suspect corpus cancer, which was proved as squamous cell carcinoma after uterine curettage. The uterine cervix appeared otherwise normal then. The disease progressed in spite of chemotherapy. The secondary examination under anesthesia showed cervical neogrowth invading upper vagina to make the diagnosis of cervical cancer. Unfortunately, she died of collapsed lung due to metastatic mediastinum tumor compression.

DISCUSSION: Special human physical character may play a role inclined to cancer development. The youngest virginity with cervical cancer was reported as 15 years old. That girl might bear special inherent characters. Here, this 34 year-old diabetic woman may bear another developed character related to diabetes mellitus. A diabetic woman with cancer may proceed unusually.

PCS-36-1

Association of Thyroid Stimulating Hormone (TSH) and Free Thyroxine (fT4) Levels with the Severity of Coronary Artery Disease in Type 2 Diabetes

Eun Ju Lee, Mi-kyung Kim, Na Han, Seung-Man Kim, Tae-nyun Kim, Tae-kyun Kim, Min-jung Kwon, Sun-hee Lee, Byoung-doo Rhee and Jeong-hyun Park
Department of Internal Medicine, College of Medicine, Inje University, Korea

AIM: Recent several studies reported that high normal range of TSH and fT4 levels have also effect on coronary atherosclerosis and correlated to severity of CAD even euthyroid state, but there were opposite results. The prediction of degree of involvement of coronary arteries in type 2 diabetes before angiography is still challenging. We try to find out the association of TSH and fT4 levels with angiographic findings of type 2 diabetes.

METHODS: Our subjects were type 2 diabetes performed coronary angiography. We measured free thyroxine (fT4) and thyroid stimulating hormone (TSH) before angiography. The severity of CAD were divided by the number of significantly involved vessels, as 0, 1, 2 and 3 vessel disease.

RESULTS: Total subjects were 465 and their mean age was 63.3 ± 10.3 years old. 5.7% and 8.0% of patients were hyperthyroidism and hypothyroidism, respectively. The mean fT4 and TSH levels of euthyroid type 2 diabetes were 1.12 ± 0.18 and 1.67 ± 0.97 , respectively. TSH and fT4 levels did not show any significant difference among groups divided by severity of coronary angiography. AUC of TSH was 0.531 ($P = 0.363$) and fT4 was 0.466 ($P = 0.318$) in ROC curve.

CONCLUSIONS: We could not find association of TSH and fT4 levels and severity of CAD in type 2 diabetes with normal thyroid function.

PCS-36-2

The Low EPA/AA may Reflect the CVD Risk in Japanese Patients with Type 2 Diabetes

Megumi Gonai¹, Mai Azuma¹, Ikue Nakadaira¹, Jun Suzuki¹, Chieko Morisawa² and Kumiko Hamano¹

¹Department of Diabetes and Endocrinology, Kanto Rosai Hospital, Japan; ²Department of Endocrinology and Diabetes, Saitama Medical Center, Japan

OBJECTIVE: Recently the ratio of the eicosapentaenoic acid and arachidonic acid (EPA/AA) is widely noticed as the novel marker of atherosclerosis, but few reports are known among patients with diabetes. We conducted the present study to characterize EPA/AA among Japanese type 2 diabetes.

METHODS: EPA/AA was measured in 236 subjects in outpatients settings. Subjects were stratified into four groups due to EPA/AA. Two groups, one with the lowest EPA/AA <0.2 , and the other with the highest EPA/AA >0.6 , were extracted. Patients taking EPA as medicine were excluded. CVD risk was assessed by the brachial-ankle pulse wave velocity (baPWV).

RESULTS: The median EPA/AA was 0.393 ± 0.244 . 88 patients out of 236 (59 male and 29 female, 59.3 ± 14.2 years old) were analyzed. The average EPA/AA and age of the Low group was 0.131 ± 0.047 , 51.0 ± 14.4 years old, the High group was 0.783 ± 0.241 and 68.3 ± 6.4 years old, respectively. The average EPA/AA was correlated weakly with the age in each group (Low: $r = 0.38$, $P = 0.01$, High: $r = 0.45$, $P = 0.002$). Extremely low EPA/AA was seen among young patients. It seemed that patients over 60 years old in the Low group had more comorbidities than those in the High group. The relationship between EPA/AA and baPWV is under investigation.

CONCLUSION: Considering the beneficial effect of EPA on insulin sensitivity or atherosclerosis, it is especially important to improve dietary habits of the young. The relationships between EPA/AA and other CVD risk factors are under investigation.

PCS-36-3

Is Insulin Resistance in the Elderly Type 2 Diabetic Patients Associated with Carotid Atherosclerosis?

Chul Sik Kim¹, J. G. Kang¹, S. J. Lee¹, S. H. Ihm¹ and K. B. Huh²

¹Department of Internal Medicine, Hallym University Sacred Heart Hospital, Korea; ²Huh Diabetes Center and the 21st Century Diabetes and Vascular Research Institute, Seoul, Korea

Currently insulin resistance itself is known to be independently associated with subclinical atherosclerosis. However, it is unclear in the elderly type 2 diabetic patients having been in the stationary insulin resistance state and progressive hyperglycemia. The aim of the study was to investigate whether

insulin resistance would be associated with carotid atherosclerosis in elderly type 2 diabetic patients.

We examined 9531 type 2 diabetic patients over than 65 years of age, consecutively enrolled in Huh Diabetes Center in Seoul, Korea. Finally 985 subjects who had been assessed for both short insulin tolerance test (SITT) and carotid intima media thickness (IMT) were included in the study. Insulin sensitivity was directly assessed by a rate constant for plasma glucose disappearance (Kitt: %/min) using short insulin tolerance test. Both carotid arteries were examined by B-mode ultrasound. Carotid intima media thickness (IMT) was measured at three points of common carotid artery 1 cm proximal to the bifurcation and the mean value of six measurements from right and left carotid arteries were used.

In multiple regression models, insulin sensitivity index (Kitt) was not significantly associated with carotid IMT ($\beta = -0.019$, $P = 0.659$) adjusting for known risk factors such as age, sex, body mass index, smoking, systolic pressure, A1C, HDL and LDL cholesterol. Instead, A1C ($\beta = 0.105$, $P = 0.007$), HDL ($\beta = -0.111$, $P = 0.005$) and LDL cholesterol ($\beta = 0.081$, $P = 0.034$) levels, traditional cardiovascular risk factors, were significantly associated with carotid IMT.

In conclusion, glycemic status and lipid profiles, not insulin resistance state, were independently associated with carotid atherosclerosis in elderly type 2 diabetic patients.

PCS-36-4

Risk Association of Glycemic Variability with Chronic Kidney Disease and Cardiovascular Disease in Type 2 Diabetes: Prospective Analysis of the Hong Kong Diabetes Registry

Wing Yan Lau¹, Luk Andrea On Yan¹, Ronald C. W. Ma², Eric S. H. Lau², Xilin Yang², Linda W. L. Yu¹, Francis C. C. Chow¹, Julianna C. N. Chan² and Wing Yee So¹

¹Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong;

²Department of Medicine, The Chinese University of Hong Kong, Hong Kong

OBJECTIVE: In type 2 diabetes, tight glycemic control lowers the risk of diabetic complications but it remains uncertain whether variability of glycemia influences outcomes. We examined the association of glycated hemoglobin (HbA1c) variability with incident chronic kidney disease (CKD) and cardiovascular disease (CVD) in a cohort of 8439 Chinese patients with type 2 diabetes.

METHODS: Intra-personal mean and standard deviation (SD) of serially measured HbA1c were calculated. SD was further adjusted for HbA1c during follow-up. CKD was defined as estimated glomerular filtration rate <60 mL/min per 1.73 m². CVD was defined as events of ischemic heart disease, heart failure, ischemic stroke or peripheral vascular disease.

RESULTS: Over a median follow-up period of 7.1 years, 19.7% and 10.0% of patients developed CKD and CVD respectively. Patients who progressed to CKD had higher mean HbA1c ($7.8 \pm 1.3\%$ vs $7.4 \pm 1.2\%$, $P < 0.001$) and SD ($1.0 \pm 0.8\%$ vs $0.8 \pm 0.6\%$, $P < 0.001$). Patients who developed CVD had higher mean HbA1c ($7.7 \pm 1.3\%$ vs $7.4 \pm 1.2\%$, $P < 0.001$) and SD ($1.4 \pm 1.1\%$ vs $1.1 \pm 0.8\%$, $P < 0.001$). Using multivariate-adjusted Cox regression analysis, adjusted SD was associated with incident CKD and CVD with corresponding hazard ratios of 1.16 [95% CI 1.11–1.22], $P < 0.0001$ and 1.27 (95% CI 1.15–1.40, $P < 0.001$), independent of mean HbA1c and other confounding variables.

CONCLUSIONS: Long-term glycemic variability expressed by SD of HbA1c predicted development of renal and cardiovascular complications.

PCS-36-5

Diagnostic Accuracy of 64-Slice Multidetector CT Coronary Angiography for the Assessment of Coronary Artery Disease in Korean Patients with Type 2 Diabetes

Junsung Moon¹, Kyu Chang Won¹, Ji Sung Yoon¹, Kyoung A. Chun², In Ho Cho² and Hyoung Woo Lee¹

¹Department of Internal Medicine, Yeungnam University College of Medicine, Korea;

²Department of Nuclear Medicine, Yeungnam University College of Medicine, Korea

OBJECTIVE: Although many studies about the availability of 64-slice multidetector computed tomography (MDCT) has been reported, there were a few researches about Asian such as Korean who is lesser obese compared with Caucasians. The aim of this study was to investigate the diagnostic usefulness of 64-slice MDCT coronary angiography for detecting coronary artery disease (CAD) in Korean patients with type 2 diabetes.

METHODS: We studied 240 symptomatic patients undergoing ICA. Seventy-four patients were type 2 diabetes (M:F = 40:33, 41.8 ± 9.5 years). Results were analyzed for significant coronary stenosis (over 50% luminal narrowing) by segment, artery, and patient.

RESULTS: Of the 4064 coronary segments studied, 4062 segments (99.9%) were assessed quantitatively by both MDCT and ICA and 706 segments were detected as significant lesion in ICA in all patients. In patients with type 2 diabetes, there were 226 significant lesions of 1109 segments in ICA. Sensitivity, specificity, and positive and negative predictive values for presence of significant stenosis of type 2 diabetes were: by segment, 89.4%, 96.4%, 85.8%, and 97.4% respectively; by artery ($n = 222$), 95.1%, 92.9%, 94.4% and 93.8%, respectively; by patients ($n = 74$), 98.4%, 100.0%, 98.4%, and 90.0%, respectively. Between with and without diabetes group, there were no significance in diagnostic accuracy. In our results, sensitivity and specificity of MDCT were not affected by obesity ($>25 \text{ kg/m}^2$) and level of coronary calcium score in both diabetics and non-diabetics.

CONCLUSION: Our results suggest that 64-slice MDCT coronary angiography in patients with T2DM may be useful for detecting CAD and its diagnostic accuracy is similar with non-diabetic patients.

PCS-36-6

T2DM and IGR Risks Among Elderly Patients with Essential Hypertension: A 10-years Cohort Study

Yupeng Li, Hui Tian, Jing Xiao, Fusheng Fang, Yinghong Shao, Banruo Sun and Xiaofei Han

Department of Geriatric Endocrinology, PLA General Hospital & Chinese Military Postgraduate Medical College, China

OBJECTIVE: To investigate the incidence of T2DM and IGR among elderly patients with and without hypertension during 10 years' follow up.

METHODS: Objects of the study are elderly patients (>60 years) who had taken health examinations every year, excluded previously diagnosed DM and IGR patients. Investigate the incidence and risk factors by Kaplan-Meier method and COX's: Proportional Hazard Analysis.

RESULTS: Total investigated subjects was 1317, among which 582 subjects were enrolled in the study. There are 384 subjects in essential hypertension (HT) group and 198 subjects in non-essential hypertension (NHT) group (including newly onset 67 hypertension subjects). During 10 years follow up, the newly onset diabetes was 27.6% in HT group and 18.7% in NHT group (RR = 1.66; 95%CI: 1.09–2.52, $P < 0.05$); incidence rate of DM among two group was 33.8‰ and 20.6‰, respectively. There is no difference in the prevalence of IGR among HT and NHT group, and also no difference in the prevalence of DM or IGR among newly onset HT group and NHT group as well. The independent risk factor of T2DM was dyslipidemia (RR = 1.459; 95%CI: 1.027–2.072, $P < 0.05$) and hypertension (RR = 1.516; 95%CI: 1.039–2.212, $P < 0.05$) base on COX's Proportional Hazard Analysis. Dyslipidemia (RR = 1.545; 95%CI: 1.087–2.195, $P < 0.05$) and hypertension (RR = 1.524; 95%CI: 1.044–2.224, $P < 0.05$) are also independent risk factors of abnormal glycometabolism (T2DM and IGR). Kaplan-Meier analysis indicates accumulative incidence of DM and abnormal glycometabolism are different between HT group and NHT group.

CONCLUSION: The DM risk is 1.66 folds higher in elderly patients with HT than in those without hypertension. hypertension and dyslipidemia are independent risk factors of DM and abnormal glycometabolism.

PCS-36-7

Mean Intima-Media Thickness, Correlated with Glucose Intolerance, is useful for Evaluating Coronary Artery Stenosis

Koji Kashima¹ and Hiroyuki Shimizu²

¹Department of Internal Medicine, Kiryu Kosei General Hospital, Japan; ²Takasaki University of Health and Welfare, Japan

OBJECTIVE: We examined the relationship between the severity of coronary stenosis and carotid artery intima-media thickness (IMT) in the subjects who visited for physical examination.

METHOD: In a total of 291 subjects, carotid arteriosclerosis was evaluated by ultrasonography. Mean-IMT and max-IMT (maximal IMT including plaque thickness) were calculated, and the correlation of various metabolic factors to mean-IMT and max-IMT was evaluated. In addition, coronary artery stenosis was also evaluated by 128 multi-slice computed tomography coronary angiography in 33 subjects.

RESULT: Both mean-IMT and max-IMT were significantly higher in diabetic (DM) subjects than subjects with normal glucose tolerance (NGT). However, there was no significant difference between the subjects with impaired glucose tolerance (IGT) and NGT in mean-IMT and max-IMT. There was a significant correlation between mean IMT and age, A1C, fasting plasma glucose levels, systolic blood pressure, BMI, waist circumference ($P < 0.001$, respectively), and HDL-cholesterol, plasma glucose levels at 120 min after 75 g oral glucose load ($P < 0.05$, respectively). An increase of mean-IMT was correlated with the severity of coronary artery stenosis. Mild ($>25\%$), moderate ($>50\%$) and severe ($>75\%$) stenosis in coronary artery was found in 18%, 18%, 9% of the subjects with normal mean IMT ($<0.8 \text{ mm}$), and 29%, 14%, 29% of the subjects with increased mean IMT ($>1.1 \text{ mm}$).

CONCLUSION: Mean-IMT is correlated with glucose intolerance, and might be associated with the severity of coronary artery stenosis. Evaluation of mean-IMT on physical examination may be useful for screening the existence of coronary artery stenosis.

PCS-36-8

Association of A1c Variability and the Presence of Coronary Artery Disease in Type 2 Diabetes

Eun Ju Lee, Mi-kyung Kim, Eun-ju Lee, Na Han, Seung-Man Kim, Tae-nyun Kim, Taekyun Kim, Min-jung Kwon, Sun-hee Lee, Byoung-doo Rhee and Jeong-hyun Park
Department of Internal Medicine, College of Medicine, Inje University, Korea

The effect of glycemic control on macrovascular complication has been still discussed because there is no discrete conclusion. Traditionally, many epidemiologic studies have used A1c as the criteria of glycemic control and tool for assessing association with diabetic complications. Recent several studies suggested postprandial glucose level or glucose fluctuation including A1c variability may be more important factors for cardiovascular disease than A1c itself at certain time. We try to find out relationship between A1c variability and severity of coronary angiography finding in T2DM. We reviewed charts of type 2 diabetes that they were followed up in our hospital at least 5 years previously and performed coronary angiography. We recorded A1c levels for over 5 years and assessed A1c variability by calculating of SD of serial A1c levels. The presence of coronary artery disease was defined as no vessel involved or one more vessel involved. Male were 47.6% and mean age was 63.6 ± 10.0 years old. Their mean A1c and SD of A1c values for previous 5 years were $7.46 \pm 1.20\%$ and $0.86 \pm 0.67\%$, respectively. Mean A1c level was significantly higher in CAD(+) group compared to CAD(−) group, but there was no difference in A1c at angiography between two groups. SD of serial A1c did not show any difference between two groups in patients with mean A1c < 7 . A1c variability was significantly higher in CAD(+) group in patients with mean A1c > 7 . SD of serial A1c was significant predictor of CAD after adjusted other factors, but mean A1c was not.

In diabetic patients whose glycemic control was not good, A1c variability was significant predictor for CAD.

PCS-37-1

QTc Interval Prolongation During Severe Hypoglycemia Without Hypokalemia in Patients with Type 2 Diabetes

Mi Yeon Kang, Jueng Min Kim, Jae Won Beom, Cheol Hwan Kim and Gun Park
Department of Internal Medicine, Saint Carollo Hospital, Korea

BACKGROUND/AIMS: To access the effects of severe hypoglycemia without hypokalemia on the electrocardiogram in patients with type 2 diabetes.

METHODS: We analysed data from adult patients with type 2 diabetes who were checked each ECG during severe hypoglycemia and recovered stage between October 1, 2011 and May 31, 2012. We only included subjects with normal serum sodium & potassium during severe hypoglycemia. We defined that severe hypoglycemia is below serum glucose 60 mg/dL and decreased mentality.

RESULTS: Nine type 2 diabetes patients (seven men, two women) were included in the study. The mean subject age was 73.2 ± 7.7 years. The mean HbA1c level was $6.07 \pm 1.19\%$. The mean duration of diabetes was 13.8 ± 9.5 years. QTc interval increased significantly during severe hypoglycemia in compare to recovered stage ($447.6 \pm 18.2 \text{ ms}$ vs $417.2 \pm 30.6 \text{ ms}$, $P < 0.05$).

However, the morphology and amplitude of the T-wave did not changed and the depression of ST segment was not found during severe hypoglycemia.

CONCLUSIONS: In our data, QTc interval prolongation during severe hypoglycemia without hypokalemia was observed. Thus, We suggest that

distinct alterations in cardiac repolarisation during severe hypoglycemia may not be associated with hypokalemia.

PCS-37-2

B Cell-Activating Factor is Associated with the Histological Severity of Nonalcoholic Fatty Liver Disease

Teruki Miyake, Shinya Furukawa, Masanori Abe, Maho Hamada, Keitarou Kawasaki, Fujimasa Tada, Shin Yamamoto, Teru Kumagi, Yoichi Hiasa, Bunzo Matsuura and Morikazu Onji

Department of Gastroenterology and Metabolism, Ehime University Graduate School of Medicine, Japan

PURPOSE: Nonalcoholic fatty liver disease (NAFLD) is recognized as the hepatic manifestation of metabolic syndrome. Furthermore, nonalcoholic steatohepatitis (NASH), which is frequently complicated with diabetes, is the risk factor of cirrhosis, liver failure, and hepatocellular carcinoma. Therefore, it is important to distinguish NASH from simple steatosis (SS). B cell-activating factor (BAFF) is expressed in adipocytes and affects insulin sensitivity. In addition, the BAFF receptor is expressed in the liver. The aim of this study was to analyze serum BAFF levels in patients with NASH and SS and to compare their respective clinical and histological findings.

METHODS: We enrolled 96 patients with NAFLD (20 with SS and 76 with NASH) and analyzed their serum BAFF levels. Comprehensive blood chemistry analysis and histological examination of liver samples were also studied.

RESULTS: Serum BAFF levels were higher in patients with NASH than in those with SS ($P = 0.016$). NASH patients with ballooning hepatocytes and advanced fibrosis had higher levels of BAFF in sera ($P = 0.016$ and $P = 0.006$, respectively). In addition, the prevalence of NASH increased significantly as the serum BAFF level increased ($P = 0.004$). Higher serum BAFF levels were found to be an independent risk factor for development of NASH (OR: 1.003, 95% CI: 1.0003–1.006; $P = 0.024$).

CONCLUSIONS: NASH patients had higher levels of serum BAFF than SS, and higher levels were associated with the presence of hepatocyte ballooning and advanced fibrosis. The serum BAFF level may be a useful tool for distinguishing NASH from SS.

PCS-37-3

Postoperative Adverse Outcomes in Surgical Patients with Diabetes: A Nationwide Population-Based Study

Yi-Chun Chou¹, Chien-Chang Liao² and Ta-Liang Chen²

¹Department of Physical Medicine and Rehabilitation, China Medical University Hospital, Taiwan; ²Department of Anesthesiology, Taipei Medical University Hospital, Taipei, Taiwan

BACKGROUND: Many studies had investigated postoperative outcomes in surgical patients with diabetes, however, they were limited to single surgery or inappropriate statistical methods. Our study was designed well to report the surgical adverse outcomes in patients with preoperative diabetes underwent any non-cardiac surgeries.

METHODS: We used the National Health Insurance Research Database to identify patients with diabetes (including type I and type II) who underwent major non-cardiac surgery in Taiwan between the years 2008 and 2010. Propensity score was performed to select matched non-diabetes patients as controls. Sociodemographic factors, operation in teaching hospital, preoperative co-existing medical conditions, types of surgery and anesthesia were matched. Six major postoperative complications and overall 30-day mortality were considered as adverse outcomes. Adjusted odds ratios (ORs) and 95% confidence intervals were estimated in the multivariate logistic regressions.

RESULTS: In 6662 diabetes cases and 6662 non-diabetes matched controls, surgical patients with diabetes had higher risks of postoperative mortality (OR = 2.14), stroke (OR = 2.01), pneumonia (OR = 1.80), septicemia (OR = 3.09), acute renal failure (OR = 4.09), acute myocardial infarction (OR = 2.65) and deep wound infection (OR = 1.50) compared with non-diabetes controls. Postoperative increased length of stay, intensive care unit stay and elevated medical expenditure were also associated with preoperative diabetes. The higher postoperative mortality was found in patients with diabetes who had more preoperative chronic diseases. Surgical patients with type I diabetes had higher postoperative mortality than type II diabetes or controls.

CONCLUSION: Patient with diabetes had increased risk of postoperative adverse events. Better management for surgical patients with diabetes is needed.

PCS-37-4

Association of Glycated Albumin with Diabetic Peripheral Neuropathy and Albuminuria in Type 2 Diabetes Mellitus Patients

Eun Sook Kim^{1,2}, Eun Young Mo², Sung Dae Moon² and Je Ho Han²

Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea, Korea

BACKGROUND: Glycated albumin (GA) is a nonenzymatically glycated protein *in vivo*, having good correlation with current glycemic control and excursion. We aimed to investigate the clinical value of GA in predicting the presence of diabetic peripheral neuropathy and albuminuria in patients with type 2 diabetes.

METHODS: A cross-sectional study was conducted on 340 subjects with type 2 diabetes (age 55.7 ± 12.1 years and diabetic duration 8.1 ± 7.7 years). Neuropathy was assessed by on Michigan Neuropathy Screening Instruments and questionnaire. Albuminuria was defined as an albumin/creatinine ratio >30 mg/g.

RESULTS: There was a significant differences in serum GA levels between subjects with and without neuropathy ($18.6 \pm 8.2\%$ vs $16.2 \pm 4.8\%$, $P = 0.002$) and subjects with and without albuminuria ($18.3 \pm 7.5\%$ vs $15.6 \pm 4.3\%$, $P < 0.001$). According to the quintiles of GA, there was a linear increase in prevalence of both peripheral neuropathy ($P < 0.001$) and albuminuria ($P < 0.001$). Subjects in the highest quintile group of GA had an odds ratio (OR) of 2.5 of for having neuropathy [95% confidence interval (CI) = 1.3–6.9] and OR 5.2 for having albuminuria (95% CI = 2.0–12.9) after adjusting for potential confounding factors. The association remained significant after further adjustments for HbA1c levels.

CONCLUSION: GA was strongly associated with of albuminuria and peripheral neuropathy in Korean patients with type 2 diabetes. Further investigation is needed to validate the predictive value of serum GA on diabetic microvascular complications.

PCS-37-5

Cytokeratin-18 Fragment Levels as a Biomarker for Nonalcoholic Fatty Liver Disease in Type 2 Diabetes

Mai Miyasato, Yuko Murase-Mishiba, Megumi Bessho, Kanako Shishikura, Hisashi Imbe, Masahiro Miyawaki, Fumihiko Nakatsuji, Chiharu Tsutsumi, Fumitaka Haseda, Hiroyuki Sano, Mineki Ohnishi, Jungo Terasaki and Toshiaki Hanafusa

Department of Internal Medicine (I), Osaka Medical College, Japan

OBJECTIVE: Cytokeratin-18 fragment (CK-18) level has been proposed as a noninvasive predictor of the histologic activity in nonalcoholic fatty liver disease (NAFLD). We assessed the usefulness of serum CK-18 level as a biomarker for NAFLD in type 2 diabetes.

METHODS: A total of 105 patients with type 2 diabetes mellitus (59 men and 46 women, age 63.5 ± 10.9 years, BMI 24.9 ± 3.7 kg/m²) were studied. Participants were divided into two groups: NAFLD group ($n = 68$) and non-NAFLD group ($n = 37$). NAFLD was diagnosed by ultrasonography. Serum CK-18 levels were measured by ELISA. Clinical variables were compared between the NAFLD and non-NAFLD group. Logistic regression analysis was used to identify independent factors associated with NAFLD. Univariate and multivariate analyses were conducted to evaluate the relationship of CK-18 and other variables.

RESULTS: CK-18 levels were significantly higher in the NAFLD group than in the non-NAFLD group [median (IQR): 125.0 (82–172) vs 80.1 (72–113) U/L, $P < 0.0001$]. BMI, ALT, and TG, levels of the NAFLD group were also higher ($P = 0.0005$, 0.002, and 0.0005, respectively) and HDL-C was lower ($P = 0.016$) than those of the non-NAFLD group. Logistic regression analysis revealed that CK-18 was the only independent determinant of NAFLD (Odds ratio 1.02, 95%CI: 1.00–1.03, $P = 0.02$). In univariate analysis, CK-18 was positively correlated with AST ($r = 0.50$, $P < 0.0001$) and ALT ($r = 0.52$, $P < 0.0001$) respectively; these correlations remained significant after adjustment for sex, age, and BMI ($r = 0.57$, $P < 0.0001$; $r = 0.58$, $P < 0.0001$).

CONCLUSION: CK-18 could be a potentially useful biomarker for diagnosis and assessment of NAFLD in type 2 diabetes.

PCS-37-6

Metformin-Associated Lactic Acidosis Following Acute Kidney Injury

Yen-Kuang Tai and Chih-Neng Hsu

Department of Internal Medicine, Yuan's General Hospital, Taiwan

OBJECTIVE: Lactic acidosis is a rare but life-threatening complication of metformin treatment. The current contraindications to metformin use have been defined for prevention of this adverse event; renal dysfunction was among the most important ones. This study aimed to explore the factors associated with the unfavorable outcome of metformin-associated lactic acidosis (MALA) and assess the impact of previous chronic kidney disease (CKD).

METHODS: We conducted a retrospective analysis of patients admitted in intensive care unit (ICU) for MALA during a 5-year period. The premorbid conditions, clinical presentations, biological data, therapeutic strategies and outcomes were recorded.

RESULTS: A total of 17 patients with MALA were identified. All of them were accompanied by acute kidney injury and associated with a 35.3% mortality rate. The factors associated with a fatal outcome were high APACHE (acute physiology and chronic health evaluation) II score ($P = 0.002$), presence of shock ($P = 0.028$), and the requirements for mechanical ventilation ($P = 0.002$) or vasopressors ($P = 0.035$). The survivor group stayed longer in the ICU than the non-survivor group ($P = 0.014$). Although patients with previous CKD had worse renal function on admission, as compared with patients without CKD, the other illness severity indicators and mortality rate were similar between the two groups.

CONCLUSION: The prognosis of MALA is mainly determined by the severity of underlying conditions. Previous renal dysfunction (CKD stage 3) has no influence on the illness severity or outcome following acute kidney injury.

PCS-37-7

Serum Fibroblast Growth Factor-21 Levels are Independently Associated with Nonalcoholic Fatty Liver Disease in Korean Men with Type 2 Diabetes

Jang Yel Shin, Mi Young Lee and Choon Hee Chung

Department of Internal Medicine, Yonsei University, Wonju College of Medicine, Korea

Elevated serum fibroblast growth factor-21 (FGF-21) was found to be associated with obesity, metabolic syndrome, and type 2 diabetes. In addition, an association between FGF-21 and nonalcoholic fatty liver disease (NAFLD) was shown in general population. This study investigated the association between serum FGF-21 and NAFLD in Korean men with type 2 diabetes.

We enrolled 135 Korean men with type 2 diabetes (mean age: 56.2 ± 9.2 years; body mass index [BMI]: 25.7 ± 2.9 kg/m²; HbA1C: $7.6 \pm 1.5\%$). Clinical and biochemical metabolic parameters were measured. Serum FGF-21 was determined by ELISA. The severity of NAFLD was assessed using liver ultrasound. High-grade (hg) NAFLD was defined as moderate or severe fatty liver disease.

All patients were divided into three subgroups: normal (17.0%), low-grade (50.4%), and high-grade (32.6%). Patients with hgNAFLD have higher values of BMI, waist circumference, HOMA-IR, triglyceride (TG), liver enzymes, and FGF-21 comparing to those with normal. FGF-21 after adjusted for age was positively correlated with BMI, serum creatinine (Cr), TG, liver enzymes, and C-reactive protein, but was negatively correlated with HDL. In multivariate regression, Cr and TG were independently associated with FGF-21. Also, BMI and FGF-21 were strongly correlated with hgNAFLD. Odds ratio (OR) of a 1-SD increase in FGF-21 predicting presence of hgNAFLD after adjusted for age was 2.38 (95% CI 1.54–3.68). The OR remained significant after further adjusted for Cr, TG, and BMI.

In conclusion, our findings suggest that serum FGF-21 is independently associated with NAFLD in Korean men with type 2 diabetes.

PCS-37-8

Periodontitis is Independently and Positively Associated with Coronary Artery Calcification in Japanese Patients with Type 2 Diabetes

Noriko Takebe, Tomoharu Oda, Riyuki Nakagawa, Mitsutaka Ono, Mizue Matsui, Takayoshi Sasai, Kan Nagasawa, Toru Takahashi, Hiroyuki Honma, Takashi Kajiwara, Haruhito Taneichi, Yoshihiko Takahashi, Kazuma Takahashi and Jo Satoh
Division of Diabetes and Metabolism, Department of Internal Medicine, Iwate Medical University, Japan

BACKGROUND AND AIMS: Few studies have observed a relationship between periodontitis and atherosclerosis in type 2 diabetic patients. Therefore, we have studied whether periodontitis is related to surrogate markers of cardiovascular diseases in 118 Japanese patients with type 2 diabetes.

MATERIALS AND METHODS: Variables analyzed were age, sex, BP, BMI, VFA, IMT, HbA1c, FIRI, serum and urinary CPR, smoking status, and coronary artery calcification (CAC) score. Periodontitis was defined by the presence of periodontal pocket (PP) depth more than 4 mm.

RESULTS: Sixty patients (51%) had periodontitis. In comparison with patients without periodontitis, those with periodontitis had significantly higher or greater log(CACS + 1), urine CPR, and prevalence of carotid plaque, whereas significantly lower or smaller % body fat, VFA, WBC counts, and TC levels. Logistic regression analysis revealed that significant predictors for the PP depth more than 4 mm (periodontitis) were increased log(CACS + 1).

In patients with periodontitis, as compared to those with the lowest tertile of the number of teeth with PP depth more than 4 mm, those with the highest tertile had significantly higher or greater VFA, FIRI, HOMA-IR, serum and urine CPR, and homocysteine. Multiple regression analysis revealed that significant predictors for the number of teeth with PP depth more than 4 mm in patients with periodontitis were serum CPR levels.

CONCLUSION: These results indicate that periodontitis was independently and positively associated with CAC in Japanese patients with type 2 diabetes. In addition, the severity of periodontitis was associated with insulin resistance in patients with periodontitis.

PCS-38-1

Effects of Glucose and Meal Ingestion on Incretin Secretion in Japanese Subjects with Normal Glucose Tolerance

Shunsuke Yamane, Norio Harada, Akihiro Hamasaki, Atsushi Muraoka, Erina Joo, Kazuyo Suzuki, Daniela Nasteska, Daisuke Tanaka, Masahito Ogura, Shin-ichi Harashima and Nobuya Inagaki

Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

OBJECTIVE: Gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) are the major incretins; their secretion after various nutrient loads are well-evaluated in Caucasians. However, little is known of the relationship between incretin secretion and differing nutritional loading in Japanese subjects. In the present study, we evaluated GIP and GLP-1 secretion in Japanese subjects with normal glucose tolerance (NGT) after glucose loading (75 g glucose and 17 g glucose) and meal ingestion.

METHODS: A total of 10 Japanese NGT subjects participated in 75 g oral glucose tolerance test (OGTT), 17 g OGTT and meal tolerance test (MTT). Plasma glucose (PG), serum insulin (IRI), serum C-peptide (CPR), plasma total GIP, and plasma total GLP-1 levels during OGTT and MTT were determined.

RESULTS: Area under the curve (AUC)-GIP was increased in proportion to the amount of glucose, and was highest in MTT, showing that GIP secretion is also stimulated by nutrients other than glucose, such as lipid. In contrast, although the larger glucose load tended to induce a larger GLP-1 release, AUC-GLP-1 was not significantly different among the three loading tests (75 g OGTT, 17 g OGTT and MTT) irrespective of the kind or amount of nutrition load.

CONCLUSION: Our results suggest that nutritional composition might have a greater effect on GIP secretion than that on GLP-1 secretion in Japanese NGT subjects.

PCS-38-2

Changes of Incretin Responses 1 month after Laparoscopic Mini-Gastric Bypass Surgery in Non-obese Patients with Type 2 Diabetes

Hyeonkyu Park¹, Myungjin Kim², Kyo-il Suh¹, Myunghi Yoo¹, Kyungul Hur² and Dongwon Byun¹

¹Department of Internal Medicine, Soonchunhyang University College of Medicine, Korea;

²Department of Surgery, Soonchunhyang University College of Medicine, Korea

Gastric bypass surgery (GBP) in morbidly obese patients often results in weight loss, increase in incretin levels, and improvement of T2DM. In Asian countries, T2DM incidence is recently increasing in non-obese as well as obese subjects. Mini-GBP involves creating a long-sleeved gastric tube along the lesser curvature, and a Billroth II type loop gastroenterostomy with the side of small bowel. We investigated the effects of mini-GBP on incretin responses to oral glucose tolerance test (OGTT) in non-obese [body mass index (BMI) <30 kg/m²] patients with T2DM. A total of 12 patients (7 M/5 F, age 45 ± 3 year, BMI 26.2 ± 0.6 kg/m²) who received laparoscopic mini-GBP were included. Total and active glucagon-like peptide-1 (GLP-1), gastric inhibitory peptide (GIP), insulin, and c-peptide levels were measured during 75-g OGTT before and 1 month after mini-GBP. One month after surgery, body weight decreased by 6.2 ± 0.7 kg, postprandial (pp) glucose levels significantly decreased. Oral glucose-stimulated insulin and c-peptide levels increased, but not significantly. Total GLP-1 levels increased [peak: 42 ± 7 vs 102 ± 10 pM/L, *P* < 0.001; area under curve (AUC): 28 ± 4 vs 59 ± 5 pM/L/min, *P* < 0.001]. Active GLP-1 levels after OGTT markedly increased 3-fold (peak: 207 ± 47 vs 619 ± 133 pg/mL, *P* < 0.001; AUC: 108 ± 18 vs 311 ± 56 pg/mL/min, *P* < 0.001). However, total GIP levels significantly decreased after mini-GBP (peak: 238 ± 28 vs 137 ± 16 pg/mL, *P* < 0.001; AUC: 184 ± 20 vs 98 ± 10 pg/mL/min, *P* < 0.001). In summary, after mini-GBP in non-obese patients with T2DM, GLP-1 levels were markedly increased, whereas GIP levels decreased. Further studies will be needed to address the long-term effects of mini-GBP on glucose homeostasis in non-obese patients with T2DM.

PCS-38-3

Effects of Mitiglinide on Incretin Hormone Responses in a Case of Impaired Glucose Tolerance Following Total Gastrectomy with Roux en Y rebuilding

Mai Kamitani¹, Hiroyuki Konya¹, Masayuki Miuchi², Taku Tsunoda¹, Hayato Fukuoka¹, Tomoyuki Katsuno², Tomoya Hamaguchi³, Yasushi Tanaka⁴, Shin Mizutani⁴, Yoshio Kanayama¹, Jun-ichiro Miyagawa² and Mitsuyoshi Namba²

¹Department of Internal Medicine, Ashiya Municipal Hospital, Japan; ²Divisions of Diabetes and Metabolism, Department of Internal Medicine, Hyogo College of Medicine, Japan;

³Divisions of Innovative Diabetes Treatment, Department of Internal Medicine, Hyogo College of Medicine, Japan; ⁴Department of Surgery, Ashiya Municipal Hospital, Japan

BACKGROUND AND METHODS: Recently, Roux-en-Y gastric bypass (RYGB) as bariatric surgery has been increasing. Some studies reported that the incretin hormone glucagon-like peptide-1 (GLP-1) in postprandial plasma concentrations increase after RYGB because of digested materials directly flow into the lower intestine. We examined preoperative and postoperative secretion of insulin, glucagon and incretin hormones by 75 g oral glucose tolerance test (OGTT) in a patient with impaired glucose tolerance (IGT) who received RYGB due to gastric cancer, and evaluated the effect of mitiglinide on these hormone responses.

RESULTS: At 1 year after RYGB, plasma insulin levels was significantly elevated at 60 min (149 μU/mL), but glucagon levels showed no significant change in 75 g OGTT compared to those before operation. Plasma levels of intact GLP-1 were elevated to 53.7 pmol/L at 30 min, and the value of AUC_{0-180 min} was markedly increased (+41%). On the contrary, the plasma level of total gastric inhibitory polypeptide (GIP) was 311.6 pg/mL at 30 min, and was gradually decreased thereafter. The value of AUC_{0-180 min} of total GIP was significantly decreased (-34%). Treatment with mitiglinide before glucose loading in this patient exhibited a significant elevation of intact GLP-1 secretion (9% increase in AUC_{0-180 min}), while total GIP secretion was further decreased (-48% decrease in AUC_{0-180 min}).

CONCLUSIONS: We demonstrated the increase of intact GLP-1 secretion, and the decrease of total GIP secretion in a case who received RYGB. The increased secretion of intact GLP-1 by mitiglinide administration suggested the direct mechanism of GLP-1 secretion from GLP-1-secreting L cells by mitiglinide.

PCS-38-4

Relationship Between Intestinal Gut Hormone and Insulin in Patients with Prader-Willi syndrome

Se Hyun Maeng¹, Dong-Kyu Jin¹, Yon Ho Choe¹, Sung Yoon Cho¹, Hae Jeong Lee², Young Bae Sohn³ and Su Jin Kim⁴

¹Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea; ²Department of Pediatrics, Samsung Changwon Hospital,

Sungkyunkwan University School of Medicine, Changwon, Korea; ³Department of Medical Genetics, Ajou University Hospital, Suwon, Korea; ⁴Department of Pediatrics, Kwandong

University College of Medicine, Myongji Hospital, Goyang, Korea

OBJECTIVE: Prader-Willi syndrome (PWS) is a common genetic cause of life-threatening obesity characterised by uncontrolled hyperphagia. We studied the effect of gut hormones regulating appetite for explaining the abnormal eating behavior in children with PWS.

METHODS: Fasting and postprandial gut hormone responses were measured in children with PWS (*n* = 18) and overweight controls (*n* = 25). Plasma samples were assayed for Peptide YY (PYY), cholecystokinin (CCK), ghrelin, amylin and insulin.

RESULTS: PYY levels showed no significant difference between the two groups. CCK and ghrelin levels increased and insulin levels decreased in PWS over 24 h. However, there were no differences in group x time interactions in PYY, CCK, ghrelin and insulin. Amylin levels between 0 and 30 min after meal were significantly lower in the children with PWS.

CONCLUSION: There was no significant differences in the response pattern of PYY, CCK, ghrelin and insulin to meals in two groups. Only amylin x time interactions were significantly different. The relatively low levels of amylin right after meal in PWS may contribute to the excessive appetite of PWS patients as compared to the overweight controls. In addition, a decrease of the insulin level in spite of obesity and elevated ghrelin levels may be the important abnormality in PWS.

PCS-38-5

Enteral Supplementation with Glutamine, Fiber, and Oligosaccharide and Incretin Secretion

Takanari Harada, Akihiro Hamasaki, Shunsuke Yamane, Norio Harada, Atsushi Muraoka, Hidemi Tsuji, Kazuyo Suzuki, Daniela Nasteska, Erina Joo, Masahiro Hishizawa, Yaeko Kondo, Kimitaka Shibue, Kazuki Sasaki, Ken-ichiro Shide and Nobuya Inagaki

Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

OBJECTIVE: Recently, it is reported that glutamine, dietary fiber and short-chain fatty acid brought by oligosaccharide modify incretin secretory profiles in human. Currently, enteral supplementation product enriched with glutamine, dietary fiber, and oligosaccharide (GFO) is available as prebiotics in clinical situation. Thus, in the present study, we examined the effects of GFO on incretin secretion.

METHODS: We recruited 20 healthy Japanese volunteers. Oral GFO (including 9 g glutamine, 15 g fiber, 18 g carbohydrates) and glucose (18 g) were administrated on separate days. Plasma or serum levels of glucose, insulin, C-peptide, GIP and GLP-1 were determined over 180 min.

RESULTS: Plasma glucose levels were higher in Glucose loading than those in GFO loading at 30 min (*P* < 0.01) and area under the curve of (AUC-) glucose in glucose loading was significantly higher than in GFO loading (*P* < 0.05). Plasma GLP-1 levels were higher in GFO loading than those in Glucose loading at 30, 60 and 120 min. AUC-GLP-1 in GFO loading was significantly higher than in Glucose loading (*P* < 0.01). In contrast, plasma GIP levels were higher rather in Glucose loading than in GFO loading at 30 and 60 min. AUC-GIP in Glucose loading was significantly higher than in GFO loading (*P* < 0.01). Serum insulin and C-peptide levels showed no significant difference at each time point.

CONCLUSION: Our results suggest that GFO has a potential of dietary supplemental intervention to improve glucose metabolism and has a favorable influence on metabolic status by modulation of incretin signaling.

PCS-39-1

Type of Cancers and Their Association to Metformin Therapy in Thai Patients with Type 2 Diabetes Mellitus (T2D)

Wannee Nitiyanant and Sasitorn Pinitphol

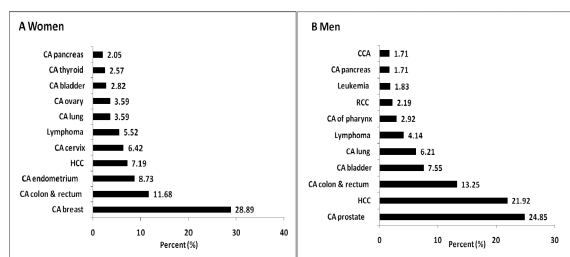
Department of Internal Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

OBJECTIVES: To explore type of and assess factors associated with cancers in Thai T2D.

METHODS: T2D patients with cancer attended out-patient services of Siriraj Hospital in 2010 were recruited. Demographic data, age at diagnosis of diabetes and cancer, treatment and type of cancer were collected.

RESULTS: One thousand six hundred T2D (51.31% males) with cancer had mean age $\pm$ SD of 67.22 ± 10.14 years. Mean $\pm$ SD of age at cancer diagnosis, duration of diabetes and cancer were 65.28 ± 10.17 , 10.64 ± 7.02 and 2.90 ± 2.50 years, respectively. Common cancers in women and men were shown in figure.

There was a correlation ($r = 0.226$, $P < 0.001$) in incident cancers to patient's age and diabetes duration. Metformin users were associated with decreased bladder cancer compared to non-users (4.5% vs 7.6%, $P < 0.016$). Prostate cancer was more prevalent in metformin users compared to non-users (27.3% vs 18.2%, $P < 0.008$).



CONCLUSION: Most common cancer in T2D was prostate cancer in men and breast cancer in women. The relationship of cancer to metformin therapy was inconsistent and inconclusive.

PCS-39-2

Evaluation of sodium and protein intake by measuring sodium or protein excretion in spot urine

Kazuo Fujisawa, Saiko Murakami, Makiko Fukunaga and Kenro Nishida

Department of Endocrine and Metabolism, Minamata City General Hospital, Japan

OBJECTIVE: Evaluation of sodium and protein intake is difficult. We tried to evaluate the sodium and protein intake by measuring sodium or protein in spot urine.

METHOD: One hundred and two patients with Type2 Diabetes were restricted daily energy and sodium intake at 1600 ± 118 kcal/day and 6 g/day, and examined daily protein, urea nitrogen and sodium excretion in pooled urine from 9th to 10th day, and in morning spot urine at 11th day. We calculated daily protein intake from 24-h urinary urea excretion by Maroni formula, and estimated protein intake and protein excretion from the ratio of urea nitrogen and creatinin in spot urine. We also estimated 24-h urinary sodium excretion with spot urine by formula from the guideline of Japan Society of Hypertension.

RESULT: There were significant correlation between protein excretion evaluated by pooled and spot urine ($r = 0.921$, $P < 0.001$), between sodium intake evaluated by pooled and spot urine ($R = 0.431$, $P < 0.001$), between protein-intake evaluated by pooled and spot urine, respectively. Estimated protein-intake by pooled and spot urine were 30.6 and 33.5 g/day among 41 subjects with protein restricted diet (30 g/day). Estimated sodium-intake by pooled and spot urine were 4.89 and 7.06 g/day.

CONCLUSION: Our findings suggest that daily protein excretion estimated by spot urine is reliable as well as by pooled urine. Evaluation of protein and sodium intake by spot urine might be a useful tool for treating outpatients especially with diabetic nephropathy.

PCS-39-3

Serum Carbohydrate Antigen 19-9 (CA 19-9) Level in Diabetic Patients and its Relation to the Metabolic Control

Kyung Ae Lee, Jae Moon Kim, Sunhee Kim, Heung Yong Jin, Hong Sun Baek and Tae Sun Park

Division of Endocrinology and Metabolism, Department of Internal Medicine, Chonbuk National University Hospital, Korea

INTRODUCTION: The aim of this study is to compare CA 19-9 levels in diabetic patients and healthy control group. And the relation of CA 19-9 levels to metabolic control in patients with diabetes was also investigated.

METHOD: Forty adult hospitalized diabetic patients and age-, sex- matched 40 healthy control group were included in the study. HbA1c, serum glucose level, duration of diabetes, c-peptide level, acute diabetic complications (diabetic ketoacidosis, hyperosmolar hyperglycemic state) and microvascular complications of DM were reviewed. CA 19-9 levels (normal range, 0–37 U/mL) were measured in all participants. Abdomen CT scan was performed in order to eliminate abdominal malignancy in the diabetic patients with high CA 19-9 levels (>37 U/mL).

RESULT: Mean CA 19-9 level significantly higher in patients with diabetes compared with control group [31.46 ± 26.07 vs 7.14 ± 4.21] ($P < 0.001$). The prevalence of high CA 19-9 levels in patients with diabetes was 27.5%. For these patients, however, abdominal CT showed no pancreatic abnormalities. CA 19-9 level was positively correlated with serum glucose level ($r = 0.24$, $P = 0.035$) and presence of acute diabetic complications ($r = 0.51$, $P < 0.001$).

CONCLUSION: Serum CA 19-9 level in diabetic patients is higher than healthy controls, especially they in acute metabolic situations. A careful interpretation of this tumor marker assay is required among diabetic patients.

PCS-39-4

Serum CA 19-9 Level Associated with Metabolic Control and Pancreatic Beta Cell Function in Diabetic Patients

Haoyong Yu, Ruixia Li, Lei Zhang, Haibing Chen, Yuqian Bao and Weiping Jia

Department of Endocrinology and Metabolism, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, China

OBJECTIVE: To evaluate whether serum carbohydrate antigen 19-9 (CA19-9) level was related with metabolic control and pancreatic beta cell function in subjects with diabetes.

METHODS: Seventy-one type 1 diabetes (T1DM), 866 type 2 diabetes (T2DM) patients and 122 healthy volunteers were enrolled in this study. Duration of diabetes, clinical and biochemical parameters were recorded. Serum CA19-9 levels (normal range, 0–35 U/mL) were measured in all participants.

RESULTS: The median serum CA 19-9 level was significantly highest in T1DM group [18.59 (11.68–39.28)], lowest in control group [4.69 (2.66–9.65)], and intermediate in T2DM group [12.07 (6.72–21.57)]. When CA19-9 values were divided into four quartiles, the upper quartile group had significantly higher fasting plasma glucose (FPG), 2-h postprandial plasma glucose (2hPG), glycated hemoglobin (HbA1c), glycated albumin (GA) and lower C-peptide 0 min (CP0), C-peptide 120 min (CP120), Δ CP (the D-value of CP120 minus CP0) compared with the lower quartile group. The serum CA 19-9 level was positively correlated with HbA1c, GA, total cholesterol (TC), and negatively correlated with Δ CP. Multiple stepwise regression analysis showed that HbA1c, type of diabetes, TC and Δ CP were independent contributors to the CA19-9.

CONCLUSION: The elevated serum CA19-9 level in diabetic patients may indicate further investigations of glycemic control, pancreatic beta cell function and TC level.

PCS-39-5

Maternal 25 Hydroxyvitamin D Level and its Correlation in Thai Gestational Diabetes Patients

Napartivaumnay Navaporn, Sathit Niramitmahapanya, Chaicharn Deerochanawong, Thongkum Suthornthepavarakul and Veerasak Sarinnapakorn

Department of Endocrinology and Metabolism, Rajavithi Hospital, Medical College of Rangsit University, Thailand

The purpose of this study was to identify 25 Hydroxyvitamin D (25OHD) level in Thai pregnant women with gestational diabetes and non-gestational diabetes.

METHOD: This prospective study was conducted in 197 pregnant women at Rajavithi hospital, a tertiary care medical center in Bangkok during October

2010 to July 2011. The plasma 25 OHD and HbA1c level during the 75 g OGTT in GDM and non GDM were evaluated. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommendation were used for diagnosing GDM in this study.

RESULT: In the selected 197 Thai pregnant age from 18 to 49, mean aged 32.1 ± 5.9 year old, the mean plasma 25OHD level was 34.3 ± 8.3 ng/dL. 3.1% had 25OHD deficiency (<20 ng/dL), 22.3% had 25OHD insufficiency ($20-29$ ng/dL) and 74.6% had normal 25OHD level. Among the 197 women, 70 patients (34.8%) were GDM. In GDM group, 29 patients (41.4%) had abnormal 25OHD level, 5.7% and 35.7% had 25 OHD deficiency and insufficiency respectively. GDM plasma 25OHD concentration were significantly lower than non GDM (32.3 ± 10.3 vs 35.5 ± 6.7 ng/dL, $P = 0.001$). Fasting blood glucose and HbA1C independently predict low level of 25OHD level in Thai GDM after applying regression model and adjusted for age, BMI, trimester and family history of DM ($P = 0.031$, $P = 0.014$ respectively). Higher pre-pregnancy BMI was associated with GDM and lower 25OHD level.

CONCLUSION: Finding from this study suggested that Thai GDM had lower level of 25OHD than non GDM. Fasting plasma glucose and HbA1C independently predict low level of 25OHD level in GDM.

PCS-39-6

Sleep-Wake Cycle Irregularities in Type 2 Diabetic Subjects

Tomoko Minami¹, Ken Kishida¹, Tohru Funahashi² and Ichihiro Shimomura¹

¹Department of Metabolic Medicine, Graduate School of Medicine, Osaka University, Japan; ²Department of Metabolism and Atherosclerosis, Graduate School of Medicine, Osaka University, Japan

OBJECTIVE: Sleep loss and circadian rhythm abnormalities are thought to be one of the underlying causes of adverse metabolic health. However, little is known about sleep-wake cycle irregularities in type 2 diabetes mellitus (T2DM). The present study compared the bedtime, waking time, and estimated sleep duration between T2DM and non-T2DM subjects.

METHODS: The study subjects were 106 consecutive outpatients with lifestyle-related diseases (males/females = 56/50), who answered a questionnaire on sleep status. Subjects were divided into two groups; non-T2DM ($n = 32$) and T2DM ($n = 74$) subjects.

RESULTS: T2DM subjects retired to bed on weekdays and holidays significantly later than non-T2DM subjects ($23:43$ vs $22:52$, $P = 0.0032$; $23:45$ vs $22:53$, $P = 0.0038$, respectively), and woke up significantly later on weekdays and holidays, compared with non-T2DM subjects ($06:39$ vs $06:08$, $P = 0.0325$; $06:58$ vs $06:24$, $P = 0.0450$, respectively). There was no significant difference in the estimated sleep duration between the two groups. Daytime sleepiness was reported significantly more commonly by T2DM subjects than non-T2DM subjects ($P = 0.0195$).

CONCLUSIONS: Circadian rhythm sleep disorders are more common in T2DM subjects than non-T2DM.

PCS-39-7

Diabetic Nephropathy Predicts Severe Hypoglycemia in Patients with Type 2 Diabetes Mellitus: A 8-year Follow Up Study

Seung-Hyun Ko¹, Jae-Seung Yun¹, Sun-Hye Ko¹, Hyuk-Sang Kwon¹, Ki-Ho Song¹, Yu-Bae Ahn¹, Sun-Hee Ko¹, Kun-Ho Yoon¹ and Yong-Moon Park²

¹Department of Internal Medicine, The Catholic University of Korea, Korea; ²Department of Preventive Medicine, The Catholic University of Korea, Korea

OBJECTIVE: We investigated factors that might influence the development of severe hypoglycemia (SH) in patients with Type 2 diabetes.

METHODS: From 1999 to 2001, patients with Type 2 diabetes aged 25–75 years were consecutively enrolled ($n = 1,734$) and followed-up in 2011 and 2012. SH was defined as hypoglycemic episodes requiring hospitalization or medical care in an emergency department. We used Cox proportional hazard regression analysis to test the association between SH episodes and potential variables.

RESULTS: At baseline, mean age and duration of diabetes were 57.1 ± 11.0 and 9.1 ± 7.3 years, respectively. After a median 8.3 years of follow-up, the incidence of SH was 1.55/100 patient-year. The SH events was higher in older patients (63.7 ± 8.9 vs 56.6 ± 9.9 year-old, $P < 0.001$) and those with a longer duration of diabetes (13.5 ± 7.5 vs 9.1 ± 6.7 years, $P < 0.001$), hypertension ($P = 0.041$), more use of insulin and sulfonylurea ($P < 0.001$), and in those who had higher levels of albuminuria ($P < 0.001$) at baseline. Cox hazard regression analysis revealed that the development of SH was significantly associated with longer diabetes duration (<5 years vs >10 years, HR 2.119, 95%

CI 1.181–3.801; $P = 0.012$), and the presence of macroalbuminuria (normo-albuminuria vs macroalbuminuria, HR 2.172, 95% CI 1.275–3.703; $P = 0.004$).

CONCLUSIONS: The development of SH was independently associated with diabetic duration and macroalbuminuria in patients with Type 2 diabetes.

PCS-39-8

The Etiology Analysis of Hypoglycemia of Emergency Department

Nan Zhang¹, Dahai Xu¹, Nan Zhang¹, Li Pang¹, Dawei Wang¹, Jing Wang¹, Xiuxian Zang¹, Dan Shi² and Yang Wu¹

¹Emergency Department, The First Hospital of Jilin University, China; ²The Hospital of Changchun University of Chinese Medicine

OBJECTIVE: To investigate the etiology of hypoglycemia of Emergency Department and instruct the clinical treatment.

METHOD: Analyze retrospectively the etiology of hypoglycemia of Emergency Department.

RESULTS: ALL 304 cases were included in the investigation. The etiology factor were respectively as follows: drug-induced 237 cases, hepatic diseases 15 cases, alcoholic hypoglycemia 13 cases, neoplasms out of pancreatic gland eight cases, severe infection six cases, subtotal gastrectomy five cases, unsection of gland pituitary five cases, B cell of pancreatic islet abnormalities five cases, hypoadrenocorticism three cases, autoimmune hypoglycemia two cases, hypothrepsia two cases.

CONCLUSION: The etiology factors of hypoglycemia of Emergency Department include many kinds of causes. Correct the hypoglycemia as soon as possible, on the same time, we should try to find the causes and treat the primary diseases to avoid the recurrent hypoglycemia.

PCS-39-9

A Case of Young Adult Onset Diabetic Patient with Optic Nerve Atrophy, Sensorineural Hearing Loss, Primary Hypogonadism and Foot Gangrene

Toshihide Izumida¹, Emiri Muranaka¹, Kanako Motoyoshi¹, Eriko Shiona¹, Chikaaki Kobashi¹, Tadashi Yamamoto¹, Yukihiko Satou¹, Tadao Ishikawa¹, Kouichi Sigeta¹, Masaharu Urakaze¹, Yuuko Nagata², Hideya Ooi³, Kanehito Nogami⁴ and Yukio Yazawa⁵

¹Department of Internal Medicine, Kamiichi General Hospital, Japan; ²Department of Ophthalmology, Kamiichi General Hospital, Japan; ³Department of Ear, Nose and Throat Disease, Kamiichi General Hospital, Japan; ⁴Department of Neurosurgery, Kamiichi General Hospital, Japan; ⁵Department of Medicine and Bioregulatory Science, Yamaguchi University, Japan

A 53-year-old man was presented to the neurological department in Kamiichi General Hospital. He had 1 week history of gait disorders, numbness in the right side of the body. His past medical history included young adult onset diabetes mellitus treated with insulin, sensory neural deafness from childhood, and optic nerve atrophy from 40 years of age. His height was 155 cm and body weight was 50.1 kg (BMI 20.8). The initial vital signs revealed blood pressure 141/63 mmHg, pulse 52 beats per minute. Physical examination on admission revealed hypoesthesia of touch sensation of right facial and right two limb and mild paresis of the right limbs, and gait ataxia. Routine laboratory examinations revealed hyperglycaemia and a mild increase in transaminase levels. Magnetic resonance imaging (MRI) showed a recent infarction in the left medulla. In addition, moderate stenosis of the left vertebral artery was demonstrated on magnetic resonance angiography (MRA). He was treated with anti-platelet agents and his condition improved substantially. Furthermore, he was absent of axillary hair growth and diagnosed as primary hypogonadism from findings of the increase in LH and FSH levels and the decrease in testosterone level. Wolfram syndrome (WFS) is a rare, autosomal recessive, neurodegenerative disorder presenting with the main clinical symptoms of childhood-onset diabetes mellitus, optic atrophy, diabetes insipidus and deafness. WFS-1 mutation of the patient was examined, but not detected. We suppose that another mutation might be in the patient because he was associated with primary hypogonadism and macroangiopathy, which are rare in WFS.

PEC-01-1

Effect of 3 weeks Low GI Food in Patients with Type II Diabetes Mellitus

Keiko Honda and Ryu Ka

Medicine Nutrition, Kagawa Nutrition University, Japan

PURPOSE: We examined the effectiveness of the glycemic control with the low GI diet in type II diabetes mellitus.

SUBJECT AND METHOD: We divided subjects into two groups: eight patients of type II diabetes mellitus (DM) and 16 healthy people (NDM). After 3-weeks normal meal (RD) intake, we compared the effect of the low GI food (LGID) intake for 3 weeks between two groups. With no body weight change during the study period, we evaluated the effect of glycoalbumin (GA), fasting glucose (FPG) and insulin (IRI) level, HbA_{1c}, serum lipids, abdominal circumference, blood pressure, at the two points of time, after LGID and RD. The NDM group was further divided into two groups, 11 of young people (Y-NDM) and five of middle aged group and compared.

RESULTS: In DM group, GA, HbA_{1c}, total cholesterol (T-ch), triglyceride (TG) were decreased ($P = 0.035, 0.042, 0.046, 0.046$, respectively), after LGID. In Y-NDM group, GA after LGID was decreased ($P = 0.006$). Comparing the decreasing rate, GA, HbA_{1c} and T-ch were larger in DM group than M-NDM and Y-NDM group ($P = 0.012, 0.046, 0.018$).

CONCLUSION: By the short-term low GI food intake in type II diabetes mellitus, GA, HbA_{1c}, T-ch and TG were decreased and improvement of glycemic control and serum lipids were suggested.

PEC-01-2

Micronutrient Status of Diabetic Patients

Unurbayar Sumya¹, Tegshee Barkhas², Purejav M.², Enkhtaivan Gombosuren² and Saibilleg Sonomtseren³

¹Department of Nutrition, Diabetes Center, Mongolia; ²Food Engineering and Biotechnology School, Mongolian University of Sciences and Technology, Mongolia; ³Department of Endocrinology, School of Medicine, Health Sciences University of Mongolia, Mongolia

AIMS: Aims of this study were to evaluate micronutrient status of diabetic patients.

METHODS: Cross-sectional study included 55 (26 male and 29 female) diabetic patients. Micronutrient status of diabetic patients was evaluated by 24 h recall method and calculated by using Com_definer_1v program. Micronutrient status compared with Recommended Dietary Allowances (RDA) or Adequate Intake (AI) and calculated Daily Value of vitamins and minerals.

RESULTS: Daily Values of Vitamin B1 (0.9 vs 1.2 mg or 75%), Vitamin B3 (14.9 vs 35 mg or 42.6%), Vitamin B5 (2.1 vs 5 mg or 42.0%), Vitamin B6 (1.1 vs 1.3 mg or 85.4%), Vitamin B9 (37.2 vs 400 µg or 9.3%), Vitamin C (24.9 vs 90 mg or 27.7%), Vitamin E (2.6 vs 15.0 mg or 17.3%), Vitamin K (42.8 vs 120 µg or 35.7%), Calcium (490.3 vs 1000 mg or 49.0%), Potassium (2071.1 vs 4700 mg or 44.1%), Magnesium (183.9 vs 400 mg or 46.0%), Molybdenum (25.1 vs 45 µg or 55.8%) and Selenium (1.6 vs 55 µg or 2.9%) were low; Vitamin B2 (1.8 vs 1.3 mg or 138.5%), Vitamin B12 (2.7 vs 2.4 µg or 112%), Phosphorus (881.8 vs 700 mg or 126%), Iron (29.4 vs 8 mg or 367%), Sodium (2541.8 vs 1500 mg or 169%), Manganese (59.8 vs 2.3 mg or 260%), and Zinc (99.6 vs 11.0 mg or 905%) were high in diabetic patients compare with RDA or AI.

CONCLUSIONS: Diabetic patients have micronutrient deficiency. Diabetic patients vitamin and mineral supplements.

PEC-01-3

A Questionnaire Survey on the Background of Diabetic Patients Undertaking Exercise Therapy

Toshihiro Amagawa, Naoko Awane, Naoko Usui, Kyoko Ogata, Yuusuke Hirota, Akino Kaji, Kuniaki Kaji, Misato Takeda, Takahiro Usui, Takaya Matsushita, Nobuteru Asahi, Tomoya Satou, Atsushi Ohno and Akio Ueki

Department of Diabetology, Endocrinology and Metabolism, Hachioji Medical Center of Tokyo Medical University, Japan

Exercise therapy for diabetic patients is based on the assumption that they can engage in daily life activities. In the clinical situation, diabetic patients often cannot undertake exercise therapy because of musculoskeletal pain. Such pain may result from orthopedic problems, prognostic symptoms after cerebrovascular disease, disuse muscle atrophy, or joint involvement. Physical therapists who are certified diabetes educators in Japan should consider exercise therapy for diabetic patients who have pain to decrease insulin resistance and enable them to engage in daily life activities. We conducted a questionnaire survey among diabetic patients whose doctors directed them to undergo exercise therapy. The questionnaire items included the presence or absence of pain, the site of pain, the trigger of pain, and whether they received orthopedic treatment or not. The responses indicated that 71% of the diabetic patients have musculoskeletal pain, but 63% received no orthopedic treatment. Only 22% of the diabetic patients were directed to have exercise therapy for improving physical activity. Our data suggest that many diabetic patients have musculoskeletal pain which precludes them from undertaking exercise

therapy. Physical therapists should initially prescribe physical therapy to relieve the pain before advising diabetic patients to have exercise therapy.

PEC-01-4

Expanding the Step-Length in Walking under Unconscious Might get the Effective HbA_{1c} Control on Impaired Glucose Tolerance?

Akira Kimura

Department of Health Sciences, Gunma PAZ College, Japan

PURPOSE: The purpose of this study is to clarify to keep a better HbA_{1c} in impaired glucose tolerance people after 1 year of the intervention. It determined subconsciously longer the step-length in walking under unconscious-behaviour (SLUB) by measuring device was used (WCEE) with the combination of sensor and ubiquitous device wearable computer.

METHODS: Thirty six subjects participated in this study. They were impaired glucose tolerance. Mean age 65 ± 6 years, 17 male genders, 19 female, and $56 \text{ kg} \pm 5$. Physiotherapists, et al explained participants how to use WCEE, how to increase the amount of physical activity in ADL at the same time. After four hours of teaching WCEE, was measured for 30 days. Outcomes were HbA_{1c} < 6.5 (NGS) after a year. Success group (SG) was performed for 2 h to increase the stride guidance in daily life. Not-success group (NG) were compared with a walking rate of the fourth week is the start of the experiment, were significantly lower than the rate of walking at 3 weeks. It set the value of SLUB average of distance per step samples were removed. The odds ratio was analyzed using a SPSSv17.

RESULTS: All were carrying out the program.

SLUB was $69.5 \pm 28(\text{cm/step})$. SG ($n = 29$); 73.4 ± 15.3 , NG ($n = 7$); 67.8 ± 10.21 , Endpoint reached, SG 82%, NG, 42%, Odds ratio is 11.5 in SG vs NG, $P = 0.015$. 95% CI is $1.7 - 78.4$.

CONCLUSION: Effect of expanding the step-length in walking under unconscious had shown the effective HbA_{1c} control on impaired glucose tolerance.

PEC-02-1

Evaluation of the Utility of Diabetes Conversation Map™ in Japanese Diabetic Patients

Yu Kouchi¹, Eitaro Nakashima¹, Rui Imamine¹, Minoru Kusama¹, Mariko Kawai¹, Makiko Watanabe¹, Chiaki Tanaka², Akio Kanai³, Takahiko Kawamura³, Takahisa Sano¹ and Nigishi Hotta¹

¹Department Diabetes and Endocrinology, Chubu Rosai Hospital, Japan; ²General Internal Department Chubu Rosai Hospital; ³Center for Preventive Medicine, Chubu Rosai Hospital

OBJECT: We evaluated the utility of Diabetes Conversation Map™ (Healthy-i) (MAP) which was introduced to our hospital recently.

RESEARCH DESIGN AND METHODS: Eighty-three inpatients who attended a diabetes education program in our hospital (average age: 60 years old, 46 men, average disease history: 11.3 years, HbA_{1c} 9.6%) were enrolled. We examined the utility of MAP using the questionnaire method before and after the participation of MAP. Statistical analyses were done by SPSS (ver. 12).

RESULTS: HbA_{1c} has improved from 9.6% to 7.6% after 3 months of MAP class ($P < 0.01$). Most of the patients who participated in the map answered 'MAP was very interesting' and 76% of the patients answered 'Having communication with other patients was interesting'. The rate of correct answers to the questions in understanding the factor of affecting blood glucose levels improved from 69.8% to 80.3%. Also, understanding the symptoms of abnormal blood glucose levels improved from 54.3% to 66.4%. Significant differences in PAID test or DTSQ test were not observed. (PAID, 50.7–51.1, $P = 0.84$. DTSQ, 28.3–30.1, $P = 0.14$).

CONCLUSION: We tried to integrated the Map method into the diabetic education program in our hospital and found significant improvement of patient's knowledge and motivation by MAP. Although we must take care not to fall into the complacency of medical staff, we need to establish a method for evaluating the patient's emotion and motivation objectively in the future.

PEC-02-2

Introduce Maps to Effectively Improve the Blood Glucose Control

Cheng-Wei Lin¹, Wan-Yu Wu¹, Yi-Ping Li¹, Shu-Fen Lai², Shu-Mih Chen¹ and Neng-Chun Yu¹

¹Neng-Chun Diabetes Clinic, Taiwan; ²Department of Medical Education and Research, Lo-Hsu Foundation, Inc., Lotung Poh-Ai Hospital

AIMS/INTRODUCTION: The Diabetes Conversation Maps are recognized education tools. The aim of this study was to induce patients' motivation for

blood glucose control by using the Diabetes Conversation Maps since the percentage of Taiwanese HbA1c $\leq 7\%$ was only 35.4% in 2011.

METHODS: We conducted a prospective randomized study with T2DM patients who have accepted personal education in the past, from August 1, 2011 to April 30, 2012. Sex, BMI and HbA1c were not limited. The primary end point measurement was HbA1c. The second end point measurements were the frequency of SMBG, knowledge of diabetes, exercise and diet change.

RESULTS: A total of 132 personal time and 26 sessions including six Conversation Maps were completed within 6 months. The average age was 61.6 years old and the male to female ratio was 48%:52%. HbA1c decreased from 8.1% to 7.6% ($N = 125$, $P < 0.0001$), frequency of SMBG increased from 2.1 to 3.2 times/week ($N = 110:66$, $P < 0.0001$), all recognition score significantly improved ($P < 0.0001 \sim 0.032$).

Sub-group analysis of Conversation Map 2: Diet and exercise showed metabolic equivalents increased from 3.3 to 6.3 mets, servings of carbohydrates intake reduced from 10.4 to 9.7 servings/day, vegetables intake increased from 2.6 to 3.2 servings/day, the trend is increasing but no significant difference ($N = 20$, all $P > 0.05$).

CONCLUSION: The study demonstrates the Diabetes Conversation Maps are an effective and interactive education tools through the power of peer conversation to facilitate and reinforce behavior change of diabetes self-management. We shall continue to carry forward and broadly apply in clinical practice.

KEYWORDS: Conversation MAP, A1C, SMBG, Group education program, Motivation

PEC-02-3

Appropriate Facilitation of Diabetes Conversation Map™ Based on the Characteristics of Japanese Diabetes Patients

Keiko Wada¹, Nahoko Mizuno¹, Shin-ichi Harashima², Hiroko Higashiyama³, Kenichiro Shide¹ and Nobuya Inagaki²

¹Department of Metabolism and Clinical Nutrition, Kyoto University Hospital, Japan;

²Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan;

³Department of Clinical Psychology, Bukkyo University, Japan

AIM: Self-management is a key component of living with diabetes. The ability is empowered when patients well communicate with healthcare professionals. However, one-way education from healthcare professionals to patients does not lead to achievement of self-management because patients usually remember little of the content of what they learn. Diabetes Conversation Map™ (MAP) is a novel educational tool to learn diabetes effectively. We previously reported that MAP improves general knowledge of diabetes, regardless of their age and gender, in Japanese patients with type 2 diabetes. Next, we surveyed diabetes comprehension level and support persons of diabetes patients, and evaluated appropriate approach in facilitation of MAP.

METHODS: Patients answered their HbA1c level, fasting blood glucose (FBG) level, post prandial glucose (PPG) level, body weight, purpose of self-care, and support persons set down on 'My Purpose Card', a questionnaire equipped in MAP, after each session of MAP program.

RESULTS: Fifty-eight diabetes patients (men 29, women 29) were recruited into the study. Mean age was 58.9 ± 14.4 , and mean diabetes duration was 9.9 ± 8.2 years. Twenty-seven patients (46.6%) filled in HbA1c, but only 7 (12.1%) were right answers. Similarly, 14 (24.1%), 7 (15.2%), and 22(37.9%) patients answered exact FBG, PPG, and body weight, respectively. As support persons, 42(72.4%), 6 (10.3%), and 9 (15.5%) patients answered families, healthcare professionals, and none, respectively.

CONCLUSIONS: These data suggested that facilitators should encourage patients to understand their diabetes conditions and make patients aware of support persons to obtain optimal benefit of MAP.

PEC-02-4

Nationwide Implementation Program of Diabetes Conversation Map™ by the Japan Association of Diabetes Education and Care: Current Status and Future Perspectives

Daisuke Yabe¹, Hiroko Higashiyama², Shin-ichi Harashima³, Naomi Kitatani⁴, Hiroko Hotta⁵, Jun Takeda⁶ and Yutaka Seino⁷

¹Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, Japan; ²Japan Association of Diabetes Education and Care, Clinical Psychology Program, Bukkyo University Graduate School of Education, Kyoto, Japan; ³Japan Association of Diabetes Education and Care, Department of Diabetes and Clinical Nutrition, Kyoto University Graduate School of Medicine, Kyoto, Japan; ⁴Japan Association of Diabetes Education and Care, Division of Metabolism and Clinical Nutrition, Kanasai Electric Power Hospital, Osaka, Japan; ⁵Japan Association of Diabetes Education and Care; ⁶Japan Association of Diabetes Education and Care; Department of Diabetes and Endocrinology, Graduate School of Medicine, Gifu University, Gifu, Japan; ⁷Japan Association of Diabetes Education and Care, Division of Diabetes, Clinical Nutrition, and Endocrinology, Kanasai Electric Power Hospital, Osaka, Japan

Diabetes Conversation Map™ (DCM) is a novel educational tool that engages a group of patients with interactive learning relevant to diabetes, and its nationwide implementation has been carried out by the Japan Association of Diabetes Education and Care (JADEC) in Japan. Here, we reports progress of JADEC's implementation program, and discuss problems and future plans.

The JADEC's nationwide implementation program was initiated from December, 2010, and 14 training sessions were performed in 10 different locations in last 15 months, in which 263 participants received certificates and DCM kits. Each training session is 2-day, and comprises 1 medical director, 1 psychological director, 3-4 trainers, 1-2 JADEC's officer, and 16-20 participants. Our questionnaire revealed 100% of participants want to use DCM in their diabetes education. It revealed, however, only 10% of participants felt fully ready to use DCM and 83% felt partially ready. Many participants feeling partially ready to use DCM requested follow-up trainings, and places to discuss with other trained participants. In addition, 26% of participants stated they could not start DCM within 1 month after training as they need to have strong efforts to convince their medical doctors and colleagues to start DCM in their institutions. Therefore, JADEC initiated follow-up sessions from February 2012, and disseminate information on DCM to healthcare professionals and patients through official magazines, Sakae and DM Ensemble as well as through diabetes-related lectures and events. These approaches could make DCM to be widely integrated into Japanese diabetes education, and help improving diabetes education in Japan.

PEC-03-1

Effect of a Newly Devised Nutrition Guidance using the Self-Efficacy Theory

Takuya Yamamoto¹, Shota Moyama², Akira Kuroe³ and Hideki Yano³

¹Division of Clinical Nutrition, Hikone Municipal Hospital, Japan; ²Department of Health and Nutrition, The University of Shiga Prefecture, Japan; ³Department of Internal Medicine, Hikone Municipal Hospital, Japan

PURPOSE: The psychological approach to nutrition education is required for diabetic patients. In this study, we devised a new nutrition guidance with the application of self-efficacy theory. We investigated the effect of our method for patients with type 2 diabetes.

METHODS: Subjects were 38 patients (16 male and 22 female) with type 2 diabetes who have not overt chronic complications such as diabetic neuropathy, nephropathy or retinopathy. At first, patients set the action target by themselves. We carried out step-by-step evaluation for the degree of achievement of their action target, calorie intake and the nutrient balance in each time of education. The targeted value of the end of the education was HbA1c6.8% (NGSP).

RESULTS: HbA1c and BMI were significantly decreased after the end of nutrition education using our guidance ($P < 0.001$). The attainment rate against the action target and the degree of improvement in both HbA1c and BMI showed a significant positive correlation ($P < 0.05$ and $P < 0.01$, respectively). The most frequent action target was on a stop of snacks (57.9%).

CONCLUSIONS: In the present study using our new nutrition guidance, setting the action target by patients themselves and continuing self-monitoring contributed to a significant improvement in BMI and HbA1c. In conclusion, our new guidance may serve an effective and helpful nutrition educational tool for the patients with type 2 diabetes.

PEC-03-2

Simplified Self-Titration Dosing Guideline is Effective to Improve Glycemic Control for Pre-Mixed Insulin Using Type 2 Diabetes in Taiwan

Hsueh Ying Lee and Chieh-Hsiang Lu

Department of Endocrinology and Metabolism, Chia-Yi Christian Hospital, Taiwan

OBJECTIVE: The aim of this study was to evaluate the effects of a simplified self-titration dosing guideline for person with pre-mix insulin using type 2 diabetes in Taiwan.

METHODS: Eighty-two patients with informed consent were randomly assigned to simplified self-adjusted dosing algorithm ($n = 40$) and standard physician-driven adjustments algorithm ($n = 42$) as a control group. Patients from experimental group were instructed to adjust their insulin dose every 3 days based on the mean of three fasting plasma glucose (FPG) values using a simple algorithm: mean FPG < 70 mg/dL, reduce dose by 2U, FPG between 70 and 120 mg/dL, no change, and FPG > 120 mg/dL, increase dose by 2U. Comparison with baseline was undertaken on 3, 6 and 9 months after intervention.

RESULTS: Mean A1c and mean fasting blood glucose of experimental group was significantly improved ($d = -1.185$, $t = -6.896$, $P = 0.000$; $d = -48.950$, $t = -3.947$, $P = 0.000$) and better than that of the control group at 3 month ($P < 0.05$). Though a slightly elevated A1c at the 6 and 9 months ($P > 0.05$), there is still significant greater reduction of A1c in experimental vs control group after 6 months ($t = -2.356$, $P = 0.021$), but no significant improved at 9 months ($P > 0.05$). There was no significant difference in the incidence of hypoglycemia between two groups (0.30 ± 0.608 vs 0.26 ± 0.587 , $z = -0.361$, $P = 0.718$).

CONCLUSION: Patients who learned simplified self-adjusted dosing skills had better glycemic control than standard physician-driven adjustments care. It is safe and easy as an additive education program for insulin treated type 2 diabetes for improving clinical outcomes. Further study is needed to see the long term effects of this approach.

PEC-03-3

The Effect of Diabetes Genetic Counseling for Adult Offspring of Patients with Type 2 Diabetes on the Attitude Toward Diabetes and its Heredity: A Randomized Controlled Trial

Masakazu Nishigaki¹, Yuri Tokunaga-Nakawatase¹, Junko Nishida² and Keiko Kazuma¹

¹Department of Adult Nursing, The University of Tokyo, School of Medicine, Japan;

²Department of Health Care Center, Social Insurance Central General Hospital, Tokyo, Japan

OBJECTIVE: To investigate the effect of diabetes genetic counseling on the attitude toward diabetes and its heredity in relatives of type 2 diabetes patients.

DESIGN: This study was an unmasked, single-center, randomized controlled trial.

SETTING: A medical check-up center at the Tokyo metropolitan area.

PARTICIPANTS: Healthy adults age between 30 and 60 years who have a family history of type 2 diabetes in their first degree relatives.

Intervention Participants in the intervention group received a brief genetic counseling session for approximately 10 min. Genetic counseling was structured based on the Health Belief Model. Both groups received a booklet for general diabetes prevention.

Outcome measures Change in risk perception and recognition of diabetes, and attitude towards its prevention. Outcomes were measured immediately and 1 week and 1 year after the session.

RESULTS: Participants who received genetic counseling recognized their higher risk, controllability and knowledge regarding a favorable lifestyle immediately after counseling, while anxiety about diabetes did not increase. These effects could be complemented by general information on prevention, but controllability was recognized only by genetic counseling.

CONCLUSION: Genetic counseling for diabetes is effective in modifying the negative perceived controllability for diabetes in healthy adults who are genetically predisposed to diabetes.

PEC-03-4

Patient-Directed Self Titration of Insulin Therapy with the Insulin Rotary Disc for Attainment of Glycaemic Goals in Patient Age >65 years in a Taiwan Primary Care Setting

Jeng-Fu Kuo, Shih-Te Tu, Yan-Chi Li, Guan-Yi Lin and Jia-Yu Tian

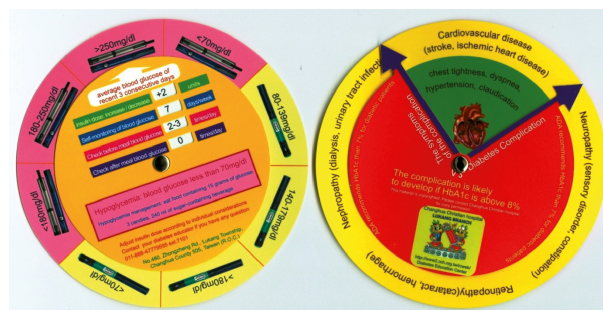
Division of Endocrinology and Metabolism, Department of Internal Medicine, Changhua Christian Hospital Lukang Branch, Taiwan

By the insulin rotary disc (IRD), our patients were taught to titrate of their insulin dose based on a simplified algorithm. This study assessed the effectiveness of IRD for patient-directed self-titration of insulin therapy for attainment of glycemic goals.

Seventy-six type 2 diabetes patients (47 patients were <65 years old and 29 were >65) under insulin therapy were included in this 24-week trial. They self adjusted their insulin dose every 3 days according to the algorithm in IRD.

The baseline average A1C was 10.0%. Baseline-adjusted HbA1c decrease for patients <65 vs >65 years old were 1.9% vs 2.1%, with final HbA1c achieving 8.3% and 7.6%, respectively. 23.4% of patients <65 years old achieved A1C < 7% compared with 27.6% of patients >65 years old. Minor hypoglycemia occurred in 14.9% and 31.0% of patients <65 vs >65 years old, respectively. Major hypoglycemia occurred in 2.1% and 0% of patients.

With a patient-centered approach and appropriate educational efforts, patients with type 2 diabetes can successfully manage their insulin therapy under the care of their physicians.



PEC-03-5

Is 'ICF Core Set for Diabetes Mellitus' Applicable to Quality of Life Evaluation of Japanese Patients with Diabetes?

Hideyo Tsutsui¹, Yoshiharu Oshida², Nobuaki Ozaki², Masataka Kusunoki³, Tetsuya Ishiguro⁴, Hideo Tawada⁵, Akira Ito⁶ and Toshiyuki Ojima¹

¹Department of Community Health and Preventive Medicine, Hamamatsu University School of Medicine, Japan; ²Research Center of Health Physical, Fitness and Sports,

Nagoya University, Japan; ³Aichi Medical University Medical Clinic, Japan; ⁴Ishiguro Medical Clinic, Japan; ⁵Tawada Hospital, Japan; ⁶Masuko Memorial Hospital, Japan

OBJECTIVE: To examine criterion validity of 'ICF Core Set for Diabetes Mellitus (DM)', and whether it can extract physical and psychosocial problems of Japanese patients with diabetes.

METHODS: The subjects were 302 patients of diabetes who are undergoing treatment regularly (Age 62 ± 13 , Men 68.2%, Type 2 DM 88.1%, HbA1c $7.1 \pm 1.6\%$). Patients were interviewed using the ICF core set for DM, which has 99 categories, and asked whether or not they had experienced problems in each category since starting diabetic treatment. In order to calculate criterion validity, patients were divided into the existence of complications and diabetic nephropathy (DMN), and HbA1c levels ($\geq 7.0\%$ vs $< 7.0\%$). In each category, the number of categories which more than 30% of patients answered as 'yes' was counted.

RESULTS: Patients with and without complications group reported problems in 25 and 11 categories, respectively, among 99 categories. Patients with and without DMN group reported problems in 27 and 15 categories, respectively, among 99 categories. Patients of HbA1c $\geq 7.0\%$ and HbA1c $< 7.0\%$ group reported problems in 32 and 21 categories, respectively, among 99 categories.

CONCLUSION: In complication group and poor glycemic control group, which can commonly be thought as one of criteria related to severe DM, they reported more categories of problems compared with the counterparts. Since criterion validity was shown, 99 categories of 'ICF core set for DM' are thought to be able to extract physical and psychosocial problems of Japanese patients with diabetes.

PEC-03-6

Application of Dialogue Tool-DAWNTM Effectively Enhanced Insulin Injection Rate and Improved Glycemic Control

Lan-Fen Lin¹, Wan-Ting Huang¹, Min-Yu Chen¹, Shu-Fen Lai², Shu-Mih Chen¹ and Neng-Chun Yu¹

¹Neng-Chun Diabetes Clinic, Taiwan; ²Department of Medical Education and Research, Lo-Hsu Foundation, Inc., Lotung Poh-Ai Hospital

AIMS/INTRODUCTION: The insulin injection rate of T2DM in Taiwan is low. This study aimed to explore the possibility of reducing barriers to effective treatment by increasing the rate of insulin injection and improve blood glucose control, using the Dialogue tool-DAWNTM.

METHODS: We conducted a prospective cross sectional study from October 1, 2011 to May 4, 2012. We enrolled type 2 diabetes who had HbA1c $\geq 7.5\%$ into two groups, insulin treated (I) and non- insulin treated (O). We analyzed the results of the Dialogue tool after 6 months. The primary end point was HbA1c and the second end points were to observe new insulin injection rate, creatinine, frequency of SMBG and cognitive differences.

RESULTS: A total of 129 cases enrolled, the average age was 58 ± 11 years old and male to female ratio was 51%:49%, duration of diabetes was 10 ± 6 years and the ratio of non-insulin treated to insulin treated patients was 68%:32%. HbA1c significantly from 8.7% to 8.2% ($P < 0.0001$), creatinine decreased significantly from 0.95 to 0.92 mg/dL ($P = 0.0093$), frequency of SMBG increased from 10.8 to 13.7 times/month ($P = 0.0621$). Cognition of insulin side effects, feelings of remorse, self-management ability and psychological injection obstacles improved 14.3%, 14%, 10.6% and 4.8% respectively.

CONCLUSION: This study demonstrated application of Dialogue tool effectively enhanced insulin injection rate and improve blood glucose control by strengthening HCP-patient communication and reducing the barriers to treatment.

KEYWORDS: DAWN, Barriers to Effective Therapy, A1C, Insulin Injection Rate, Self-Management

PEC-04-1

Diabetes Nurses' Perception of Barriers and Adherence of Patients on Insulin Therapy

Margaret Choy Wan Chan, Jasmine Shew, Pei Kwee Lim and Brenda Lim

Association of Diabetes Educators Singapore, Singapore

BACKGROUND: Intensive insulin therapy is effective in the treatment of patients with diabetes by slowing down the disease progression and preventing complications. However, the timely initiation and adherence to insulin therapy is often hindered and compromise the management of diabetes resulting in sub-optimal glycaemic control.

OBJECTIVES: To explore diabetes nurses' (DEs) perception on barriers and issues in adherence to insulin therapy faced by their patients with diabetes.

METHOD: A survey questionnaire was conducted from 28 April 2012 to 9 May 2012 amongst 51 DEs from Association of Diabetes Educators Singapore. A randomized convenient sampling obtained after the weekends education events. Data were analyzed using Microsoft Excel.

RESULTS: The three most commonly perceived reasons of the barriers were fear of needles, lack of family support and financial difficulty. Once insulin is initiated, DEs reported 65% patient adherence to daily injection, 90% reported patients omission of insulin dose. The frequency in missing insulin dose was about once to four times a month. The two main reasons for non-adherence to insulin therapy were due to inconvenience to bring insulin outdoor and forgetting to inject. One method suggested by DEs to increase the adherence to insulin therapy was to provide better user-friendly insulin delivery devices to accommodate patients' daily lifestyle.

CONCLUSION: The barriers and adherence to insulin therapy has been linked to the insulin delivery devices. DEs should continue to seek out innovative insulin delivery devices to assist their patients in adhering to daily injections to achieve optimal glycaemic control.

PEC-04-2

About the Effect of the Diabetes Classroom using the Hotel Lunch Buffet

Shigeko Inoue¹ and Akiko Nishimura²

¹Dietician, Nakatani-naika Clinic, Japan; ²Yamanashi-Pref. University

CONTEXT: As one of the diabetes classrooms of the diet cure, the patient receives cooking training with a menu of the appropriate quantity that a dietician prepared for. In the diabetes classroom of our clinic, I carried out the diabetes classrooms of 600 from 500 kcal with French food by the cooperation of the restaurant chef. But, I think that it is important that patients choose food and calculate energy which they eat. Therefore I tried the lesson using the hotel lunch buffet.

PURPOSE: I examined the effect of the diabetes classroom using the lunch buffet.

METHOD: The participants are the type 2 diabetes patients of our clinic, and their friends. They choose a dish among the lunch buffet of the hotel freely and, ahead of a meal, eat vegetables for 5 min.

They calculated the approximate amount of energy of the thing which they ate.

They did the SMBG measurement before and after a meal. The measuring instrument used an ultra one-touch view of J&J Co., Ltd.

RESULT AND CONCLUSION: The second classroom significantly increased the ratio of the participant who chose the proper quantity (1% of levels of significance). The patient who ate more than 1000 kcal noticed that he usually overate himself. There was the case that had lower blood glucose level than it which was usual after a meal. It is thought that they ate vegetables ahead of a meal for five minutes.

I think that this classroom is useful for the self-control of diabetes.

PEC-04-3

Assessing the Improvement of Insulin Injection Technique and Lipohypertrophy from Periodic Re-education and Injection Sites Inspection: A 2.5-year Evaluation

Shu-Mih Chen¹, Shu-Hua Feng¹, Yi-Hui Li¹, Min-Yu Chen¹, Amy Youhying Lin², Shu-Fen Lai³ and Neng-Chun Yu¹

¹Neng-Chun Diabetes Clinic, Taiwan; ²BD, Franklin Lakes, NJ, USA; ³Department of Medical Education and Research, Lo-Hsu Foundation, Inc., Lotung Poh-Ai Hospital

AIMS/INTRODUCTION: Despite current recommendation of annual examination on injection site, no literature described the effectiveness of implementing regular education on injection technique by HCP/certified diabetes educator (CDE) This study investigated the impact of inspect and regular health education strategy to reinforce proper injection techniques to improve patient outcomes.

METHODS: A prospective cross-sectional randomized survey study was conducted from 07/2009 to 01/2012 in patients with diabetes on any insulin injection regimen in diabetes clinic in Taiwan. Injection techniques and injection areas were inspected by CDE at every 3 months visit using evaluation form.

RESULTS: A total of 1417 patients was surveyed with 512, 487 and 418 patients in each annual examination, respectively. Demographics: 60.6 ± 16.0 years; 47.8% males; 92.7% T2DM; duration of diabetes: 15.6 ± 8.1 years; duration of injection: 5.6 ± 4.7 years. There was no significant difference in the demographics between the three groups. Improvement in all injection techniques was observed ($P < 0.0001$), except local injection site massage ($P = 0.3292$). Bleeding and bruising decreased significantly ($P < 0.0001$). Of each group, lipohypertrophy reduced from 30% to 19% and 11% ($P < 0.0001$). Pen needle users increased from 46% to 50% and 67%. No significant change in A1C, BMI, and injection frequency was observed.

CONCLUSION: This is the first study that showed the improvement of injection technique through periodic inspection and education by CDE and this appears related to reduction in lipohypertrophy.

KEYWORDS: Insulin Injection, A1C, Re-education and Inspection, Lipohypertrophy, Long-Term Evaluation

PEC-04-4

The Difference Depending on the Experience of Home Visiting Nurses in Difficulties and Educational Preferences of Diabetics Care

Kyoko Uchiumi¹, Mitsuko Ushikubo², Mitsue Iida³, Akemi Takagi⁴, Kaai Aso⁵ and Chie Isomi⁶

¹School of Nursing, Dokkyo Medical University, Japan; ²Faculty of Medicine, School of Health Science, Gunma University, Japan; ³School of Nursing, Gunma Prefectural College of Health Science, Japan; ⁴Out Patient Clinic, Maebashi Red Cross Hospital, Japan; ⁵Faculty of Medical Science School of Nursing, University of Fukui, Japan; ⁶School of Nursing, Kyoto Tachibana University, Japan

OBJECTIVE: The objective was to identify the difference depending on years of experience of home visiting nurses (hereafter HVNs) in difficulties and educational preferences of nursing to diabetics and their family.

METHODS: The research was conducted by Questionnaire survey by post. The data were included: attributes of subject; difficulty and educational preferences in 51 items of nursing to diabetics by HVNs.

RESULTS: One hundred and twenty-six responses were received (response rate: 65.9%). The years of experience of HVNs ranged from 2–216 months (median: 65 months).

In terms of difficulty in nursing to diabetics and their family, significant differences were observed in three items between HVNs with <1 year of experience and those with >1 year. Significant differences were identified in five items between HVNs with <4 years' experience and those with >4 years, and between those with <5 years' experience and those with >5 years. In terms of multiple comparison that was conducted by dividing HVNs' years of experience into seven groups, the group with 5 years' experience showed more items that indicated significant differences than the other groups.

As regards educational preferences, the most significant differences were identified between HVNs with <3 years' experience and those with >3 years. In terms of multiple comparison, significant differences were identified in the group with 4 years' experience between those 5 years' experience.

CONCLUSION: These results suggest we should be taken into consideration 5 years' experience in a HVNs' education program.

PEC-04-5

Cost-Effectiveness of School Based Self-Management Education among Patients with Type 2 Diabetes in China

Bo Xie¹, Min Jia², Chang-ping Ju², Jing Han², Hui Jin², Li-li Liu² and Zi-lin Sun²

¹Institute of Diabetes, Medical School, Southeast University, China; ²Institute of Diabetes, Medical School, Department of Endocrinology, Zhongda Hospital, Southeast University, China

OBJECTIVE: To assess the cost-effectiveness of a school based self-management education for ongoing intervention compared with usual care in patients with type 2 diabetes in China.

METHODS: We undertook a cost-utility analysis that used data from a 24 month, multicentre, randomized controlled trial and compared the effects of a school based self-management education (SBSME) ($n = 292$) and usual care ($n = 234$) on diabetes-related outcomes in eight hospitals in Jiang Su, China. SBSME uses a 20 h structured group education delivered in the school by a professional educator group and subsequent regular follow-up (website, telephones, short messages, etc) to provide surveillance, patient education. Main outcome measures were changes from baseline in: Incremental cost and quality-adjusted life-years (QALYs) derived from changes in scores on a Quality of Life for Diabetes Scale.

RESULTS: Compare to usual care, the intervention was associated with an annual increase of 0.024 in mean quality-adjusted life-years per patient and savings of RMB 39.66 in mean healthcare cost per patient respectively. There is no significant differences in final cost at endpoints between intervention and control group. The incremental cost effectiveness ratio was 5092.97 RMB. Results from sensitivity analysis suggest that the SBSME intervention is cost effective even under more modest assumptions.

CONCLUSION: Our results suggest that the SBSME intervention is likely to be cost effective compared with usual care. Because a considerable proportion of costs were fixed, cost-utility and cost-effectiveness estimates would likely be substantially improved in a scaled-up SBSME program.

KEYWORDS: Tye 2 diabetes; self-management; cost-effectiveness analysis; cost-utility analysis

PEC-04-6

The Lole of Family Nutritional Support in Japanese Patients with Diabetes Mellitus

Naomi Kitatani, Masahiro Iwasaki, Tomoko Tuji, Daisuke Yabe, Takanori Hyo, Koin Watanabe, Takeshi Kurose and Yutaka Seino

Division of Clinical Nutrition Kansai, Kansai Electric Power Hospital, Japan

AIMS: An important finding of the diabetes control and complications trial (DCCT), and UK Prospective Diabetes Study is self-care behavior as part of program of good blood control. Fisher et al. suggested that four groups of factors probably account for most of the variability in self-care in patients with diabetes over time: patient characteristics, the patients family, the practitioner and health system, and the community/work setting. Of these factors, characteristics of the patient's family, which is the primary social context of disease management, is the least investigated.

METHODS: Medical record data, which were recruited for analysis, if their HbA1c were constant for 6 months, and their changes were within 2%, were obtained from outpatients of Kansai Electric Power Hospital.

RESULTS: Among 125 participants 72 were male and 53 were female. Mean age was 65.0 ± 10.6 years, duration of diabetes was 13.5 ± 9.2 years, average HbA1c was $8.1 \pm 1.8\%$, average BMI was 24.4 ± 4.2 . The five items are as follows: No.1 Do you think diet therapy is essential for the treatment of diabetes? No.2 Are you on diabetic diet therapy? No. 3 Is there any person who support or advise your diabetic diet therapy? No.4 Who support your diet therapy? No.5 What kind of support do they do? Effect of family nutritional support on metabolic control in patients with type 2 diabetes. HbA1c 8.1%(N0), 7.5%(YES) HbA1c ($P < 0.01$).

CONCLUSIONS: Family nutritional support is significantly associated with metabolic outcome of diabetic patients. Self-care practices in disease management should be assessed on the family settings in the patients with type2 diabetes.

PEC-04-7

To Investigate the Factors Associated with Quality of Life and Psychological Distress Among People with Type 2 Diabetes Mellitus

Meng-Han Shih¹, Fu-Li Chen² and Kwang-Wen Chen³

¹Division of Endocrinology and Metabolism, Chang Gung Memorial Hospital, Taiwan;

²Department of Public Health, Fu Jen Catholic University, Taiwan; ³Department of

Internal Medicine, Saint Paul's Hospital, Taiwan

OBJECTIVE: To investigate the association factors linked to quality of life (QoL), and emotional status among people with type 2 diabetes.

METHODS: Adult people with type 2 diabetes were enrolled for demographic review and questionnaire studies with WHOQOL-BREF, the Center for Epidemiologic Studies Depression Scale (CES-D), and State-Trait Anxiety Inventory (STAI).

RESULTS: There were 258 subjects (132 M, 126 F) participated the study with age between 18 and 83 years (mean age 56.28 ± 14.55 years), and a mean duration of diabetes was 8.07 ± 6.83 years. There were 74 (28.7%) having insulin treatment and 165 (64%) overweight (BMI > 25). Mean HbA1c was $7.96 \pm 1.72\%$. The mean Score of QoL was 53.74 ± 8.83 , mean scale of CES-D 13.36 ± 9.60 and mean Score of STAI 37.07 ± 11.24 . QoL was associated with exercise habitus, income and marriage status. The major factors associated with scale of depression were sex (female), exercise habitus, and age; the major factors associated with score of anxiety were sex, exercise habitus, marriage, education, religion, and age. QoL and anxiety were not affected in patients with insulin treatment, but their score of physical condition and scale of depression were lower.

CONCLUSION: The factors influencing QoL and emotional status are complex, however healthier life style with regular exercise is important. Insulin treatment did not affect QoL and anxiety is shown in this study. Whereas the people on insulin treatment might have worse physical status and depression which should be more concerned.

PEC-05-1

Seasonal Variation in Hypoglycemia in Diabetics – Patient Education before Summer and Drug Adjustment until Autumn –

Kosuke Amano¹, Kumiko Natsume¹, Kana Kato¹, Taku Tsunekawa², Risako Watanabe², Minemori Watanabe² and Ataru Okumura²

¹Department of Clinical Laboratory, Okazaki City Hospital, Japan; ²Department of Endocrinology and Diabetes, Okazaki City Hospital, Japan

OBJECTIVE: Although it is already known that there is seasonal fluctuation in hypoglycemia, the causative factors of seasonality have not yet been identified.

The aim of this study is to clarify latent factors in seasonal variation contributing to hypoglycemia.

METHODS: We retrospectively studied consecutive 305 patients with hypoglycemia (<2.8 mmol/L) visiting our emergency room in a 650-bed district-wide hospital in 2009–2011. Among 220 of those patients with a history of diabetes, we investigated probable factors classified into the following, (1) dietary factors: little food intake, skipping of meal or accidental overdose of hypoglycemic agents, (2) physiological factors: inappropriate prescription of oral hypoglycemic agents in aged above 60 years in spite of lower eGFR (<60 mL/min/1.73 m²), 3) Others.

RESULTS: Seasonal variations were significant in dietary and physiological factors. The number of patients who had dietary factors was 10 in winter, 21 in spring, 29 in summer, and 27 in autumn. The number of patients who had physiological factors was 14 in winter, 12 in spring, five in summer, and seven in autumn. Hypoglycemia induced by dietary factors increased threefold in summer more than in winter, while physiological factors were prominent in winter. No seasonality was identified in age, gender and types of diabetes.

CONCLUSION: We concluded that dietary and physiological factors were two major factors driving the seasonal fluctuation in hypoglycemia for diabetics. Patient education before summer concerning meals and drug readjustment until autumn based on renal function might contribute to a reduction of hypoglycemia in countries with seasons.

PEC-05-2

Clinical Characteristics of Type 2 Diabetic Patients with Anti-Diabetic Drugs Induced Severe Hypoglycemia

Ming-Chao Lee¹, Shu-Hwa Hsiao², Ming-Yan Tsai³, Shu-Chun Hu¹ and Ta-Jen Wu¹

¹Department of Internal Medicine, National Cheng Kung University Hospital, Taiwan;

²Department of Pharmacy, National Cheng Kung University Hospital, Taiwan; ³Nursing Department, National Cheng Kung University Hospital, Taiwan

OBJECTIVE: To evaluate the risk factors associated with severe hypoglycemia (SH) in patients with type 2 diabetes mellitus (T2DM).

MATERIAL AND METHODS: One hundred forty-five T2DM patients with a confirmed diagnosis of anti-diabetic drug induced SH and 1450 matched T2DM patients without SH were included in a nested case-control study at a medical center during January 2009 to December 2011. Demographic and clinical variables were analyzed for Odds Ratio.

RESULTS: Between SH and control group, age (71.5 ± 10.6 years vs 62.0 ± 11.6 years; $P < 0.0001$), BMI (23.1 ± 5.0 vs 26.1 ± 4.1; $P < 0.0001$), eGFR (56 ± 43 vs 84 ± 27, $P < 0.0001$), and A1c (6.7 ± 1.4% vs 8.1 ± 1.6%; $P < 0.0001$) are significantly different. Among co-morbidities, CAD [OR 3.67 (2.35–5.73); $P < 0.0001$], CHF [OR 10.89 (5.74–20.7); $P < 0.0001$], dementia [OR 10.57 (5.32–21.0); $P < 0.0001$], Parkinsonism [OR 9.35 (3.55–24.63); $P < 0.0001$], CVA [OR 13.11 (7.44–23.09); $P < 0.0001$], hemodialysis [OR 9.53 (3.81–23.85); $P < 0.0001$], and chronic lung disease [OR 7.60 (3.31–17.43); $P < 0.0001$], cancers [OR 2.06 (1.19–3.56); $P < 0.05$] are all significant risk factors associated with SH. Binominal logistic model excluded Parkinsonism, hemodialysis, and cancers.

CONCLUSIONS: The presence of diabetic complications and other concurrent disease such as chronic lung disease or dementia increased risk of SH in T2DM patients. In addition to age, BMI, and glycemic control, educators should pay more attention to such concurrent disorders to reduce risk of SH.

PEC-05-3

Effectiveness of Carbohydrate Counting; Improved Glycemic Control of 78-year-old Patient with Recurrent Hypoglycemia

Shigemi Tamate¹ and Daisuke Matsuda²

¹Department of Nutrition, Higashi Yamato Hospital, Japan; ²Department of Diabetes Mellitus and Endocrine Diseases, Higashi Yamato Hospital, Japan

OBJECTIVE: Regardless of the insulin consolidation therapy, the patient was experiencing painful hypoglycemia and hyperglycemia cycle after total pancreatectomy and partial gastrectomy. She had limited volume of food intake and was hesitated to continue insulin consolidation therapy further.

Therefore, the purpose of our therapy was to relieve above symptoms by offering dietary advice using carbohydrate counting, given her family can fully support the proposed plan.

METHOD: As an initial consultation, we calculated her insulin-carbohydrate ratio using the meal records and associated blood glucose levels: 0.8 for breakfast, 0.6 for lunch and dinner, and necessary adjustment had been made in line with the past advice.

During the course of therapy it was observed that the patient was experiencing hypoglycemia more often after the breakfast. To improve this situation, we switched insulin detemir to insulin glargine, while insulin correction and a series of delicate adjustment had been contemplated through a volume of food intake.

RESULTS: Frequency of hypoglycemia symptom had been tremendously improved to the level that patient faces the situation only once a month.

CONCLUSION: Carbohydrate counting method is effective for aged diabetic patients with unstable dietary intake when instructions are accurately followed.

PEC-05-4

Hypoglycemia and Body Weight Issues: Enlightenment from Taiwan Subgroup Analysis of Real-Life Effectiveness and Care Patterns of Diabetes Management (RECAP-DM) Study

Chih-Yuan Wang¹, Ching-Ling Lin², Tien-Shiang Huang¹, Ming-Nan Chien³, Sheng-Hwu Hsieh⁵, Yu-Yao Huang⁶, Kuang-Chung Shih⁷, Shih-Te Tu⁸, Chwen-Tzuei Chang⁹, Chien-Ning Huang¹⁰, Chien-Wen Chou¹¹, Ta-Jen Wu¹², Rue-Tsuan Liu¹³, Hing-Chung Lam¹⁴, Ching-Fai Kwok¹⁵, Chen-Chun Fu¹⁶ and Wayne H.-H. Sheu¹⁷

¹Department of Internal Medicine, National Taiwan University Hospital, Taiwan;

²Department of Internal Medicine, Cathay General Hospital, Taipei, Taiwan;

³Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan; ⁴Division of Endocrinology and Metabolism, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan; ⁵Department of Internal Medicine, Chung-Gang Memorial Hospital, Lin-Ko, Taiwan; ⁶Department of Internal Medicine, Taipei Veteran General Hospital, Taipei, Taiwan; ⁷Department of Internal Medicine, Chung-Hua Christian Hospital, Chung-Hua, Taiwan; ⁸Department of Internal Medicine, China Medical Hospital, Taichung, Taiwan; ⁹Department of Internal Medicine, Chung-Shan Medical University Hospital, Taichung, Taiwan; ¹⁰Department of Internal Medicine, Chi-Mei General Hospital, Tainan, Taiwan; ¹¹Department of Internal Medicine, Cheng-Kung University Hospital, Tainan, Taiwan; ¹²Department of Internal Medicine, Chung-Gang Memorial Hospital, Kaohsiung, Taiwan; ¹³Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; ¹⁴Division of Endocrinology and Metabolism, Department of Internal Medicine, Taipei Veteran General Hospital; ¹⁵Department of Internal Medicine, Tzu-Chi General Hospital, Hua-Lien, Taiwan; ¹⁶Department of Internal Medicine, Taichung Veteran General Hospital, Taichung, Taiwan

Type 2 diabetes mellitus is an important issue globally. Dysglycemic control usually resulted in chronic cardiovascular, cerebrovascular and nephropathic complications. Improving control in HbA1c level below 7% in order to minimize the risk of developing complications is strongly recommended by standard medical care in American Diabetes Association. Meanwhile, hypoglycemia together with body weight gain is recognized as the most important barriers in adequate control of type 2 diabetes mellitus. Hypoglycemia can manifest symptoms of varying degrees of severity, and obesity due to body weight gain after therapeutic intervention may play the pivotal role in motivation of glycemic control. The association of obesity/hypoglycemia and cardiovascular morbidity/mortality has been widely discussed in recent years. Here, we present a post-hoc Taiwan subgroup analysis of these data collected in the RECAP-DM study to indicate that we need to pay more attention and concern on body weight gain and hypoglycemia for type 2 diabetes in Taiwan. In this study, we found no significant difference was observed in treatment-related satisfaction between Taiwanese patients in the issue of body weight gain and hypoglycemia. On the other hand, we found statistically significant correlation of HOMA-% and HOMA-IR between different levels of weight gain (<5, 5–9, 9–

15, and >15 kg). We found more attention to such issue in weight change and hypoglycemia should be concerned in type 2 diabetic patients. Future interventions and therapeutic options should emphasize the probable patients' unawareness or neglect on the issues of body weight gain and hypoglycemia.

PEC-05-5

Nearly 70% of Japanese Type 2 Diabetes Patients on Insulin Analogues Report Hypoglycaemia, Causing Missed Doses and Significant Concerns

Yoshihito Atsumi¹, Meryl Brod², Anthony Barnett³ and Mark Peyrot⁴

¹Saiseikai Diabetes Center, Saiseikai Central Hospital, Tokyo, Japan; ²The Brod Group, Mill Valley, CA, USA; ³Heart of England NHS Foundation Trust and University of Birmingham, Birmingham, UK; ⁴Loyola University Maryland, Baltimore, MD, USA

OBJECTIVES: To understand the impact of self-treated hypoglycemia (hypo) in a country where insulin analogue (IA) treatment is widely initiated at diagnosis of type 2 diabetes (T2DM), Japanese patients and diabetes prescribers were included in a global online survey (GAPP2TM).

METHODS: Japanese responses from 355 T2DM IA patients and 222 prescribers were compared with 2687 patients and 1000 prescribers from other GAPP2TM countries (US, Canada, UK, Germany, Denmark).

RESULTS: Significantly fewer Japanese patients reported hypos than GAPP2 patients (ever: 69% vs 82%; last 30 days: 27% vs 37%), and significantly fewer recent events were nocturnal (14% vs 26%). Significantly more Japanese patients worried about hypos, especially when driving (55% vs 38%) and working (40% vs 26%). Conversely, Japanese prescribers reported relatively low patient worry about hypos (driving 9.2%; work 11.5%), similar to GAPP2 prescribers.

In response to hypos, Japanese patients were more likely than GAPP2 patients to have missed (11% vs 8%) a basal insulin (BI) dose and significantly less likely to have reduced (6% vs 13%) a BI dose or increased their glucose monitoring (28% vs 47%).

Japanese prescribers described significantly lower levels of patient under-reporting of hypo frequency (17.1% vs 34.8%) and severity (15.3% vs 28.3%) than GAPP2 prescribers. Fifty-six percent of Japanese prescribers reported contact at least once a month by IA patients after hypos.

CONCLUSIONS: Japanese patients report lower overall hypo rates, which may reflect local clinician HbA1c target-setting. Additional guidance from physicians on managing hypoglycaemia may reduce patient worry and inappropriate missed doses of BI post-event.

PEC-06-1

Insulin Adherence Behaviors and Barriers in Japanese Population Based on the Global Attitudes of Patients and Physicians in Insulin Therapy Study

Shin-ichi Harashima and Nobuya Inagaki

Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

OBJECTIVE: We evaluated Japanese patient and physician beliefs regarding insulin therapy by analyzing data from Global Attitudes of Patients and Physicians in Insulin Therapy (GAPP) survey.

METHODS: Of the 1250 physicians and 1530 diabetes patients from eight countries who participated in the GAPP survey, 100 Japanese physicians (50 specialists, 50 primary care physicians) and 150 Japanese diabetes patients (15 type 1, 135 type 2) were included in the present sub-analysis. The survey was conducted via a web-based interview for physicians and via a computer-assisted telephone interview for patients.

RESULTS: Sub-analysis showed that 44% of Japanese patients missed their insulin doses or did not take their insulin as prescribed; this percentage was higher than the global average of 35%. The main reason for poor adherence was related to difficulty in scheduling (e.g. too busy, travelling, etc.). Further, the fact that 67% of the patients experienced hypoglycemic symptoms during the past year suggested that concern or fear of hypoglycemia may pose barriers to the timely introduction of insulin therapy and adequate blood glucose control. Many patients and physicians were of the opinion that the current regimens of insulin therapy did not fit into the dynamic lifestyle of the patients.

CONCLUSION: The present analysis indicated that a significant proportion of Japanese diabetes patients receiving insulin therapy missed their insulin doses or did not take their insulin as prescribed. More flexible regimens of insulin therapy that can reduce the risk of hypoglycemia and are less likely to affect the lifestyle of patients are warranted.

PEC-06-2

Quality of Life in Adolescents with Type 1 Diabetes and Relationship to Some Psychosocial Factors

Adel Eladi¹ and Hoda Atwa²

¹Special Education, Postgraduate Collage, Arabian Gulf University, Bahrain; ²Pediatrics, Faculty of Medicine, Suez Canal University, Egypt

BACKGROUND: Treatment of type1 diabetes often disrupts a child's usual activities, requires disease focused behaviors from child and family.

AIM: To assess quality of life in children with T1D and their family.

SUBJECTS AND METHODS: Eighty children with type1 diabetes and their family were included. Quality of life was assessed by PedsQL Diabetes care profile an instrument that assesses psychosocial factors related to diabetes was used.

RESULTS: The child with T1D perception of QOL was higher than parent perception. The mean total score of PedsQL was (69.5 ± 10.3 and 67.2 ± 8.6) respectively. The child with T1D QOL was lower than their sibling (69.5 ± 10.3 and 73 ± 2.5). Parent QOL was lowest among family (66.5 ± 3.7). Good metabolic control was associated with better QOL. Diabetic children with high QOL had higher mother education, better diet adherence, understanding management practice and lower self monitoring of blood glucose barriers. Higher mother education and lower hypoglycemic or DKA attacks were good predictor of high QOL in Sibling of diabetic children.

CONCLUSION: Diabetes disrupts QOL of children with T1D and their family.

PEC-06-3

Knowledge and Attitudes Associated with Self Care Practices among Chinese Type 2 Diabetics: A Systematic Review

Qilin Liu, Martin Chi Sang Wong and Harry Haoxiang Wang

Division of Family Medicine and Primary Health Care, Chinese University of Hong Kong / The Jockey Club School of Public Health and Primary Care, Hong Kong

OBJECTIVE: To assess and summarize evidence and gaps in literature regarding diabetes self care in China with focus on Knowledge, Attitudes and Practices (KAP).

METHODS: Using knowledge, attitude, practice, diabetes and Chinese as key words, self care as subheading, all articles were obtained from PubMed, Embase, MEDLINE and EBSCO databases from January 2000 to May 2012. Articles identified were further selected based on pre-determined criteria, including study design, subjects' characteristics, issued year, language and outcome measurements.

RESULTS: Among 19 recruited articles, most (16) were non-experimental descriptive studies, seven were of cross-sectional design with appropriate sample size. Only three were randomized control trials with follow-up period longer than 3 months. Four common major variables influencing diabetes control were addressed, namely demographic information (4), diabetes related knowledge (12), attitudes towards treatments (19) and skills to self management (8). Other variables indentified were perceived social support, language preference and self efficacy. Summarizing all these findings, Chinese patients had limited knowledge of diabetes self care, believing dietary control and regular exercise but unable to stick to these lifestyle measures. For medication treatments, attitudes, especially Chinese health belief, as well as fare and worry, towards therapeutic effectiveness and side effects significantly influenced self care practice.

CONCLUSION: KAP serve as important predictors to evaluate diabetes control, while among Chinese patents, patients' health belief and self efficacy towards effectiveness of treatments were directly correlated with optimal diabetes control. Future studies need investigating functional characteristics of social support and provider-patients communication along with diabetes management in China.

PEC-06-4

Impact of Cultural Views of Self and Perceived Emotional Support on Diabetes Self-Care

Kaori Ikeda¹, Shimpei Fujimoto², Yukiko Uchida³, Shiho Takahara¹, Andrew Carroll⁴, Beth Morling⁴ and Nobuya Inagaki¹

¹Department of Diabetes and Clinical Nutrition, Kyoto University, Japan; ²Department of Endocrinology, Metabolism, and Nephrology, Kochi Medical School, Kochi University, Japan; ³Kokoro Research Center, Kyoto University, Japan; ⁴Department of Psychology, University of Delaware, USA

In diabetes self-care, cultural aspect is important. From the perspective of social and cultural psychology, people's identities, including cultural identities

affect their behaviors and emotions. In the European-American cultural contexts, independent views of self are predominant and one's behavior is attributable to one's own intention and ability. In Asian cultural contexts, interdependent views of self are predominant and behavior is framed in terms of contexts and social relationships. In addition, perceived emotional support (PES) was demonstrated to be more effective in interdependent Asian cultures than in independent Euro-American cultures. Thus, we performed two studies to elucidate influence of Asians' interdependence on their diabetes self-care activity. In study 1, we compared impact of interdependence on diabetes related distress and adherence to self-care activity between Japanese (JP) and American (US) patients with type 2 diabetes. In study 2, we examined association between self-care strategy and HbA1c in JP. One hundred and fifty-one JP were enrolled in Kyoto University hospital and 41 US in Cristiana Care Health System (Delaware). Age and HbA1c (mean $\pm$ SD) were 61 ± 9 years and $7.6 \pm 1.1\%$ in JP, and 58 ± 10 years and $7.6 \pm 1.7\%$ in US, respectively. In JP, higher interdependence and lower PES independently predicted higher distress, and higher PES and higher self-efficacy predicted higher adherence. PES was stronger predictor of adherence in JP than in US. Of the three self-care strategies (control situations; adjust oneself to situations; receive willing support from people around), adjusting oneself to situations and receiving willing support were associated with better HbA1c in JP.

PEC-06-5

Self-Efficacy, Self-Management Behaviors, Knowledge and Quality of Life in Adults with Type 2 Diabetes Mellitus

Min Jia¹, Bo Xie², Chang-ping Ju², Jing Han², Hui Jin³, Li-li Liu² and Zi-lin Sun²

¹Department of Endocrinology, Southeast University, China; ²Institute of Diabetes, Medical School, Department of Endocrinology, Zhongda Hospital, Southeast University, China;

OBJECTIVE: The objective was to evaluate the relationships between diabetes management self-efficacy, diabetes self-management behaviors, the knowledge of diabetes and the quality of life (QoL).

METHODS: A total of 391 subjects with type 2 diabetes were invited to participate in the study during their regular visits to outpatient clinics. Diabetes management self-efficacy, diabetes self-management behaviors, knowledge of diabetes and QoL were all evaluated by corresponding specific scales. The quality of life was also analyzed from five dimensions: disease impact, physiology impact, psychological impact, social role and health satisfaction. Demographic and clinical data were collected at the same time.

RESULTS: Overall, respondents reported a moderate to low quality of life. Multiple regression analyses revealed that self-efficacy, knowledge, self-management behaviors, duration of diabetes were more significant after adjustment for other factors. Among them self-efficacy was the most important one to the total score as well as to the five dimensions. Self-efficacy and knowledge predicted better QoL, while self-management behavior was a predictor for poor QoL, and among these behaviors, blood sugar testing affect most. Even if the number of diabetes complications did not affect QoL much, subjects with complications of neuropathy, foot, or cerebrovascular disease reported lower QoL.

CONCLUSION: Knowing more about diabetes and getting better self-efficacy help patients with type 2 diabetes achieve higher quality of life. Concerning too much about the disease and strictly controlling their behaviors could decline the quality of life, and finding the balance between them may be the work we should do in the future.

PEC-06-6

The Common Characteristics of Daily Life Pattern on Poor Control Days between Type 1 and Type 2 Diabetic Patients

Shu Chun Chien¹, Nobue Nakamura², Wazumi Yoshiko¹ and Kumiko Kuroda¹

¹Center for Education and Research in Nursing Practice, Graduate School of Nursing, Chiba University, Japan; ²Maternal and Child Nursing Division of Child Nursing

OBJECTIVE: The purpose of this study is to identify what kind of life patterns induce poor control days of both Type 1 and Type 2 patients.

METHODS: Participants included one Type 1 and one Type 2 patient. Three IT instruments were utilized to collect patients' daily life data. They included: Glucose meter, digital camera for recording meals and a pedometer called Lifecoder for monitoring exercise. Using Lifecoder, the total steps walked and the amount of calories burned from exercise could be collected. Based on the graphs activities, participants' daily rhythm could be predicted.

The data of IT instruments was delivered to a researcher every month for over 6 months. The researcher interviewed the participants to clear up any questions and to discuss their lives over the past month. All data was assessed on a daily basis for 6 months. Analysis was focused on poor control days.

RESULTS: A common characteristic showed that for both Type 1 and Type 2 patient, night exercise was greater than daytime exercise despite the distance walked being more than 10,000 steps and calories from meals had not changed remarkably. That means the daily rhythm was disturbed in poor control days that affects the action of insulin.

CONCLUSION: Blood sugar is the result of daily activities and it also influences subsequent activities. Analysis of the relationship between daily life pattern and blood sugar levels is helpful in identifying the real problems for both Type 1 and Type 2 patients.

PEC-07-1

Evaluation of a Novel Glucose Area Under the Curve (AUC) Monitoring System: Comparison to AUC Measured by CGM

Satoshi Ugi¹, Katsutaro Morino¹, Yoshihiko Nishio², Kazuhiro Ikeda¹, Osamu Sekine¹, Takeshi Yoshizaki¹, Toshiyuki Sato³, Seiki Okada³, Yasuo Kikkawa³, Toshihiro Watanabe³, Samiko Hosoya³, Hiromu Nakajima⁴, Atsunori Kashiwagi¹ and Hiroshi Maegawa¹

¹Department of Medicine, Shiga University of Medical Science, Japan; ²Graduate School of Medical and Dental Sciences, Kagoshima University, Japan; ³Sysmex Corporation, Japan; ⁴Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan

AIM: We have newly developed the monitoring system for glucose area under the curve (AUC) using minimally invasive interstitial fluid extraction technology (MIET), which enables us to perceive the complete glucose excursion as the area measured without blood sampling. In this study, we compared glucose AUCs measured using MIET with those measured by CGM for 2-8 h.

METHODS: Twenty diabetic patients underwent CGM (CGMS-Gold, Medtronic) and were simultaneously measured glucose AUC using MIET. MIET consists of the following two steps. First, a plastic microneedle array is applied to the skin of the forearm as the pretreatment to enhance transdermal interstitial fluid glucose (IG) extraction. Second, a hydrogel patch is placed on the pretreated area to accumulate IG for a predefined period. Hydrogel patches were replaced by new ones every 2 or 4 h for 8 h. After the extraction of IG, accumulated glucose levels in the hydrogel patches were measured to predict IG-AUC. Extracted sodium ion levels were simultaneously measured for the calibration.

RESULTS: Predicted AUC using MIET correlated well with that using CGM ($r = 0.93$) over a wide AUC range for 8 h. The enhanced extraction rate of IG after pretreatment was stable for 8 h. The painless nature of the technique was confirmed by responses of patients to questionnaires.

CONCLUSION: We confirmed that extracted IG using MIET correlated well with the IG measured by CGM for 8 h. This glucose AUC monitoring system can be applied to the management of postprandial glycemic control without blood sampling.

PEC-07-2

Clinical Implication of 1,5-Anhydroglucitol as a Marker for Assessment of Short-Term Changes in Glycemic Variability of Type 1 Diabetes

Hannah Seok, Hyun Min Kim, Sun-Ok Song, Ji Hye Huh, Byung-Wan Lee, Eun Seok Kang, Hyun Chul Lee and Bong Soo Cha
Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine, Korea

OBJECTIVE: Glycemic variability of type 1 diabetes is usually more severe than type 2 diabetes. However, serum marker for glycemic variability has not been established. The aim of this study was to demonstrate the usefulness of 1,5-anhydroglucitol (1,5-AG) as a marker reflecting short-term changes in glycemic variability of type 1 diabetes.

METHODS: Fourteen patients with type 1 diabetes treated by multiple insulin injections (MDI) or continuous subcutaneous insulin infusion (CSII) were enrolled. For evaluation of glycemic variability, continuous glucose monitoring system (CGMS) was applied for 72 h. Based on the results of CGMS, insulin dose adjustment was done for 2 weeks, and CGMS was repeated thereafter. The changes of serum glycemic markers including 1,5-AG, HbA1c and glycated albumin were also evaluated.

RESULTS: The change of 1,5-AG level was significantly correlated with the changes of mean postmeal maximum glucose (MPMG) and lability index (LI) ($r = -0.578$ and -0.596 ; all $P < 0.05$). And the changes of 1,5-AG showed a trend towards correlation with the changes of continuous overlapping net glycemic action with 1 h time (CONGA-1), mean amplitude of glucose excursions (MAGE) and the area under the curve for glucose above 180 mg/dL (AUC-180) ($r = -0.532$, -0.530 and -0.490 ; $P = 0.050$, 0.051 and 0.075 , respectively). The change of glycated albumin was correlated with only change of AUC-180. And the change of HbA1c did not show any correlation with the changes of CGMS variables.

CONCLUSION: 1,5-AG could be a valuable marker for assessment of short-term changes in glycemic variability of type 1 diabetes.

PEC-07-3

The Effect of Color-Indicated Self-Monitoring of Blood Glucose (SMBG) on Glycemic Control in Type 2 Diabetes Patients

Akiko Nishimura¹, Ikumi Honda¹, Shinichi Harashima², Yoshiyuki Shimizu¹, Norio Harada², Kazuaki Nagashima², Yoshihito Fujita², Shunsuke Yamane², Akihiro Hamasaki², Daisuke Tanaka², Masahito Ogura², Kiminori Hosoda¹ and Nobuya Inagaki²

¹Department of Human Health Science, Graduate School of Medicine, Kyoto University, Japan; ²Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Japan

OBJECTIVE: Color is known to directly affect emotions, feelings and behaviors in humans. It produces different cognitive learning motivations; Red produces avoidance motivation and blue produces approach motivation. Thus, we conducted a clinical research study to determine the effect of color on glycemic control and the value of color indicator on SMBG in type 2 diabetes patients.

METHODS: The study is a prospective, 24-week, single center, 2×2 factorial randomized comparison study to evaluate the efficacy of color-indicated SMBG on glycemic control in insulin- or GLP-1 receptor agonists-treated type 2 diabetes. Outpatients of Kyoto University hospital were recruited and randomized into four groups; no color indication and no color record, color indication and no color record, no color indication and color record, and color indication and color record. OneTouch^(R) UltraVueTM was used; Red or blue was displayed on the meter or marked on self-monitoring note when blood glucose (BG) is over 160 or <70 mg/dL, respectively. The primary endpoint was change in HbA1c in 24-week. The secondary endpoints were dropout rate, treatment change, and improvement in self-management. Subjects answered the questionnaire about self-management performance at 0-, 4-, 12- and 24-week. The study protocol was approved by the Institutional Review Board of Kyoto University Hospital, and registered on University hospital Medical Information Network in Japan (UMIN00003589). Written informed consent was obtained from all subjects.

RESULTS AND CONCLUSIONS: We present the study protocol and the progress of the study. We also show the results of self-management performance at the entry.

PEC-07-4

SMBG Associated with High Glycemic Goal and Low Adverse Events in Discharged Patients with Insulin Therapy

Jhao-Kun Liou¹, Tzu-Fan Huang², Jhao-Kun Liou¹, Yi-Ping Chen¹, Ching-Hui Chen¹, Pei-Jhen Liang¹, Li-Jung Cheng¹, Ching-Wen Wu¹, Shih-Te Tu³ and Ming-Chia Hsieh³
¹Health Management System Development and Telecare Center, Changhua Christian Hospital, Taiwan; ²Changhua Christian Hospital Diabetes Education Center, Changhua, Taiwan; ³Changhua Christian Hospital Endocrine and Metabolism Department, Changhua, Taiwan

BACKGROUND AND PURPOSE: Self monitoring blood glucose (SMBG) is an important component of modern therapy for type 2 DM patients with insulin therapy. But until now, not any important research to investigate the role of discharge patients with insulin therapy using SMBG.

METHODS: We collected 199 discharged patients with insulin therapy and diabetes education in Changhua Christian Hospital from March 2011 to April 2012. To isolate two groups with using SMBG or not. Therefore, characters, A1C of admission and discharged, the occurrence of severe hypoglycemia in emergency and re-hospitalization were investigated through electronic chart review.

RESULT: In this retrospect study, participants incidence were 3.3 years, male and female were 49% and 51%, occurrence of DKA and HHNK hospitalized

proportion were 3% and 6%. Survey on discharge patients ($n = 100$, 51%) had use glucose meter. We found two groups using SMBG or not that HbA1C were reduce 4.3 ± 2.7 and 1.8 ± 2.2 (respectively, $P < 0.001$), HbA1C $<7.0\%$ were 61% and 10.1% (respectively, $P < 0.001$), discharge patients re-entering the emergency were 2 and 0 times and admission again were 25 and 10 patients, respectively.

CONCLUSION: In our founding, SMBG associated with high glycemic goal and low adverse events in discharged patients with insulin therapy. We expected more participants to include this study and observe during a long time.

PEC-07-5

Self-Monitoring of Blood Glucose (SMBG) Improves Glycemic Control in Oral Hypoglycemic Agents (OHA)-Treated Type 2 Diabetes (SMBG-OHA Study)

Shin-ichi Harashima, Toru Fukushima, Masahito Ogura, Shunsuke Yamane, Daisuke Tanaka, Norio Harada, Akihiro Hamasaki, Yoshito Fujita, Kazuaki Nagashima, Kentaro Toyoda and Nobuya Inagaki

Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, Kyoto, Japan

BACKGROUND: We conducted a clinical research study to determine the effect of SMBG on glycemic control and the value of a putatively less painful blood sampling technique on SMBG in OHA-treated type 2 diabetes (T2D) patients because SMBG was not broadly applied in non-insulin-treated patients in Japan.

METHODS: One hundred thirty-seven subjects were recruited for the 24-week, prospective, comparison study and randomized into three groups: 46, no SMBG group; 46, fingertip group; and 45, palm group. The primary endpoint was change in HbA1c. The secondary endpoints were SMBG compliance, dropout rate, treatment changes, and patient's and physician's satisfaction.

RESULTS: Six subjects in fingertip group (13.2%) and one subject in palm group (2.2%) were dropped because of pain. A1C level of all subjects at 24-week was decreased more in fingertip (-0.23%) and palm group (-0.16%) than that in no SMBG group ($+0.31\%$) ($P < 0.05$). SMBG compliance was higher in fingertip group (2.17 times/day) than that in palm group (1.65 times/day) ($P < 0.05$). A1C level of treatment-unchanged subjects was decreased more in fingertip (-0.25%) and palm group (-0.21%) than that in no SMBG group ($+0.30\%$) ($P < 0.05$). SMBG compliance was higher in fingertip group (2.24 times/day) than that in palm group (1.65 times/day) ($P < 0.05$). Patient's questionnaire showed that 84.1% of fingertip group and 90.2% of palm group were satisfied with SMBG. Physician's satisfaction was higher in palm group (94.0%) than that in fingertip group (80.0%) ($P < 0.05$).

CONCLUSION: SMBG is beneficial for glycemic control and palm blood sampling is a useful procedure for OHA-treated T2D.

PEC-07-6

Emotional Change of Patients after Switching to Continuous Subcutaneous Insulin Injection

Noriko Nakayama¹, Yoshiyuki Hamamoto², Shinji Sato³, Hisato Tatsuoka², Kanta Fujimoto², Yoshiharu Wada², Atsuko Matsuoka², Hiroki Ikeda⁴, Yukiko Kawasaki², Sachiko Honjo² and Hiroyuki Koshiyama²

¹Nursing Department, Kitano Hospital, Japan; ²Center of Diabetes and Endocrinology, Kitano Hospital, Japan; ³Osaka Sangyo University, Japan; ⁴The Seimeikai Ikeda Hospital, Japan

BACKGROUND: We investigated the change in the emotional distress of patient, specific to diabetes after switching the insulin therapy from multiple daily injections (MDI) to continuous subcutaneous insulin infusion (CSII).

METHODS: The study included a total of consecutive six patients who changed their insulin therapy from MDI to CSII during April 2010 to September 2011 in our institute. The Problem Areas in Diabetes (PAID) questionnaire were performed before and 3 months after switching to CSII.

RESULTS: Mean age was 42.8 ± 6.2 years (five female and one male), and the mean period of MDI was 17.3 ± 8.3 years. After CSII, the mean HbA1c was decreased from 7.2% to 6.6%, and the mean score of PAID was changed from 57.8 to 39.0 points. Although 'Taking up too much of mental and physical energy' score did not change (3.0–3.0 points), all other 19 categories showed a reduction. In particular, 'Worrying about the possibility of complications' score showed a decrease from 3.8 to 3.0 points ($P = 0.059$).

DISCUSSION: The 'user-friendliness' of CSII may improve patient's feeling by making them feel free about the timing of insulin injection in relation to meal. Our results suggest that change of insulin therapy from MDI to CSII does not affect the mental and physical energy spent because of diabetes, but the anxiety about its complications and the melancholy due to living with diabetes may be decreased.

PEC-07-7

SEBIA Quantitative HbA1c Capillary Electrophoresis Instrument: A new instrument for monitoring diabetes control

Paul Frank Williams^{1,2} and Kim Lee²

¹Discipline of Medicine, University of Sydney, Australia; ²Department of Endocrinology, Royal Prince Alfred Hospital, Australia

Monitoring HbA1c requires tight CV's, BioRad HPLC has previously been the only method that reported variant haemoglobins. SEBIA launched a capillary electrophoresis method for HbA1c that also reported variants, and in this study we compared the SEBIA Capillarys and BioRad Variant II Nu.

Over 120 samples the concordance correlation coefficient was 0.996, Pearson Precision Coefficient of 0.997 and a bias correction factor of 0.999, demonstrating the strong agreement between the two methods. Individual capillaries had CV's between 0.69% and 1.7% (*N* = 16). Inter assay variation was between 0.45% and 1.34% (*N*-16) and Intra assay variation between 0.86% and 1.6% (*N* = 16).

HbA1c was linear over 5-fold dilution of haemoglobin (Hb). Labile, carbamylated HbA1c, or bilirubin did not interfere with HbA1c. Output showed major Hb variants and the analysis software flagged abnormal profiles. The instrument has both NGSP and IFCC certification.

We thank Diagnostic Solutions for providing the instrument and the reagents.

Interassay variation

Variant II	N = 12	SEBIA	N = 128 (8x16) ±
Mean ± SD	CV %	Mean ± SD	CV %
5.49 ± 0.07	0.01	5.49 ± 0.04	0.79
6.02 ± 0.09	0.014	8.52 ± 0.11	1.34
9.77 ± 0.16	1.63	5.97 ± 0.03	0.45
11.98 ± 0.13	1.08	8.2 ± 0.05	0.61

PEC-08-1

Role of Diabetes Nurses in Post-Discharge Stabilization of Patients Admitted for Uncontrolled Diabetes Mellitus

SCV Hung, AYY Ho, ST Chiu, HF Ng, CK Cheung, MF Chow and CCK Woo

New Territories West (NTW) Diabetes Centre, Department of Geriatrics and Medicine, Pok Oi Hospital, Hong Kong

INTRODUCTION: Uncontrolled diabetes mellitus is a common reason of hospitalizations in which patients were frequently started with insulin therapy. However, insulin requirement can change rapidly after discharge. Diabetes nurses play important roles in filling the gap between discharge and first medical clinic visit.

OBJECTIVE: To evaluate the outcomes of nurse-led service for patients discharged from hospitalization due to uncontrolled diabetes.

METHOD: We recruited 87 consecutive patients admitted to medical wards for uncontrolled diabetes from October 2010 to October 2011. After discharge, diabetic nurses followed them in structured nurse clinics with telephone consultations in between. Weekly case conferences were held with endocrinologists to discuss the progress.

RESULT: There were 30 female and 57 male (mean age 58.5 ± 16.4) in this cohort, 61 of them were known diabetics. Mean duration of diabetes was 12.3 ± 7.4 years with 61% had diabetic complications. Eighty-six patients were discharged on insulin. The average length of stay was 4.5 days. Overall, the mean number of tele-consultations and nurse clinic visits per patient were 2.1 and 2, respectively. Insulin dosages were adjusted in 53 patients (27 within 2 weeks of discharge). Mean haemoglobin A1c before and after hospitalizations were 12.0 ± 2.9% and 8.6 ± 2.3% (Paired *t*-test,

P < 0.0001). Number of 28-day readmissions was 9, two of which were related to glycaemic control.

CONCLUSION: Diabetes nurses, supported by endocrinologists, play important roles in managing patients discharged for uncontrolled diabetes. The current model was safe and effective.

PEC-08-2

The Issues of Self-Improvement: A Comparison of Diabetes Care Nurses Practical Abilities Self-Assessments for Each Qualification

Natsuko Seto¹, Kazuya Taira¹, Soshiro Ogata¹, Hidetoki Ishii², Mizuyo Okura¹, Yasuko Shimizu¹ and Harue Masaki³

¹Graduate School of Medicine, Osaka University, Japan; ²Graduate School of Education and Human Development, Nagoya University, Japan; ³Graduate School of Nursing, Chiba University, Japan

PURPOSE: This study compares diabetes nursing practical abilities self-assessments for each qualification to gain insight into the issue of self-improvement.

METHODS: (1) Diabetes certified nurses (DCN) and all nursing staff of the hospital ward with the most patients hospitalized for the treatment of diabetes were subject to an anonymous self-administered survey by mail. (2) The nine factors revealed through reliability and validity tests of data obtained from 1056 people working as diabetes nurses were analyzed by one-way ANOVA to compare self-assessment of nursing practical abilities for each of the following qualifications: DCN, certified diabetes educators of Japan (CDEJ), and local certified diabetes educators of Japan (LCDE). Furthermore this study was conducted with the approval of the ethics committees.

RESULTS: (1) Results were significantly higher (*P* < 0.05) in order of LCDE < CDEJ < DCN for the following six factors: Specialized nursing using the nursing process, Specialty of nursing as a component of the health professional team, Confidence in ability to practice by self-study, Patient outcome after nursing assistance, Staff education based on expertise and skills (2) DCN was significantly higher than CDEJ and LCDE (*P* < 0.05), and although CDEJ was higher than LCDE there was no significant difference between the two, with regards to the following three factors: Specialty through activities inside and outside the institution, Development of staff by education, Strategy to attain an activity environment based on the evaluation.

CONCLUSION: From these results we gained an insight into the issues of self-improvement for each qualification in terms of diabetes nursing practical abilities.

PEC-08-3

Establishment of a Structured Education Program for Women with Gestational Diabetes

Huang-Chun Yeh¹, Kwang-Wen Chen² and Ching-Ju Wang¹

¹Department of Nursing, Saint Paul's Hospital, Taiwan; ²Department of Internal Medicine, Saint Paul's Hospital, Taiwan

OBJECTIVE: Diabetes education and nutritional counseling are necessary for every woman with GDM, however not well provided in clinical practice in Taiwan. We develop a structured education program for women with GDM and compare it with usual care.

METHODS: Women with GDM were approximately 3:1 randomized assigned to receive either a structured education program including designed follow-up schedule, education curriculum, and laboratory check-up or usual prenatal care.

RESULTS: Fourteen women with a structured education program (Gr A) and five women with usual prenatal care (Gr B) were enrolled and compared. Better knowledge and healthier behavior change were shown in questionnaire studies in Gr A than Gr B. Laboratory data including AC sugar, HbA1C and lipids profile including total cholesterol, LDL-C, HDL-C, triglyceride were not significantly different in both group. Macrosomia (>4000 g) were found 1 (7.1%) in Gr A and 1 (20%) in Gr B with no statistical significance. At postpartum follow up, they were very high risk for hyperglycemia were shown in our participants and there were five, one, and two cases in GR A and one, one, and two cases in Gr B with IFG, IGT and DM, respectively.

CONCLUSION: We established a structured education program which is feasible for most women with GDM. There is no significant difference in

laboratory changes and fetal outcomes in women receiving structured education program, but having better diabetes knowledge and healthier behavior change which are fundamental for future prevention of diabetes.

PEC-08-4

Difficulties of Diabetic Care for Foreigners Living in Japan

Reika Usui¹, Mayumi Hakogi¹, Kaori Nakama², Fumie Okazaki¹, Reiko Tokunaga¹, Kazuko Nin³, Takashi Asakura⁴, Hiroshi Takamura², Miyuki Nogawa¹, Yuko Watanabe¹, Hitomi Fujii¹ and Takaichi Miyakawa¹

¹Tama-Center Mirai Clinic, Japan; ²Takamura Naika Clinic, Japan; ³Human Health Sciences, Faculty of Medicine, Kyoto University; ⁴Tokyo Gakugei University Laboratory of Health and Social Behavior

AIMS AND METHODS: Today, we have a lot of socio-cultural as well as language barriers among 2,000,000 immigrants in Japan. In the health care field, this can be a serious disadvantage. We investigated the difficulties perceived by them by semi-structured interviews asking about the cultural differences and difficulties living with diabetes in Japan. We obtained informed consent and recorded to be analyzed word for word.

RESULTS: Fifteen people from Korea, China, Taiwan, India, Nepal, Philippines, Egypt, Peru, the U.S.A, Barbados, and Ghana. Age; 56.2, HbA1c; 7.2%, living in Japan for 19 years. Occupations; security guard, house-keeping, demolition work, non-government organization, etc. Some experienced discrimination and financial difficulties. Most obtained medical information from doctors, some English speakers used the internet. Those who had lower level education seemed to have difficulties grasping concept of the disease. In India, Peru, the Philippines, people are not accustomed to eating vegetables. Some did not recognize diabetes as a chronic disease, include regular clinic visits. Muslims practiced Ramadan, and Hindus meditated in Japanese temples. They occasionally had meetings with people of their own countries; however seldom had close Japanese friends.

CONCLUSION: They had less close relationships among their peers and health care providers. This may be kept away from occasional 'know-how' or tips of diabetes self care. The reason could be a language barrier and lack of understanding and respect to their cultural background forming their own values.

We are now planning to make leaflets, and hold meetings of foreign patients' association.

PEC-08-5

Towards the Establishment of an Effective System for Diabetic Patient Consultation at Nights and on Holidays

Taiko Terashima¹, Mizue Fujii², Yuko Yoshitani¹ and Sadako Yoshimura³

¹Department of Nursing, The Japanese Red Cross Hokkaido College of Nursing, Japan;

²Department of Nursing, Sapporo City University, Japan; ³Faculty of Health Sciences, Hokkaido University, Japan

OBJECTIVE: At nights and on holidays, nurses are the first to respond to telephone calls or visits by diabetic patients suffering from hypoglycemia or who have problems with insulin administration. The purpose of this study was to clarify problems in current consultation systems used in institutions for diabetic patients in order to establish an effective consultation system by nurses.

METHODS: Questionnaires were sent by mail in November 2007 to nursing managers in 715 institutions. The questionnaire including items on (1) outline of the facility, (2) presence/absence of a telephone consultation service at nights and on holidays and the initial responders to telephone.

RESULTS: Information in questionnaires obtained from 224 educational institutions certified by the Japan Diabetes Society was used for analysis. Respondents were divided into a positive group (52.5%) and negative group (22.8%) according to positive or negative answers to both of the following questions concerning future prospects: (1) Will consultation needs increase in the future? and (2) Will efforts be made to enhance the quality of consultation services provided by nurses? There was a large percentage of institutions to which respondents in the positive group belonged that had <200 beds and a telephone consultation service and that had a higher frequency of initial responses by ward nurses than by nighttime emergency outpatient nurses or physicians on duty.

CONCLUSION: The results suggest that a system using nurses with experience in diabetes management is better than an outpatient emergency room for diabetic patient consultations at nights and on holidays.

PEC-08-6

Effect of Applying Self-Regulation Theory on the Control of Postprandial Glucose in T2DM Patients

Yueh Chu Wu¹, Yi-Sun Yang¹, Ying-Li Lu¹, Chien-Ning Huang¹, Yu-Ju Chen¹, Yu-Tze Lin¹, Ching -Lu Li² and Edy Kornelius³

¹Chung Shang Medical University Hospital, Taiwan; ²Diabetes Education Center, Chung Shang Medical University Hospital, Taiwan; ³Division of Endocrinology and Metabolism, Department of Internal Medicine

OBJECTIVE: Self-Regulation Theory (SRT) is a system of self-conscious healthmanagement. We evaluated the effectiveness of applying SRT to type 2 diabetic patients (T2DM) on the understanding of postprandial blood glucose (PBG) changes, preconceptions of drug and diet therapy, in order to enhance self-care behavior and improve glycemic control.

METHODS: From October to December in 2011, T2DM patients who visited the medical center at central Taiwan were recruited if hemoglobin A1C (HbA1C) levels were above 8% while taking at least two types of oral anti-diabetic drugs. They were required to perform self-monitoring of blood glucose (SMBG) over a 6-month period of investigation. Patients who actively controlled PBG by applying SRT attended small group courses. Physiological indices like HbA1C, fasting blood glucose (FBG), PBG and SMBG behavior were compared before and after intervention.

RESULTS: Thirty subjects were in the study group while 30 in the control group. In the study group, mean HbA1C decreased from 9.3% to 7.7%, FBG decreased from 203.2 to 151.4 mg/dL, PBG decreased from 276 to 172.3 mg/dL, SMBG frequency increased from 0.13 to 13.1 times per week, exercise frequency increased from 61.6 to 164 min per week, and carbohydrate intake decreased from 271.5 to 193.9 g/day. All changes were statistically significant ($P < 0.05$) in the study group, whereas the control group did not.

CONCLUSION: Patients may become more active in changing dietary and SMBG behaviors after participating in small group activities. Through telephone follow-up, investigators may strengthen patients self-care behavior, thus to improve their glycemic control.

PEC-08-7

Education Prescription in Patients with Type 2 Diabetes Mellitus; Obedience and Efficacy

Sunghwan Suh, Mi Yeon Kim, Sang-Man Jin, Se Won Kim, Hye Jeong Kim, Ji Cheol Bae, Myung-Shik Lee, Moon Kyu Lee and Jae Hyeon Kim

Department of Internal Medicine, Samsung Medical Center, Korea

BACKGROUND: Modifying one's life style is a basic component in the management of diabetes.

METHODS: We conducted a retrospective study to investigate the prescription obedience of diabetes education and effect of education on glycemic control during 2009 in Samsung Medical Center, Seoul, Korea.

RESULTS: Among the 588 patients who were included in the analysis, 433 received education. The overall obedience rate was 74%. There was significant difference in hemoglobin A1c change between the educated subjects and subjects without education (From 7.74 ± 1.25 at baseline to 7.14 ± 1.02 at 3 months and 7.24 ± 1.24 at 12 months after education in noncompliant group vs From 7.84 ± 1.54 at baseline to 6.79 ± 1.06 at 3 months and 6.97 ± 1.20 at 12 month after education, $P = 0.0013$). The decrease in hemoglobin A1c was more evident in the subjects with short diabetes duration ($P = 0.032$ in subjects with short duration) than in subjects with long diabetes duration ($P = 0.183$ in those with long duration).

CONCLUSION: This result implies that large percent of patient refused to get the diabetes education despite the prescription of their physicians. Furthermore, diabetes education was more effective in patients with short duration of diabetes in clinical practice. Therefore diabetes education after diagnosis should be done as early as possible and more intensive education is needed to have effect on diabetes management in patients with long standing diabetes.

PEC-09-1

Diabetes Basics Supporting Students with Diabetes: A Collaboration

Michelle Trute¹, Andrea Sanders², Kirsty MacDougall², Helen O'Neill² and Taryn Black²

¹CEO, Diabetes Queensland, Australia; ²Diabetes Queensland, Australia

Diabetes self-care is complex and balancing the array of diabetes self-care behaviors can be frustrating for children and adolescents. These frustrations

can be compounded by difficulties getting the support they need while at school. Research also suggests that schools find it difficult to provide support for children with diabetes. In many instances, school staffs are not educated regarding diabetes care needs and therefore are often ill equipped to support students. Inadequate management can lead to serious adverse health consequences in both the short and long term.

OBJECTIVE: To build capacity of school staff to better support and improve health outcomes for students with diabetes in Queensland schools.

METHOD: In partnership with the Department of Education, Training and Employment (DETE) and major children diabetes services of Queensland, the 'Students with Diabetes: Guidelines for Queensland schools' was developed. As a result, the Diabetes Basics program was designed to support the school guidelines through delivery of education and resources to Queensland Schools. The program focuses on building capacity, educating school staff and developing effective relationships between the parents, schools and health services in supporting students with diabetes.

RESULT: The school guidelines have successfully been incorporated into Government policy on supporting children with diabetes. Results have indicated that Diabetes Basic program builds the capacity of school staff to better support students with diabetes.

CONCLUSION: The Diabetes Basics Program is an effective way to deliver consistent education and support to schools and strengthened communication between health services, parents and schools throughout Queensland.

PEC-09-2

Development of a Picture Book for Young Children with Type 1 Diabetes to Facilitate Child-Mother Communication and Self-Care

Nobue Nakamura¹, Keiko Ideno², Tomo Kanamaru³, Hiroe Tani⁴, Noriko Shirahata⁵, Yuriko Kanematsu⁵, Kanako Utsumi¹, Aya Nakai¹ and Naho Sato¹

¹Department of Maternal and Child Nursing, Chiba University Graduate School of Nursing, Japan; ²Toho University School of Nursing, Japan; ³Chiba University Hospital, Japan; ⁴Tokushima University Graduate School of Health Bio Science, Japan; ⁵Iwate Prefectural University Faculty of Nursing, Japan

OBJECTIVE: Mothers of young children with type 1 diabetes are confronted with both complex diabetes management and raising children. Young children with diabetes gradually become interested in diabetes care and they want to share in this through daily repetition. Effective child-mother interaction is required to improve children's self-care competency. We developed a picture book for young children with diabetes to facilitate child-mother communication and self-care.

METHODS: We explored essential factors in the learning process of self-care behavior in young children with diabetes through a systematic literature review. Based on the factors we discovered, we developed a corresponding picture book. This picture book was sent to diabetes clinics and peer support groups along with postcards to collect feedback.

RESULTS: Emotion and interest in self-care behavior, the ability to learn technical skills and knowledge about diabetes management were essential factors in the learning process of self-care behavior in young children with diabetes. Emotion and interest in self-care behavior focused on insulin injection, blood glucose testing, diet, and hypoglycemia. Based on these findings, we developed a picture book for young children with diabetes. The end of the picture book included a message intended to assist mothers with fostering children's motivation, coping with children's unstable emotions and hypoglycemia, enjoying meal time, creating a safe environment at kindergarten, and taking the perspective of next developmental stage.

CONCLUSION: The picture book was found to be an effective tool to facilitate child-mother communication and self-care of young children with diabetes because they could clearly understand the content.

PEC-09-3

Can Lifestyle Modification Reduce the Fasting Plasma Glucose for Overweight & Obesity children? A Systematic Review

Angela Shin-Yu Lien¹, Jia-Ling Tsai¹, Tzu-Ying Chen¹ and Bih-Shya Gau²

¹College of Medicine, School of Nursing, Chang Gung University, Taiwan; ²Department of Nursing, College of Medicine, National Taiwan University, Taiwan

BACKGROUND: Obesity and young type 2 diabetes mellitus increased globally after 1990. However, the effect for lifestyle modification on fasting plasma glucose or diabetes mellitus was not well-known for children.

METHODS: With the methodology of the Cochrane Collaboration, systematic review from the evidence of randomized control trials and clinical control trials was undertaken. Electronic databases and hand search form Cochrane Library, MEDLINE, PsychInfo between 1965 and April, 2012 was performed under the Mesh terms and key words of childhood overweight or obesity, lifestyle, diabetes, exercise, physical activity or fitness. Overweight or obese children with age 5-18 were included with the measurement of fasting plasma glucose and lifestyle modification such as diet control, healthy nutrition, exercise or fitness or physical activities. If subjects with below diseases (neurosurgical, cardiovascular, diabetes mellitus, eating disorders, malnutrition, and psychosocial or physical disability), or intervention other than lifestyle modification such as breastfeeding or medications, were excluded.

RESULTS: There were 44 articles screened out, but only five trials met all inclusion and exclusion criteria with 342 children in intervention group and 240 in control group. Three studies showed positive and significant results, one positive but non-significant results, and one negative but non-significant result.

CONCLUSION: Unlike the studies for adults with consistently positive and significant reports, lifestyle modification may be effective in reduce fasting plasma glucose level of overweight children. A larger and more comprehensive program with survey will be expected to reduce fasting plasma glucose or the onset of diabetes mellitus in youth.

PEC-09-4

Type 2 Diabetes Mellitus in a Child with Selective Mutism: A Case Report

Jiro Takeuchi¹, Mayu Takeuchi², Fumiko Tanaka³, Takeshi Hattori², Taizo Yamamoto², Ayako Hanashima³, Nobuyuki Kishi⁴, Yoshiki Ishisaka⁵, Daisuke Jyonen¹, Mioko Mori¹, Yasuhiro Mizushima¹, Akihiro Kataoka¹ and Yoshihiro Wakazono¹

¹Department of Pediatrics, Kyoto Katsura Hospital, Japan; ²Department of Diabetes and Endocrinology, Kyoto Katsura Hospital, Japan; ³Department of Mental Care Consultant, Kyoto Katsura Hospital, Japan; ⁴Department of Pediatrics, Kyoto Katsura Hospital, Japan; ⁵Department of Child Psychiatry, Kyoto Katsura Hospital, Japan

The case is a 14-year-old male patient. His family has impaired glucose tolerance. The patient's perinatal history revealed late child-bearing, premature birth, and low birth-weight. No particular finding had been recognized by urinalysis at health check-ups until an abrupt loss of body weight (BW), 19 kg in 6 months, was noticed by a school teacher at the age of 10. He was diagnosed as having type 2 DM, based on data of body height 160.0 cm, BW 62.0 kg, body mass index 24.2, plasma glucose 28.7 mmol/L, HbA1c 12.9%, β -hydroxybutyric acid 1307 μ mol/L, and glutamate decarboxylase antibody undetectable. Insulin therapy was started on hospitalization, but discontinued in ambulant. The BW increased substantially, and the nutrition and exercise therapy was intensified, but the patient remained inferiorly adherent to the therapy. Because of low reactivity and slow response in dialogue, he was examined on the Wechsler intelligence scale for children, third edition. His performance intelligence quotient and processing speed were evaluated as low as 73 and 69, respectively, though the verbal intelligence quotient was 91. The patient was thus diagnosed as selective mutism complicated with type 2 DM. Since the patient's psychosomatic problem seemed to be related to his life-style, additional interventions, i.e. counseling by clinical psychologist, behavior-recognized therapy and family therapy, were introduced. These multidisciplinary treatments induced a gradual improvement of reactivity despite persistent difficulties in difficulty in management.

PEC-09-5

Prevalence of Thyroid Antibodies in Thai Type 1 Diabetes Mellitus Children and Adolescents

Worraporn Tantichattanon, Jeerunda Santiprabhob, Pairunyar Nakavachara and Supawadee Likitmaskul

Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Thailand

OBJECTIVE: Type 1 diabetes mellitus is frequently associated with autoimmune thyroid disease and increased prevalence of thyroid antibodies. The prevalence of thyroid antibodies is varying according to nationality from 3.7% to 33%, which has not been reported in Thai type 1 diabetic children. We have, therefore, investigated the prevalence of thyroid antibodies in children with type 1 diabetes mellitus in Thailand.

METHODS: Anti-thyroglobulin(anti-TG) and anti-thyroid peroxidase(anti-TPO) were measured cross-sectionally in 110 Thai type 1 diabetic patients at

diabetic clinic, Department of Pediatrics, Siriraj hospital during November 2009 to October 2010. Serum T3, free T4 and TSH were measured in all patients regardless of history of thyroid disease

RESULTS: Of 110 young diabetic patients (64 females and 46 males), anti-TG and anti-TPO were positive in 17 (15.5%) and 25 (22.7%) patients, respectively. Fifteen patients (13.6%) were positive for both antibodies and 27 patients (24.5%) were positive for anti-TG and/or anti-TPO. There were seven patients who have been diagnosed thyroid disease before study, four were diagnosed hyperthyroidism and the remainder were hypothyroidism. All of them were positive for anti-TG and/or anti-TPO. Two of 20 patients, who had thyroid antibodies without previous history of thyroid disease, were subclinical hypothyroidism. One of 83 patients without thyroid antibodies, was subclinical hyperthyroidism. There was a female preponderance for type 1 diabetic patients with thyroid antibodies (female:male, 32.9:13.04%, $P = 0.017$). Goiter was noted in 8 (7.27%) patients and all of them were positive for thyroid antibodies.

CONCLUSIONS: The prevalence of thyroid antibodies in Thai type 1 diabetic children and adolescent was 24.5%. The frequency of thyroid antibodies was increased in female patients.

PEC-10-1

Long Term Effect of Switch from Insulin to Liraglutide Treatment on QOL of Patients with Type 2 Diabetes Mellitus

Kayo Yokota¹, Daisuke Yabe², Naomi Kitatani³, Takanori Hyo², Koin Watanabe², Ryota Usui², Hitoshi Kuwata², Shuichi Fujiwara², Minoru Matsumoto², Akihiro Yasuhara², Masahiro Iwasaki³, Takeshi Kurose² and Yutaka Seino²

¹Division of Nursing, Kansai Electric Power Hospital, Japan; ²Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, Japan; ³Division of Nutrition, Kansai Electric Power Hospital, Japan

AIMS: In order to investigate the effect of switching from insulin to liraglutide on changes of QOL in patients with type 2 diabetes mellitus, we have evaluated patients' anxiety, burdens and difficulties in their daily lives before and after liraglutide treatment.

METHODS: Study Subjects; 60 outpatients with type-2 diabetes mellitus whose treatment were switched from insulin to liraglutide.

Data Collection; 29 questionnaires on QOL were asked a year before and after liraglutide treatment, including anxiety for new treatments, QOL changes such as burdens for preparing meals, exercise, and treatment.

Data analysis; Responses to questions were made with a 7-point Likert scale. Impact and worry scales are rated from 1 (absolutely yes) to 7 (absolutely no). Comparisons of two groups were evaluated using student *t*-test.

RESULTS: Sixty outpatients (M/F, 41/18) who were treated with insulin were in this study. Average age of 60 outpatients was 62 ± 10 . Duration of diabetes mellitus was 11.4 ± 8.4 years. Average HbA1c (NGSP) was $7.8 \pm 0.98\%$. After recruited a year liraglutide treatment HbA1c decreased to $7.12 \pm 1.02\%$. The patients had strong anxiety about hypoglycemia before Liraglutide. In addition, anxiety for hyperglycemia decreased as well after liraglutide treatment. Using liraglutide the burden of injection before eating was also reduced. Anxiety, burdens, difficulties have all decreased by introduction of liraglutide.

CONCLUSIONS: Switch from insulin to liraglutide can reduce the frequency and difficulty of self-injection and the time burden of diabetes to improve QOL.

One daily injection of liraglutide can enhance dining by making meal composition and punctuality less critical. In addition, hypoglycemic episodes and the progress complications are reduced, which can lessen anxiety to improve QOL.

PEC-10-2

Achieving Remarkable Results in Diabetic Patient Care

Hui-Min Hsieh¹, Hsiu-Ying Cheng¹, Chiu-Mi Chang¹, Chi-Sung Hsu¹, Hsien-Yu Ho¹, Yu-Lien Liu², Yu-Ling Lin³ and Cheng-Hsiu Lin³

¹Diet and Nutrition Department, Fong-Yuan Hospital, Taiwan; ²Nursing Department, Fong-Yuan Hospital, Taiwan; ³Endocrinology & Metabolism Department, Fong-Yuan Hospital, Taiwan

OBJECTIVE: The Endocrinology & Metabolism Team of Fong-Yuan Hospital incorporated the Balanced Scorecard strategic management method into the treatment and management of diabetic patient conditions. The strategy enabled the implementation of a value-based system in patient treatment and the selection of the best procedure for the patient.

METHODS: The hospital provided financial support to enhance the core capacity of the team members. The team conducted ward rounds, made professional presentations, and developed new services to foster learning and growth of the team. Moreover, the hospital planned a discussion forum for the integrated outpatient care system, thus making it possible to provide patients with a more thorough diabetic treatment and care program and to enhance quality of patient care services. The hospital also expanded the shared caring network case acceptance range for diabetic patients; in turn, it improved the attendance rate of patient groups and bolstered customer satisfaction.

RESULTS: In 2011, the diabetes care quality indicators of HbA1C, blood pressure, low density lipoprotein reached the target level. The analysis of patients taking medicine at the right time and proper dosage improved from 77.6% to 90.3%. The team received an 'excellent' rating from the Bureau of Health Promotion.

CONCLUSION: Achieving a consensus, the team created a vertical organization procedure flow. The team integrated resources with the activity-oriented team strategy to enhance core growth and foster the implementation of health management. It continued to make breakthroughs and innovate on medical service, thereby producing the optimal value for the shared care of diabetic patients.

PEC-10-3

A Proposal of an Effective Method to Develop a Team Approach in Diabetes Education

Shigeru Kusaka¹, Katsuko Maeda², Etsuko Kawada², Sachiko Yoshimi², Mariko Matsuura², Chiemi Hayashi², Kae Tamura³, Yoshiyasu Hirayama⁴, Kazuhiro Ogino⁵, Keiko Matsumoto⁶, Tatsunori Fukazawa⁷, Fumiko Kimura¹, Mariko Fujimoto⁸, Shoko Sasaki⁸, Chihiro Ebihara¹, Ken Ebihara⁹, Makoto Sawamura⁹, Keiko Ebihara², Masahiro Mizuno¹, Shinji Miki¹⁰ and Tadasumi Nakano⁹

¹Department of Internal Medicine, Mitsubishi Kyoto Hospital, Japan; ²Department of Nursing, Mitsubishi Kyoto Hospital, Japan; ³Department of Pharmacy, Mitsubishi Kyoto Hospital, Japan; ⁴Department of Rehabilitation, Mitsubishi Kyoto Hospital, Japan; ⁵Department of Clinical Laboratory, Mitsubishi Kyoto Hospital, Japan; ⁶Department of Nutrition, Mitsubishi Kyoto Hospital, Japan; ⁷Patient Support Center, Mitsubishi Kyoto Hospital, Japan; ⁸Department of Obstetrics and Gynecology, Mitsubishi Kyoto Hospital, Japan; ⁹Department of Diabetology, Mitsubishi Kyoto Hospital, Japan; ¹⁰Department of Cardiology, Mitsubishi Kyoto Hospital, Japan

OBJECTIVE: The aim of our presentation is to show that we can develop a fulfilling and practical team approach in diabetes education even in a short term.

METHODS: Our hospital had an existing embryonic small group consisted of medical and paramedical personnel in charge of diabetes education for the admitted patients with diabetes mellitus. We set up a committee dealing with promotion of appropriate diabetes treatment and tried to develop newly organized diabetes care team ("Team Diabetes") by dividing the small group into six functional subgroups for better diabetes education.

RESULTS: (1) 'Class for diabetes team' started the class for helping diabetes education for outpatients, (2) 'Outpatient insulin therapy introduction team' produced clinical path and safely introduced insulin or incretin therapy, (3) 'Round and conference team' prepared information sheets related to hospitalized patients with diabetes, practiced team round and held case conference on clinical and psycho-behavioral problems associated with medical treatment, (4) 'Diabetes education team for hospitalized patients' produced a text on diabetes treatment, care and education for improvement of daily life living of the patients, (5) 'Skill-up team for diabetes-educator' set up improvement of diabetes education and (6) 'Gestational diabetes team' developed new flow chart of treatment according to new criteria for diagnosis. Scheduled team meetings were held once a week with the team members. Committee instructed the team members to maintain the correct orientation of the team approach.

CONCLUSIONS: We have developed a safe and effective team approach by developing a small group into several functional subgroups for diabetes education in a short term.

PEC-10-4

Clinical Characteristics of Diabetic Patients Beyond Age of 85 in Japanese Populations

Toshiya Matsuda¹, Shinya Furukawa², Shin Yamamoto², Teruki Miyake², Teruhisa Ueda², Teru Kumagi², Tetsuji Niiya³, Hisaka Minami⁴, Takenori Sakai⁵, Hiroaki Miyaoka⁶, Bunzo Matsuura² and Morikazu Onji²

¹Ehime University School of Medicine, Japan; ²Department of Gastroenterology and Metabolism, Ehime University Graduate School of Medicine, Japan; ³Matsuyama Shimin Hospital; ⁴Ehime Niihama Hospital; ⁵Yawatahama General Hospital; ⁶Saiseikai Matsuyama Hospital

BACKGROUND: The population of diabetic patients in elderly is increasing in developed countries along with the increase in elderly population. The treatment goals for diabetic patients in elderly are reported to maintain physical activities and quality of life, and to prevent diabetic complications. However, there is no report on clinical characteristics of diabetic patients beyond age of 85.

AIM: To assess the clinical characteristics of diabetic patients beyond age of 85 in Japanese populations.

POPULATION AND METHOD: The patients over the age of 85 within the DOGO study (a multicenter prospective cohort study that includes 890 T2DM) were enrolled in this analysis. Data collection included body mass index (BMI), blood glucose levels, HbA1c (NGSP), use of diabetic medications and diabetic complications. All participants completed self-administered questionnaires about duration of T2DM, smoking, drinking, stress and social condition.

RESULTS: There were 40 patients with T2DM over the age of 85 (mean 87.1 years, 40% male). Mean BMI was 23.5 and mean HbA1c was 7.3%. The most common complication was hypertension (80%). Exercise habit was observed in 40%. Thirty-two percent of patients were stressed from their daily life but male patients who had consultants to consult about their daily life were less stressed compared to those who did not have such ($P < 0.05$).

CONCLUSIONS: Our study identified the clinical characteristics of diabetic patients beyond age of 85 in Japanese populations: the control of HbA1c was relatively good; hypertension was the most common complication; and having consultants could reduce stress from their daily life in male patients.

PEC-11-1

Diabetes Nursing for the Patients' Objective Self-Awareness

Mizuyo Ookura, Chisono Kameishi, Nathuko Seto and Yasuko Simizu
Health Sciences, Osaka University Graduate School, Japan

OBJECTIVES: Continued self-care is crucial in managing diabetes mellitus (DM) because it can delay DM progression and proactively prevent DM complications. For the continued self-care, the diabetic should take objectivity his disease as his own are important. This report tells about nursing assist how these can be achieved.

METHODS: Data were obtained using semi-structured interviews of five diabetes specialist nurses (DSN) certified by the Nursing Association, within the ethical guidelines, and were analyzed using the qualitative synthesis method (KJ method).

RESULTS: Following were obtained based on the responses of the nurses

1. Nurses are not confident that they truly understand the patients, although they try to do so.
2. Nurses think about making the patients self-aware very carefully.
3. Patients ask for recognition when they give their best.
4. When patients get recognition and become invulnerable, they become calm and ready to notice changes in their health.
5. Nurses a trial-and-error method with patients.
6. Nurses are willing to accept patients' self-determination by preparing themselves for the worst.
7. Nurses are not always conscious of making the patients self-aware.

CONCLUSION: It is obvious that the seven findings above are correlated. At the same time, however, to what extent and how they are correlated is not necessarily certain. Therefore, the relationship between these findings should be structured, and these findings and the structure should be best utilized for more practical nursing assistance.

PEC-11-2

Effect of Difference in Exercise Education Method with Accelerometer on Clinical Data of Pre-Diabetes Patients

yeo-jin Moon¹, Sun-Woo Kim², Sung-Woo Park², Ki-Won Oh², Won-Young Lee², Chul-Young Park², Eun-Jung Rhee² and Se-Eun Park²

¹Diabetes Mellitus Center, Kangbuk Samsung Hospital, Korea; ²Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Korea

The study examined what effect did it have on clinical data of pre-diabetes patients to make a difference in exercise education method by using accelerometer lifecorder that could monitor physical activity. Fourteen pre-diabetes patients were made to put on lifecorder, and were classified into randomized seven of experimental group, and seven of control group. Physical activity analysis and education on importance and increase of physical activity were carried out for EG, and physical activity analysis and general exercise education were carried out for CG once a month for 3 months. Clinical data after exercise education was analyzed by carrying out independent *t*-test, paired sample *t*-test of level of change for fbs, hba1c, bp, total-ch, tg, bmi, waist, physical activity cal, total energy expenditure, total steps and total physical activity time, with SPSS 19.0 at $P < 0.05$. Average age of all subjects was 43.3 ± 0.1 years old, duration was 1.3 ± 1.6 years, and clinical data didn't have significant difference between EG and CG. After exercise education, fbs, hba1c, bp, total-ch, tg, bmi, waist, pa, tee, ts and tpat were improved in EG and bml, waist, pa and tee were improved in CG. Rate of change after exercise education inside group showed more significant rate of change for EG, and TAT and TS were most significantly increased in physical activity rate of change. It is hard to represent effect of education due to a small number of subjects, but it may be useful in improving clinical data to carry out exercise education through monitoring physical activity, and setting up goal of individual physical activity. It can be deemed that physical activity is improved and obesity is consequently improved, by using equipment to monitor physical activity as education tool alone.

PEC-11-3

The Effects of a Care Program to Support Self-Adjustment of Insulin Administration for Outpatients with Type-1 Diabetes

Mutsuko Kubota¹, Mariko Kawaharada², Kazuko Saeki², Yukari Shindo², Michiyo Hirano² and Hikaru Honda²

¹Graduate School of Health Sciences, Hokkaido University, Japan; ²Faculty of Health Science, Hokkaido University, Japan

OBJECTIVE: The aim of this study was to examine the effects of a care program to support self-adjustment of insulin administration (hereinafter referred to as self adjustment) for outpatients with type-1 diabetes, by means of a randomized controlled trial.

METHODS: The subjects were 19 patients with type 1 diabetes, aged between 20 and 70, who visited hospitals in northern Japan, and were randomly assigned to either an intervention group ($n = 10$) or a control group ($n = 9$). The care program consists of three phases: (1) pattern management of blood glucose, (2) skill acquisition of self-adjustment and rehearsal, (3) practice of self-adjustment and feedback. Four individual consultations concerning pattern management of blood glucose are provided to the patients in the intervention group at intervals of 1 month. Before starting the intervention in November 2011, a baseline survey was conducted. After the consultations finish in May 2012, a post-survey is scheduled to be conducted. The items to be evaluated are HbA1c, BMI, the reliability and validity of Instrument of Diabetes self-care Agency (IDSCA), and Problem Area in Diabetes (PAID). The study was conducted with permission from and in line with the ethical regulations of the Board of Ethics for Medical Studies at Hokkaido University's Faculty of Health Sciences.

RESULTS AND DISCUSSION: The mean age of the participants was 44.1 years old and 21% of the participants were male. There were no significant differences in characteristics between the groups.

Currently, we are in the middle of intervening with patients about this study.

PEC-11-4

A Study of Patient Intention of Self-Monitoring of Blood Glucose in Type 2 Diabetes

Ching-Wen Wu¹, Chiao-Yun Chen¹, Yi-Yu Chen¹, Pei-Jhen Liang¹, Ya-Yu Tseng¹, Pei-Wen Huang¹ and Shih-Li Su²

¹Diabetes Case Management Center, Changhua Christian Hospital, Taiwan; ²Divisions of Endocrinology and Metabolism, Changhua Christian Hospital, Taiwan

OBJECTIVE: This research wants to study the impacts of diabetes patient's cognitive and service quality after the medical institute offering a blood glucose test for type 2 diabetes depending on the patient's intention of using.

RESEARCH DESIGN AND METHODS: The age of patients was around 20–80 years. All had self monitoring experience. The questionnaire is desired by literature review and the real clinical situations. The 202 effective questionnaires are composed of on cognition, service quality, satisfaction, intention and sample question presented using a five-point score Likert item. The analysis method includes descriptive statistics, factor analysis, reliability, validity, regression analysis and one way analysis of variance.

RESULTS: The study results show blood testing cognition question average 3.8 point. There are not significant correlation of satisfaction and intention. There are significant effect between service quality and motif intention ($P < 0.05$), especially, the hospital educational service. The perceived quality is higher compared other glucose meter's channel, and strong intention to use ($P < 0.05$). The glucose meter quality and behavior intention were also high associated ($P < 0.05$).

CONCLUSIONS: The study results show glucose testing benefit item to exceed four points, but, it don't produce using intention. The knowledge provision is necessary, but can't change behavior. The service and perceived quality play the major role for participants' willing to continue self blood glucose tests. Therefore, the patient needs to stimulate their intrinsic motivations by diabetes educator via these directions.

PEC-11-5

Diabetes Counseling Study at St. Mary's Hospital (1) Need of Psychological Approach for Japanese Diabetic Out Patients

Yosie Togawa¹, Sakiko Kimura¹, Yasuhiro Nakashima¹, Rika Fukuzawa¹, Toru Motoyama¹, Kayoko Kakei¹, Ryota Funatsu¹, Akiko Mukasa¹, Kiyohide Nuno², Yuichi Satou² and Rie Sakuragi³

¹Department of Clinical Psychology, St. Mary's Hospital, Japan; ²Division of Diabetes, St. Mary's Hospital, Japan; ³Health Center, St. Mary's Hospital, Japan

OBJECTIVE: To investigate the need of psychological approach for diabetic out patients with hyperglycemia and/or obesity.

SUBJECTS: Diabetic out patients who had HbA1c $\geq 8.4\%$ (Group A; $n = 161$), BMI ≥ 30 kg/m² (Group B; $n = 73$), HbA1c $\geq 8.4\%$ and BMI ≥ 30 kg/m² (Group C; $n = 32$), BMI < 18.5 kg/m² (Group D; $n = 18$), psychological problem (Group E; $n = 16$).

METHODS: Emotional burden was evaluated by problem area in diabetes (PAID), and well-being was evaluated by WHO-5. Psychologists explained the results of PAID and WHO-5 to the patients and asked their will for counseling.

RESULTS: PAID score was highest in Group C, but not significant. WHO-5 score of Group C was significantly lower than that of Group A or B, and near to that of Group E. Frequency of high PAID score (≥ 55) and/or low WHO-5 (< 50), which indicate the potential needs of psychological approach, was 37%, 30%, 59%, 56% and 56% in Group A to E, respectively. Frequency of those hoped for counseling was 20%, 18%, 25%, 22% and 13% in Group A to E, respectively. According to the item of PAID and WHO-5, Group C was associated with uncomfortable social situations, poor relaxation and less sleep, significantly.

CONCLUSION: There is high need of psychological approach for diabetic out patients with hyperglycemia or obesity, especially for patients with both of them. But the patients who hoped for counseling were not so many. We have to make appropriate roots to touch their heart.

PEC-11-6

Duration of Diabetes Influence the Efficacy of Insulin Therapy in Subjects with Type 2 Diabetes

Soo Kyoung Kim, Jong Ryeal Hahm, Tae Sik Jung, Jung Hwa Jung and Soon Il Chung
Department of Internal Medicine, Gyeongsang National University School of Medicine, Korea

OBJECTIVE: To investigate which factors are associated with the efficacy of insulin therapy in subjects with type 2 diabetes.

METHODS: Fifty-four patients with type 2 diabetes are enrolled (mean age, 60.5 ± 9.4 years; body mass index, 24.8 ± 3.4 kg/m²; median diabetic duration, 16 years (range 2–30); 27 males and 27 females). A questionnaire regarding clinical characteristics and self-care management behaviors was asked, and HbA1c, fasting blood glucose level, lipid profile, and status of diabetic complications were abstracted from the patient's records. Poor glycemic control was defined as HbA1c $> 8.0\%$.

RESULTS: Of the total 54 patients, 44.2% had HbA1c $> 8.0\%$. Fasting serum C-peptide level, triglyceride level, and duration of diabetes (> 16 years) were significantly different between good glycemic control and poor glycemic control groups. In the multivariate analysis, longer duration of diabetes was significantly associated with poor glycemic control ($P = 0.037$).

CONCLUSION: Glycemic control was poor in subjects with type 2 diabetes. Longer duration of diabetes was associated with poor glycemic control.

PEC-12-1

The Intervention of Personalized Health Education can Enhance Insulin Injection Rate and Ameliorate the Healthcare Quality of Patient's Self-Management

Liu Su Yen, Chen Ming Hui and Chen Jia Lin

Department of Nursing, Chi Mei Foundation Hospital, Taiwan

The objective of this program is to increase the injection rate for patients who require insulin injection treatment, and further improve the quality of healthcare while reducing the medical cost. The onset criteria is type 2 diabetic patients who were diagnosed by physician as necessary to transform into insulin treatment; using two or more than three oral anti-diabetic agent with A1C > 8.0 mg/dL; or have poor liver and kidney functions. The duration of this program is from December 1, 2010 to March 31, 2011. Utilize convenient sampling method to take out-patients or patients for the ward. Engage individual healthcare education and insulin healthcare treatment. Apply bilateral one by one interaction approach to convey healthcare education and consultation for a total of 66 patients in the program. Patient follow-up via telephone interviews and clinical revisits. Host three focus groups for insulin injection cases to conduct health education. Physicians will present the theory of insulin injection to emphasize the intention of insulin injection. Health educator will review the skill of insulin injection. The result of this program indicated a 95.5% switch on insulin injection, and 92.1% sustainable injection rate. HbA1C, fasting blood glucose and post prandial glucose tests have significant variation after the intervention of the activity.

The result demonstrate that individual healthcare education plus focus group health education can achieve better sustainable injection for insulin injection treatment and ameliorate blood sugar figures under sustainable follow-up to achieve superior life quality.

PEC-12-2

The Communication Style Inventory can be a Useful Tool in the Diabetic Education Program

Sonei Shojima, Tetsuji Niiya, Kenichi Manabe, Akiko Ogawa, Eriko Kawamoto, Takashi Sekikawa and Shinya Furukawa

Department of Internal Medicine, Matsuyama Shimin Hospital, Japan

BACKGROUND AND AIMS: The communication style inventory (CSI) is a simple and convenient method for identifying personal characteristics by four characteristics: Controller, Promoter, Supporter, and Analyzer. By evaluating the four elements, we can estimate the patients' character to some extent, in order to approach and communicate with them especially in diabetic education program. In our retrospective cohort study, we investigated if there are some relationships between the patients' characteristics and their clinical condition.

MATERIALS AND METHODS: We enrolled 149 type 2 diabetic patients who were admitted to our hospital in a 2-week diabetic education program (age:

60.6 ± 10.7 years; Male/Female: 93/56; HbA1c: 9.1% ± 2.1%). CSI was performed at the beginning of the program.

RESULTS: Controllers were less depressive than Non-Controllers (SDS score: 38.2 vs 44.8; $P = 0.0002$). In addition, male Controllers smoked more heavily than Non-Controllers (Brinkman index: 1290.8 vs 649.1; $P < 0.0001$). Promoters were less depressive (SDS score: 37.0 vs 45.5; $P < 0.0001$) than Non-Promoters. Female Promoters had more visceral fat than female Non-Promoters (visceral fat area (VFA): 121.7 vs 92.0 cm²; $P < 0.05$). Male Analyzers had lower HbA1c levels than male Non-Analyzers (HbA1c: 9.1% vs 10.1%; $P < 0.05$). No significant clinical differences were found between Supporters and Non-Supporters.

CONCLUSION: On the basis of the results of this retrospective analysis, it was suggested that the characteristics of type 2 diabetic patients could be related to their clinical condition.

PEC-12-3

Effectiveness of Insulin Rotary Disk and Empowerment for Improving the Glycemic Control of Type 2 Diabetic Patients

Kuan-yi Lin, Yan-Chi Li, Jeng-Fu Kuo, Shih-Te Tu and Jia-Yu Tian

Changhua Christian Hospital Lukang Branch, Changhua, Taiwan

OBJECTIVE: To help empowerment, we developed an Insulin Rotary Disk (IRD) as a creative tool which encourages patients to adjust insulin dosage according to self-monitored blood glucose (SMBG) levels.

METHODS: The intervention group was adjustment of insulin dosage as indicated on the IRD, based on the 3-day average SMBG level. The control group had insulin dosage adjusted by the physician during clinic visits. The improvements in A1C levels in both groups were compared after 3 months of intervention.

RESULTS: A total of 159 patients were enrolled. The intervention group consisted of 83 patients. The control group consisted of 76 patients. After 3 months, A1C level decreased from 10.07% to 8.17% was significant ($P < 0.001$) in the intervention group. A1C level decreased from 9.65% to 8.99% was significant difference ($P < 0.05$) in the control group. The intervention group had significantly greater improvement in A1C level compared to the control group ($P < 0.001$).



CONCLUSION: In addition to improving glycermic control, it enabled to develop self-management skills and achieve self-care goals.

PEC-12-4

The Usefulness of the Unique Diabetes Education which Utilized Classical Rakugo of Japan

Toshinori Nimura

Department of Internal Medicine, Kouseiren Chita Kousei Hospital, Japan

OBJECTIVE: The symptoms of diabetes were shown at the 2nd week of the visit to Japan of the 22-year-old woman (BMI 20.7) from China for purposes of training for 2 years. She was not able to speak and read Japanese. As for her laboratory data, blood sugar was 517 mg/dL and HbA1c (NGSP) was 13.8%. She was hospitalized in our hospital. Diabetes education which utilized rakugo was practiced to her who looked sad every day. This effect was examined.

METHODS: I have utilized rakugo and practiced diabetes education for these 15 years. Classical rakugo is one of the traditional performing arts of Japan. Rakugo is loaded with humor and healing. This time, five classical rakugo stories were utilized and performed. Every scene of the important point of rakugo was made the slide, and the subtitles of her native language were put in.

RESULTS: Her expression dark and filled with a feeling of disappointment became bright. She said smiling that rakugo was very good and she would live with a smiling face every day.

CONCLUSION: Unique diabetes education is performed all over the world. This time, diabetes education which utilized rakugo was performed to the 22-year-old woman who visited to Japan from China and looked sad. By this education, she became bright and said, 'I think that I will make a living with a smiling face from now on'. 'It was thought that diabetes education which utilized rakugo was the method of being meaningful'.

PEC-12-5

Glucose Meters Comparison Program: Experience from a Medical Center in Taiwan

Shu-Ting Yang, Ya-Wen Tsai, Chia-Chen Chiu, Han-Chun Hsieh, Hung-An Wei and Li-Ching Wu

Department of Pathology, Chi-Mei Foundation Medical Center, Taiwan

Blood glucose meter is a common home-used device to diabetes patients and it helps one to perform day-to-day blood sugar management. Therefore, not only a qualified meter, also proper handling skill and maintaining knowledge are all determining factors that affect accuracy of the device.

The aims of the study were to explore the accuracy of current home-used device, and survey if one had correct knowledge of using devices and proper hands-on techniques.

Participants were invited to bring devices to compare accuracy with Hitachi 7600 module in an ISO 15,189 certified clinical laboratory. In addition, a questionnaire was given to assess eleven items of operating and maintaining knowledge and twelve hands-on techniques.

A total of 82 subjects (43 male/39 female) were recruited. Seventy-seven percent of participants operated the glucose device by themselves, but 58% had not monitored glucose regularly. There were 14(17%) devices did not meet the requirement of ISO 15197:2003. Participants with uncertified meters had a lower score of knowledge than those whose devices are certified (uncertified group vs certified group; 6.8 ± 2.9 vs 7.6 ± 2.1). However, two groups had a similar score on hands-on techniques.

Of eleven items of operating knowledge, the least three scores received were the sense of (1) running control solutions, (2) keeping the reaction area clean, and (3) low battery affect the reading.

In conclusion, the study demonstrated most users are not familiar with device-maintaining process and this may lead to biased results. The study suggested continuous education and devices comparison program be more approachable to users.

PEC-12-6

Got Suga: An Innovative Theatre Based Solution to Tackling Diabetes in Australian Indigenous Communities

Michelle Trute¹, Michael Adams², Lucille Chalmers³, Ted Dean³ and Taryn Black³

Diabetes Queensland, Australia

Indigenous Australians are 3.4 times more likely to have diabetes than other Australians and are more likely to suffer the severe complications. The Aboriginal and Torres Strait Islander death rate from diabetes is up to 17 times that of non-indigenous Australians, mainly due to high levels of cardiovascular and kidney disease. Culturally appropriate education programs are critical in addressing this alarming situation.

OBJECTIVE: Improve diabetes outcomes through education programs that empower Indigenous communities to better understand diabetes and find their own solutions to addressing the diabetes epidemic.

METHODS: Got Suga is a multi layered program that combines a diabetes education workshop with social marketing strategies that provide culturally appropriate education about diabetes. The workshop uses Theatre for Change, an innovative approach that involves the community in playing out scenes and developing solutions to issues that impact on their health. The social marketing strategies include a series of radio plays that explore different themes in diabetes education and self-management. The plays are broadcast on community radio and supported by print resources that re-enforce key diabetes management messages.

RESULTS: The program has been successfully delivered in rural and metro communities across Queensland. Evaluation results show that participants had increased knowledge of important aspects of diabetes and improved awareness of health services available to support them in their community.

CONCLUSIONS: Interactive, theatre based diabetes education programs are an effective way of building diabetes knowledge and community capacity to tackle the issue of type 2 diabetes in Australian Indigenous communities.

PEC-13-1

Effect of Applying Self-Regulation Theory on Initiation of Insulin Therapy in T2DM Patients

Yi-Sun Yang¹, Yueh-Chu Wu², Ying-Li Lu³, Chien-Ning Huang³, Yu Ju Chen², Yu-Tze Lin², Ching -Lu Li² and Edy Kornelius³

¹Chung Shang Medical University Hospital, Taiwan; ²Diabetes Education Center, Taiwan;

³Division of Endocrinology and Metabolism, Department of Internal Medicine

OBJECTIVE: Self-Regulation Theory (SRT) is a system of self-conscious health management. We evaluated the effectiveness of SRT on type 2 diabetic (T2DM) patients' knowledge, drug therapy, preconceptions and feelings about diabetes, and acceptance of insulin therapy for glycemic control.

METHODS: From Oct. to Dec. in 2011, T2DM patients who visited the medical center at central Taiwan were recruited if hemoglobin A1C (HbA1C) levels were above 8% while taking at least two types of oral anti-diabetic drugs (OAD) combination initiated on basal insulin therapy. They were required to perform self-monitoring of blood glucose (SMBG) over a 6 month-period of investigation, followed via telephone interviews and instructed to adjust insulin dosage every 3 days according to fasting blood glucose (FBG) to achieve preset targets. SRT was applied to patients who actively adjusted insulin dosage. Effectiveness of glycemic control was compared to the controls who had insulin dosage adjusted by clinic physicians.

RESULTS: There were 31 subjects in the study and 30 in the control group. In study group, by active insulin adjustments and SMBG, the mean HbA1C decreased from 10.1% to 8.3%, FBG decreased from 229 to 131.9 mg/dL, basal insulin dosage increased from 13.8 to 19.2 units, and SMBG frequency increased from 2.5% to 13.9% times/week. All changes were statistically significant ($P < 0.05$) in the study group, whereas the control group did not.

CONCLUSION: Prompt intervention is important when patient requires intensive therapy with insulin. Reducing misconceptions and inducing early acceptance of insulin therapy increase the improvement of glycemic control.

PEC-13-2

About the Self-Administration Instruction of the Type 2 Diabetes Patient Whom Control of the Blood Glucose Level Worsens in the Winter Season

Shigeko Inoue

Nakataninaika Clinic, Japan

CONTEXT: The type 2 diabetes patients continue increasing in Japan. Importance of exercise and how to get meals has pointed out for a long time.

In our clinic, there are the patients whom control of diabetes changes on the seasons. We paid attention to the patient that HbA1c turned worse in winter every year.

PURPOSE: I clarify the cause that control of the blood glucose level worsens in winter of this patient.

And we support the self-control of the patient.

METHOD: We examined everyday active mass with the pedometer which a patient could record automatically for one year to clarify summer and winter difference in active mass.

I estimated meal intake amount of energy at the time of his going to hospital.

RESULT AND CONCLUSION: The winter intake amount of energy did not have the significant difference in the summer.

There is a significant increase of the consumption energy of activity in the summer (1% of level of significance).

Nagano prefecture is cold in winter, and it increased to be in the room, and the work of the field decreased, and active mass decreased.

The significant difference of amount of meal was not seen winter and summer. But, because the cooking such as 'New Year dishes' continues in winter, the attention of the meal is necessary.

PEC-13-3

To Identify the Needs to Education in People with Diabetes During the Waiting at Outpatient Clinics

Chun-Chun Chung¹ and Kwang-Wen Chen²

¹Department of Nursing, Saint Paul's Hospital, Taiwan; ²Department of Internal Medicine, Saint Paul's Hospital, Taiwan

OBJECTIVE: We perform this study to understand the needs to diabetes education in the people with diabetes during their long waiting time for clinics.

METHODS: The questionnaire was formed with the dimensions including their activity during the waiting, preferred mode of education, and the topics interested.

RESULTS: There were 98 participants (58 M, 40 F), ages between 49 and 81 years (mean 63.6 ± 14.7 years) completed the questionnaires. There were 67 (68.4%) subjects whose education was below the level of high school. The average waiting time was 57 ± 23 min. The activity during the waiting was categorized and rated as purposeless 33.7% ($n = 33$), watching television 26.5% ($n = 26$), preparing for meeting their doctors 24.5% ($n = 24$), and reading 15.3% ($n = 15$). About mode of education, the patients preferred lectures 48.0% ($n = 47$), TV 42.8% ($n = 42$), leaflets 34.6% ($n = 34$) and posters 15.3% ($n = 15$). About lecture from professionals, they preferred from physicians 49.0% ($n = 48$), nurses 31.6% ($n = 31$), dietitians 19.4% ($n = 19$). About the topics preferred were pathogenesis and prevention of diabetes (80.5%), pharmacological education (78.8%), nutritional education (73.1%) and daily care for elder (67.5%).

CONCLUSIONS: According the results of the questionnaire, we may set up the education program for people with diabetes during their waiting hour for clinics. Lectures from physicians or other professionals are preferred and information about the pathogenesis and prevention of diabetes, pharmacological and nutritional treatment, and daily care for elder are most required.

PEC-13-4

Evaluation Psychometric Properties of a Mongolian Version of the Problem Areas in Diabetes Scale in Newly Diagnosed Type 2 Diabetes

Shatarbal Bujinlham¹, Enkhjargal Yanjmaa¹, Sergelenchimeg Sundev² and Tserendagva Dalkh³

¹HSUM Mongolia, Mongolia; ²Clinical Nursing Department, School of Health Technology, HSUM; ³Admin Department, School of Health Technology, HSUM

OBJECTIVE: Examine psychometric properties of a Mongolian version of the PAID scale in patients with Type 2 diabetes in Mongolia.

METHODS: This study subjects were 150 Mongolian diabetics, aged 23–64 years old, who visited the Diabetes centers and Level II hospitals in Ulaanbaatar.

The cross-sectional survey was conducted between May 2011 and April 2012. The participants with type 2 diabetes were referred within, from May to August as newly diagnosed and included only the ones who met inclusion criteria and agreed with informed consent. We evaluated a Mongolian version of Polonsky's Problem Areas in Diabetes (PAID) stress questionnaire in baseline, 3, 6 months follow-up by educated and non-educated groups. Statistical analysis was performed with the SPSS 16 software.

RESULTS: At the baseline study were PAID Questionnaire in educated group 45 ± 17.4 , at the 3 months 43.1 ± 14.1 , and 6 months decreased 42.3 ± 13.6 . However psychosocial status which includes satisfaction of health care service, anxiety of their disease depression related blood glucose reactions eating family and regular self management was significantly different between educated and non educated groups.

CONCLUSION: Problem Areas in Diabetes Mongolian version were significantly different during the in non-educated newly diagnosed diabetic mellitus patients in Mongolia

PEC-13-5

Enhance Diabetes Self-Management Skills Program

Hsiu-Jen Tsai¹, Ming-Juan Shan¹, Chi-Chun Chi-Chun¹, Ling-Ting Huang¹, Ya-wen Yang², Chih-Chien Wang³, Yu-He Shan⁴ and Ching-Wo Yang⁴

¹Center of Diabetes Education, Show Chwan Memorial Hospital, Taiwan; ²Department of Nutrition, Show Chwan Memorial Hospital, Taiwan; ³Medical Department, Show Chwan Memorial Hospital, Taiwan; ⁴Department of Nursing, Show Chwan Memorial Hospital, Taiwan

PURPOSE: Self-management is a multiple caring behavior consisting physical, psychological and social care activities. Taking medicine, diet control,

symptom management and doing exercise are important factors of a chronic disease self-management. It's tested the longer changed behavior can keep diabetes in a good condition and prevent or postpone to having complications.

METHOD: By holding group activities, establishment of a case of self-management education program can strengthen the behavior by nurses through questionnaire to reiterate the importance of blood glucose monitoring and exercise. Nutritionists offer the overall knowledge and guidance of staple food. Team leader conduct interviews by phone weekly to strengthen the monitoring of blood glucose and staple food intake behavior change techniques.

RESULT: Conclusions through project implementation can successfully enhance the skill of diabetes self-management. Self-monitoring blood glucose by patients will be 1 times/week 22%, increased to 68% after; regular exercise five times a week 48% to 83%; correctly identify the staple food with the correct intake of staple food from 9% increase to 49%

CONCLUSION: Self-management of blood sugar is a necessary action to preventing from complications. Through the implementation of this program, blood glucose monitoring and exercise frequency and proper identification of the staple food and the right intake of staple food are improved significantly. Enhance the right attitude of the diabetes and positive behavior can enhance the self-management ability of patient to control blood sugar purpose and having a better life.

PEC-13-6

Activities of Diabetes Mellitus Support Team in Our Hospital

Mayumi Adachi¹, Sigemi Tamate², Akiko Simoji³, Yumi Kaneda³, Yoshinori Okano⁴, Seito Nakamura⁵ and Daisuke Matsuda⁶

¹Department of Rehabilitation Medicine, Higasiyamato Hospital, Japan; ²Department of Nutrition; ³Nursing Department; ⁴Department of Clinical Laboratory; ⁵Department of Pharmacy; ⁶Department of Diabetes Mellitus & Endocrine Diseases

BACKGROUND: Currently, patients with diabetes has increased dramatically in the world. It has become a problem in Japan too. Our hospital organized Diabetes Mellitus Support Team [DMST], and has supported diabetic patients and Diabetes Mellitus. I would like to announce what the team has contributed.

OBJECT: According to the diagnostic criteria of diabetes.

METHODS: (1) Weekly, co-medical members of DMST extract the object patients. (2) Considering the necessary support to the objects at the conference. (3) To create a plan for support of the objects at the meeting and submit it to the doctor. With DMST members, including the doctor, go the rounds at the objects. (4) Issuing a prescription to each medical professions to determine the comprehensive support needed to the Objects.

RESULT: Ninety-seven patients were examined for about half a year. However, only 62% of them were successfully conducted an examination and the average value of their HbA1c was 8.1%. The examination is still in the process.

CONSIDERATION: Respiration Support Team and Nutrition Support Team is often working on putting the effort in The medical institutions since they obtain remuneration for medical care. Like our hospital, it is rare that has introduced a DMST system to support hospitals in Japan.

Once again, those 97 patients were not been treated for diabetes mellitus.

They were treated for other health problems. No staff was questioned the value of their blood sugar. It means the worsening of diabetes, and treatment delay. We would like to continue activities to protect the patient's quality of life.

PEC-13-7

To Explore the Telephone Counseling Intervention on Diabetes Self-Care Behavior of Effectiveness

Hsiu-Jen Tsai¹, Chi-Chun Hou¹, Ling-Ting Huang¹, Ming-Juan Shan¹, Chih-Chien Wang², Ching-Wo Yang³ and Yu-He Shan³

¹Center of Diabetes Education, Show Chwan Memorial Hospital, Taiwan; ²Medical Department, Show Chwan Memorial Hospital, Taiwan; ³Department of Nursing, Show Chwan Memorial Hospital, Taiwan

PURPOSE: The evidence shows that telephone consultation can effectively enhance the frequency of self-monitoring of blood glucose, foot checking and weight monitoring and medication compliance degree, improving blood glucose levels, increasing self-care performance satisfaction. We hope to improve patients' diabetes awareness and self-care knowledge and skills through group health education and regular telephone consultation up care. Diabetes will be well managed by reducing the risk of high and low blood sugar.

METHOD: For insulin-treated patients, by group education, teaching and guidance and feedback to demonstrate the skills of blood glucose monitoring

education programs. Educator will conduct three consecutive months once a week telephone interviews to track cases of diet, exercise, blood glucose monitoring values frequency and offer in time teaching.

RESULTS: After 3-month tracking, the frequency of self-monitoring per person per week increases about 1 times, the ratio increased from 36.36% to 63.64% (21), $P < 0.03$ statistical differences. Exercise increased by 60.6–75.8%, the weekly average exercise frequency increased by 1.06 times to achieve significant differences ($P < 0.03$); Comparison of body weight before and after health education the group overall weight loss of 12 kg to reach groups is a weight loss of 5 kg target.

CONCLUSION: The Professional telephone consultation timely and intervention. Finally patients can improve self-care ability and self-confidence and slow down the danger caused by the high and low blood sugar, improve quality of life, to achieve the goal of glycemic control.

PEC-14-1

Plan to Our Clinical Path for the Medical Treatment Fee from the Tendency of our Diabetic Nephropathy Patients

Chikako Hibino and Hiroshi Tamura

Department of Internal Medicine, Hiroshi Tamura's Hilltop Clinic, Japan

Our clinic is no hospitalization. Not only diabetes, but also the internal medicine, circulatory organ, respiratory apparatus and allergy department. We are four nurses have the Certified Diabetes Educators, two Registered Dietitians, seven smoking cessation authorization leaders. We have been activated our diabetic group. Japanese medical treatment fee from April 2012, diabetes dialysis prevention instruction management charges (350 points a month = 3500 yen) started calculating. We are investigated of our calculated diabetic nephropathy patients (both of diabetic over second-stage renal disease and HbA1c (NGSP) ≤ 6.5), and planning our clinical path. Fifty-eight patients with diabetic nephropathy that it is registered from November 2004 to March 2012, and also continued treatment. Thirty-eight patients (65%) need to calculate the diabetes dialysis prevention instruction management charges. Twenty-six male (age 59 ± 14 , HbA1c 7.0 ± 0.7) was larger than that of 12 female (age 65 ± 12 , HbA1c 6.9 ± 0.3) ($P < 0.01$). Also, 26 patients (68%, age 57 ± 12) are the second stage renal-stage, the third-stage 11% ($n = 4$, age 64 ± 16), the forth-stage 21% ($n = 8$, age 72 ± 12). Between the stage division and the average age had correlation ($y = 7.47x + 49.00$, $R^2 = 0.99$). Thirty-one patients (82%) received the nutrition consultation.

CONCLUSION: The patients of diabetes dialysis prevention instruction management charges might be the dialysis. The average age of diabetic nephropathy patient starts dialysis was 66.1 years old from the investigate of Japan Society for dialysis therapy in 2010. We suggested that our diabetic nephropathy management patients (average age 57) who has been the second-stage might be starting dialysis after 10 years. We need to plan to the clinical path shouldn't be the short-period, it is a long-term clinical path.

PEC-14-2

Periodontitis Among Type 2 Diabetic Patients

Solongo Gurkhaajav¹, Bayarchimeg Batbayar¹ and Sainbileg Sonomtseren²

¹School of Dentistry, Health Sciences University of Mongolia, Mongolia; ²Department of Endocrinology, School of Medicine, Health Sciences University of Mongolia, Mongolia

AIMS: The aim this study was to determine periodontitis among Type 2 DM patients.

METHOD: Case-control study included 21 Type 2 DM patients and 21 Non-diabetics (healthy subjects). Periodontitis was diagnosed by clinical examination such as periodontal probe (depth of periodontal pocket), index of oral health and moving teeth.

RESULTS: We studied Diabetic and Non-diabetic 35–75 years old patients. Depths of periodontal pockets were different (with normal depth or 2–3 mm 0.0% and 76.12%, with depth 4–6 mm 52.38% and 19.04% and with depth > 6 mm 47.61% and 4.84%) between Diabetic and Non-diabetic groups. Diabetic and Non-diabetics with good oral health index were 9.52% and 4.0% but, with bad oral health index were 90.47% and 96.0%. 85.71% of Type 2 DM patients and 28.57% of Non-diabetics have moving teeth.

CONCLUSIONS: Individuals with type 2 diabetes have higher degree of periodontal inflammation.

PEC-14-3

How do the Patients with Diabetic Nephropathy Understand Their Disease?

Noriko Kato and Mitsutoshi Kato

Kato Clinic of Internal Medicine, Japan

OBJECT: We investigate the outpatients who have diabetic nephropathy, how much do they understand their disease.

RESULT: Two hundred and thirty-nine out diabetic patients were get the lessons and did the questioner. The diabetologist diagnosis the patients, how is their stage of diabetic nephropathy. Nurse teaches them about the examination, and dietitian teaches how much salt and protein intake. (1) 80% of them know diabetic nephropathy. (2) 74% of them know protein urine were occur from the kidney disorder. (3) 50% know they have nephropathy. (4) could understand the stages of diabetic nephropathy is a bit of fit 92% it was. (5) adversely affect blood pressure or kidney is the intakes of salt will understand the fit a little 98% and good. (6) Is able to understand the bad kidney diseases fit little intakes of protein 95% is used (7) has changed during the execution is 62%, (8) is going to change 33% in still not enough guidance. But that very came to care about results of urine tests of 67%, little 30% is a. Hydronephrosis in merger CV of investigated the presence of families to live together, tell the because of the high risk of nephropathy in that the family is important.

OBSERVATIONS: Medical staff to teach prevention of dialysis on diabetic patients in the team is important, but in desirable to confirm the understanding of the patient coached in such surveys. Further important to convey to the family, and to utilize in the future leaders.

PEC-14-4

Constipation in Diabetic Neuropathy Patients and Current Coping Strategies

Akane Hatanaka¹, Kanako Ejiri², Chiyo Murauchi², Midori Okubo², Akemi Ono², Naomi Nishimura² and Keiko Tsuneyoshi²

¹Department of Nursing, Iseikai Hospital, Japan; ²The "Hanshin Club," The Organization of Certified Nurses (CN) of Diabetes Care, Japan

OBJECTIVE: This study aims to elucidate how diabetic neuropathy patients cope with constipation.

METHODS: Study subject were 37 patients (24 male, 13 female, average age 65.2 years, diabetic morbidity 19.3 years, and average HbA1c value 9.8%) diagnosed with diabetic neuropathy undergoing a nursing consultation with a certified nurse. Patients were assessed using the Japanese edition of the Constipation Assessment Scale (long term version) to study awareness and coping strategies regarding constipation.

RESULTS: All patients had a CAS score between 8 and 15, giving a mean score of 10.1. This score was higher than the mean of 2.13 given for healthy elderly (over 60 years of age) during previous studies, although 22 patients were aware that they suffered from constipation, and 34 patients were taking measures to manage their constipation. Coping strategies chiefly consisted of: fluid, dairy or laxative intake by 17 patients; abdominal massage by 15 patients and moderate exercise and intake of dietary fiber by 14 patients. Although coping strategy types were limited, they could be adapted to suit the individual.

CONCLUSION: Neuropathy patients have a high rate of severe constipation. Regardless of whether patients are aware of their constipation or not, medical staff should work actively to support the control of symptoms and find a coping strategy suited to the individual patient.

PEC-14-5

Practice of Foot Care Education by CNS for the Prevention of Diabetic Foot

Kayo Yokota¹ and Sanae Iha²

¹Division of Nursing, Kansai Electric Power Hospital, Japan; ²Division of Nursing, Shiga University of Medical Science, University Hospital, Japan

AIMS: Report practice of foot care education by Certified Nurse Specialist in Chronic Care Nursing (CNS) for the prevention of diabetic foot.

METHOD: Provided in-hospital and out-of-hospital education about skill and knowledge about foot care to nurses, who finished training for the prevention of diabetes complication or are interested in foot care.

RESULTS: Fifty nurses participated in out-of-hospital education and 40 nurses participated in in-hospital education. Regarding out-of-hospital education, we built up knowledge and skill of foot care and educated improving assessment

ability. Fifty percent of participants have established outpatient department for foot care and have implemented foot care for outpatients.

Regarding in-hospital education, we provided education about basic knowledge and skill training. Participants got better understanding about foot care and acquired skills for nail care and skin care.

CONCLUSION: Education for the prevention of diabetic foot by CNS led improvement of knowledge and skill as well as learning nursing-care to sustain and improve the QOL of patient's life.

PEC-15-1

Quality of Life in Mongolian Children and Teenagers with Type 1 Diabetes

Gerelchimeg Tsagaantsooj¹, Undram Lkhagvaa¹ and Sainbileg Sonomtseren²

¹Department of Public Health, Health Science University of Mongolia, Mongolia;

²Department of Endocrinology

OBJECTIVE: The aim of this research was to determine the quality of life of the children and adolescent with type 1 diabetes

RESEARCH DESIGN AND METHODS: Study participants included 17 parents of children with diabetes, 4–12 years of age, and 13 adolescents with type 1 diabetes. Parents and adolescents completed the Pediatric Quality of Life Inventory (PedsQL), including five domains (problems with diabetes, problems with treatment 1 and 2, problems with worry and problems with communication).

RESULTS: PedsQL responses from youth with type 1 diabetes and their parents show living with type 1 diabetes is difficult to control and they always dreaded of complications. After controlling for age, duration of diabetes, sex and characteristics of diabetes treatment did not predict quality of life.

CONCLUSION: The problem which is affecting the quality of the children and teenagers life with type 1 diabetes is their fear of complication, diabetes and food management.

PEC-15-2

The Utilization of Traditional Chinese Medicine Among Patients with Diabetes in Taiwan

Chien-Chang Liao¹ and Chun-Chuan Shih²

¹Department of Anesthesiology, Taipei Medical University Hospital, Taiwan; ²The School of Chinese Medicine for Post-Baccalaureate, I-Shou University, Kaohsiung County, Taiwan

BACKGROUND: The increasing use of complementary, alternative medicine and traditional Chinese medicine (TCM) has attracted attention. However, the patterns of TCM use among diabetes were still unknown. The objective of this study is to report the prevalence of TCM and associated factors among patients with diabetes in Taiwan.

METHODS: Claims data of 1,000,000 insured subjects randomly selected from the National Health Insurance Research Database of Taiwan were used to identify adults with newly diagnosed diabetes in 2000–2009. We investigate the 1-year use of TCM after the diagnosis of diabetes among patients aged 20 years and older. Multivariate logistic regression was used to estimate odds ratios and 95% confidence intervals of factors associated with TCM use.

RESULTS: The 1-year prevalence of TCM use in patients with diabetes was high. We found that factors associated with TCM use among patients with diabetes included age, sex, low-income status, living area with high TCM physicians, and having more chronic diseases.

CONCLUSION: Our study investigated sociodemographic factors associated with TCM use in patients with diabetes. Further studies need to assess the impact of medical pluralism and the interaction between Chinese herbal medicine and biomedical medication.

PEC-15-3

Association Between Shift Work with Glycemic Control in Chinese Type 2 Diabetic Patients

Jenny Yuying Zhang¹, Rebecca Wong¹, Harriet Chung², Risa Ozaki¹, Andrea Luk¹, Enoch Wu¹, Ronald Ma¹, Wing Yee So¹, Francis Chow¹, Juliana Chan³ and Alice Kong¹

¹Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong; ²Yao Chung Kit Diabetes Assessment Centre, Hong Kong Institute of Diabetes and Obesity, The Chinese University of Hong Kong, Hong Kong; ³Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Yao Chung Kit Diabetes Assessment Centre, The Chinese University of Hong Kong; Asia Diabetes Foundation, Hong Kong

OBJECTIVE: To evaluate the association between shift work with glycemic control in Hong Kong Chinese type 2 diabetic (T2D) patients.

METHODS: Chinese T2D patients attending a hospital clinic were invited to complete validated questionnaires to evaluate their sleep habits during comprehensive assessment for diabetes complications using the Joint Asia Diabetes Evaluation (JADE) Program. The latter is a web-based program incorporating a validated risk engine, care protocols, feedback charts and decision support.

RESULTS: Between January 2010 and February 2012, we recruited 1911 T2D subjects (58.3% men) with a mean age of 54.7 ± 15.7 years (mean $\pm$ SD) and median disease duration of 6 years. Amongst 1111 (58.1%) patients actively employed, 14.0% undertook regular shift work within 1 year of assessment. Compared to those without regular shift work, patients with regular shift work were younger (51.5 ± 9.5 vs 54.9 ± 8.6 years, $P = 0.037$), more likely to be men (68.2% vs 57.0%, $P = 0.003$) and less likely to engage in regular physical activity (exercise ≥ 5 times/week, 23.1% vs 35.1%, $P = 0.001$). After adjustment for age, gender, disease duration, sleep duration, physical activity, use of alcohol and tobacco, insulin treatment and diet compliance, patients with shift work had higher HbA1c level ($7.8 \pm 1.7\%$ vs $7.4 \pm 1.4\%$, $P = 0.005$) and were less likely to achieve glycemic goal (HbA1c $< 7.0\%$) (Odds ratio: 0.68, 95% confidence interval: 0.48–0.97, $P = 0.032$) than those without shift work.

CONCLUSION: Shift work is associated with suboptimal glycemic control in Chinese T2D patients.

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PEC-15-4

Feelings about Blood Sugar Control in Type-2 Diabetes Patients with Cancer

Naoko Higo¹, Sachiko Mitsuki², Hiroya Iwase³, Mayuko Kadono¹, Masahiro Yamazaki¹, Michiaki Fukui¹, Goji Hasegawa¹ and Naoto Nakamura¹

¹Kyoto Prefectural University of Medicine Hospital, Japan; ²School of Nursing, Kyoto Prefectural University of Medicine, Japan; ³Endocrinology and Metabolism, Kyoto Prefectural University of Medicine, Japan

PURPOSE: Clarifying feelings about blood sugar control in type-2 diabetes patients with cancer.

SUBJECTS: Thirty-four type-2 diabetes patients with cancer, age 50–60; 34 type-2 diabetes patients without cancer, age 50–60; all currently receiving treatment at this facility.

METHOD: Questionnaire survey during exam. The survey was conducted using a Self-Efficacy Scale for dietary control in diabetes patients, the Locus of Control Scale, and a written questionnaire.

FINDINGS: Valid response received from: 34 type-2 diabetes patients with cancer (27 male, seven female, average age 61.9 years); 34 type-2 diabetes patients without cancer (27 male, seven female, average age 61.6 years). (1) No significant difference in self-efficacy of dietary management. (2) No significant difference in locus of control. (3) In the patients with cancer, response to 'Do you wish to concentrate on treatment for both cancer and diabetes?' were biased towards the positives of 'strongly agree' and 'somewhat agree'; self-efficacy was significantly greater in 'strongly agree' than in 'somewhat agree' (Wilcoxon rank-sum test $P = 0.0055$).

DISCUSSION: Findings suggested that type-2 diabetes patients with cancer have the same level of self-efficacy and locus of control as patients without cancer, and that they want treatment for both cancer and diabetes.

PEC-15-5

Glycaemic Profile of Diabetic Patients

Sarnai Otgonbayar¹, Telmen Boldbaatar¹, Byambatseren Jambaljav², Tsetsegee Dagvadorj², Bayanjargal B.³ and Sainbileg Sonomtseren¹

¹School of Medicine, Health Sciences University of Mongolia, Mongolia; ²First State Clinical Hospital, Mongolia; ³Food Engineering and Biotechnology School, Mongolian University of Sciences and Technology, Mongolia

AIMS: Aim of this study was to evaluate glycaemic profile (SMBG) of hospitalized DM patients.

METHODS: This study included 44 DM patients (27 male and 17 female). We measured blood glucose level of DM patients seven times (fasting or before and after 2 h breakfast, before and after 2 h lunch, before and after 2 h dinner and bedtime) on first day of hospitalization by SMBG.

RESULTS: DM patients mean age was 52.63 ± 11.11 (27–75) years old and mean diabetes duration was 5.85 ± 4.74 (0–21) years. By SMBG results DM patients mean blood glucose levels were high such as fasting or before breakfast 11.92 ± 5.25 (4.6–29.3) mmol/L, after 2 h breakfast 13.49 ± 5.98

(4.2–32.1) mmol/L, before lunch 13.69 ± 7.30 (4.9–Hi) mmol/L, after 2 h lunch 14.44 ± 7.14 (4.5–32.2) mmol/L, before dinner 14.37 ± 7.29 (4.6–Hi) mmol/L, after dinner 15.54 ± 7.41 (5.9–30.6) mmol/L, bedtime 15.09 ± 7.89 (4.9–Hi) mmol/L.

CONCLUSIONS: Glycaemic profile or blood glucose levels of diabetic patients on first day of hospitalization were high by SMBG.

PEC-15-6

Recurrent Episodes of Hyperosmolar Hyperglycemic State Complicated with Acute Kidney Injury: A Case Report

Pei-Yin Chen¹, Yi-Ling Liang¹ and Ta-Jen Wu²

¹Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Taiwan; ²Department of Internal Medicine, National Cheng-Kung University, Medical College and Hospital, Taiwan

A 78-year-old man without diabetic history was found consciousness disturbance and then hyperosmolar hyperglycemic state (HHS) was diagnosed. The initial plasma glucose level was 1323 mg/dL. After this first episode of HHS, basal insulin combined with oral hypoglycemic agent was prescribed, and the regimen was shifted to premixed insulin therapy 7 months later. In spite of regular medication with insulin injection and self-monitoring blood glucose (SMBG), the glucose control was very poor. The data of SMBG highly fluctuated, and his HbA1c ranged from 11.8% to 17.1%. He experienced six additional episodes of HHS during the following 9 months. The clinical characteristics of the six episodes were very similar. They all showed highly elevated glucose levels (ranged from 1038 to 1487 mg/dL) and ran a very rapid clinical course in 1–2 days. The consciousness and hyperglycemia crisis usually improved within 2–4 days. Acute renal failure also returned to normal soon. In conclusion, we report a rare case of recurrent HHS episodes.

PHE-01-1

Withdrawn

PHE-01-2

Correlation Between Anthropometry and Dietary Habits of Teenage School Children in the Chiayi Region of Taiwan

Hsiang-Hsun Chuang, Hui-Yi You, Shi-Zhe Hua and Chieh-Hsiang Lu

Division of Endocrinology and Metabolism, Department of Internal Medicine, Chiayi Christian Hospital, Taiwan

OBJECTIVE: In recent years, obesity and the metabolic syndrome have become an emerging problem among children and adolescents. According to a 2005 survey, approximately 26.3% of school children in the Chiayi region are overweight and obese, representing the highest prevalence in the country. Therefore, this study was aimed to investigate the correlation between anthropometry and dietary habits in school-age children from the Chiayi region of Taiwan.

METHODS AND TOOLS: Junior high school students from eight municipal schools in Chiayi city were invited as study subjects. A total of 1110 students with the informed consent were interviewed using an adolescent metabolic syndrome questionnaire survey.

RESULTS: Mean body mass index (BMI) of junior high school children in Chiayi city was 20.99 ± 3.75 , the 90th percentile BMI was 25.67. According to the National criteria, 50.53% were normal weight, and 29.68% were overweight or obese. Thirty-five percent of male and 19.8% of female students were overweight, 24.47% of male and 10.55% of female students were obese.

Dietary habits were significantly different ($P < 0.05$) in both sex in mean daily number of meals, consumption of school lunch, sleep time, amount of water consumption, preference for vegetable intake, preference for fried foods, frequency of snack consumption, speed of eating.

CONCLUSION: Since the dietary habits of male and female school children in the Chiayi region were different, these groups require different interventions and gender-specific public health education. Both government, educational institutions and medical professionals should devote efforts and cooperatively help improve adolescent health.

PHE-01-3

Association Between an Increase in Waist Circumference and the Number of Cardiovascular Risk Factors in Men under 65 years of Age and Women under 50 years

Teruyo Okazawa¹, Yutaka Kamura¹, Minoru Iwata¹, Kazuyuki Tobe¹, Hiromi Katou² and Yumi Matsushita³

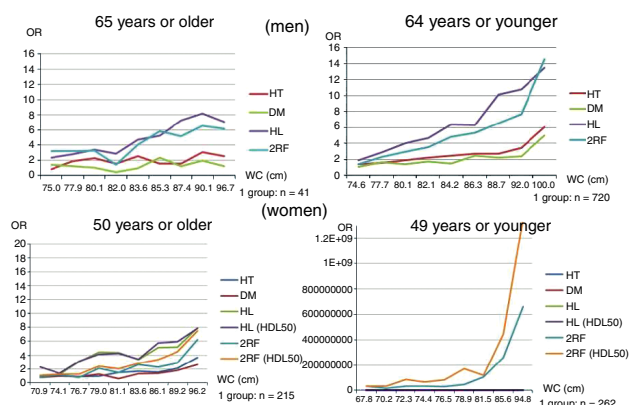
¹The First Department of Internal Medicine, University of Toyama, Japan; ²Department of Internal Medicine, Shikaihoken Takaoka Hospital, Japan; ³Department of Clinical Research Coordination, National Center for Global Health and Medicine, Japan

OBJECTIVE: The relationship between waist circumference (WC) and cardiovascular risk factor (RF) clustering was investigated according to sex and age.

METHODS: The study population consisted of 12,389 Japanese individuals who were not taking medication for cardiovascular RFs. Fasting blood tests were performed for each individual. The WC values were divided into deciles; a WC of <70 cm was used as a reference for calculating the odds ratios (ORs). The number of individuals with two or more RFs is shown using the OR for each decile.

RESULTS: The number of RFs increased with an increasing WC among men under 65 years of age and among women under 50 years of age. This trend became stronger as the WC increased. The relevance of this trend decreased in men aged 65 years or older and in women aged 50 years or older.

Association between an increase in waist circumference and the number of cardiovascular risk factors



PHE-01-4

The Metabolic Syndrome: Prevalence and Associated Risk Factors in adults in Jilin Province of China

Qi Wei, Jie Sun, Liu Yulian, Liu Xingxing, Wang Chunyan and Niu Junqi

Department of Cadre, The First Hospital of Jilin University, China

OBJECTIVE: To evaluate the prevalence of metabolic syndrome (MS) and risk factors in Jilin Province in China.

METHODS: A cross-sectional study named the health and nutrition examination survey of Jilin province was performed. And there are 7554 subjects aged from 18- to 78-year involved in this survey. The definition of MS is referred to the International Diabetes Federation (IDF) 2005 definition. Logistic regression analysis was used to identify risk factors of hypertension.

RESULTS: The prevalence of MS is 31.2% in Jilin Province in China. And the age specific prevalence of MS is 4.66%, 16.70% and 9.85% for age from 18- to 44-year, 45-year to 59-year and 60- to 78-year, respectively. There is significant difference between urban and rural area ($P < 0.001$), the urban is 20.28% and country is 10.93%. The metabolic syndrome was present in 0, 1.43%, 9.32%, and 2.33% of normal-weight, overweight, obesity and over-obesity men, respectively; And for women is 0, 4.42%, 11.22%, and 2.49%, respectively. In a binary logistic regression, old age, current smoking, high monthly income, high carbohydrate intake, urban area, and family history of MS were associated with increased odds of the metabolic syndrome, and the odd ratio [95% confidence interval (CI)] is 1.04 (95%CI: 1.03–1.05), 1.46 (95%CI: 1.11–1.92), 1.09 (95%CI: 1.03–1.14), 1.32 (95%CI: 1.11–1.56), 1.61 (95%CI: 1.39–1.86), and 1.71 (95%CI: 1.03–2.81), respectively. But no relationship with physical activity, type of occupation, drink and education in this study.

CONCLUSION: The prevalence of the metabolic syndrome was higher in Jilin province than in southern China, and higher in urban than rural residents.

PHE-01-5

Prevalence of Metabolic Syndrome According to Increasing Fasting Blood Glucose Level in Korean Nondiabetic Individuals Within Normal Range of Fasting Blood Glucose

Hyun Jin Moon, Jae Min Lee, Hea Min Yu, Kang Seo Park and Seong Kyu Lee

Division of Endocrinology, Department of Internal Medicine, Eulji University Hospital, Daejeon, Korea

INTRODUCTION: Metabolic syndrome is a well-known predictor of diabetes or cardiovascular disease. However, studies about prevalence of metabolic syndrome in subjects with normal fasting glucose are limited. We investigated the association between fasting glucose level and metabolic syndrome in normal fasting glucose subjects.

METHODS: Twenty four thousand six hundred and three individuals underwent health check-up in Eulji medical center from January 2006 to June 2007. Patients with uncontrolled diabetes mellitus, hypertension, thyroid function abnormalities, kidney disease, abnormal liver function test were excluded. Data of fasting glucose and waist circumference, blood pressure, lipid profile were obtained. Subjects who have normal fasting glucose level were divided into four groups according to quartile of fasting glucose level and the metabolic parameters and prevalence rate of metabolic syndrome was compared between each group.

RESULTS: Twenty thousand eight hundred subjects had normal fasting glucose level and the mean fasting glucose level was 85.64 mg/dL. Among them, 7.4% ($n = 1539$) had metabolic syndrome (1187 men vs 352 women, $P < 0.01$). As fasting blood glucose level increased, the prevalence of metabolic syndrome increased significantly ($P < 0.01$) and the metabolic parameters such as waist circumference, systolic blood pressure, diastolic blood pressure, triglyceride showed positive correlation ($P < 0.01$) and high density lipoprotein level showed negative correlation ($P = 0.01$).

CONCLUSION: As fasting glucose level increased within normal range, it was associated with a derangement in metabolic parameters and a high prevalence of metabolic syndrome. The result shows that raised fasting glucose level, even though in the reference range, can be a useful tool for detecting derangement in metabolic markers and predicting the occurrence of metabolic syndrome.

PHE-01-6

Decreased Physical Activity is Associated with a Clustering of Metabolic Risk Factors in Non-Obese Japanese Individuals

Wataru Kaino, Kaoru Takase, Kyouko Tada, Shigeru Karasawa, Kiriko Wada, Wataru Kameda, Shinzi Susa, Toshihide Oozumi, Makoto Daimon and Takeo Kato
Department of Neurology, Hematology, Metabolism, Endocrinology and Diabetology, Yamagata University School of Medicine, Japan

OBJECTIVE: The metabolic syndrome (MetS) is a complex of interrelated risk factors for cardiovascular disease (CVD). Although obesity is the essential factor for the diagnosis of MetS in Japan, those without obesity but with a clustering of several other metabolic risk factors also appeared to be at risk for CVD. We examined here lifestyle characteristics different between those with and without a clustering of metabolic factors (C-MetRF) in non-obese subjects as well as in obese subjects.

METHODS: From a population-based cross-sectional study of Japanese people over 40 years old, the Takahata study, 1601 subjects (mean age: 61.9 ± 10.3 years; men/women: 710/891) were recruited. Their status of daily nutritional intake and current physical activity were estimated using the brief self-administered diet history questionnaire and the Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire, respectively. Subjects with C-MetRF were defined based on the presence of ≥ 2 of the non-essential risk factors for the diagnosis of MetS in Japan.

RESULTS: The subjects with C-MetRF had no tendency to take more energy, fat and salt compared with those without. While, they had less physical activity than those without in men (26.9 ± 5.4 vs 28.6 ± 6.6 METs $\times$ hour, $P = 0.005$) both with obesity ($P = 0.038$) and without ($P = 0.046$). This fact was not significantly observed in women, but energy expenditure at work and housework was tended to be less in the subjects with C-MetRF (11.6 ± 7.8 vs 14 ± 8.7 , $P = 0.053$).

CONCLUSION: Decreased physical activity but not increased energy consumption seems to be a risk factor for C-MetRF in Japanese individuals, especially in men.

PHE-02-1**The Prevalence and Clinical Implications of Painful Diabetic Neuropathy in Korea**

Kyung Soo Ko¹, Jung Min Kim¹, Jong Chul Won¹, Chong Hwa Kim², Hyuk-Sang Kwon³, Ji-Hyun Lee⁴, Tae Sun Park⁵ and Bong-Yun Cha³

¹Department of Internal Medicine, Inje University Sanggye Paik Hospital, Korea;

²Department of Internal Medicine, Sejong General Hospital, Bucheon, Korea; ³Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea;

⁴Department of Internal Medicine, College of Medicine, Daegu Catholic University, Daegu, Korea; ⁵Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, Korea

BACKGROUND: Painful diabetic neuropathy (PDN) has implications for patient's morbidity. However, data on the prevalence and risk factors of DPNP in Korea are limited. To determine the prevalence and risk factors and evaluate the sleep impairment and quality of life in patients with PDN among the patients with diabetic peripheral neuropathy (DN).

METHODS: Data from Korean Diabetes Association Neuropathy Study group, a total of 3999 type 2 diabetic patients were evaluated. PDN was diagnosed by using visual analogue scales (VAS) and medication history. The patients were asked to answer the Brief Pain Inventory-Sort Form (BPI-SF), Medical Outcomes Study Sleep measure (MOS-Sleep), and EuroQol (EQ-5D) and VAS.

RESULTS: Among the patients with DN ($n = 1338$, 33.5%), 65.3% ($n = 874$) were found to be PDN (overall 26.2% of studied patients). PDN was independently associated with duration of diabetes, and nephropathy and hypertension. All measures about pain severity and interference were higher in patients with PDN compared to those without PDN. Patients with PDN reported much impaired sleep and lower EQ-5D and VAS scores compared to those without PDN. Multivariate analysis revealed that presence of macrovascular complication and hypertension was independently associated with indices of BPI-SF, MOS-Sleep, and EQ-5D and VAS.

CONCLUSION: PDN patients had far advanced diabetic complications, which associated with decreased sleep adequacy and quality of life. There is a clear need for further research relating to prevention and treatment of DPN including the issues of sleep and quality of life.

PHE-02-2**A Study of Risk Factors of Diabetic Foot Complications in Mongolia**

Battsetseg Lkhagvasuren, Enkhjargal Yanjmaa and Ulziisaikhan Batchuluun

Endocrinology Department of Ahtan Clinical Hospital, Mongolia

OBJECTIVES: To evaluate some risk factors of diabetic foot complication in type 2 diabetic patients.

METHODS: This cross sectional study was conducted in UB- I, II, Ahtan clinical hospital, outpatient hospitals are Sukhbaatar, Bayanzurkh, Chingeltei, Bayangol districts of Ulaanbaatar city. A total of 158 type 2 diabetic patients were randomly selected using the questionnaire, anthropometric measurement and clinical testing of peripheral neuropathy, peripheral vascular disease based on WHO standard methods.

RESULTS: This study subjects were over the 35 years old and from them 77 (48.7%) male, 81 (51.3%) female. The mean age of participants 54 ± 10.4 years and diabetes duration of 12 ± 4.6 years. Using diabetic foot complication diagnosing standard methods the patients 71(44.9%) were in risk of diabetes foot complications and we can subdivide patients: 15 (21.42%)- have peripheral neuropathy, 27 (38.58%)- have peripheral vascular disease, 29 (40.01%)- duplicated mixed form.

Diabetes duration increased by systolic blood pressure significantly increasing ($P < 0.001$, OR = 4.1) and related to ankle brachial index decrease by diabetes foot complications.

CONCLUSION: For the diabetic patients long diabetes duration, high blood pressure, reducing the ankle brachial index are becoming the risk factors for the diabetic foot complication.

KEYWORDS: Diabetic foot complication, peripheral vascular disease, peripheral neuropathy, foot ulcer, foot amputation, osteomyelitis, gangrene

PHE-02-3**Factors Associated with Cardiovascular Disease in Korean Diabetic Patients: The Korea National Health and Nutrition Examination Survey (KNHANES) 2009–2010**

Ohk Hyun Ryu¹, Sunghwa Lee², Sung Hee Ihm¹, Jae Myung Yu¹, Doo-Man Kim¹, Hyung Joon Yoo¹ and Moon-Gi Choi¹

¹Department of Internal Medicine, Hallym University College of Medicine, Korea;

²Gangneung Health Center, Korea

BACKGROUND AND AIM: Cardiovascular disease (CVD) is a major cause of morbidity or mortality among diabetic patients. The purpose of this study was to evaluate the risk factors for CVD in Korean diabetic patients.

METHODS: We analyzed the Korea National Health and Nutrition Examination Survey (KNHANES) which was conducted in 2009–2010. We selected the data of 30-year or more old subjects ($n = 12,650$) who were diagnosed as diabetes by physicians previously ($n = 1072$; men = 524, women = 548). The history of stroke, myocardial infarction, or angina pectoris was defined as CVD. Univariate and multivariate logistic regression analysis was performed to identify and select the related factors to CVD.

RESULTS: The age and diabetes duration were 63.3 ± 11.1 and 8.4 ± 7.7 years in diabetic participants, respectively. The number of participants who had CVD history was 135. In univariate analysis, age, duration of hypertension, presence of hypertension, house income, frequency of alcohol drinking, presence of dyslipidemia, and level of cholesterol were significantly related to CVD. In multivariate logistic regression analysis, duration of hypertension ($P < 0.001$), presence of dyslipidemia ($P = 0.001$), level of cholesterol ($P = 0.002$), age ($P = 0.011$) was related to CVD in diabetic participants.

CONCLUSION: In Korean diabetic patients, duration of hypertension, presence of dyslipidemia, level of cholesterol, and age were related to CVD. Multifactorial intervention, including hypertension and dyslipidemia, is necessary for the prevention of CVD in Korean diabetic patients.

PHE-02-4**Non High-Density Lipoprotein Cholesterol is Associated Closely with Albuminuria in Chinese Type 2 Diabetic Patients with Normal Renal Function**

Fei Gao, Jie Min Pan, Yuqian Bao, Lei Zhang, Yinfang Tu and Weiping Jia

Department of Endocrinology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai Diabetes Institution, Shanghai Clinical Medicine Center for Diabetes, China

BACKGROUND: Urinary albumin excretion rate (UAER) is a remarkable index reflecting the progression of kidney disease in diabetic subjects. The link between UAER and lipid metabolism is still unclear. The correlation of Apolipoprotein B (ApoB) to albuminuria has been investigated. It was recommended that non high density lipoprotein cholesterol (non HDL-c) as a surrogate marker for ApoB.

OBJECTIVE: We sought to evaluate the relationship of UAER with lipid profile, especially with non HDL-c in type 2 diabetic patients without renal dysfunction.

METHODS: A total of 507 type 2 diabetic patients with normal renal function participated in this study. Twenty-four hour urine samples were collected for UAER measurement. Blood samples were collected for lipid parameters and HbA1c measurement.

RESULTS: The patients with albuminuria had greater levels of non HDL-c and ApoB. The frequencies of albuminuria among the four quartiles of lipid parameters, ie, triglycerides, total cholesterol, non-HDL-c, and ApoB, demonstrated significant linear test for trend ($P < 0.01$). After adjustment, UAER was significantly correlated with total cholesterol, triglycerides, ApoB, and non-HDL-c but not with low-density lipoprotein cholesterol (LDL-c) or lipoprotein (a) [Lp(a)]. Stepwise regression analysis showed that age ($b = 0.255$, $P = 0.000$), systolic blood pressure ($b = 0.261$, $P = 0.000$), non-HDL-c ($b = 0.164$, $P = 0.000$), and duration of diabetes ($b = 0.105$, $P = 0.024$) were independently correlated with UAER in diabetic patients without renal dysfunction.

CONCLUSION: Compared with the lipid parameters of total cholesterol, triglycerides, HDL-c, LDL-c, ApoB, Apolipoprotein A-I and Lp(a), non-HDL-c was more closely associated with albuminuria in Chinese type 2 diabetic patients without impaired renal function.

PHE-02-5

Cardiovascular Risk Management of Diabetes Patient in South Korea

Doo-Man Kim¹, Shingon Kim², Donghyuk Cho³, Chonghwa Kim⁴, Cheoshik Kim⁵, Wonyoung Lee⁶, Geujang Won⁷ and Youngju Kim⁸

¹Department of Internal Medicine, Hallym University College of Medicine, Korea;

²Department of Internal Medicine/Korea University, Anam Hospital, Seoul, Korea;

³Department of Internal Medicine/Chonnam National University Hospital, Gwangju, Korea;

⁴Department of Internal Medicine/Sejong General Hospital, Gyeonggi-do, Korea;

⁵Department of Internal Medicine/Hallym University Sacred Heart Hospital, Gyeonggi-do, Korea;

⁶Department of Internal Medicine/Kangbuk Samsung Hospital, Seoul, Korea;

⁷Department of Internal Medicine/Yeungnam University Medical Center, Daegu, Korea;

⁸Pfizer Pharmaceuticals Korea Ltd., Seoul, Korea

A prospective, observational study was carried out in 22 hospitals in Korea. Six hundred and twenty-two type 2 diabetes patients aged > 40 years were assessed by Carotid Ultrasound (CUS) and United Kingdom Prospective Diabetes Study (UKPDS) risk engine. CV high risk from CUS was defined as carotid intima-media thickness >1 mm or plaque presence. Before and 6 months after the test, patients completed a questionnaire on health-related behaviors and physicians collected data on treatment patterns.

Among 622 (mean age: 60.02 years), 271 (43.5%) and 66 (10.6%) patients were stratified as CV high risk from CUS and UKPDS, respectively. Approximately 40% of patients at moderate and low risk from UKPDS were determined as high risk from CUS. The awareness of high risk from CUS altered physician's treatment patterns ($P = 0.021$) for managing major CV risk factors: blood pressure (BP) and lipid. Along with CUS, risk levels by UKPDS also impacted physician's behavior: more changes of treatment pattern in high than in low risk level for BP (12.0% vs 15.6%) and lipid (13.8% vs 21.6%). Patients noted increased health-related behaviors: smoking cessation and dietary changes ($P < 0.005$, respectively) in 6 month follow up than before CUS and bigger in high risk.

This study identified NIT could detect more CV high risk patients than risk calculation. However, awareness of CV high risk itself has a positive impact on physician and patient behavior, regardless of assessment methods. Therefore, assessing CV risks using varied methods with the patient could be better for risk management in diabetes patient.

PHE-03-1

Diabetes, Drug Use and Cancer- The Hong Kong Diabetes Registry

Wing Yee So, Ronald Ma, Winnie Lau, Andrea Luk, Alice Kong, Francis Chow, Xilin Yang, Eric Lau and Juliana Chan

Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

Hyperglycemia is associated with increased risk of all-site cancer which may be mediated through the renin-angiotensin system (RAS) and 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGCR) pathways.

METHODS: We examined the joint associations of optimal glycemic control ($A1c < 7\%$) and use of RAS and HMGCR inhibitors on incident cancer in Chinese type 2 diabetic patients without history of cancer and exposure to these drugs.

RESULTS: After a median (interquartile range) period of 4.91 (2.81–6.98) years, 271 of 6103 patients developed cancer. Apart from older age, longer disease duration and higher tobacco and alcohol usage, incident cancer was associated with systolic blood pressure [137(25) vs 134(27) mmHg, $P < 0.001$], albuminuria [3.45 (14.2) vs 2.06 (10.5) mg/mmol, $P = 0.002$], low triglyceride [1.23 (0.77) vs 1.34 (1.02) mmol/L, $P = 0.001$] and low estimated glomerular filtration rate [98.8 (37.3) vs 103.1 (41.6) mL/min/1.73 m², $P = 0.018$] compared to non-cancer. Patients with incident cancer were less likely to be started on statins (22.5% vs 38.6%, $P < 0.001$), fibrates (5.9% vs 10.2%, $P = 0.02$), metformin (63.8% vs 74.5%, $P < 0.001$) and thiazolidinedione (TZD) (0.7% vs 6.8%, $P < 0.001$) than those without. After adjusting for covariates, new treatment with metformin [hazard ratio (95% confidence intervals): 0.39 (0.25–0.61), $P < 0.001$], TZD [0.18 (0.04–0.72), $P = 0.015$], sulphonylurea [0.44 (0.27–0.73), $P = 0.014$], insulin [0.58 (0.38–0.89), $P = 0.01$], statins [0.47 (0.31–0.70), $P < 0.001$] and RAS inhibitors [0.55 (0.39–0.78), $P < 0.001$] were associated with reduced cancer risk. Patients with all three risk factors ($A1c \geq 7\%$, non-use of RAS and statins) had 4-fold adjusted higher risk of cancer than those without any [incidence per 1000-person-years for 0 vs 1 vs 2 vs 3 risk factors: 3.40 (0.07–6.72); 6.34 (4.19–8.50); 8.40 (6.60–10.20), 13.08 (9.82–16.34) respectively, $P < 0.001$].

CONCLUSIONS: Hyperglycemia may be causally linked with cancer which can be attenuated by optimal glycemic control and inhibition of the RAS and HMGCR pathways.

PHE-03-2

Association Between Diabetes and Hearing Impairment in a Japanese General Population

Yusuke Kabeya, Kiyoe Kato, Masuomi Tomita, Takeshi Katsuki, Yoichi Oikawa, Akira Shimada and Yoshihito Atsumi

Department of Internal Medicine, Saiseikai Central Hospital, Japan

OBJECTIVE: The association between diabetes and hearing impairment has been rarely investigated in an Asian general population. The aim of the present study was to examine the association, controlling for the confounding effects of age, gender, smoking status and metabolic factors.

METHODS: We conducted a cross-sectional study in the medical check-up unit of Saiseikai Central Hospital. A total of 2753 participants who underwent a medical checkup at Saiseikai Central Hospital from May 2008 to December 2010 were included in the analysis. Logistic regression analysis was performed to examine the associations between diabetes and the presence of high- (4000 Hz) and low- (1000 Hz) frequency hearing impairment.

RESULTS: High- and low-frequency hearing impairment were found in 403 and 189 participants, respectively. A total of 468 participants were classified as having diabetes. After the adjustment for possible confounders, diabetes was significantly associated with an increased risk of having high-frequency hearing impairment with the odds ratio of 1.33 (95% CI = 1.02–1.75). On the other hand, a significant association was not observed between diabetes and low-frequency hearing impairment.

CONCLUSION: The present study demonstrated that diabetes was modestly and significantly associated with the presence of high-frequency hearing impairment. To our knowledge, this is the first study to report that diabetes is associated with hearing impairment independently of multiple lifestyle factors in a large sample of Asian general population. However, the causal association has not been confirmed because of the cross-sectional design. Further research should be performed to figure out the mechanism of the association.

PHE-03-3

Number of Remaining Teeth and the Impact on Health Among Rural Residents with Diabetes: A Cross-Sectional Observational Study

Jui-Chu Huang^{1,2}, Yun-Shing Peng², Su-Er Guo³ and Mei-Yen Chen³

¹Department of Internal Medicine, Chang Gung Memorial Hospital, Taiwan; ²Division of Endocrinology and Metabolism, Department of Internal Medicine, Chang Gung Memorial Hospital, Taiwan; ³College of Nursing and Chronic Diseases and Health Promotion Research Center, Chang Gung University of Science and Technology, Taiwan

BACKGROUND: There has been limited research describing the relationship between the number of remaining teeth (NRT) and the impact on health among rural residents with type 2 diabetes mellitus (T2DM). The aim of this study was to explore the prevalence and determinant factors associated with NRT among individuals with T2DM in Taiwan.

METHODS: This cross-sectional, observational study was conducted on 703 residents with T2DM who were participants in a longitudinal cohort study investigating the effect of health promotion in the prevention of diabetic foot among residents in rural communities in central Taiwan.

RESULTS: More than half of the participants presented with the lowest NRT. The NRT was significantly correlated to age, brachial pressure grading, Michigan Neuropathy Screening Instrument (MNSI), and ankle brachial pressure index (ABI); but not duration of diabetes, waist circumference, blood glucose status, or lipid profiles. Dental flossing and diurnal teeth brushing were potential determining factors for the NRT, especially among rural people aged from 51 to 80 years.

CONCLUSIONS: We found a potential predictive role of the NRT as a common indicator of diabetic foot. Further studies are needed to understand the relationship between oral health status and late diabetic complications.

PHE-03-4

An Observational Prospective Study of Cancer in Japanese Subjects with Diabetes with Special Reference to Pancreatic Cancer

Sachiko Honjo, Yukiko Kawasaki, Yoshiyuki Hamamoto, Hisato Tatsuoka, Kanta Fujimoto, Atsuko Matsuoka, Kanako Mori, Hiroki Ikeda, Yohiharu Wada and Hiroyuki Koshiyama

Center for Diabetes & Endocrinology, The Tazuke Kofukai Foundation Medical Research Institute Kitano Hospital, Japan

OBJECTIVE: We prospectively investigated the frequency and type of cancer in Japanese subjects with diabetes.

METHODS: Subjects included a total of 3968 consecutive patients with diabetes, who visited our clinic during 36 months from January 2009 to December 2011.

RESULTS: A total of 101 patients (2.5%) were newly diagnosed to have cancer. The mean age was 70 ± 9 (SD) years and male/female ratio was 67/34. The most frequent site of cancer was colon ($n = 23$) followed by pancreas ($n = 16$), stomach ($n = 16$), lung ($n = 10$), liver ($n = 9$), and others. The A1C at the diagnosis of cancer was $8.0 \pm 1.7\%$. The therapeutic variations (diet and exercise only 14.9%, oral antidiabetic drugs (OADs) 47.5%, and insulin 37.6%) of the patients with cancer were not significantly different from those without malignancy in our clinic.

In the cases with pancreatic cancer ($n = 16$), eight of 16 of them were found to have new-onset diabetes. The patients with pancreatic cancer had greater maximum BMI in the history compared to those without cancer (28.3 vs 25.7 kg/m², $P < 0.05$). However, they have shown rapid weight loss (mean -7.0 kg/1 year) before the cancer was diagnosed. The mean A1C was significantly higher in the patients with pancreatic cancer than that in the patients with other cancers (9.4% vs 7.7% , $P < 0.05$).

CONCLUSION: The present registry indicated that the incidence of cancer was considerably high in Japanese patients with diabetes. It is suggested that the risk factors for pancreatic cancer in subjects with diabetes are the aggravation of glycemic control and loss of body weight despite of greater BMI.

PHE-03-5

Association Between Sleep Condition and Glycaemic Control Among Patient with Type 2 Diabetes

Jo Jo Yee Mei Kwan¹, Kai Chow Choi², Doris Sau Fung Yu², Grace Sau Ping Yeung¹ and Vincent Tok Fai Yeung¹

¹Centre for Diabetes Education and Management, Our Lady of Maryknoll Hospital, Hong Kong; ²The Nethersole School of Nursing, The Chinese University of Hong Kong, Hong Kong

OBJECTIVE: To examine the relationship between sleep condition and glycaemic control among patients with type 2 diabetes in Hong Kong.

METHODS: Subjects were recruited from one community hospital and five family medical clinics in Hong Kong. The sleep condition was measured by Pittsburgh Sleep Quality Index (PSQI) while glycaemic control was measured by haemoglobin A_{1c}.

RESULTS: Five hundred and forty-eight subjects were recruited (male 46%, female 54%). Mean age was 63.8 and mean diabetes duration was 9 years. Majority of them (77%) were using oral anti-diabetic drugs as the treatment modality. The mean haemoglobin A_{1c} level was 7.3% and mean PSQI was 5.85 which exceeded the normal cut-off value at 5. On examining the bivariate association between HbA_{1c} and patient characteristics, we noted that HbA_{1c} level was correlated positively with PSQI ($P < 0.001$) and duration of diabetes ($P = 0.011$); but correlated negatively with age ($P < 0.001$). Significant difference was also noted between A_{1c} level and employment status ($P = 0.001$) and treatment modality ($P < 0.001$). Multivariate analysis using linear regression model was tested again to predict the level of haemoglobin A_{1c} and Pittsburgh Sleep Quality Index. The model showed that A_{1c} level was still associated positively with PSQI after adjustment for the factors mentioned above.

CONCLUSION: As the association is recognized between sleep condition and glycaemic control for people suffering from type 2 diabetes, care and patient education strategies to improve quality and quantity of sleep could be an adjunctive measure in optimizing the management of diabetes.

PHE-03-6

Scale Development for Self-perception of Health by Diabetics; Sense of Ill-being

Miyoko Nakano

School of Nursing and Rehabilitation Sciences, Showa University, Japan

OBJECTIVE: To develop sense of ill-being [SOI] scale for diabetics.

METHODS: In the literature on health, SOI is defined as 'the sense of being disease-stricken with pain and suffering that is directly attributable or related to the disease.' From interview data and reference materials, a 520-item pool was arranged. After reviewing them for content validity, 45 items were chosen. The preliminary survey was conducted on 110 diabetics. Final scale was created through a process of statistical review and content validity examination. To evaluate the scales' validity and reliability, the survey was conducted on 300 diabetics. With regard to validity, in order to confirm the one-dimensionality of the scale, principal component analysis was conducted. Subscale of the Health Questionnaire [HQ] was used to examine the validity of the scale in terms of the predicted relationship between the concepts. Coefficient alpha and test-retest reliability coefficient were used to evaluate reliability.

RESULTS: For preliminary survey, we obtained 107 responses to analyze. Ten-item final scale was created. To evaluate the scales' validity and reliability, 263 responses were using. As only the first principal components were extracted through principal component analysis, the one-dimensionality of SOI was supported. The validity was supported through the relationship with the HQ subscale ($r = -0.71$, $P < 0.01$). As for reliability, coefficient alpha was 0.93, test-retest reliability was 0.80. From these results the reliability was supported.

CONCLUSION: With their validity and reliability supported, the developed scale can be regarded as convenient scale that enables the evaluation of SOI using 10 items without a subscale.

PHE-03-7

Association Between Mental Health and Diabetes form Korean National Health and Nutrition Examination Survey (2008–2010)

Sangmo Hong, Jung Hwan Park, Yong Soo Park, Dong Sun Kim, Woong Hwan Choi, You Hern Ahn and Chang Beom Lee

Endocrinology and Metabolism, Hanyang University College of Medicine, Korea

The prevalence of depression in diabetes patients is known to increase. However, in patients with diabetes in Korea is reported to be associated with depression are rare. In this study, we studied the relationship between diabetes and the depressive mood and suicidal ideation.

We used the data form Korean National Health and Nutrition Examination Survey (KNHANES, 2008–2010). We studied the association between 'depressive mood' and suicidal idea, health-related quality of life, and diabetes. Health-related quality of life was evaluated by EQ-5D.

Patients with diabetes were significantly higher the prevalence of depressive mood (18% vs 14%, $P < 0.001$) and suicidal idea (22% vs 17%, $P < 0.001$) than normal glucose tolerance patients. In diabetic patients, the EQ-5D index of patients with depressive mood (0.78 ± 0.23) showed significantly reduced than without depression mood (0.90 ± 0.15 , $P < 0.001$). After adjusted wit age sex, diabetes patients were associated with depressive mood ($P = 0.04$) and suicidal idea ($P = 0.009$). However, there was no relationship between depressive mood and suicidal idea and diabetes.

According to the results, depression mood and suicidal idea is higher patients with diabetes than without diabetes, and these relations were associated with the health-related quality of life. Therefore, blood sugar control in diabetes care, as well as considering the quality of life of patients is considered to require treatment.

PHE-04-1

A Short Message Service Intervention to Prevent Diabetes for Chinese Professional Drivers: A Single-blinded, Randomized Controlled Trial

Carlos K. H. Wong¹, Colman S. C. Fung¹, S. C. Siu², Yvonne Y. C. Lo¹, K. W. Wong², Daniel Y. T. Fong³ and Cindy L. K. Lam¹

¹Department of Family Medicine and Primary Care, The University of Hong Kong, Hong Kong; ²Department of Medicine and Rehabilitation, Tung Wah Eastern Hospital, Hong Kong; ³School of Nursing, The University of Hong Kong, Hong Kong

OBJECTIVE: The aim of this trial was to determine the efficacy of using short-messaging service (SMS) to provide Diabetes information and reminders of

healthy lifestyle modification in reducing the risk of developing diabetes at 12 and 24 months in pre-diabetes.

METHODS: A single-blinded, randomized controlled trial was conducted in Hong Kong between 05/2009 and 04/2012. Chinese professional drivers with impaired glucose tolerance (IGT) were randomly allocated to either a SMS program with a total of 64 messages comprising knowledge and lifestyle modification on diabetes; or to a control group with usual care. The primary outcome was the incidence rate of diabetes at 12 and 24 months period. All analyses were undertaken on an intention-to-treat approach.

RESULTS: One hundred and eight professional drivers were recruited, of whom 54 IGT were randomly allocated to the intervention group and 54 to the control group. Fewer subjects developed diabetes at 12 months in the intervention group compared to the control group (5.56% vs 16.00%), relative risk (RR) of diabetes onset being 0.35 (95% CI: 0.10–1.24) and number needed to treat (NNT) for preventing diabetes being 9.57. At 24 months, the RR remained <1 but was increased to 0.62 (95% CI: 0.24–1.61) while NNT increased to 10.58.

CONCLUSIONS: The SMS intervention might help reducing pre-diabetic patients to reduce the risk of developing diabetes at 12 months but the effect was not sustained at 24 months. Additional measures are needed to be integrated into the preventive care to further prevent or slow down the progression from IGT to diabetes.

PHE-04-2

Impact of the Type of Glycation Product, HbA1c or Glycated Albumin (GA), on the Diagnosis of Glucose Tolerance (GT)

Sumie Okahata, Kentaro Sakamoto and Teruo Shiba

Division of Diabetes and Metabolism, Toho University Ohashi Medical Center, Tokyo, Japan

BACKGROUND AND AIM: HbA1c has recently been recommended as an index for assessing GT. Little is known, however, about the application of glycated products to subjects close to the diagnostic borders of diabetes.

METHOD: GT was assessed using either of two different glycated products, HbA1c or GA, and the assessments thus attained were evaluated based on the results of the 75 g-OGTT. Subjects undergoing OGTT as part of a general health examination were recruited to the analyses. HbA1c was examined in 3485 participants and GA was examined in 1,996. The subjects were classified into four GT categories according to their HbA1c or GA: low risk, high risk, mild diabetes, and overt diabetes.

RESULTS: GT assessments with HbA1c and GA both resulted in discordant 2 h-plasma glucose values (2hPG) in comparisons between genders, adiposity levels, and age groups. Men and obese persons showed consistently higher 2hPG in all GT categories assessed by either HbA1c or GA. The discrepancy between genders in the GT assessment with HbA1c tended to be smaller than that in the assessment with GA. The 2hPG was 153 mg/dL in non-obese subjects in the GA-assessed mild-diabetes and 173 mg/dL in women in the HbA1c-assessed mild-diabetes. This suggested over-diagnosis of diabetes, as the PG were far lower than 200 mg/dL. Little discrepancy in 2hPG was noted in the comparison between ages in either the HbA1c- or GA-assessed group.

CONCLUSION: The 2hPG differed widely by adiposity and by gender. Diagnosis of glucose intolerance with glycated products is suggested to screen each different population in terms of GT.

PHE-04-3

Diabetes Screening Activities to Enhance the Four Indicator

Hsiu-Jen Tsai¹, Wen-Chin Lee², Ling-Ting Huang¹, Chi-Chun Hou¹, Yung-Hsiang Yeh², Tsai-hsia Hsieh³ and Ching-Wo Yang³

¹Center of Diabetes Education, Show Chwan Memorial Hospital, Taiwan; ²Medical Department, Show Chwan Memorial Hospital, Taiwan; ³Department of Nursing, Show Chwan Memorial Hospital, Taiwan

PURPOSE: Studies confirmed that early good control of diabetes can continuously to prevent related complications. In addition to focusing on the control of high blood sugar, other risk factors must also be strictly attentive and screened. Annual monitoring of glycosylated hemoglobin, fasting blood lipids test, nephropathy examination, and retinal examination for diabetes outpatient, is patient's right and physician's responsibility.

METHODS: Therefore, analysis to confirm the truth through reason, development of improving the problem-oriented strategies the medical department; the establishment that prompt screening box of health indicators,

the report query system: to enhance the screening of four indicators to improve quality of patients' health care.

RESULTS: Through policy advocacy, information of out-patient medical orders popsup from the window, and then orders are taken, four indicators achieve obvious results. Four indicators of diabetes through monitoring query system, each indicators rise significantly, compared in the same period of the year 99–100. Glycosylated hemoglobin test of the whole hospital increases from 81.38% to 89.31%; fasting lipid testing increases from 72.25% to 81.94%; fundus examination increases from 43.65% to 79.86%; urine microalbumin testing also from 39.94 up to 80.90%.

CONCLUSIONS: Patients trust physicians with their health problems, so physicians have the responsibility to care for the patient's health to prevent the complication, so the pop-up alert system diabetes patients benefit by advocacy of early screening, four indicators significantly increases diabetes screening rates, and achieve early diagnosis of diabetes.

PHE-04-4

Effect of a Diabetes Diagnosis on Quality of Life in the Japanese Population

Yukiko Nonoyama¹, Mayumi Yamamoto^{1,2}, Shino Oba³, Chisato Nagata⁴, Kazuki Matsui⁵ and Jun Takeda¹

¹Department of Diabetes and Endocrinology, Gifu University Graduate School of Medicine, Japan; ²Health Administration Center, Gifu University, Japan; ³Department of Health Promotion Research, National Institute of Public Health, Saitama, Japan;

⁴Department of Epidemiology and Preventive Medicine, Gifu University Graduate School of Medicine, Japan; ⁵Midori Hospital, Gifu, Japan

OBJECTIVE: To evaluate the difference in the quality of life (QOL) between people in whom diabetes has been diagnosed and those in whom diabetes has not been diagnosed.

METHODS: Of 2260 men and 3010 women who were randomly selected and invited to participate in 'the survey of diabetes in Gifu City', blood glucose levels were measured in 452 men and 659 women. Further, these subjects answered questions regarding diabetes diagnosis and QOL using the World Health Organization (WHO) questionnaire WHOQOL-26. Data were analyzed using the chi-square test and multi-regression analysis.

RESULTS: The QOL score in subjects with diabetes previously diagnosed at medical institutes was lower than that in subjects without previous diagnosis of diabetes. Among the subjects with a previous diabetes diagnosis, those who were educated regarding the required lifestyle changes had the trends of lowering QOL score. However, the QOL score did not show a strong correlation with blood glucose levels determined by HbA1c. Lowered in QOL scores were significant not only in sum of score but also in the physical section and general section.

CONCLUSION: A previous diabetes diagnosis may affect the QOL of the Japanese populations in a manner not related with treatment. From this study, QOL scores may be affected by a previous diabetes diagnosis. A diabetes diagnosis and the necessity for a change in lifestyle might suppress the QOL. These findings suggest that the manner in which patients are initially educated is very important for controlling diabetes while maintaining a good QOL.

PHE-04-5

Outreach Program To Raise Awareness and Change Lifestyle (OPAL) For Prevention of Chronic Diseases

Wai Chi Fu¹, Vanessa W. S. Ng², Harriet H. Y. Chung¹, Cindy W. C. Lui¹, Miho C. Yue³, Jenny Y. Y. Zhang³, Yi Sui³, Nicola Brown³, Patrick T. S. Wong³, Risa Ozaki² and Juliana C. N. Chan²

¹Yao Chung Kit Diabetes Assessment Centre, Hong Kong Institute of Diabetes and Obesity, Chinese University of Hong Kong, Hong Kong; ²Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong; ³Asia Diabetes Foundation, Hong Kong

OBJECTIVE: We examined the effects of an outreach program targeting at young-to-middle-aged people on detection of diabetes and behavioral change.

METHODS: We used validated risk score, clinical measurements and capillary blood glucose testing to identify high risk subjects. All subjects were given a pamphlet containing simple health messages. We contacted agreeable high risk subjects 6 weeks later regarding follow up actions.

RESULTS: During a 12-month period in 2011–2, we conducted 22 health surveys involving 2727 subjects (mean ± SD: age: 50 ± 14 years, 25.4% male).

Of these 83% had at least one risk factor for diabetes [36% family history; 56% general obesity (BMI ≥ 23 kg/m²); 41% central obesity; 11% gestational diabetes; 23% known hypertension; 22% known dyslipidemia and 3% known cardiovascular disease]. Using a cutoff point of 16, 20% were at high risk for diabetes ($n = 545$). We contacted the agreeable subjects by phone and enquired about action items (intake of sweetened sugar beverages and fibres, sleep habits, physical activity, medical follow-up, losing weight). At the time of analysis, we contacted 289 subjects and 205 responded. Of these, 72% reported improvement in at least one item. Non-responders to call had higher waist and risk scores than responders. Amongst responders, those who took action had higher waist and BMI than those who did not.

CONCLUSION: An outreach program identified high percentage of young-to-middle aged subjects harboring risk factors for diabetes/prediabetes. Increased awareness and risk communication resulted in behavioral changes although there remained barriers in reaching out some subjects despite their high risk profile.

PHE-04-6

'A Worksite Body Weight' Intervention by Telecare

Yi-Ping Chen¹, Jhao-Kun Liou¹, Yu-Chin Huang², Ching-Hui Chen¹, Tzu-Fan Huang¹, Shi-Dou Lin¹, Shang-Ren Hsu¹, Ming-Chia Hsieh¹ and Shih-Te Tu¹

¹Division of Endocrinology and Metabolism, Changhua Christian Hospital, Taiwan;

²Bariatric Surgery and Diabetes Health Management Center, Changhua, Taiwan

INTRODUCTION: General office staff work long time and less activities, resulting in heavier body weight. In this study, we evaluated the effect of worksite bodyweight intervened by telecare on overweight or obesity employees.

METHOD: This study was recruited BMI more than 24 kg/m² employees with a company during 8 weeks of long distance health care. The program includes (1) physician and dietitian clinical visits in initiation and finish (2) nutrition education by video camera. Through this model, by the subjects themselves and health management, transit measurements records to hospital in real time and deal with employees consulting. Both before and after the intervention participators were collected body weight, waist, blood pressure, triglycerol, total cholesterol and to investigate health knowledge. Statistical analysis was by one-way variation test.

RESULTS: During 8 week of tele-healthcare services, participators total body weight and waist reduced 77.4 kg and 4.21 cm ($P < 0.05$). Total cholesterol and TG were reduced 22 and 33 mg/dL, systolic pressure and diastolic pressure were lowered 8.52 mmHg and 13.25 mmHg, averaged BMI was reduced 2.35 (respectively, $P < 0.05$) All of subjects have get more correct health knowledge than initiation.

CONCLUSION: It could help management of participants at worksite to get health knowledge and effectly to reduce body weight, waist, cholesterol, triglycerol, blood pressure by telecare services. We expect to recruit more employees as well as evaluate the effect of worksite bodyweight intervened by telecare in a long time study.

PHE-05-1

Who are Caring for Patients with Childhood-Onset Adult Type 1 Diabetes in Japan? Pediatric or Adult Diabetologists? The DERI Mortality Study

Yoshiko Onda, Aya Morimoto, Rimei Nishimura, Hironari Sano, Kazunori Utsunomiya and Naoko Tajima

Division of Diabetes and Endocrinology, Department of Internal Medicine, Jikei University School of Medicine, Japan

OBJECTIVE: To investigate the status of care for patients with T1DM by their attending physicians 25 years after diagnosis.

METHODS: Of the 1387 patients registered with two nationwide type 1 diabetes surveys in Japan who were diagnosed as having T1DM at <18 years of age between 1965 and 1979, the present study included a total of 859 patients whose attending physicians were confirmed. We evaluated the percentage of the attending physicians as they were accounted for by pediatric (PED), adult diabetology (AD), and other specialists (OS).

RESULTS: The mean age at diagnosis was 8.5 ± 4.1 (SD) years, with a duration of diabetes 25.2 ± 4.0 years. Their mean attained age was 33.7 ± 5.8 years. Of these, 16.4% consulted PED, 81.3% consulted ADC, and 2.3% OS. By their age at diagnosis, of the 667 patients diagnosed at <12 years old (y.o), 19.5% consulted PED, 78.7% ADC, and 1.8% OS, while, of those diagnosed at ≥ 12 y.o, 5.7% consulted PED, 90.1% ADC, and 4.1% OS.

By their attained age, of the 244 patients whose attained age <30 y.o, 29.1% consulted PED, 68.9% ADC, and 2.1% OS. Of the 615 patients whose attained age was ≥ 30 y.o, 11.4% consulted PED, 86.2% ADC, and 2.4% OS. Logistic regression analyses revealed that younger age and more recent year of diagnosis were predictors of these patients consulting PED.

CONCLUSIONS: Even 25 years after diagnosis, 16.4% consulted PED. About 10% of patients ≥ 30 years of age still consulted PED in Japan.

PHE-05-2

An Exploration of the Number of People with Type 1 Diabetes and Coverage of Care in China

David Russel Whiting¹, Helen McGuire¹, Katarzyna Kissimova-Skarbek¹, Puhong Zhang², Till Seuring³, Florencia Aguirre¹, Yangfeng Wu², Shaoda Lin³, Jianping Weng⁴ and Linong Ji⁵

¹Policy and Programmes, International Diabetes Federation, Belgium; ²The George Institute, Beijing, China; ³The First Affiliated Hospital of Shantou University Medical College; ⁴The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China; ⁵Peking University People's Hospital, Beijing, China

BACKGROUND: The DIAMOND study in 1998 was limited to children under the age of 15 years, and current estimates of the number of people with T1D China may therefore be under-estimated.

METHODS: Patients: Type 1 diabetes with age of onset <35 years in Beijing and Shantou during a 3 month period in 2011. Recorded place of birth, place of residence, and year of diagnosis. In addition a list of patients with T1D who attended in the previous 3 years was compiled and patients followed-up to determine current vital status.

RESULTS: Five hundred and ninety-nine patients were enrolled (Beijing $n = 359$, Shantou $n = 240$), 84 and 40 were aged 0–14 years and resident in Beijing and Shantou respectively, and 189 and 141 were aged 15 plus and resident in Beijing and Shantou.

One hundred and thirty-three children under the age of 15 years resident in Beijing recorded on the 3-year list. Extrapolating to China the estimated number of children under 15 years with type 1 diabetes is 9023. Applying a similar approach to those over the age of 15 years suggests there are at least 42,800 people of all ages with T1D.

CONCLUSION: The estimated number of people with T1D under the age of 15 years in China is similar to the estimate from the IDF diabetes Atlas. There appears to be a considerable number of people with T1D over the age of 15 years and this group needs to be considered when planning services.

PHE-05-3

Diabetes Mellitus in South Asia: A Scientific Evaluation of the Research Output

Priyanga Ranasinghe¹, Ranil Jayawardena² and Prasad Katulanda³

¹Department of Pharmacology, Faculty of Medicine, University of Colombo, Sri Lanka;

²Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Qld, Australia; ³Diabetes Research Unit, Department of Clinical Medicine, Faculty of Medicine, University of Colombo, Sri Lanka

BACKGROUND: Diabetes in South Asia (SA) represents a different disease entity in onset, progression and complications. To systematically analyzed the medical research output on diabetes from SA.

METHODS: The online SciVerse Scopus database was searched using the following search terms; 'diabetes' and 'diabetes mellitus' in the article 'Title', 'Abstract' or 'Keywords', in conjunction with the names of each regional country in 'Author Affiliation'.

RESULTS: Total number of publication was 8,478. A significant majority was from India (85.1%) and Pakistan (9.6%). The contribution to the global diabetes research output was 2.1%. Publications from SA have dramatically increased after year 2007, 58.7% of the publication between years 2000–2010 were after 2007. Majority were Research articles (75.9%) and Reviews (12.9%), with only 90 (1.1%) clinical trials. Publications predominantly appeared in local national journals. Indian authors and institutions had the most number of articles and highest h-index. Total number intra-regional collaborative studies were 136 (1.6%). Only 39 articles (0.46%) had >100 citations.

CONCLUSIONS: Regional research output on diabetes mellitus is unsatisfactory, with only minimal contribution to global research. Publications were not highly cited and there were only a minimal number of RCTs.

Regional scientist must collaborate and focus on practical and culturally acceptable interventional studies on diabetes mellitus in the coming decades.

PHE-05-4

Incidence of Diabetes Mellitus in a Korean Rural Population and its Risk Factors: The Chungju Metabolic Disease Cohort (CMC) Study

Jeong-Ah Shin¹, Jin-Hee Lee², Sun-Young Lim², Hee-Sung Ha³, Hyuk-Sang Kwon¹, Yong-Moon Park³, Won-Chul Lee³, Moo-Il Kang¹, Hyeon-Woo Yim³, Ho-Young Son¹, Hun-Sung Kim¹ and Kun-Ho Yoon¹

¹Department of Endocrinology and Metabolism, The Catholic University of Korea School of Medicine, Korea; ²Catholic Institute of U-Healthcare, The Catholic University of Korea, Korea; ³Preventive Medicine, College of Medicine, The Catholic University of Korea, Korea

AIMS: The objective of this study was to determine the incidence of type 2 diabetes in a Korean population living in a rural area and its association with various clinical characteristics.

METHODS: The Chungju Metabolic Disease Cohort (CMC) study is an ongoing community-based study of metabolic diseases including diabetes, metabolic syndrome, and osteoporosis. The baseline examination was carried out during 2003–2006 in 11,672 participants aged 40 years over living in the rural area of Chungju city, South Korea. Among these, 6347 participants visited for follow-up examination in 2007–2010. Final analysis is performed in 5534 subjects who did not have diabetes at baseline study and could get all follow-up data.

RESULTS: In this 4-year prospective cohort study, the age- and sex-adjusted cumulative incidence of diabetes was 10.6% (95% CI 9.8–11.5) in total participants. The age-adjusted incidence was similar in male subjects (11.35%) and female subjects (10.20%). Regression analysis revealed that age over 60 years, family history of diabetes, high waist circumference (WC), hypertension, fasting plasma glucose (FPG), increased triglyceride (TG) were significant risk factors for the development of diabetes.

CONCLUSIONS: We found that an incidence of diabetes mellitus was 10.6% in Korean rural population for 4-year follow-up period. Age over 60 years, family history of diabetes, increased abdominal obesity, hypertension, FPG, high TG were predictive of diabetes.

PHE-05-5

The Association Between Serum Amylase and the Incidence of Type 2 Diabetes

Kyoko Kogawa Sato¹, Tomoshige Hayashi¹, Shinichiro Uehara¹, Hideo Koh¹, Isseki Maeda¹, Ginji Endo¹, Keiko Oue², Yoshiko Nakamura², Hiroshi Kambe² and Kanji Fukuda²

¹Department of Preventive Medicine and Environmental Health, Osaka City University Graduate School of Medicine, Japan; ²Kansai Health Administration Center, Nippon Telegraph and Telephone West Corporation, Japan

OBJECTIVE: Serum amylase is the index of the exocrine pancreas. A few cross-sectional studies have reported that patients with type 1 diabetes or type 2 diabetes had decreased serum amylase. Our purpose is to examine prospectively the relationship between serum amylase and the incidence of type 2 diabetes.

METHODS: Study participants included 8470 nondiabetic Japanese men aged 40–55 years at entry. Type 2 diabetes was diagnosed if the fasting plasma glucose (FPG) level was ≥ 126 mg/dL, HbA1c was $\geq 6.5\%$, or if subjects were taking diabetes medications. Participants were classified into quintiles of serum amylase levels: quintile 1 (-72 IU/L), quintile 2 ($73-86$ IU/L), quintile 3 ($87-99$ IU/L), quintile 4 ($100-118$ IU/L), and quintile 5 (119 IU/L).

RESULTS: During the 42,227 person-years of follow-up, we confirmed 868 cases. Lower serum amylase level was associated with an increased risk of type 2 diabetes. In Cox proportional hazards model, after adjusting for age, body mass index, the FPG level, estimated glomerular filtration rate, alcohol consumption, smoking habit, walk to work, regular leisure-time physical activity, and family history of diabetes, the hazard ratios of the incidence of type 2 diabetes were 1.30 (95% CI, 1.06–1.60, $P = 0.012$) for quintile 1, 1.15 (0.92–1.43, $P = 0.197$) for quintile 2, 1.00 for quintile 3 (Reference category), 1.01 (0.80–1.27, $P = 0.949$) for quintile 4, and 1.16 (0.92–1.46, $P = 0.221$) for quintile 5.

CONCLUSION: We concluded that low serum amylase had an increased risk of type 2 diabetes.

PHE-05-6

Research on the Current Situation of T2DM in Ganzhou City

Shumei Li¹, Xiaoting Luo², Minghua Dong¹, Wei Qiu¹, Lixia Jiang³, Zhengchu Huang⁴, Jian Li⁴, Qin Huang⁵, Qinfeng Wu¹, You Guo¹ and Shuiqin Chen²

¹Department of Epidemiology, Gannan Medical College, China; ²Department of Biochemistry and Molecular Biology, Gannan Medical College, China; ³Clinic Laboratory, The First Affiliated Hospital of Gannan Medical College, China; ⁴Department of Anatomy, Gannan Medical College, China; ⁵Emergency Department, The First Affiliated Hospital of Gannan Medical College, China

OBJECTIVE: To understand the prevalence of type 2 diabetes mellitus (T2DM) in the residents of Ganzhou.

METHODS: Nine thousand eight hundred and one Chinese adults (age: 35–64) from 2009 to 2010 were investigated through multiple hierarchy random sampling method; Diagnosis of T2DM, impairment of fasting serum glucose (IFG) and hypertension was employed by diagnosis criteria of WHO in 1999; diagnosis of hyperlipidemia, overweight and obesity was adopted by Chinese diagnostic criteria.

RESULTS: The prevalence of T2DM and IFG in Ganzhou was respectively 7.68% and 13.1%, the prevalence of T2DM in the overweight and obesity population was respectively 9.6% and 14.9% and higher than in the BMI normal population (6.7%, $P < 0.001$); the prevalence of IFG in the overweight and obesity population was respectively 21.5% and 25.5% and higher than the BMI normal population (16.2%, $P < 0.01$); the prevalence of T2DM and IFG in the hypertension population was respectively 12.4% and 23.7% and higher than the non-hypertension normal population (7.0%, $P < 0.001$; 17.1%, $P < 0.001$); the prevalence of T2DM and IFG in the hyperlipidemia population was respectively 12.3% and 23.7% and higher than the non-hyperlipidemia normal population (6.2%, $P < 0.001$; 17.7%, $P < 0.001$).

CONCLUSION: The prevalence of T2DM and IFG in Ganzhou were further higher than the Chinese average level in 2002 but lower than in the Chinese corresponding time period; overweight, obesity, hypertension, hyperlipidemia and so on had close correlation with T2DM; the health education should be emphasized for the residents in the moderate or small city which the economy was changing; and early screen T2DM in order to depress the prevalence of T2DM.

PHE-05-7

Depression and Suicidal Ideation Among Adults with Diabetes Mellitus

Seung Jin Han, Min Suk Lee, Hae Jin Kim, Kwan Woo Lee and Dae Jung Kim

Department of Endocrinology & Metabolism, Ajou University School of Medicine, Korea

OBJECTIVE: We aimed at investigating the prevalence of depression and suicidal ideation among adults with diabetes mellitus in Korea and compare it to non-diabetic subjects.

METHODS: We used data from the 4th Korea National Health and Nutrition Examination Survey. We analyzed data of 17,065 subjects aged more than 20 years, after excluding non-respondents to the questionnaire on diabetes, depression and suicidal ideation. The presence of diabetes and depression were defined by a self-reported questionnaire asking if the participants had ever been diagnosed with diabetes or depression by a medical doctor. Suicidal ideation was assessed by a self-reported questionnaire asking if the participants had ever had any suicidal thoughts.

RESULTS: Suicidal ideation was reported by 16.5% of Korean adults. The prevalence of depression was higher in diabetic subjects compared to non-diabetic subjects (15.0% vs 11.5%, $P < 0.001$). The prevalence of suicidal ideation was significantly higher in subjects with diabetes [23.5% vs 16.0%, Odds ratio (OR) 1.168, $P = 0.057$] and subjects with depression (45.1% vs 12.7%, OR 4.43, $P < 0.001$) compared to subjects without diabetes or depression respectively. Compared with the subgroup of those without diabetes or depression, the risk of suicidal ideation was significantly higher in the subgroup of diabetic subjects without depression, non-diabetic subjects with depression, and diabetic subjects with depression respectively (OR 1.24 vs 4.37 vs 4.07).

CONCLUSION: We concluded that diabetes was strongly associated with depression and suicidal ideation. Therefore, we should evaluate the presence of depression in patients with diabetes.

PHE-05-8

Initiation of Oral Antihyperglycemic and Statin Therapy in Previously Untreated Patients with Type 2 Diabetes

Michael J. Davies¹, Peter Sun², Kaan Tunceli¹, Qiaoyi Zhang¹, Thomas Seck¹, Kristy Iglay¹, Baishali Ambegaonkar¹ and Larry Radican¹

¹Merck Sharp & Dohme Corp., USA; ²Kailo Research Group, USA

OBJECTIVE: To assess the time from the first diagnosis of type 2 diabetes (T2DM) to initiation of oral antihyperglycemic and statin therapy.

METHODS: In a retrospective electronic medical record analysis, US patients ≥ 18 years were included if they had the first T2DM diagnosis between 1 January 2004 and 31 December 2005, had a last pre-index HbA_{1c} value $\geq 7\%$, and had not received any antihyperglycemic agents in the year prior to T2DM diagnosis. In addition, patients had to be eligible for statin therapy per 2008 American Diabetes Association recommendations, but untreated in the year prior to diagnosis. Patients had to have medical records for 1 year prior to and at least 2 years after diagnosis date. Initiation of an oral antihyperglycemic agent and statin was determined by prescription records.

RESULTS: Of the selected patients ($N = 2,254$), mean age was 58 years, mean HbA_{1c} was 8.5%, and mean untreated LDL-cholesterol was 115 mg/dL at baseline. In addition, 21% of patients had pre-existing overt cardiovascular disease and 40% had a diagnosis of dyslipidemia. Over the 2-year follow-up period, 66.1% and 41.9% of patients initiated treatment with an oral antihyperglycemic agent and statin, respectively, with those with higher levels of baseline HbA_{1c} (i.e., $\geq 9\%$) or LDL-cholesterol (i.e., ≥ 130 mg/dL) more likely to initiate treatment.

CONCLUSION: Treatment with an oral antihyperglycemic agent and/or statin was suboptimal in previously untreated patients with T2DM who were eligible for both antihyperglycemic and statin therapy. Of those treated, patients initiated treatment with an oral antihyperglycemic agent more often than with a statin.

PHE-06-1

A Nested Case-Control Study on the Relation of Type 2 Diabetes Mellitus Between Lifestyle and 7 Gene Single Nucleotide Polymorphisms

Minghua Dong¹, Shumei Li¹, Xiaoting Luo², Qin Huang³, Wei Qiu¹, Lixia Jiang⁴, Zhengchun Huang⁵, Jian Li⁵, Qinfeng Wu¹, You Guo¹ and Jun Nie⁶

¹Department of Epidemiology, Gannan Medical College, China; ²Department of Biochemistry and Molecular Biology, Gannan Medical College, China; ³Emergency Department, The First Affiliated Hospital of Gannan Medical College, China; ⁴Clinic Laboratory, The First Affiliated Hospital of Gannan Medical College, China; ⁵Department of Anatomy, Gannan Medical College, China; ⁶Department of Epidemiology, Southern Medical University, China

OBJECTIVE: Lifestyle and individual differences in SNPs could affect susceptibility to T2DM, but previous studies have most assessed only either lifestyle or genes instead of combining the two factors, so our aim was to find some risk factors of T2DM in lifestyle and some genes SNPs distribution.

METHODS: We studied 9801 persons aged from 35 to 64 without previous T2DM in Ganzhou city from 2009 to 2011. Physical examination and blood samples collecting was done in the base line survey. We compared some lifestyle factors and seven gene SNPs (TCF7L2-rs11196218; SLC30A8-rs2466293; SLC30A8-rs11558471; CDKAL1-rs10946398; CDKAL1-rs9465871; IGF2BP2-rs1470579; IGF2BP2-rs11705701) distribution in individuals who went on to develop T2DM with those matched controls who remained event free.

RESULTS: The prevalence rate of T2DM of the three groups (BMI < 24; 24–28; > 28 kg/m²) are 7.3%, 9.9% and 17.2% for male, 6.2%, 9.3%, 14.4% for female, respectively. Results show that SLC30A8-rs11558471 G allele may have a certain relationship with T2DM (G/A OR = 1.338, 95%CI: 1.042, 1.718). Other genes in this test is not found significantly. Alcohol intake more than 40 mL daily vs less among male found statistically significant result (OR = 1.724, 95%CI: 1.017–2.922%). Milk intake more than 200 mL daily vs less among female found statistically significant (OR = 2.559, 95%CI: 1.216–5.381%). Daily intake of vegetables more than 150 g vs less found statistically significant result (OR = 0.601, 95%CI: 0.403–0.896).

CONCLUSION: High BMI is a risk factor among male and female. Over drinking is a risk factor for male and over milk intake is a risk factor for female. Enough fresh vegetable intake is a protective factor for individuals. This study demonstrates that the SLC30A8 rs- rs11558471 G allele confers susceptibility to T2DM in Chinese.

PHE-06-2

The Risk Factor for Type 2 Diabetes in Koreans

Hyeseo Chung and Sam Kwon

Department of Internal Medicine, Sungkyunkwan University School of Medicine, Korea

OBJECTIVE: The aim of study was to evaluate the risk of obesity and body fat distribution to incidence of type 2 diabetes in Koreans.

METHODS: We analysed the anthropometric and laboratory data of 66,510 non-diabetic Korean adults (40,160 men and 26,350 women). Diabetes were defined as fasting glucose > 7.0 mmol/L and HbA_{1c} $> 6.5\%$ and prediabetes were defined as fasting glucose > 5.6 mmol/L or $5.7\% < \text{HbA}_{1c} < 6.4\%$.

RESULTS: Of the 66,510 adults, 1500 subjects (2.26%) detected diabetes and 14,787 subjects (22.23%) detected prediabetes. The general obesity (BMI, fat mass, percent body fat) and central obesity (waist circumference) were risk factor of type 2 diabetes in Korea. Logistic regression models for detecting undiagnosed type 2 diabetes; men: $\text{Ln}(\text{probability}/[1-\text{Probability}]) = -29.416 + 0.036(\text{age}(\text{years})) + 0.102(\text{percent body fat}(\%)) + 0.25(\text{Waist circumference}(\text{cm})) + 0.190(\text{Fasting glucose}(\text{mg/dL}))$ women: $\text{Ln}(\text{probability}/[1-\text{Probability}]) = -30.506 + 0.116(\text{age}(\text{years})) + 0.411(\text{fat mass}) + 0.007(\text{Waist circumference}(\text{cm})) + 0.199(\text{Fasting glucose}(\text{mg/dL})) + 0.102(\text{hs-CRP})$.

CONCLUSIONS: Age, fat mass (or percent body fat) and waist circumference were good predictor of type 2 diabetes risk in Koreans.

PHE-06-3

Visceral Adiposity, Not Abdominal Subcutaneous Fat Area, is Associated with Glucose Intolerance in Japanese: The Ohtori study

Hideaki Sokooshi, Daisuke Horiuchi, Yudai Matsuoka, Kei Yura, Shinichiro Uehara, Kyoko Sato, Ginji Endo, Yonezo Hikita and Tomoshige Hayashi

Department of Preventive Medicine and Environmental Health, Osaka City University Graduate School of Medicine, Japan

OBJECTIVE: Visceral adiposity is considered to have a key role in cardiometabolic diseases. The purpose of this study is to investigate cross-sectionally the association between visceral adiposity directly measured by computed tomography (CT) and the prevalence of impaired fasting glucose (IFG) or type 2 diabetes independent of abdominal subcutaneous fat area (ASFA) and insulin sensitivity in Japanese men and women.

METHODS: We enrolled 1588 Japanese men and women who were between 27 and 77 years of age. Intra-abdominal fat area (IAFA) and ASFA was measured by CT. Type 2 diabetes was defined as a fasting plasma glucose level ≥ 126 mg/dL, HbA_{1c} $\geq 6.5\%$, or taking hypoglycemic medications or insulin. IFG was defined as fasting plasma glucose level ≥ 110 and < 126 mg/dL with no history of diabetes.

RESULTS: We confirmed 146 cases of IFG and 104 cases of type 2 diabetes. Greater IAFA was associated with an increased odds of glucose intolerance. After adjusting for age, gender, family history of diabetes, ASFA, regular physical exercise, smoking status, immunoreactive insulin (IRI), and square-root of IRI, multiple-adjusted odds ratios of type 2 diabetes for IAFA were 2.11 (95% confidence interval, 0.94–4.73) for tertile 2 and 2.70 (1.14–6.38) for tertile 3 compared with tertile 1. Multiple-adjusted odds ratios of IFG or type 2 diabetes for IAFA were 3.14 (1.71–5.95) for tertile 2 and 6.42 (3.38–12.19) for tertile 3 compared with tertile 1.

CONCLUSIONS: Greater visceral adiposity increases the odds of IFG or type 2 diabetes independent of abdominal subcutaneous fat and insulin sensitivity.

PHE-06-4

Association of Single Nucleotide Polymorphism rs7754840 of CDKAL1 and Type 2 Diabetes Mellitus: A Meta Analysis

Xiaoting Luo¹, Qin Huang², Minghua Dong³ and Shumei Li³

¹Department of Biochemistry and Molecular Biology, Gannan Medical College, China;

²Emergency Department of the 1st Affiliated Hospital, Gannan Medical College, China;

³Department of Epidemiology, Gannan Medical College, China

OBJECTIVE: To assess the association between single nucleotide polymorphism rs7754840 of CDKAL1 (cyclin-dependent kinase5 regulatory subunit associated protein 1-like 1) and type 2 diabetes mellitus (T2DM), a literature-based search was conducted to collect data.

METHODS: The PubMed and Chinese Wanfang databases were systematically reviewed for studies published from January 2002 to May 2012. The odds ratio (OR) and 95% confidence intervals (CI) were used to assess the

strength of association between rs7754840 polymorphism and T2DM. Meta analysis was carried out by Stata 11.0 software. Publication bias was estimated by Egger's analysis and funnel plots.

RESULTS: A total of 20 reports were collected, among of them only seven studies with 6349 cases and 5179 controls match the inclusion criteria and were enrolled in this meta-analysis. Significant heterogeneity between studies was found ($P = 0.004$, $I^2 = 69.1\%$). A random effect model by DerSimonian-Laird method was performed for meta-analysis and generated a combined OR = 1.39 (95%CI = 1.27–1.52) for the risk of rs7754840. Egger analysis and funnel plots indicated no publication bias for the SNP rs7754840 which indicated reliability of the pooled results.

CONCLUSION: The meta-analysis indicated that rs7754840 polymorphism of CDKAL1 was significantly associated with the risk of T2DM.

PHE-06-5

Cigarette Smoking is a Risk Factor for Impaired Insulin Secretion, but not Insulin Resistance, in Japanese Men: the Saku Cohort Study

Akiko Morimoto¹, Yukako Tatsumi¹, Kijyo Deura², Shoichi Mizuno², Yuko Ohno¹ and Shaw Watanabe³

¹Department of Mathematical Health Science, Graduate School of Medicine, Osaka University, Japan; ²Saku Central Hospital, Nagano, Japan; ³Life Science Promoting Association, Tokyo, Japan

OBJECTIVE: To assess the impact of smoking on impaired insulin secretion and insulin resistance in Japanese men.

METHODS: This cohort study included 1199 men aged 30–79 years without diabetes, impaired insulin secretion, and insulin resistance at baseline who underwent a comprehensive medical check-up between April 2006 and March 2007 at Saku Central Hospital. Smoking status was categorized as current, ex-smoker, and never-smoker. Insulinogenic index and homeostasis model assessment-insulin resistance were determined using a standard 75-g oral glucose tolerance test. The Japan Diabetes Society criteria were used to define impaired insulin secretion and insulin resistance. Participants were followed up until March 2011.

RESULTS: Four hundred and forty-nine and 99 men developed impaired insulin secretion and insulin resistance during 3403 and 4092 person-years follow-up, respectively. The multivariable-adjusted hazard ratios (HRs) for impaired insulin secretion were 1.06 (95% CI 0.84–1.33) in ex-smokers and 1.95 (1.44–2.63) in current smokers compared with never-smokers after adjusting for age, familial history of diabetes, alcohol consumption, exercise, systolic blood pressure, triglyceride, γ -glutamyltransferase, waist circumference, leukocyte count, changes in smoking status, and changes in waist circumference. The number of pack-years was positively associated with the risk for impaired insulin secretion in a dose-dependent manner (P for trend <0.001). The multivariable-adjusted HRs for insulin resistance were 0.95 (0.56–1.61) in ex-smokers and 1.11 (0.67–1.79) in current smokers compared with never-smokers.

CONCLUSIONS: Cigarette smoking is a modifiable risk factor for impaired insulin secretion. The findings may also be important for other Asian populations, which have lower insulin secreting ability.

PHE-06-6

Incidence of Type 2 Diabetes for the Metabolic Syndrome Components: The Chungju Metabolic Disease Cohort (CMC) Study

Jin-Hee Lee¹, Sun-Young Lim¹, Jeong-Ah Shin², Hee-Seung Ha³, Hyuk-Sang Kwon², Yong-Moon Park³, Won-Chul Lee³, Moo-Il Kang², Hyun-Woo Yim³, Ho-Young Son² and Kun-Ho Yoon²

¹Catholic Institute of U-Healthcare, The Catholic University of Korea, Korea; ²Department of Endocrinology and Metabolism, The Catholic University of Korea, Korea; ³Department of Preventive Medicine, The Catholic University of Korea, Korea

AIM: The aim of this study is to investigate risk of T2DM incidence by conceivable combination of metabolic syndrome (Mets) components in Korean rural population.

METHODS: This CMC study is an ongoing community-based prospective cohort study. A total of 5530 subjects (2113 men, 3417 women) age 40 and older, free of T2DM at baseline were included in the present study. We estimated the cumulative incidence of T2DM according to Mets traits for 4 years.

RESULTS: At baseline, the prevalence of Mets was 24.6% in men and 43.4% in women. The cumulative incidence of T2DM was 19.7%, 5.6% in individuals with/without Mets respectively, and increased with the number of Mets

components. However, individuals with only impaired fasting glucose (IFG) had higher incidence than those who had two- or three- or four- components except IFG. Also, in comparison with Mets, diabetes incidence in individuals with IFG at baseline was highly presented (32.8% vs 19.7%).

CONCLUSIONS: The cumulative incidence for T2DM was high in individuals with Mets, however, it varied considerably depending on the specific combination of Mets components. IFG was the key feature for T2DM incidence regardless of the presence of Mets in Korean rural population.

PHE-06-7

Impact of Protein Intake on the Incidence of Type 2 Diabetes Mellitus in a Japanese Population: The Saku Cohort Study

Yukako Tatsumi¹, Akiko Morimoto¹, Kijyo Deura², Shoichi Mizuno², Yuko Ohno¹ and Shaw Watanabe³

¹Department of Mathematical Health Science, Graduate School of Medicine, Osaka University, Japan; ²Saku Central Hospital, Nagano, Japan; ³Life Science Promoting Association, Tokyo, Japan

OBJECTIVE: To investigate the association of protein intake for incidence of type 2 diabetes mellitus (T2DM) in a Japanese population.

METHODS: Our investigation included 1651 community residents aged 30–79 years who had six eligibility criteria at baseline examination from April 2008 to March 2009: (1) a fasting plasma glucose level <7.0 mmol/L; (2) a 2-h plasma glucose level after a standard 75-g OGTT <11.1 mmol/L; (3) no history of diabetes; (4) body mass index <25.0 kg/m²; (5) waist circumference <90 cm; and (6) not work on the improvement of the lifestyle recently. We assessed the intake of meat and fish from the questionnaire. We followed the participants until March 2011. T2DM was determined from fasting and 2-h post-load levels of plasma glucose. The association between protein intake and diabetes incidence was investigated using Cox proportional hazards models by sex. We adjusted for multivariable including age.

RESULTS: The mean follow-up was 1.8 years and 208 individuals developed T2DM. Among men, the multivariate-adjusted hazard ratios and 95% confidential intervals for incidence of T2DM were 2.40 (1.24–4.67) in participants who intake meet higher than 50 g and 1.13 (0.74–1.71) in those who intake meet lower than 50 g compared with those who intake meet about 50 g. Fish intake was not significantly associated with incidence of T2DM. Among women, the intake of meat and fish were not significantly associated with incidence of T2DM.

CONCLUSION: Higher intake of meat was associated with the higher risk for incidence of T2DM in Japanese men.

PHE-06-8

National Trends in Antidiabetic Treatment in Taiwan, 2000–2009

Chia-Hsueh Chang¹, Yi-Der Jiang¹, Ching-Hu Chung², Low-Tone Ho³ and Lee-Ming Chuang¹

¹Internal Medicine, National Taiwan University Hospital, Taiwan; ²Department of Pharmacology and Toxicology, Tsu-Chi University; ³Department of Internal Medicine, Taipei Veterans Hospital

BACKGROUND/PURPOSE: The impact of the introduction of newer anti-diabetic agents on the treatment pattern in the booming diabetic population remains unclear. We examined the patterns and temporal trends of anti-diabetic drugs use in Taiwan, with particular emphasis on combination therapy.

METHODS: We searched the Taiwan National Health Insurance Database during 2000–2009 to identify outpatient prescriptions of anti-diabetic drugs, including human insulins and insulin analogues, sulfonylureas, glinides, metformin, thiazolidinediones, alpha-glucosidase inhibitors, and dipeptidyl peptidase-4 inhibitors. Glucose-lowering treatments were classified according to pattern (oral agents only, insulins only, oral agents and insulins combination) and number of different classes of anti-diabetic drugs. Insulin therapy and two oral diabetic drugs combination therapy were further classified according to individual drug combination patterns.

RESULTS: Although metformin remained the mainstay of anti-diabetic treatment, patients receiving combination therapy of oral glucose-lowering agents with or without insulin significantly increased from approximately 40% in 2000 to 60% in 2009, particularly with the newer agents including glinides, alpha-glucosidase inhibitors, and long-acting insulin analogues. Use of sulfonylureas and thiazolidinediones decreased substantially. For insulin therapy, the most commonly prescribed drugs were premix insulin analogues

and basal insulin analogues, accounting for one-third of total insulin prescriptions in 2009.

CONCLUSION: We found an increasing complexity of anti-diabetic therapy during the past decade in Taiwan. Further studies are needed to evaluate whether this treatment pattern will lead to improved clinical outcome in a cost-effectiveness way.

PHE-07-1

Trends in the Prevalence of Metabolic Syndrome Among the Population with Diabetes and Pre-Diabetes in Korea: 1998–2009 Korean National Health and Nutrition Examination Survey (KNHANES)

Seung-Hyun Ko¹, Ki-Ho Song¹, Hyuk-Sang Kwon¹, Jung-Min Lee¹, Sung-Rae Kim¹, Hyeon-Woo Yim², Won-Cul Lee² and Yong-Moon Park²

¹Department of Internal Medicine, The Catholic University of Korea, Korea; ²Department of Preventive Medicine, The Catholic University of Korea

To investigate the trends in the prevalence of metabolic syndrome (MetS) and its components among the population with diabetes and pre-diabetes in Korean adults.

Using data from the Korean National Health and Nutrition Examination Survey (1998–2009), including adults (aged 30 years or older) with diabetes ($n = 2637$) and pre-diabetes ($n = 5943$), we analyzed changes in the prevalence of metabolic syndrome (MetS) and its components. MetS was defined according to the revised NCEP-ATP III guideline with modified Asian criteria (waist circumference (WC) >90 cm in men or >80 cm in women).

MetS prevalence increased significantly from 56.3% in 1998, 64.7% in 2001, and 69.8% in 2005 to 73.2% in 2009 for diabetic men; from 45.6% in 1998, 52.1% in 2001, and 62.4% in 2005 to 56.8% in 2009 for pre-diabetic men (both $P < 0.001$). High WC ($P = 0.009$), low HDL cholesterol ($P < 0.001$), and high triglycerides ($P = 0.011$) increased significantly in diabetic men, whereas low HDL cholesterol ($P = 0.001$) only increased significantly in diabetic women. In addition, high WC ($P = 0.001$), low HDL cholesterol ($P < 0.001$), and high triglycerides ($P = 0.032$), and high blood pressure ($P = 0.018$) increased significantly in pre-diabetic men, whereas low HDL cholesterol ($P = 0.001$) and high triglycerides ($P = 0.012$) increased significantly in pre-diabetic women. Low HDL cholesterol was the most increased MetS component in both diabetic and pre-diabetic men.

Increasing prevalence of MetS and its components among diabetic and pre-diabetic men need intensive interventions to reduce cardiovascular morbidity and mortality.

PHE-07-2

The Relationship Between Different Definitions of Metabolic Syndrome with Albuminuria and Diabetic Retinopathy

Pang Can¹, Gao Xin², Jia Lili³, Hou Xuhong¹, Liu Wei⁴, Bao Yuqian¹ and Jia Weiping¹

¹Department of Endocrinology and Metabolism, Shanghai Sixth People's Hospital, China; ²Department of Endocrinology and Metabolism, Fudan University Affiliated Zhongshan University; ³Department of Ophthalmology, Shanghai Jiaotong University Affiliated Sixth People's Hospital, China; ⁴Department of Endocrinology and Metabolism, Shanghai Jiaotong University Affiliated Renji University

AIMS: To estimate the association of albuminuria and retinopathy with metabolic syndrome (MS) under different definitions.

METHODS: A total of 3211 Chinese subject were recruited from Shanghai communities. Albuminuria was defined as an elevated morning urine albumin-to-creatinine ratio (30 mg/g or higher). Diabetic retinopathy was

identified with nonmydriatic retinal photographs according to the Diabetic Retinopathy Disease Severity Scale. MS was defined according to criteria of International Diabetes Federation (IDF), NCEP Adult Treatment Panel III (ATP III) and Chinese Diabetes Society (CDS), separately. Logistic regression was performed to analyze the contribution of metabolic components to albuminuria and retinopathy.

RESULTS: For isolated albuminuria, blood pressure over 130/85 mmHg and MS definition of CDS were both significant risk factors. For isolated diabetic retinopathy, blood pressure over 130/85 mmHg, hyperglycemia and MS definition of CDS or IDF were significant contributive factors. Hyperglycemia was a unique risk factors for subjects with albuminuria combined of retinopathy.

CONCLUSIONS: Albuminuria and diabetic retinopathy in Chinese were highly associated with MS definition of CDS.

PHE-07-3

The Effects of Physical Activity on Metabolic Syndrome: From the 2009 Cross-Sectional Study on Working Men in Tokushima

Takako Ichihara¹, Ayako Tamura¹, Yumi Kuwamura¹, Takako Minagawa¹, Nanako Aki², Chisato Kosugi², Akiko Hata², Emi Shuto³, Tohru Sakai³ and Makoto Funaki²

¹Nursing, Health Biosciences/The University of Tokushima Graduate School, Japan; ²Clinical Research Center for Diabetes, Tokushima University Hospital, Japan; ³Public Health and Applied Nutrition, The University of Tokushima Graduate School, Japan

A cross-sectional study was conducted to investigate an association between physical activity in daily life and metabolic syndrome (MetS) on working men aged 20–60 years in Tokushima. Physical activity, diet, medical history, physical measurements of each participant was evaluated. For an evaluation of the physical activity, the Japanese version of the International Physical Activity Questionnaire (IPAQ; long version) was used. According to a criteria for MetS in Japan, 78 participants out of 476 were diagnosed with MetS. Logistic regression analysis revealed an association between MetS and the following three parameters of physical activity: (1) Number of days walking was a major mode of transport per week; (2) Frequency of elevator usage; and (3) The duration of free time spent on moderate activity per day. These findings suggest that frequency of walking as a mode of transport, frequency of stair use and length of time spent on moderate activity may serve to prevent MetS.

PHE-07-4

The Association Between Food Intake and Potential Metabolic Syndrome Cases in Taiwanese

Shu-Hui Hu¹, Yu-Kuei Chen², Yi-Hsin Yang¹, Mei-Ling Liao³, Ming-Feng Hou¹, Chih-Jen Huang¹ and Sue-Joan Chang⁴

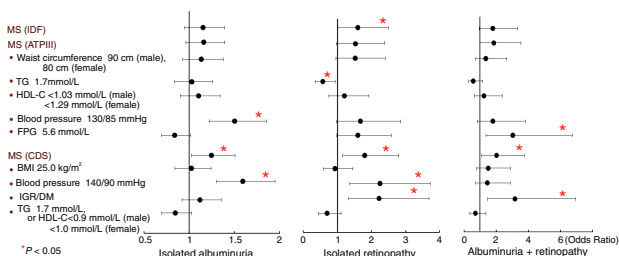
¹Cancer Center, Kaohsiung Medical University Hospital, Taiwan; ²Department of Food Science and Nutrition, Meiho University, Pingtung, Taiwan; ³Department of Nutrition, Lishin Hospital, Tao-Yuan, Taiwan; ⁴Department of Life Sciences, National Cheng Kung University, Tainan, Taiwan

OBJECTIVE: Metabolic syndrome (MS) has gained the moment in the realm of preventive over the past decade. Several studies have reported the importance of dietary factors in the development of MS.

METHODS: A community-based case-control study was conducted between 2008 and 2009. A total of 61 subjects with 40 potential MS cases and 21 healthy controls completed a structure questionnaire, including questions of food frequencies. Potential MS case was defined that the subject has one of abnormalities syndrome, including glucose intolerance, increased triglycerides, decreased HDL cholesterol, Central obesity and hypertension.

RESULTS: Although the frequent consumption of coffee, milk, meat and seafood was not significantly associated with the risk of potential MS, subjects who reported more one time per week (>1 time) frequent consumption of beverages with sugar had an increased risk of potential MS compared to those who consumption less one time per week [crude odds ratio (COR) = 4.9; 95% CI = 1.2–19.7]. Subjects who reported water consumption of more than five cups per day had an increased risk of MS compared to those who did not consumption over five cup of day (COR = 3.7; 95% CI = 1.0–13.4). The water consumption may contain sugar beverage.

CONCLUSION: These results suggest that high-frequency intake of beverage with sugar might increase the risk of potential MS. The results also imply that water intake might be a risk factor for potential MS. We suggest that sugar-water consumption is a dietary risk for MS.



PHE-07-5

Comparison of C-Reactive Protein, Gamma Glutamyltransferase, and Homocysteine in Detecting Metabolic Syndrome in Korean Adults

Yang Ho Kang, A. Ra Jo, Dong Won Yi and Seok Man Son

Department of Internal Medicine, Pusan National University School of Medicine, Korea

OBJECTIVE: Metabolic syndrome (MetS) is closely associated with low grade systemic inflammation. High sensitivity C-reactive protein (hs-CRP), gamma glutamyltransferase (GGT), and homocysteine were inflammatory markers, which have been reported their elevated serum levels in Mets. The aim of this study was to evaluate and compare the validity of these three markers in detecting Mets in Korean adults.

METHODS: Total 234 subjects who visited the Center for Health Promotion in Pusan National University Yangsan Hospital for routine health check-up were analyzed. We defined metabolic syndrome using ATP III criteria.

RESULTS: All serum levels of three markers were significantly elevated in MetS. In the components of Mets, hs-CRP levels were significantly elevated in subjects with central obesity, hypertension, and lowHDL. GGT levels were significantly elevated in subjects with central obesity, hypertension, and hyperTG. Homocysteine levels were significantly elevated in subjects with hypertension and hyperTG. In multivariate logistic regression analyses, hs-CRP showed the most highly elevated odd ratio (OR) of the highest quartiles for MetS among three markers (hs-CRP, OR. 4.97, $P = 0.004$; GGT, OR 4.21, $P = 0.016$; homocysteine, OR 1.99, $P = 0.271$)

CONCLUSION: These limited data showed that elevated hs-CRP levels may be more useful inflammatory risk factor in detecting MetS compared with GGT or homocysteine.

PHE-07-6

Metabolic Syndrome Prevalence Among Health Workers of the National Central Hospital of Mongolia

Tsetsgee Davaadorj, Byambatseren Jambaljav and Yanjmaa Sankhuv

Department of Endocrinology, National Central Hospital, Mongolia

GOAL: To detect, asses and plan treatment for metabolic syndrome among physicians, nurses and health workers of the National Central Hospital.

METHODOLOGY: Following basic measurements were taken:

1. Blood pressure
2. Waist measurement
3. Body mass index
4. Fat measurement
5. Blood glucose level
6. Fat measurement

RESULT: Sixty-eight percent of the participant either are overweight or obese (1st level), over 40s 52% have high blood pressure and 56% have larger waist circumference than normal, and 62.3% have either high or very high body fat. From the result we can conclude that over 50% of the participants have metabolic syndrome. Therefore they have high risk to develop T2DM and other complications such as heart diseases and other. Further we will select 50 people and develop individual recommendation on healthy diet and exercise.

PHE-07-7

Leukocyte Counts Combined with C-Reactive Protein or Adiponectin Increase the Risk For Metabolic Syndrome in Elderly People

Jung Hee Kim, Sung Hee Choi, Seon Mee Kang, Soo Lim, Yoon Ji Kim, Won Sang Yoo, Ah Reum Khang, Kyong Soo Park and Hak Chul Jang

Department of Internal Medicine, Seoul National University College of Medicine, Korea

OBJECTIVE: The prevalence of metabolic syndrome increases with aging. Metabolic syndrome has been known to be associated with inflammatory process which is mediated by inflammatory cells and cytokines. We aimed to elucidate the combined effect of leukocyte and C-reactive protein (CRP) or adiponectin on metabolic syndrome in Korean elderly population.

METHODS: We recruited 439 men and 561 women aged >65 years without infectious or inflammatory disease who participated in Korean Longitudinal Study on Health and Aging (KLoSHA). We measured leukocyte count, fasting glucose, insulin, lipid profile, CRP and adiponectin. Metabolic syndrome was defined according to the modified NCEP-ATP III criteria.

RESULTS: Glycated hemoglobin, Fasting plasma glucose, HOMA-IR and triglyceride were positively associated with leukocyte counts. HDL cholesterol

level was inversely associated with leukocyte counts. Leukocyte counts were positively associated with CRP ($r = 0.222$) and negatively with adiponectin ($r = -0.153$). Subjects with higher leukocyte counts were consistently higher risk for metabolic syndrome than those with lower leukocyte counts in both genders even after adjusted for age, smoking and BMI. Within the lowest adiponectin tertile and the highest hsCRP tertile, subjects within the highest WBC tertile had a higher risk than those within the second WBC tertiles.

CONCLUSION: Higher leukocyte count might be an indicator of metabolic syndrome combined with CRP or adiponectin in elderly people.

PHE-08-1

HbA1c and Second Hour Glucose Level After Oral Glucose Tolerance Test between the Individuals in the Pre-Impaired Glucose Tolerance State and with Normal Oral Glucose Tolerance Test

Pilar Torres Salvador, Chandy Lou Malong, Mary Jane Tanchee, Sjoberg Kho, Bien Matawaran and Leilani Mercado-Asis

Department of Internal Medicine, University of Santo Tomas Hospital, Philippines

OBJECTIVES: To compare HbA1c of individuals with pre-IGT to those with normal OGTT and to correlate the HbA1c with second hour glucose and insulin levels in both groups.

METHODS: Records of 125 patients who underwent 75-g OGTT were reviewed. Demographic profile of patients such as age and BMI were determined and tabulated as mean $\pm$ SD. Patients with normal second hour glucose and insulin level and normal second hour glucose with elevated insulin level were included in the study. The HbA1c two groups was compared using *t*-test. Correlation between the second hour blood glucose and insulin with the HbA1c was done using the pearson correlation analysis.

RESULTS: Sixty-five patients satisfied the inclusion criteria. There were 33 subjects with normal OGTT (51%) and 32 subjects with pre-IGT (49%). The age and BMI were not significantly different (34 ± 12 vs 42 ± 14 years, 27 ± 6 vs 29 ± 6 kg/m²) respectively. The second hour glucose was higher in the pre-IGT group (90 vs 128 mg/dL, $P = 0.045$) with higher second hour insulin (17 vs 89 uIU/mL, $P = 0.001$). The HbA1c of the pre-IGT group was significantly higher than in the normal OGTT group (5.15% vs 6.28% , $P = 0.023$). A positive correlation was noted in the HbA1c and second hour blood glucose level ($P = 0.031$) but not with the second hour insulin level ($P = 0.937$).

CONCLUSION: HbA1c, second hour blood glucose and second hour insulin were significantly higher in the pre-IGT group compared with normal OGTT. A positive correlation was demonstrated between the HbA1c and second hour glucose levels among the pre-IGT group.

PHE-08-2

Risk of Diabetes from Quantity or Quality Sleep is Associated with Obesity in Japanese Workers

Toshiko Kita¹, Eiji Yoshioka², Yasuaki Saijo², Hiroki Satoh³, Mariko Kawaharada⁴ and Reiko Kishi¹

¹Center for Environmental and Health Sciences, Hokkaido University, Japan; ²Department of Health Science, Asahikawa Medical University, Japan; ³Department of Medical Management and Informatics, Hokkaido Information University, Japan; ⁴Department of Comprehensive Development Nursing, Faculty of Health Sciences, Hokkaido University, Japan

OBJECTIVE: To investigate whether a difference in risk for diabetes exists in Japanese workers regarding sleep conditions and the presence or absence of obesity.

METHODS: The researchers conducted a prospective occupational-based study of local government employees in Sapporo, Japan. Between April 2003 and March 2004, 3569 non-diabetic participants aged 35–55 years, underwent annual health checkups and completed a self-administered questionnaire which included information on quantity/quality sleep and BMI at baseline. To be obesity was defined as BMI ≥ 25 kg/m². New developed diabetes was defined as taking medication for diabetes or a fasting plasma glucose level of ≥ 126 mg/dL at follow-up (2007–2008).

RESULTS: A total of 121 (3.4%) new cases of diabetes were reported. In multivariate logistic regression models of workers with obesity, and after adjustment for potential confounding factors, the odds ratio (95% CI) for developing diabetes was 5.16 (1.11–23.91) in those with a sleep duration ≤ 5 h compared to those with >7 h, and 5.46 (1.57–18.95) in those with self-

perceived insufficient sleep duration. In those without obesity, the association with sleep duration was not observed, but the odds ratio was 4.16 (1.17–14.83) in those with awakening during the night, and 4.92 (1.30–18.56) in those with self-perceived insufficient sleep duration.

CONCLUSIONS: The effect on the risk differed from with/without obesity in Japanese workers. Ensuring a quantitatively adequate sleep for those with obesity and a solid sleep for those without obesity may be effective to prevent the developing diabetes.

PHE-08-3

Waist-To-Height Ratio has the Best Anthropometric Association with Diabetes Among Adults from a Developing South Asian Country

Ranil Jayawardena¹, Priyanga Ranasinghe¹, Prasad Katulanda¹, Sherif Rizvi¹ and Mathews David²

¹Diabetes Research Unit, University of Colombo, Sri Lanka; ²University of Oxford, UK

Conventional anthropometric indices have poor sensitivity and specificity for detecting people with diabetes. We aimed to investigate the sensitivity and specificity of Waist-to-height ratio (WHtR) as a predictor of diabetes in a sub-population of South Asian adults and compare it with conventional anthropometric indices such as; body mass index (BMI), waist circumference (WC) and waist to hip ratio (WHR).

A total of 5000 subjects recruited from a nationally-representative community-based sample using multi-stage random method. Weight, height, WC and hip circumference were measured using standard techniques. In addition, over night fasting blood was collected and 2 h oral glucose tolerance test was performed to diagnosed diabetes. Receiver-operating characteristic (ROC) curves were performed and area under the curve (AUC) was calculated for each of the anthropometric indices.

Response rate was near 90%. The mean WHtR in all adults was 0.496 (± 0.077), males (0.477 ± 0.065) had a significant lower WHtR than females (0.508 ± 0.081) ($P < 0.001$). Urban adults has a significantly higher WHtR than their rural counterparts, while WHtR progressively increased with age. WHtR was observed in those with diabetes (0.547 ± 0.068) than those without (0.489 ± 0.075). WHtR had a strong correlation with all traditional anthropometric indices and highest association was observed with WC. The AUC of WHtR (0.73) was significantly higher than that of BMI (0.67), WC (0.71) and WHR (0.69) in the prediction of diabetes mellitus in all adults and for both males and females.

Among Sri Lankan adults, WHtR had a greater sensitivity and specificity in predicting diabetes than traditional anthropometric indices.

PHE-08-4

Evaluation of a Minimally Invasive Glucose Monitoring System for Glucose Intolerance Screening During Health Checkups

Shigenobu Egawa¹, Ikuko Baba¹, Toshiyuki Sato², Seiki Okada², Samiko Hosoya², Yasuhito Ohnishi², Mina Kamei², Hiroyuki Koga², Kazuhiko Sakaguchi³ and Hiromu Nakajima⁴

¹Fukuoka Institute of Occupational Health, Japan; ²Sysmex Corporation, Japan; ³Division of Diabetes, Metabolism and Endocrinology, Kobe University, Japan; ⁴Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan

AIMS: Detection of postprandial hyperglycemia at an early stage of diabetes is crucial for effective diabetes management. However, the indices used during routine checkups are relatively insensitive to glucose intolerance in the early stage. We have developed a new system for monitoring glucose area under the curve (AUC) using minimally invasive interstitial fluid extraction technology (MIET) to evaluate postprandial hyperglycemia without blood sampling. In this study, the system was evaluated in nondiabetic subjects during routine checkups.

METHODS: One hundreds volunteers without previous diagnosis of diabetes, were subjected to two types of meal test during routine checkups. FPG, HbA1c, glycoalbumin (GA), 1, 5-anhydroglucitol, and urinary glucose levels were measured before the meal. The glucose AUC monitoring system was applied for 2 h after the meal. Capillary blood glucose was measured at 1 and 2 h after the meal as references.

RESULTS: The glucose AUC measured by MIET correlated well with AUC calculated by blood glucose ($r = 0.83$). Moreover, a good correlation between glucose AUC and peak glucose levels was confirmed ($r = 0.79$). Glucose intolerance characterized by elevated blood glucose was distinguished from normal glucose tolerance using MIET better than by FPG, HbA1c, and other

indices. Furthermore, the volunteer questionnaire confirmed that MIET can be done without any pain.

CONCLUSION: We confirmed that MIET is a good technique for measuring glucose AUC, a screening marker for glucose intolerance during routine checkups. Therefore, this easy-to-use system can be clinically useful in screening postprandial hyperglycemia without blood sampling.

PHE-08-5

The Clinical Characteristics of Metabolic Syndrome Associated with Prediabetic Patients

SoYoung Park¹, Mi-Kyoung Park¹, Young-Jin Park², Seong-Ho Han², Joo-Sung Park², Hye-Jeong Lee³ and Duk Kyu Kim¹

¹Department of Internal Medicine, Dong-A University College of Medicine, Korea;

²Department of Family Medicine, Dong-A University College of Medicine, Korea;

³Department of Pharmacology, Dong-A University College of Medicine, Korea

OBJECT: Prediabetic patients are known to have increased risk for diabetes and accompanied by many metabolic abnormalities and cardiovascular risks. Thus, they may have various clinical manifestations. We evaluated prevalence of metabolic syndrome (MS) in prediabetic patients and categorized prediabetic patients with MS into four groups according to their major metabolic component to find out whether clinical manifestations are different between them.

METHOD: We screened peoples who visited Health Examination Center, Dong-A University Hospital, from 2010 to 2011. Among them, 204 were selected, divided into two groups, prediabetes and normal glucose group matched by age and sex. We compared prevalence of MS according to NCEP-ATP III criteria. We divided prediabetic patients with MS into four categorical groups, hypertensive (without dyslipidemia), dyslipidemic (without hypertension), mixed (with hypertension and dyslipidemia) and complete group (all components of MS). We evaluated prevalence of osteoporosis and fatty liver, liver function test, inflammatory marker, tumor markers in all groups.

RESULTS: The prevalence of MS was significantly higher in prediabetes group (40.1%) than normal glucose group (5.8%) ($P < 0.0001$). Between four groups, there were no significant differences in age and BMI. The prevalence of fatty liver was significantly higher in mixed group (91%) than hypertensive group (33%) ($P < 0.046$). But there were no significant differences between groups regarding osteoporosis, liver function test, inflammatory marker, tumor markers.

CONCLUSION: The prevalence of MS is significantly higher in prediabetes than in normal glucose group in our study. Among prediabetic patients with MS, those with both hypertension and dyslipidemia have more risk of fatty liver than hypertension alone.

PHE-08-6

Blood Glucose Level, HbA1c and Lifestyle in College Students

Chieko Suzuki and Yoshie Yokote

Department of Nursing, Okayama Prefectural University, Japan

The present study aimed at clarifying the relationships between bloodglucose level, HbA1c and lifestyle in young people. Subjects comprised 154 university students (69 males and 85 females) between 18 and 30 years of age. The questionnaire consisted of demographic data (age, sex, BMI), knowledge of diabetes and awareness and behavior related to 'diet', 'exercise', 'sleep' and 'stress'. Blood glucose levels and HbA1c in the serum were also measured. Statistical analysis was performed using unpaired *t*-test and one-way ANOVA. The HbA1c percentage was evaluated using HbA1c (NGSP). As a result, all the participants had normal glucose levels (between 47 and 234 mg/dL) and HbA1c percentages (between 4.7% and 6.1%) except that one participant had a glucose level above normal. However, 52 participants (33.8%) had an HbA1c level of $\geq 5.6\%$, 8 (5.2%) had a fasting blood glucose level of ≥ 100 mg/dL, and 5 (3.2%) met both criteria. In other words, a total of 65 participants were found to need health guidance according to the health guidance program of the Ministry of Health, Labour and Welfare, although the abdominal circumference measurement was excluded. There was no significant difference in the BMI, knowledge, awareness, and behavior scores between those with a slightly higher glucose level and the rest of the participants. However, 141 participants (91.6%) who wanted, but failed, to change their behaviors had a significantly lower average score in 'exercise' and 'diet' than the rest. Findings suggest that there may be incipient diabetics among university students who need to have support for lifestyle improvement.

PHE-08-7

Predicting Young-Onset Type 2 Diabetes with Metabolic Syndrome Components in Healthy Young Taiwanese

Chung-Ze Wu¹, Jiunn-Diann Lin¹, Yen-Lin Chen², Chun-Hsien Hsu³ and Dee Pei⁴

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, Taiwan; ²Department of Pathology, Cardinal Tien Hospital, Xindian, Medical School, Catholic Fu Jen University; ³Department of Family Medicine, Cardinal Tien Hospital, Xindian, Medical School, Catholic Fu Jen University; ⁴Department of Internal Medicine, Cardinal Tien Hospital, Xindian, Medical School, Catholic Fu Jen University

OBJECTIVE: Increased incidence of young type 2 diabetes mellitus (YDM) is an important health problem in Taiwan as well as many other countries. In this study, we identified which one of the metabolic syndrome (MetS) components could be used to predict YDM after a 2.3-year follow-up.

METHODS: MetS components were measured in 12,501 healthy young adults (18–27 years old). They were followed up for 2–10 years (mean: 30.1 ± 20.0 months) to determine the occurrence of YDM. Cox proportional hazard model was used to evaluate which one of the MetS components could predict YDM.

RESULTS: At the end of the follow-up, there were 18 young adults (11 males and seven females) developed YDM. In young men, FPG, waist circumference (WC), and triglyceride (TG) were significant factors to predict YDM. In the same time, FPG, WC, TG, and systolic blood pressure (SBP) were significant factors for young women. After putting all the significant factors into the Cox multivariable regression for adjustment, FPG (HR: 1.044 in males, 1.048 in females) and WC (HR: 1.052 in males, 1.119 in females) were still significant factors in both young men and women.

CONCLUSION: Among MetS components, FPG and WC are the most important factors which can predict future YDM in young males and females.

PHE-08-8

Early Insulin Spike and Associated Hypoglycemia (Relationship with Diabetes Development)

Kyoko Hirai¹ and Junichi Takahashi²

¹HIRAI Clinic, Japan; ²Joto Central Hospital, Japan

BACKGROUND AND AIMS: With the aim of improving insulin secretory patterns, patterns of abnormal glucose tolerance were classified by insulin secretory patterns according to a 75 g oral glucose tolerance test (OGTT), and treatment primarily focused on dietary instructions was provided.

MATERIALS AND METHODS: A 75 g OGTT was conducted on 83 Japanese people aged between 19 and 65 years without critical symptoms and a previous history of diabetes. The instructions were given mainly on the size and content of meals, mealtime, time interval between meals and consumption sequence to the extent that their daily life was not significantly impacted.

RESULTS: Of 83 people investigated, an early insulin spike was observed in 33 subjects. The OGTT conducted after 3 months or more revealed that the peak insulin level decreased in cases where an insulin spike was observed previously.

CONCLUSION: Excessive insulin secretion in the form of a spike detected in 120 min after OGTT was considered to cause hypoglycemia for 120–180 min. The investigation also suggested that impaired glucose tolerance should not be assessed solely by the blood glucose level, which represents a result of insulin secretion, but by insulin fluctuations.

Excessive insulin secretion even in the form of a spike in Japanese people who tend to have low insulin levels may lead to insulin depletion and accelerate development of diabetes. A glucose spike is considered to exist before any insulin spike. It is therefore deemed necessary to promote OGTT as well as customized dietary instructions in order to prevent diabetes.

PHE-08-9

Study of Fasting Blood Glucose with Obesity Status in Premenopausal Women in the Age Group of 45-49 years

Pranita Ashok, Asmita Phadke, B. Balsubramanian and A. R. Joshi

Physiology, Bharati vidyapeeth Medical College, Pune, India

OBJECTIVES: The association between type 2 Diabetes Mellitus and Obesity is very close. Obesity is common in women aged between 45 and 49 years. Prevalence of prediabetes i.e. Impaired Fasting Glucose also seems to be higher in women than men in the Indian population. The present work is planned to

study the prediabetic status in preobese and obese in premenopausal women with the help of estimation of Fasting Blood Glucose (FBG) levels.

METHODS: Fasting Fasting Blood Glucose levels and BMI were estimated in 194 asymptomatic premenopausal women with no family history of Type 2 Diabetes Mellitus (DM). The subjects are divided in Control (I), Preobese (IIa) & Obese group (IIb). The results are analyzed statistically ANOVA test.

RESULT: Mean FBG levels in preobese and obese group are higher than control group. There is significant difference between BMI & Fasting Blood glucose levels in Premenopausal women. In a nutshell obesity without menopause also act as a important predictor for type 2 DM.

CONCLUSION: Thus in premenopausal women lifestyle modifications may prove as important means for prevention of obesity & type 2 DM in postmenopausal women where worsening of the effect can be prevented due to irreversible hormonal changes.

PHE-09-1

Serum Resistin is Mainly Associated with Circulating Neutrophil and Monocyte Counts: The Toon Health Study

Ryoichi Kawamura¹, Wataru Nishida¹, Isao Saito², Yasuharu Tabara³, Yasunori Takata¹, Mayo Aibiki¹, Maki Shiba¹, Yukinobu Nomi¹, Yuko Kadota¹, Ai Okamoto⁴, Tatsuya Nishimiya⁴, Hiroshi Onuma¹, Tetsuro Miki⁵, Takeshi Tanigawa² and Haruhiko Osawa¹
¹Department of Molecular and Genetic Medicine, Ehime University Graduate School of Medicine, Japan; ²Department of Public Health, Ehime University Graduate School of Medicine, Japan; ³Department of Basic Medical Research and Education, Ehime University Graduate School of Medicine, Japan; ⁴Department of Clinical Laboratory, Ehime University Hospital, Japan; ⁵Department of Geriatric Medicine, Ehime University Graduate School of Medicine, Japan

OBJECTIVE: Resistin, secreted from adipocytes, antagonizes the action of insulin in mice. Circulating resistin is also associated with inflammation and cardiovascular diseases. In humans, resistin is predominantly expressed in macrophages, and its expression and secretion are induced by inflammatory stimuli. However, the relation between serum resistin and complete blood cell count or differential white blood cell (WBC) count in general populations remains to be elucidated.

METHODS: The Toon Health Study is a cohort study for surveying risk factors for cardiovascular diseases and diabetes in community based subjects. In this study, 1109 residents aged 30–79 years were enrolled from 2009 to 2010. The 1108 participants whose serum resistin was measured by ELISA were analyzed. Resistin was natural log-transformed for statistical analysis.

RESULTS: Serum resistin was positively correlated with total WBC, red blood cell, and platelet counts [correlation coefficient (R); 0.33 ($P < 0.0001$), 0.11 ($P = 0.0004$), and 0.12 ($P < 0.0001$), respectively]. Precisely, analysis of WBC components showed that serum resistin was increased with the increased neutrophil and monocyte counts (neutrophil, $R\ 0.34$; monocyte, $R\ 0.20$; both $P < 0.0001$). These associations did not change after adjusted for age, sex, smoking, and other metabolic risk factors. There were modest correlations between serum resistin and lymphocyte, eosinophil, or basophil counts ($R\ 0.09$, 0.11 , and 0.16 , respectively), with the caution that the percentage of basophil in total WBC was very low.

CONCLUSION: Serum resistin was mainly associated with neutrophil and monocyte counts in the general Japanese population.

PHE-09-2

Liver Enzymes and Vitamin D Levels in Metabolically Healthy but Obese (MHO) Individuals

Ho Cheol Hong, Jae Hee Ahn, Hae Yoon Choi, Yoon Jung Kim, Chai Ryoung Eun, Nam Hoon Kim, Joo Hyung Kim, Sae Jeong Yang, Hye Jin Yoo, Hee Young Kim, Ji A. Seo, Nan Hee Kim, Sin Gon Kim, Sei Hyun Baik, Dong Seop Choi and Kyung Mook Choi
Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, Korea University, Seoul, Korea

Increased liver enzymes and decreased vitamin D levels are associated with insulin resistance and type 2 DM. This study examined liver enzymes and vitamin D levels in metabolically healthy but obese (MHO) individuals and compared the values with those of other body size phenotypes in the Korean population. A total of 16,190 people over the age of 18 were analyzed using data from the Fourth Korea National Health and Nutrition Examination Survey. Body size phenotypes were classified into four groups by BMI, diabetes status, and the number of metabolic syndrome components present in an individual. The prevalence of MHO individuals was 14.9% in the entire population and 47.7% in the obese population. In a correlation analysis

adjusted for age, gender and BMI, AST and ALT levels were positively correlated with insulin resistance and cardiometabolic risk factors of metabolic syndrome, whereas vitamin D levels were negatively correlated with these variables. MHO subjects had significantly lower concentrations of AST and ALT compared to metabolically abnormal obese (MAO) subjects, although vitamin D levels were not significantly different between the two groups. Furthermore, a multiple logistic regression analysis revealed that MHO subjects had lower risk of liver function abnormality compared to MAO subjects after adjusting for potential confounding factors. However, the risk of vitamin D deficiency was not significantly different between groups with different body size phenotypes. Although both liver enzymes and vitamin D levels are related to insulin resistance and metabolic syndrome, only liver enzymes were independently associated with MHO phenotype.

PHE-09-3

Serum Adiponectin Complexes and Abdominal Obesity Among Population-Based Elementary Schoolchildren in Japan

Hirota Ochiai¹, Takako Shirasawa¹, Rimei Nishimura², Aya Morimoto², Tadashi Ohtsu¹, Hiromi Hoshino¹, Naoko Tajima³ and Akatsuki Kokaze¹
¹Department of Public Health, Showa University School of Medicine, Japan; ²Division of Diabetes, Metabolism and Endocrinology, Department of Internal Medicine, Jikei University School of Medicine, Japan; ³Jikei University School of Medicine, Japan

OBJECTIVE: The objective of the present study was to investigate the relationship between serum adiponectin complexes and abdominal obesity among population-based elementary schoolchildren in Japan.

METHODS: Subjects included all fourth-grade schoolchildren (9 or 10 years of age) in Ina-town, Saitama prefecture, Japan, during 2005–2008. Information about each subject's lifestyle and family was collected using a self-administered questionnaire. Measurements of height, weight, and waist circumference (WC) were made for each child. Blood samples were drawn from the subjects to measure high-, medium-, and low- molecular weight adiponectin (HMW-adn, MMW-adn, and LMW-adn) levels. Abdominal obesity was defined as a waist-to-height ratio of 0.5 or more or a WC of 75 cm or more, according to the metabolic syndrome criteria for children and adolescents in Japan. To calculate the odds ratio (OR) and 95% confidence interval of abdominal obesity, a logistic regression model was used.

RESULTS: Data from 1654 children (846 boys and 808 girls) were analyzed. The proportion of abdominal obesity was 11.6% among boys and 9.2% among girls. For all three adiponectin isoforms, levels less than the median value significantly increased ORs of abdominal obesity among boys (adjusted OR: 2.56 for HMW-adn, 2.44 for MMW-adn, 1.79 for LMW-adn). In girls, levels less than the median value significantly increased OR of abdominal obesity, but only for HMW-adn (adjusted OR: 1.93).

CONCLUSION: Abdominal obesity was significantly associated with lower HMW-adn level regardless of sex. This study also suggested that HMW-adn was more affected by abdominal obesity than MMW-adn and LMW-adn.

PHE-09-4

The Association Between Metabolic Syndrome and Sleep Quality in a Chinese Population

Hao-Chang Hung¹, Yi-Ching Yang², Horng-Yih Ou¹, Jin-Shang Wu², Feng-Hwa Lu² and Chih-Jen Chang²

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, National Cheng Kung University Hospital, Taiwan; ²Department of Family Medicine, National Cheng Kung University Hospital, Taiwan

BACKGROUND: Both short and long sleep duration increase the risk of metabolic syndrome. However, there is limited research on the association between metabolic syndrome and sleep quality. The aim of this study is to investigate this association in a Chinese population.

METHODS: Subjects were recruited from the Prevention Health Center of National Cheng Kung University Hospital. Anthropometric data and metabolic parameters were measured. The diagnosis of metabolic syndrome was according to the statement of the American Heart Association/National Heart, Lung, and Blood Institute. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI).

RESULTS: Of the total 3251 subjects, 763 (24%) had metabolic syndrome. The global PSQI scores were 6.7 ± 3.1 and 6.2 ± 2.4 in subjects with and without metabolic syndrome, respectively ($P < 0.001$). The multivariate linear regression analysis showed that age, female gender, metabolic syndrome, smoking

habit, and habitual exercise were independently associated factors of the global PSQI score.

CONCLUSIONS: Metabolic syndrome was associated with higher global PSQI score. In clinical practice, subjects with metabolic syndrome should be evaluated for the presence of sleep disturbance.

PHE-09-5

Regional Body Fat Distribution and Prevalence of Diabetes

Yoshimi Tatsukawa¹, Michiko Yamada¹ and Shuhei Nakanishi²

¹Department of Clinical Studies, Radiation Effects Research Foundation, Japan;

²Department of Molecular and Internal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Japan

BACKGROUND: There is a limited number of studies regarding association between peripheral fat and diabetes among the Japanese population, although the positive association between abdominal obesity and risk factors in diabetes/cardiovascular disease is well established.

PURPOSE: The purpose of this cross-sectional study is to investigate association between trunk and peripheral (arms and legs) fat mass and prevalence of diabetes.

METHODS: We analyzed 1838 participants (591 men and 1247 women, average age of 65.5 years) during the period 1994–1996 in the Hiroshima Adult Health Study, consisting of atomic bomb survivors and their controls who had body-composition information from dual-energy X-ray absorptiometry. The fat-mass percentages for trunk, arms, and legs were calculated by dividing each of the specific body part's fat mass by total soft tissue mass (i.e. total body mass excluding bone mineral mass).

RESULTS: There was found to be positive associations between percentage of trunk fat and prevalence of diabetes in both sexes, although any significant association was diminished for women after BMI was added as an adjustment factor. Significant negative associations between percentage of leg fat and prevalence of diabetes were observed in both sexes, after adjustment for conventional risk factors including age, BMI, and radiation dose. Negative association between percentage of arm fat and prevalence of diabetes were suggested in women.

CONSIDERATION: Peripheral fat was suggested to have protective effects on prevalence of diabetes. We will need to verify the effects of peripheral fat on risk of diabetes with a longitudinal study design.

PHE-09-6

Study on Body Composition Analysis Among Adults with Different Body Weight

Hua Shu¹, Yansong Zheng², Chunlin Li¹, Yanhui Lu¹, Minyan Liu¹ and Xiaohong He²

¹Department of Geriatric Endocrinology, Chinese PLA General Hospital and Military Postgraduate Medical College, China; ²Department of Health Examination Center, PLA General Hospital, China

OBJECTIVE: The aim of the study is to investigate the characteristic of body composition among male and female adults with different body weight.

METHODS: We performed a study on 61,379 healthy adults (39,855 male and 21,527 female) referred to the health examination center of Chinese PLA general hospital between May/2005 to February/2011. BMI, body composition including body fat, water, muscle, protein, mineral salt content were measured by anthropometric measurements and bioelectrical impedance analysis (BIA). The data was analysed among groups divided by gender, age and BMI.

RESULTS: (1) The prevalence of overweight and obesity defined by BMI is significantly higher in the male group than in the female group ($P < 0.01$); (2) Within a certain age range (<60 in male, <70 in female), the prevalence of both overweight and obesity defined by BMI is increased with age ($P < 0.01$); (3) The fat mass percentage is significantly higher in female than in male (95% CI 24.6–37.4% vs 18.7–31.3%, $P < 0.01$); (4) Body fat mass percentage progressively elevates with increase of BMI, while there is a decreasing trend of the rest body composition. The male subjects have higher percentage of muscle, water and mineral salt ($P < 0.01$), while the percentage of protein is higher in the female group ($P < 0.01$).

CONCLUSION: (1) The female has more fat mass than male under the same level of BMI. So it is more reasonable to introduce adiposity for the evaluation of obesity, especially in women. (2) There might be an relationship between the increased risk of cardiovascular and cerebrovascular diseases, impaired

glucose tolerance, dyslipidemia and higher fat mass percentage, modification of body composition in obesity adults.

PHE-10-1

A Regional Study of the Association Between Insulin Secretory Capacity and Insulin Resistance Among Elderly with HbA1c (JDS value) of 5.1–6.1%

Hironari Sano¹, Rimei Nishimura¹, Juri Shida², Mariko Kazamaki², Kiyotaka Ando¹, Daisuke Tsujino¹, Kentaro Taki¹, Shinichiro Ishikawa², Naoko Tajima¹ and Kazunori Utsunomiya¹

¹Division of Diabetes, Metabolism and Endocrinology, Department of Internal Medicine, Jikei University School of Medicine, Japan; ²Department of Internal Medicine, Tsunan Hospital, Japan

OBJECTIVE: The aim of this study was to assess the association between insulin secretory capacity and insulin resistance of the elderly based on data obtained from the Tsunan Hospital, which is the only medical institution in a rice-producing town.

SUBJECTS: The subjects were residents of Tsunan Town aged 65 years or older who underwent a complete physical examination at the Tsunan Hospital and had never received any treatment for diabetes mellitus.

METHODS: Physical measurements and blood tests were performed from April 2010 to March 2011. The HbA1c 5.1–5.4% group (Group A) and 5.8–6.1% (Group B) were extracted, and the HOMA- β and HOMA-IR levels were determined for each group.

RESULTS: Three hundred and sixty-four (72.0 $\pm$ 5.2 years) were 65 years or older. A total of 149 persons were extracted for Group A and 51 persons were extracted for Group B. HOMA- β level was significantly lower in Group B (45.2 $\pm$ 20.9) than in Group A (56.6 $\pm$ 27.2) ($P < 0.01$). No significant difference in HOMA-IR level was detected between Group A (1.1 $\pm$ 0.1) and Group B (1.3 $\pm$ 0.7). Among individuals with BMI > 24 (36 in Group A and 19 in Group B), no significant difference in HOMA-IR was noted between Group A (1.5 $\pm$ 0.8) and Group B (1.6 $\pm$ 0.5).

CONCLUSIONS: The progression of glucose metabolism disorder from an HbA1c of 5.1–5.4% to 5.8–6.1% seemed to be associated with decreased insulin secretory capacity, rather than with increased insulin resistance, in elderly.

PHE-10-2

The Risk of Hypoglycemia due to Jointed Usage of Blood Sugar Lowering Medications and Herbs on Diabetes: A Population-Based Study

Ying-Ling Chen¹, Mark Hou¹, Nian-Ze Hu² and Sheng-Chieh Huang³

¹Department of Chinese Medicine, Changhua Christian Hospital, Taiwan; ²Department of Information Management, National Formosa University, Taiwan; ³Department of Electrical and Control Engineering, National Chiao Tung University, Taiwan

Recently there has been a growing interest in Traditional Chinese medicine (TCM) for diabetes control. Many diabetic patients seek TCM to improve their quality of life while receiving conventional treatments. Studies have shown some Chinese herbs and formula could reduce blood sugar level, such as Panax ginseng and Byakko-kaninjin-to. Thus the combining use of herbs and drugs might cause unexpected hypoglycemia. Taiwan National Health Insurance program produced the National Health Insurance Research Database (NHIRD) which covering nearly the whole population of Taiwan. The study was to investigate the demographic characteristics and frequency on the jointed usage of herbs and drugs by analyzing the NHIRD dataset.

The study sample was screened from the NHIRD according to the diabetes-related ICD9 code 250.xx, 23 frequent used diabetic medications and TCM treating code in the year of 2005. Genders, ages, residencies, TCM prescriptions and concurrent diseases of the sample were explored. Data were analyzed by Microsoft SQL Server 2005 Enterprise and Excel 2003 edition.

The result showed 27,217 (0.11%) patients out of 25.68 million people received herb and drug for diabetes at the same time. Sixty-two percent of the patient lived in five metropolitans of Taiwan. Among 106,266 TCM prescriptions there were 28% containing at least one sugar-lowering herb. Bai-Hu-Chai-Shen-Tang was the most popular formula prescribed. Hypertension is the number one co-disease of the sample. In conclusion, nearly 1/3 of the TCM prescriptions contained blood sugar lowering herbs, it indicated potential risk of unexpected hypoglycemia existed and special care should be taken into consideration.

PHE-10-3

5-Year Temporal Change in HbA1c in Japanese General Population

Yayoi Yamamoto¹, Tomoko Nakagami¹, Yasuhiko Iwamoto², Yasuko Uchigata¹ and Nobuo Yoshiike³

¹Diabetes Center, Tokyo Women's Medical University, Japan; ²Tokyo Women's Medical University, Tokyo, Japan; ³Department of Nutrition, Aomori University of Health and Welfare, Aomori, Japan

OBJECTIVE: The aim is to examine 5-year temporal change in HbA1c from 1997 to 2002 in Japan, by using cross-sectional data from the Japan National Diabetes Survey conducted in 1997 and 2002.

METHODS: The study comprises 4553 men and 6852 women aged 20 years and older. The data and proportions of people classified by five groups on HbA1c (< 5.6 , 5.6–5.9, 6.0–6.4, $\geq 6.5\%$, medicated DM) were compared between two survey years. The stepwise multivariate regression model with age, body mass index (BMI), systolic blood pressure (SBP), total cholesterol (TC), survey year, antihypertensive medication, exercise habits, foot step, smoking status, and alcohol habits as independent variables was fitted to identify risk factors for HbA1c in people without medicated DM.

RESULTS: The proportion of HbA1c 5.6–6.4% group was significantly increased and HbA1c $< 5.6\%$ group was decreased. HbA1c $\geq 6.5\%$ group was significantly decreased in women. The median HbA1c shifted from 5.3% to 5.5% in both sexes. When adjusting for age, In men, mean HbA1c was significantly increased in BMI < 30 kg/m² group. In women, mean HbA1c was increased in BMI < 25 kg/m² group. When adjusted for BMI, mean HbA1c was significantly increased in men < 40 years old and women < 50 years old. Identified risk factors for HbA1c increase were age, BMI, TC, smoking status, no alcohol habits and survey year in men, age, BMI, TC, SBP, no alcohol habits and survey year in women.

CONCLUSIONS: The median HbA1c increased by 0.2% from 1997 to 2002. This was partly due to an elevation of HbA1c in young-middle aged or non-obese individuals.

PHE-10-4

Association of 11 β -Hydroxysteroid Dehydrogenase Type 1 Gene Polymorphisms with Serum Alanine Aminotransferase Activity

Seong-Su Moon and Young-Sil Lee

Department of Internal Medicine, College of Medicine, Dongguk University, Korea

11 β -Hydroxysteroid dehydrogenase type 1 (HSD11B1), which converts inactive glucocorticoid to active glucocorticoid, plays a critical role in pathogenesis of both non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome. Serum alanine aminotransferase (ALT), an indicator of hepatocellular injury, has been suggested as a surrogate marker for NAFLD. A study was conducted to examine the association of common single nucleotide polymorphisms (SNPs) in HSD11B1 [IVS3-29G/T (rs12086634), IVS4-11120A/G (rs1000283)] with serum ALT level in 756 Korean subjects (348 males and 408 females). ALT values were divided into two groups; elevated (> 33 U/L in males, > 25 U/L in females) and normal (≤ 33 U/L in males, ≤ 25 U/L in females). SNPs showed a significant association with elevated ALT in the total study population. According to results of logistic regression analysis adjusted for age, body mass index, smoking status, alcohol consumption, and metabolic syndrome, the GT + GG genotype for rs12086634 and the GA + AA genotype for rs1000283 showed significantly higher frequencies among subjects with elevated ALT, compared with the TT and GG genotypes, respectively (GT/GG vs TT; OR 1.685, 95% CI 1.175–2.416, $P = 0.005$, GA/AA vs GG; OR 2.143, 95% CI 1.454–3.158, $P < 0.001$, respectively). In conclusion, HSD11B1 polymorphisms (rs12086634 and rs1000283) are associated with elevated levels of ALT. Findings from this study suggest a possible association between HSD11B1 polymorphisms and hepatocellular injury, such as that seen in patients with NAFLD.

PHE-10-5

Incretin and Insulin Secretions in Japanese-Americans with Normal Glucose Tolerance: Data from Hawaii-Los Angeles-Hiroshima study

Tsuguka Shiwa, Yuko Monzen, Maiko Mouri, Yasuyuki Mitama, Mami Shiwa, Mitsunobu Kubota, Masatoshi Hirano, Shusaku Maeda, Masayasu Yoneda, Tomokazu Awaya and Shuhei Nakanishi

Department of Molecular and Internal Medicine, Hiroshima University, Japan

OBJECTIVE: The incretins are hormones that work to increase insulin secretion. We have reported that Japanese-Americans, primarily exposed to a

westernized lifestyle, have increased incidence of hyperinsulinemia compared with Japanese living in Japan even under normal glucose tolerance (NGT) and similar BMI. In this study, we compared secretions of both insulin and incretin hormones between Japanese-Americans and Japanese with NGT.

RESEARCH DESIGN AND METHODS: Thirty-seven Japanese-Americans and 35 Japanese subjects diagnosed with NGT by 75 g glucose tolerance test were recruited. We examined serum insulin, plasma active GLP-1 and total GIP during a 120-min period after ingestion of 75 g glucose.

RESULTS: Data are expressed as mean levels with standard deviation. Although serum glucose levels did not differ between the two groups during the examination except for fasting glucose levels, the 60-min and 120-min insulin secretion was significantly higher in the Japanese-Americans than in the Japanese subjects, even after adjustment was made for age and gender (fasting glucose levels: 93.4 ± 5.8 vs 87.4 ± 7.0 mg/dL, $P = 0.004$, 60-min insulin levels: 98.2 ± 62.8 vs 65.6 ± 54.8 μ U/mL, $P = 0.039$, 120-min insulin levels: 54.5 ± 35.3 vs 36.3 ± 26.3 μ U/mL, $P = 0.016$, respectively). On the other hand, active GLP-1 and total GIP had similar secretion levels between the two groups.

CONCLUSIONS: Japanese-Americans have excessive insulin secretion without marked increase in incretin secretions from 60- to 120-min period after 75 g glucose ingestion.

PHE-10-6

Enhanced Response of Incretin Hormones to Oral Glucose Tolerance Test in Patients with Crohn's Disease and with Ulcerative Colitis

Yoshiyuki Hamamoto¹, Sachiko Honjo¹, Yukiko Kawasaki¹, Kanta Fujimoto¹, Hisato Tatsuoka¹, Kanako Mori², Hiroki Ikeda¹, Yoshiharu Wada¹ and Hiroyuki Koshiyama¹
¹Center for Diabetes and Endocrinology, Kitano Hospital, The Tazuke Kofukai Foundation Medical Research Institute, Japan; ²Department of Diabetes and Clinical Nutrition, Kyoto University, Japan

OBJECTIVE: It is not known how the incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are affected in patients with Crohn's disease (CD) or ulcerative colitis (UC).

METHODS: Subjects included seven patients with CD without history of operation, six patients with UC, and seven healthy controls. Plasma glucose (PG), insulin (IRI), glucagon, as well as active GLP-1 (aGLP-1) and GIP levels measured with specific immunoassay, in response to 75 g oral glucose load were determined. Insulin resistance and insulin secretion were also determined using the homeostasis model assessment (HOMA) and the insulinogenic index (IGI).

RESULTS: There was no significant difference in PG response, insulin sensitivity and insulin secretion among the groups. Although the peak stimulated aGLP-1 values were not significantly different, aGLP-1 values at 60 min were significantly higher in the patients with CD and UC than controls (4.53 ± 2.17 , 3.86 ± 1.14 , and 2.73 ± 0.65 pM/L, respectively $P < 0.05$). GIP values at fasting and 60 min were significantly higher in patients with CD (49.2 ± 22.1 and 274.1 ± 90.7 pg/mL) than controls (27.4 ± 7.6 and 178.7 ± 58.7 pg/mL, $P < 0.05$) while there was no difference in the patients with UC. There was no difference in glucagon response among the groups.

CONCLUSION: In patients with CD, increased GLP-1 and GIP response to oral glucose load, and in patients with UC, increased GLP-1 response were observed. No difference of PG response, insulin sensitivity and insulin secretion was detected in either of CD and UC.

PHE-11-1

Cost-Benefit Analysis of Community-Based Screening for Diabetic Retinopathy among Chinese type 2 diabetes in Kinmen, Taiwan

Tao-Hsin Tung and Jorn-Hon Liu
Cheng-Hsin General Hospital, Taiwan

The purpose of this study is to explore whether it is worthwhile to launch a routine diabetic retinopathy (DR) screening for blindness prevention among Chinese type 2 diabetes from different perspective based on the population-based study in Kinmen, Taiwan. A total of 971 community dwelling adults previously diagnosed with type 2 diabetes in 1991–1993 underwent DR screening in 1999–2002 by a panel of ophthalmologists using on-site indirect ophthalmoscopy and 45-degree color fundus retinal photographs. The cost-benefit analysis is used to evaluate the DR screening. In terms of benefit-cost ratio, the different screening programs for DR could save New Taiwan Dollars (NTD) from 14.38 to 36.83 in discounted costs for each dollar incurred in different screening years from the societal viewpoint for Taiwan and save NTD

from 0.81 to 1.80 in different screening years from health care payer's perspective. The average estimate of willingness-to-pay to translate into benefit yields NTD from 937.8 to 4689 benefits per case due to DR screening in different screening years during 10-year follow-up. The net present value of the DR screening were NTD from –167,318 to –307,251.2 in different screening years. In conclusion, it is worthwhile to initial a routine DR screening of Chinese type 2 diabetes for blindness prevention from the societal perspective but not from consumer decision based on the willingness-to-pay perspective.

PHE-11-2

High Prevalence of Previously Undiagnosed T2DM with Ketoacidosis in Diabetic Emergency at a University Hospital

Hisamitsu Ishihara, Nana Ohkawara, Shinobu Shoji, Suguru Yamaguchi, Fujiko Egashira, Mayumi Okamoto and Mitsuhiro Nakazaki
Division of Diabetes and Metabolic Diseases, Nihon University School of Medicine, Japan

In our university hospital, located very close to the center of Tokyo, we had noticed that increasing number of type 2 diabetes (T2DM) patients were first diagnosed when they had been hospitalized because of severe hyperglycemia with ketosis or ketoacidosis. Therefore, we analyzed 93 cases who were hospitalized between January 2009 and April 2012 due to severe hyperglycemia (higher than 300 mg/dL) and keto(acid)osis (serum 3-hydroxybutyrate (3HB) higher than 500 μ mol/L). Average blood glucose levels were 625 (307–1485) and 603 (301–1766) and average serum 3-HB were 5,637 (1152–13,803) and 3015 (830–11,700) for 40 type 1 diabetes (T1DM) and 53 T2DM patients, respectively. T1DM patients distributed evenly through teens to 60s and T2DM showed peak distribution at 30s–40s. Importantly, approximately 60% of all T2DM patients and especially 80% of patients aged between 30 and 49 were first diagnosed with diabetes. Most of them did not take physical checkup because it was not provided due to their being relatively young or because they are unwilling to take the system even though sponsored by employers or the government. We speculated that the rise in previously undiagnosed T2DM patients in diabetic emergency is because of, in addition to general increases in diabetes, (1) low rate of physical checkup in patients in the prime of their lives, (2) easy accessibility to soft drinks in the city and (3) possibly the ketosis-prone trait in Asians. Educational campaigns or better systems for citizens might be needed.

PHE-11-3

Study on Health Management of Elders with Type 2 Diabetes Mellitus in Community

Xiaolin Wang, Xiaoqin Li and Qiang Guo
Department of Endocrinology, General Hospital of Lanzhou Petrochemical, China

PURPOSE: To explore the model of health management in elders with type 2 diabetes by making use of the theories and techniques of health management, and figure out the resolution of problems such as the lower social security conditions in community elders.

METHODS: A population-based cross-sectional survey was designed to investigate chronic diseases of 5312 community residents, more than 65 years old in Lanzhou petrochemical community, from whom 534 type 2 diabetic patients were screened out their age rang from 64 to 78 years. Demographic characteristics, self-care behavior, diabetes control, medication and diabetic knowledge was assessed. We trained the general physicians in the community who participated in the program about the theory and practice of health management. General physicians in the community did the diabetic health management under the direction of experts. The details of management consisted of health education, quantificational dietary, quantificational exercises, reasonable medicine and self-monitoring.

RESULTS: The 140 individuals who were effective to the study consisted of 56 men (40.0%) and 84 women (60%) with type 2 diabetes, who were an average age of (71.50 ± 3.10) years. After community intervention, patients were more improved with their diabetic knowledge ($P < 0.05$). The levels of fasting blood sugar and blood sugar 2 h after meals were both decreased significantly ($P < 0.05$). There was significant improvements in both mean and standardized rate of hemoglobin of glycosylation ($P < 0.05$). Blood pressure and body mass index decreased significantly after intervention ($P < 0.05$). Results of multiple regression analysis indicated that dietary control and coping style have significant effects on diabetic control ($P < 0.05$).

CONCLUSIONS: Integrated care management of community, offering individualized treatment plan had significantly effect for diabetes control of community elders with type 2 diabetes.

PHE-11-4

Services Performance of Institutions of Diabetes Health Promotion in Taiwan

Sheau-Wen Yeh¹, Chien-Yu Lin¹ and Shu-Ti Chiou^{1,2}

¹Department of Health, Bureau of Health Promotion, Taiwan; ²Institute of Public Health, National Yang-Ming University, Taipei, Taiwan

OBJECTIVE: Taiwan government designated some medical institutions (i.e., diabetes health promotion institutes) to implement a 'patient-centered team care' model, in which multi-disciplinary professionals were teamed up to provide quality care and health promotion intervention. This study aimed to present services performance of diabetes health promotion institutions (DHPI) in Taiwan.

METHODS: Since 2006, the Bureau of Health Promotion developed diabetes health promotion institutions (DHPI) certification system. Accreditation criteria include structure, education service, accountability and health promotion program, which the institutes were required to report in detail annually. Patient surveys were also conducted in 2006 ($n = 6869$) and 2011 ($n = 5599$) to evaluate and ensure the quality of diabetes.

RESULTS: During 2006–2011, the total number of DHPI increased from 136 to 174. In the meantime, improved the follow-up rate in each performance indicator: A1C < 7% (32.3–34.5%), BP < 130/80 mmHg (30.9–37.7%), LDL-C < 100 mg/dL (33.3–47.9%), four-time A1C measurement (48.7–69.5%), annual lipid profile (82.0–87.1%), urine microalbumin (43.0–72.3%), retinal examination (74.9–80.6%), foot examination (73.1–82.3%).

CONCLUSION: The DHPI policy guided health institutes to develop a variety of creative health promotion programs. The preliminary results showed that the DHPI programs took a positive effect of on lifestyle change among high risk individuals, expanded their cases coverage and improved accountability. It is a consistent and effective policy to provide a national network for diabetes management and prevention in Taiwan.

PHE-11-5

Characteristics of Diabetic Patients Living in Free Shelters

Yukihiro Sekiguchi¹, Kuniko Noda², Naoko Nakajima¹, Yuuko Shimamura¹, Tetsuo Murakami¹ and Kiyoko Takahashi¹

¹Internal Medicine, Saitama Co-operative Hospital, Japan; ²Healthcare Information Management, Saitama Co-operative Hospital, Japan

OBJECTIVES: The number of welfare recipients has been increasing in Japan, reaching 2.1 million in 2012, the highest number recorded so far. In contrast, the number of homeless is decreasing and more people are entering free shelters. We investigated the feature of diabetic patients in shelters and discuss the characteristics of their diabetes.

METHODS: Of patients diagnosed from January 2006 through November 2011, the medical records of 85 diabetic patients in shelters were investigated to obtain data on their chief complaints and HbA1c at the first hospital visit, complications, disease duration, and outcomes.

RESULTS: As the chief complaints at the first visit, there were 65 (76.5%) who presented with subjective symptoms such as thirst, visual impairment, or lower extremity numbness, with only 20 (23.5%) who were still continuing with their previous treatment. At the first visit, the mean HbA1c was 8.9% (NGSP), and retinopathy and nephropathy were observed as complications in 24 (28.2%) and 12 (14.1%) patients, respectively. In regard to the disease duration, 29 patients (34.1%) were found to be diabetic for the first time. During the observation, 26 (30.6%) visited until the end, 24 (28.2%) changed their hospitals/addresses, 25 (29.4%) discontinued their treatment, and 10 (11.8%) died.

CONCLUSION: Destitute diabetic patients often lack consciousness of the disease and visit the hospital only after exacerbation of symptoms. Therefore, they tend to be not too enthusiastic about the treatment and often discontinue the treatment. To prevent this, it is important to conduct medical examination or educational activities in home shelters.

PHE-11-6

The Combination of Share Care and Telecare Improves Glycemic Control in Remote Community Health Centers

Jhao-Kun Liou¹, Yi-Ping Chen¹, Ching-Hui Chen¹, Tzu-Fan Huang¹, Shih-Te Tu² and Ming-Chia Hsieh²

¹Health Management System Development and Telecare Center, Changhua Christian Hospital, Taiwan; ²Division of Endocrinology and Metabolism, Department of Internal Medicine, Changhua Christian Hospital, Changhua, Taiwan

OBJECTIVE: Share care has been defined as the joint participation of primary and specialty care practitioners in the planned delivery of care for patients with a chronic condition. We performed the share care and telecare program in the remote community health centers in Changhua County to evaluate the effect of combination on patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS: Participants were recruited from six community health centers and were randomized to either diabetes share care with telecare (total 54 patients), a 6 month, six-session curriculum and using glucose electronic management system, or community-based diabetes care (total 41 patients). We used multivariable analyses to estimate the association between share care with Telecare and usual care.

RESULTS: Mixed liner regression model results showed a significant reduction in HbA1C in the share care group from baseline to 6 month compare with usual care ($\Delta 0.70 \pm 1.31$ mg/dL, and $\Delta 0.07 \pm 1.02$ mg/dL, respectively, P -value < 0.05). Diabetes care self-management blood glucose (SMBG) sequence was improvement at 6 months in the share care group compared with usual care group ($\Delta -4.11 \pm 2.54$ times/week, and $\Delta -0.59 \pm 1.96$ times/week, respectively, P -value < 0.001). Although share care was associated with improvement metabolic control, we observed no additional metabolic benefit.

CONCLUSIONS: Share care with Telecare was associated with improved self-management and performance in electronic management system use augmented the impact of share care on glycemic control outcomes but not on metabolic outcomes. Optimal identification of the best share care with telecare model of evidence to diabetes care will require longer follow-up or new care delivery models.

LB-01

Effect of Early and Long-Term Metformin Administration on Metabolic Profile of High-Fat Diet, Streptozotocin-Treated Diabetic Rats

Shuguang Pang¹, Congcong Wang¹, Xianping Huang¹, Xiaoli Ma², Yongmei Sun¹, Yong Lu¹, Dongjie Xiao², Lulu Wang¹, Youmei Li¹ and Mei Li¹

¹Endocrinology Department, Jinan Central Hospital Affiliated to Shandong University, China; ²Central Laboratory, Jinan Central Hospital Affiliated to Shandong University, China

OBJECTIVE: To develop a type 2 diabetic rat model and study the different influences of early and late metformin administration on metabolic parameters, especially serum bile acids.

METHODS: One hundred Wistar male rats were randomly assigned to either standard diet (SD, $n = 20$) or high fat diet (HFD, $n = 80$) for 6 weeks. Twenty rats in HFD group were randomly selected to have metformin therapy till the end as early intervention group (EI group). Oral Glucose Tolerance Tests were administrated at the end of 6 weeks. The successfully HFD-induced insulin resistance rats were given a single intraperitoneal injection of STZ at 35 mg/kg body weight in 0.1 mol/L citrate buffered saline. Three days after the injection of STZ, rats that exhibited fasting glucose levels >200 mg/dL were considered diabetic. Then 20 diabetic rats were randomly assigned to metformin gavage for 4 weeks till the end as late intervention group (LI group).

RESULTS: Metabolic disorders were improved by early and late metformin administration to a different extent. Noticeably, the effects of early and late metformin administration as well as the duration of metformin administration on serum bile acid concentrations were different.

CONCLUSION: Our study indicated that a combination of HFD and a single low-dose STZ injection proved to be a better way for developing a rat model of type 2 diabetes. Early and late metformin administration resulted in different changes of metabolic profile, especially serum bile acid. Metformin might improve the glucose and lipid metabolism by pathways related with bile acids.

LB-02

Clinical Value of Lipoprotein (a) on the Early Diagnosis of Diabetic Nephropathy

Shuguang Pang, Youmei Li and Mei Li

Jinan Central Hospital Affiliated to Shandong University, China

OBJECTIVE: To explore the correlation between serum Lipoprotein (a) and each factor, and its clinical value on the early diagnosis of type 2 diabetic nephropathy (T2DN).

METHODS: There were total 149 cases in this study, divided into three groups A (36 patients only with T2DM) and B (83 patients with diabetic nephropathy), and 30 normal controls (NC). The Levels of LP(a), triglyceride (TG), total cholesterol (TCH), high density lipoprotein cholesterol (HDL), low density lipoprotein (LDL) were measured respectively in each group. Receiver operating characteristic curve (ROC curve) analysis was used to determine the optimal cutoff identifying patients in group B.

RESULTS: The Levels of LP(a) increased obviously in groups A and group B, ($P < 0.01$). LP(a) was closely related to urinary albumin (UMA) γ -glutamyltransferase (GGT). The area under the ROC curve of LP(a) was 0.818, and the optimal value of cutoff point was 200 mg/L, its sensitivity and specificity was 77.4% and 76.8%.

CONCLUSIONS: LP(a) could be an independent risk factor for diabetic nephropathy, it may become a marker to predict and diagnosis of T2DN early.

KEYWORDS: lipoprotein (a), diabetic nephropathy, type 2 diabetes mellitus.

LB-03

Prospective Study of Risk Factors for Development of Type 2 Diabetes in Adult: 10 Year Follow-Up of Population Study in Keelung

Li-Sheng Chen¹, Bih-Tsuen Hsu², Ming-Fang Yen¹, Yueh-Hsia Chiu³, Ching-Yuan Fann⁴, Ting-Ting Wang¹ and Hsiu-Hsi Chen⁵

¹School of Oral Hygiene, College of Oral Medicine, Taipei Medical University, Taiwan;

²Health Bureau of Keelung City, Taiwan; ³Department and Graduate Institute of Health Care Management, Chang Gung University, Taiwan; ⁴Department of Nutrition and Health Sciences, Kainan University, Taiwan; ⁵Graduate Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taiwan

OBJECTIVE: Very few studies revealed the risk factors for development of type 2 diabetes based on long-term observation. This study aims to assess the risk factors for the development of type 2 diabetes based on the Taiwanese screening cohort with longitudinal follow up.

METHODS: An longitudinal and perspective cohort follow-up design was conducted in this study. After excluding the prevalent cases ($N = 9288$) at first screen, we enrolled a total of 98,213 participants with type 2 diabetes free to collect the baseline characteristics including age, gender, body mass index, education level, life styles, and hepatitis virus carriers followed with periodical repeated screens to ascertain type 2 diabetes. Poisson regression model was applied to assess the risk of type 2 diabetes development.

RESULTS: The total of 3867 newly cases and 1.08% of annual standardized incidence for type 2 diabetes were found during the 10 year follow-up. Factors affecting the incidence of type 2 diabetes include age (aRR = 1.035, 95% CI: 1.032–1.038), BMI (aRR = 1.57, 95% CI: 1.45–1.71), hypertension (aRR = 1.46, 95% CI: 1.36–1.57), smoking (aRR = 1.16, 95% CI: 1.06–1.28), betel quid chewing (aRR = 1.31, 95% CI: 1.07–1.60), central obesity (1.75, 95% CI: 1.61–1.91), cholesterol (aRR = 1.28, 95% CI: 1.11–1.48), triglyceride (aRR = 1.80, 95% CI: 1.67–1.93), and anti HCV (aRR = 1.27, 95% CI: 1.08–1.49) in the multivariable Poisson regression model.

CONCLUSIONS: The risk factors for type 2 diabetes development were revealed in this study. The result was very useful to apply the life-style modification based on the light of risk factors from our findings to reduce the incidence of type 2 diabetes in terms of population-based type 2 diabetes preventive approaches.

LB-04

The Effect of Life Style Modification in Subjects with Metabolic Syndrome in Outpatient Department of Regional Hospital

Hsiao Lien Chen¹, Wai-Kin Chan², Pei-Chen Hsu³, Yi-Jen Wu³, Huan-Wen Chen¹, Pai-Lien Chen⁴ and Dia-Sue Wu³

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Lotung Poh-Ai Hospital, Taiwan; ²Department of Internal Medicine, Chang Gung Medical Hospital, Linkou, Taiwan; ³Department of Dietitian, Lotung Poh-Ai Hospital, Taiwan; ⁴Division of Endocrinology and Metabolism, Department of Internal Medicine, Lotung Saint Mary's Hospital, Taiwan

OBJECTIVE: Metabolic syndrome is a group of risk factors that raises risk for heart disease and other health problems, such as diabetes and stroke. This

study aimed to investigate the effects of lifestyle modification on weight, waist circumference, blood sugar and lipid profile in subjects with metabolic syndrome.

METHODS: During 12 weeks period of lifestyle modification, we provided individual or group sessions designed to modify eating and activity habits. We measured height, body weight, BMI, and waist circumference, blood sugar and lipid profile at baseline and 12-week after intervention period.

RESULTS: One eighty six participants (29.8% male, and 70% female) were completed intervention period. In an intention-to-treat analysis from pre to post tests, there were significant reductions in average body weight 0.63 kg ($P = 0.004$), BMI 0.23 kg/m² ($P = 0.004$), waist circumference 0.79 cm ($P = 0.013$) and fasting blood glucose 3.7 mg/dL ($P = 0.027$) in male group. In female group, significant reductions in average body weight 0.23 kg ($P = 0.025$), BMI 0.1 kg/m² ($P = 0.025$), total cholesterol 24.41 mg/dL ($P = 0.002$), TG 23.07 mg/dL ($P = 0.040$) at 12-week compared to baseline. But, there were no significant differences in triglyceride and HDL in male group and waist circumference, fasting blood glucose and HDL in female group.

CONCLUSION: Results showed that life style modification can improve metabolic syndrome and prevention of metabolic-related chronic diseases. Long-term effects of the life style modification remain to be investigated.

LB-05

Quality of Life in Children with Type 1 Diabetes and Their Family and Relationship to Some Psychosocial Factors

Adel Eladl¹ and Hoda Atwa²

¹Especial Education, Arabian Gulf University, Bahrain; ²Pediatrics Department, Faculty of Medicine, Suez Canal University, Egypt

BACKGROUND: Treatment of type 1 diabetes often disrupts a child's usual activities, requires disease focused behaviors from child and family.

AIM: To assess quality of life in children with T1D and their family.

SUBJECTS AND METHODS: Eighty children with type 1 diabetes and their family were included. Quality of life was assessed by PedsQL. Diabetes care profile an instrument that assesses psychosocial factors related to diabetes was used.

RESULTS: The child with T1D perception of QOL was higher than parent perception. The mean total score of PedsQL was (69.5 $\pm$ 10.3 and 67.2 $\pm$ 8.6) respectively. The child with T1D QOL was lower than their sibling (69.5 $\pm$ 10.3 and 73 $\pm$ 2.5). Parent QOL was lowest among family (66.5 $\pm$ 3.7). Good metabolic control was associated with better QOL. Diabetic children with high QOL had higher mother education, better diet adherence, understanding management practice and lower self monitoring of blood glucose barriers. Higher mother education and lower hypoglycemic or DKA attacks were good predictor of high QOL in Sibling of diabetic children.

CONCLUSION: Diabetes disrupts QOL of children with T1D and their family.

LB-06

The Effectiveness of Diabetes Management Software for Glycemic Control in Diabetic Patients

Yu Ju Chen

Department of Nursing, Chung Shan Medical University Hospital, Taiwan

PURPOSE: This study aimed to investigate the effectiveness of using DM management software on glycemic control and to evaluate whether patients' willingness to perform self-monitoring of blood glucose could be promoted.

METHODS: We collected a total of 30 diabetic patients who undertook diabetes management software to manage blood sugar levels and accompanying health education. Patients were continuously followed up for 3 months. Along with a questionnaire survey, the measurements of fasting blood glucose and glycosylated hemoglobin were recorded before and after the study. The blood glucose curves were printed by specialists' assistance followed by the accompanying health education provided by nursing practitioners before visiting the doctors for the subsequent discussion of further treatment guidelines.

RESULTS: The levels of fasting blood glucose were reduced from 187 to 142 mg/dL and glycated hemoglobin was decreased from 8.8% to 7.5% for diabetic patients, showing statistically significant differences for both measurements.

CONCLUSION: The willingness of diabetic patients undertook self-monitoring of blood glucose was increased by using the management software and accompanying health education, which consequently improved the control of blood glucose for diabetic patients.

LB-07

Effectiveness of Oral Hygiene Instruction (OHI) in Improving Periodontal Disease Among Subjects with Diabetes Mellitus (DM): A Randomized Controlled Trial

Hongmin Lai^{1,2}, Ming-Te Lo³, Amy Ming-Fang Yen⁴, Li-Sheng Chen⁴, Jean Ching-Yuan Fann⁵, Sherry Yueh-Hsia Chiu⁶ and Hsiu-Hsi Chen³
¹Elite Dental Clinic, Taipei, Taiwan; ²Taipei Medical University, Taipei, Taiwan; ³Graduate Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan; ⁴School of Oral Hygiene, College of Oral Medicine, Taipei Medical University, Taipei, Taiwan; ⁵Department of Health Industry Management, School of Healthcare Management, Kainan University, Taiwan; ⁶Department of Health Care Management, College of Management, Chang Gung University, TaoYuan, Taiwan

BACKGROUND: It is not clear about the additional benefit of applying oral hygiene instruction (OHI) in patients with PD, particularly for impaired fasting glucose (IFG) or diabetes mellitus (DM).

AIM: A randomized controlled trial was conducted to assess the efficacy of OHI in treating PD in subjects with hyperglycemia.

METHOD: Aged 35–54 years with IFG or DM history from the participants enrolled in the Keelung Community-based Integrated Screening (KCIS) program between 2006 and 2007. A total 138 subjects with baseline CPI ≥ 2 were randomly assigned to two arms, study group with core treatment together with OHI and the control group with core treatment only. OHI consist of the illustration of dental plaque, Bass tooth brushing method, and the procedure of dental floss. The primary outcomes consist of Community Periodontal Index (CPI) and Bleeding on Probing (BOP). After intervention, each participant was followed at 1 and 3 months to keep record of CPI and BOP. Wilcoxon rank sum test and multiple linear mixed model were applied to assess the difference of CPI and BOP between two groups.

RESULTS: There were lacking of statistically significant difference in CPI or BOP at both 1- and 3-month follow-up. The study group yielded lower CPI than the control group, but the difference of CPI was not statistically significant (difference = -0.04881, *P*-value = 0.6869) at 1-month follow-up. Nor was that of BOP (difference = -0.2075, *P*-value = 0.1917) with respect to CPI or BOP.

CONCLUSION: The OHI is not effective in ameliorating PD while it was combined with dental scaling and root planing.

LB-08

Associations of Insulin Injection Devices and Techniques with Lipohypertrophy in Diabetic Patients

Yu Ju Chen

Department of Nursing, Chung Shan Medical University Hospital, Taiwan

PURPOSE: This study aimed to investigate the incidence of lipohypertrophy among insulin users of pens and syringes, and to analyze the associations with injection technique used.

METHODS: Participants were divided into two groups according to their uses of prefilled pens or syringes. Survey was conducted using the three parts of scoping checklist developed by the Taiwanese Association of Diabetes Educators, with additional details concerning injection technique used. Surveys and biochemical measurements were performed during January 01, 2011, and November 30, 2011.

RESULTS: A total of 82 diabetic patients were enrolled. The users of pen device and syringe accounted for 70.7% and 29.3%. Subcutaneous lipohypertrophy was presented in 20 patients (24.4%). Abdomen was the most common area chosen for injections (89.0%), followed by thigh (52.4%), arm (0.5%) and hip area (18.3%). Although the incidence of lipohypertrophy was slightly higher in pen users vs syringe users (25.9% vs 20.8%), the difference did not reach significance. A significantly higher risk of subcutaneous lipohypertrophy was associated with incorrect injection technique in the abdomen.

CONCLUSIONS: Incorrect insulin technique was significantly associated with higher risk of developing lipohypertrophy. Health providers have a vital role in educating people with diabetes about injection techniques to achieving

optimal glycemic control. Insulin injection technique is important and should be inspected regularly with patients through motivational interviewing.

LB-09

Epidemiology of Type 2 Diabetes with a Community-Based Longitudinal Cohort

Ching-Yuan Fann¹, Jean Ching-Yuan Fann², Bih-Tsuen Hsu³, Hsiu-Hsi Chen⁴, Amy Ming-Fang Yen⁵, Sherry Yueh-Hsia Chiu⁶ and Sam Li-Sheng Chen⁵
¹Health Industry Management, Kainan University School of Healthcare Management, Taiwan; ²Department of Health Industry Management, School of Healthcare Management, Kainan University, Taiwan; ³Keelung City Public Health Bureau, Taiwan; ⁴Graduate Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taiwan; ⁵School of Oral Hygiene, College of Oral Medicine, Taipei Medical University, Taiwan; ⁶Department and Graduate Institute of Health Care Management, Chang Gung University, Taiwan

BACKGROUND: Epidemiological findings about type 2 diabetes have been documented largely. However, there are still lacking evidence from long-term longitudinal and community-based study. The epidemiology profile for impaired glucose tolerance (IGT) is relatively rare, although it's crucial for early prevention of diabetes and also for modeling the natural history of diabetes.

AIM: The aim of this study was to investigate the prevalence and incidence of IGT and type 2 diabetes based on Keelung Community-based Integrated Screening (KCIS).

METHODS: A total of 107,501 subjects attended KCIS program between 2000 and 2009. Among them, 52% had been undertaken repeated screening. Subjects with fasting glucose higher than 126 mg/dL were identified as cases of type 2 diabetes. Those with fasting glucose 110–125 mg/dL before 2005 and 100–125 mg/dL after 2006 were referred for oral glucose tolerance test (OGTT) to identify cases of IGT or type 2 diabetes.

RESULTS: The age-standardized prevalence of type 2 diabetes and IGT were 6.95% (male 7.7%; female 6.53%) and 0.51% (male 0.51%; female 0.40%), respectively. The age-standardized incidence of type 2 diabetes was 1.087% (male 1.295%; female 0.983%). The transition rate was 0.83% from normal to IGT, 1.33% from normal to type 2 diabetes, 17.46% from IGT to type 2 diabetes, but as high as up to 35% for regression from IGT to normal.

CONCLUSION: Investigating the epidemiological profile for incidence and prevalence of IGT and type 2 diabetes with longitudinal and community-based cohort is valuable for public health decision-making and the modeling for natural history of diabetes.

LB-10

Natural History of Pre-Diabetes and Diabetes: A Community-Based Cohort Study

Ming-Fang Yen¹, Bi-Tsuen Hsu², Hsiu-Hsi Chen³, Sam Li-Sheng Chen¹, Sherry Yueh-Hsia Chiu⁴ and Ching-Yuan Fann⁵

¹School of Oral Hygiene, College of Oral Medicine, Taipei Medical University, Taiwan; ²Keelung City Public Health Bureau, Keelung, Taiwan; ³Graduate Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan; ⁴Department and Graduate Institute of Health Care Management, Chang Gung University, Tao-Yuan, Taiwan; ⁵Department of Nutrition and Health Sciences, Kainan University, Tao-Yuan, Taiwan

OBJECTIVE: To quantify the natural history of pre-diabetes and diabetes (DM) using a community-based cohort.

MATERIALS: A total of 107,501 subjects attending Keelung Community-based Integrated screening program between 1999 and 2009 were enrolled. Fasting glucose was tested in each screening activity. Those with fasting glucose of 100–125 mg/dL were referred to uptake oral glucose tolerance test. We used continuous-time Markov model to quantify the disease natural history for pre-diabetes and diabetes.

RESULTS: The estimated annual incidence rate of impaired fasting glucose (IFG) increased from 2.5% for male aged 30–39 years to 9.5% for those aged 70 years or older. The corresponding figures for female were lower, from 1.6% for young to 8.8% for elderly. Impaired glucose tolerance (IGT) had roughly 1.6-fold (95% CI: 1.3–2.0) risk of transferring to DM for both gender. Around 8.6% and 14.4% patients with IFG progressed to DM for non-IGT and IGT cases respectively in male, and 7.9% and 13.0% respectively for female. Around half of IFG subjects would regress to normal per year. For subjects negative for IFG, the incidence rate of type 2 diabetes was 0.1–3.0% from young to old men, and 0.1–2.4% from young to old women.

CONCLUSION: The natural history of pre-diabetes and diabetes was elucidated using a community-based cohort. The results indicated male had higher incidence rate of IFG and of type 2 diabetes, and faster progression rate from IFG to type 2 diabetes than female. Regardless of gender, the regression rate from IFG was around half.

LB-11

The Different Effect Between Simvastatin Intervention and Treatment on Fasting Plasma Glucose in Streptozotocin Induced Diabetic Rats

Shuguang Pang¹, Lulu Wang², Guanglan Duan¹, Xianping Huang¹, Yong Lu¹, Qiang Jiang¹ and Su Hu¹

¹Endocrinology Department, Jinan Central Hospital Affiliated to Shandong University, China; ²Endocrinology Department, Shandong University School of Medicine, Jinan Central Hospital Affiliated to Shandong University, China

Statins have been proven beneficial in reducing the risk of cardiovascular events in numerous patients, providing an apparently low risk approach to improve cardiovascular health. Recent studies have shown that statin may exert pleiotropic effects on glucose metabolism in animal models and humans. Most studies investigated the effect of treatment with simvastatin on glucose homeostasis in diabetes patients. However, there are few reports about the difference between intervention and treatment with simvastatin on glucose metabolism, especially on the fasting plasma glucose. The target of the present study is to investigate the difference between intervention and treatment with simvastatin on FPG in STZ-induced diabetic rats. Our findings show that the simvastatin intervention rats were more easily induced to be diabetic rats and had a higher FPG compared with simvastatin treatment group. The results

indicate that simvastatin intervention rats have an adverse effect on glucose homeostasis, especially on FPG.

LB-12

Carpenter-Coustan Criteria Compared with the National Diabetes Data Group Thresholds for Gestational Diabetes Mellitus in Taiwanese Women

Mei-Chun Lu and Panchalli Wang

Department of Obstetrics and Gynecology, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Taiwan

To compare pregnancy outcomes in women with gestational diabetes mellitus (GDM) diagnosed by the National Diabetes Data Group (NDDG) thresholds with women meeting the Carpenter-Coustan (C&C) thresholds but not the NDDG criteria. This is a 6-year retrospective cohort study of women screened for GDM at one teaching hospital in Taiwan. All women followed the 1-h 50-g glucose challenge test (GCT) and 3-h oral glucose tolerance test. Pregnancy outcomes were examined using multivariable logistic regression analyses. Of the 10,109 singleton pregnancies, 7986 (79.0%), 1506 (14.9%), 212 (2.1%), 405 (4.0%) were classified into four groups: 50-g GCT negative, 50-g GCT positive and NDDG and C&C negative, GDM by C&C not NDDG, GDM by NDDG, respectively. Compared with women with 50-g GCT negative, women with GDM by C&C but not NDDG criteria had higher odds of preterm labor (aOR 1.61, 95% CI 1.03–2.52) and macrosomia (aOR 2.98, 95% CI 1.18–7.55). In Taiwanese women, we suggested using the C&C diagnostic thresholds for GDM to reduce the adverse outcomes.

Table Adjusted odds ratios for outcomes between 50-g GCT negative, 50-g GCT positive and NDDG and C&C negative, GDM by C&C not NDDG and GDM by NDDG group

	Number	50-g GCT negative	50-g GCT positive and NDDG and C&C negative	GDM by C&C not NDDG	GDM by NDDG
Caesarean section	3253	1	1.02 (0.90–1.15)	1.13 (0.85–1.51)	1.15 (0.93–1.42)
Prolong labor	1547	1	1.04 (0.89–1.21)	0.68 (0.44–1.06)	0.76 (0.56–1.04)
Shoulder dystocia	62	1	0.59 (0.23–1.48)	1.87 (0.45–7.81)	1.49 (0.45–4.95)
Preterm labor (week < 37)	725	1	1.07 (0.87–1.33)	1.61 (1.03–2.52)	2.22 (1.65–2.99)
3rd/4th-degree perineal laceration	369	1	0.99 (0.73–1.33)	1.00 (0.46–2.17)	0.91 (0.50–1.65)
Postpartum hemorrhage	91	1	1.15 (0.65–2.03)	2.17 (0.78–6.06)	0.81 (0.25–2.66)
PIH or preeclampsia	323	1	1.47 (1.10–1.96)	1.63 (0.87–3.05)	2.14 (1.40–3.27)
Macrosomia (>4000 g)	106	1	1.82 (1.11–2.97)	2.98 (1.18–7.55)	3.85 (2.03–7.28)
Neonatal death or NICU	695	1	0.96 (0.77–1.21)	1.39 (0.86–2.26)	2.33 (1.72–3.15)

GCT, glucose challenge test; NDDG, the National Diabetes Data Group criteria; C&C, the Carpenter-Coustan criteria; PIH, pregnancy-induced hypertension; NICU, neonatal intensive care unit; OR, odds ratio; CI, confidence interval.

Data are presented as adjusted OR (95% CI).

Adjusted OR is the OR adjusted for group differences in parity, maternal age, BMI at delivery, year of delivery.

LB-13

Influencing Factors of CNS and CNSS on the Establishment of a Nursing Care Outpatient Department

Mariko Shiramizu¹, Yuki Mase¹, Ryoko Okui¹, Tomoko Sugimoto², Yuriko Kanematsu³, Kyoko Yanai⁴ and Akiko Yoneda⁵

¹School of Nursing, Faculty of Health and Social Services, Kanagawa University of Human Services, Japan; ²School of Nursing, Faculty of Health Science, Chiba Prefectural University of Health Science, Japan; ³Former Faculty of Nursing, Iwate Prefectural University, Japan; ⁴City Kawasaki Ida Hospital, Japan; ⁵Hiratsuka Kyosai Hospital, Japan

OBJECTIVE: The present study aimed to clarify the actual situations and factors related to the establishment of nursing care outpatient departments for diabetes patients.

METHODS: The subject institutions for the survey were medical institutions where the nurses in diabetes nursing certified by Japanese Nursing Association and the certified nurse specialists in chronic care nursing specialized in diabetes nursing are working. The method of survey was done by an unscripted, self-registered questionnaire to be sent by mail. We employed SPSS 15.0 for windows, and performed chi-squared-test and logistic regression analysis.

RESULTS: We obtained the responses from 92 nurses (52.6%). The number of CNs was 84 (91.3%). The number of the institution having a nursing outpatient department was 54 (58.7%), and the ratio of the institutions having the facility for CNs was 59.5%, and that for CNSs was 50.0%. In comparison of Group of Institutions having a nursing outpatient department with Group of not having such a department, the reply of putting in practice "a patient-participating program" and "a post-program follow-up by nurses" were significantly high in number ($\chi^2 = 9.01$, $P = 0.004$), ($\chi^2 = 5.203$, $P = 0.032$). As a result of the logistic regression analysis, the two variables of "We have a diabetes-specialized outpatient department by physicians" and "We have a patient-participating program" showed a significant relation.

CONCLUSION: For promoting the establishment of a nursing outpatient department, it is necessary to improve the diabetes-specialized outpatient service system and to make the educational program more active and continual.

LB-14

Effectiveness of Periodontal Non-Surgical Treatment for Hyperglycemia/Type 2 Diabetes: A Randomized Controlled Trial Among Middle Aged 35–54 Based on Keelung Community-Based Integrated Screening

Sherry Yueh-Hsia Chiu¹, Hongmin Lai², Ming-Te Lo³, Huei-Shian Tsau³, Amy Ming-Fang Yen⁴, Li-Sheng Chen⁴, Jean Ching-Yuan Fann⁵ and Hsiu-Hsi Chen³

¹Department of Health Care Management, College of Management, Chang Gung University, Taiwan; ²Elite Dental Clinic, Taipei, Taiwan & Taipei Medical University, Taipei, Taiwan; ³Graduate Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan; ⁴School of Oral Hygiene, College of Oral Medicine, Taipei Medical University, Taipei, Taiwan; ⁵Department of Health Industry Management, School of Healthcare Management, Kainan University, Taoyuan, Taiwan

BACKGROUND: The association between diabetes and periodontal disease has also been proved. While dental scaling and root planing is effective in treating early periodontal disease (PD), little is known about the intervention effect for periodontal disease prevention using non-surgical treatment among

pre-diabetes/diabetes, especially for middle aged 35–54. **AIMS:** The aim of this study is to evaluate the effectiveness of periodontal non-surgical treatment on hyperglycemia/DM using randomized controlled trial (RCT) with 2-month follow-up based on the Keelung Community-based Integrated Screening (KCIS) program.

STUDY DESIGN: Those aged 35–54 with hyperglycemia/diabetes were invited to participate the RCT for dental non-surgical effect addition to oral hygiene education. The non-surgical intervention was carried out for the severest sextant. Pre-test of knowledge and initial periodontal status were examined first for both groups. Periodontal non-surgical intervention was implemented following oral hygiene education in intervention group. The main outcome was measured by periodontal community periodontal index (CPI). The linear mixed model was applied to assess the difference of CPI between the study and control groups

RESULTS: Among participants 404 randomly allocating into two groups, 312 subjects completed this trial. The result showed the significant improvement of knowledge of oral hygiene in post-test compared with pre-test in both groups. Taking the pre-treatment CPI into account, the non-surgical intervention significantly reduced the CPI in treated sextant after 2 months follow-up (coefficient = -0.8273). The striking reduction of CPI was revealed in hyperglycemia compared with diabetes (coefficient = -0.8597, -0.7968).

CONCLUSION: The periodontal non-surgical intervention could significantly improve the periodontal status for aged 35–54 with hyperglycemia/DM subjects.

LB-15

Seasonal Variation in Glycosylated Hemoglobin in Mainland China

Shuguang Pang¹, Mei Li¹, Guanglan Duan², Zhiping Qu², Yong Lu¹, Qiang Jiang¹, Su Hu¹, Jingjing Ma¹, Youmei Li¹, Lulu Wang¹ and Congcong Wang¹

¹Endocrinology Department, Jinan Central Hospital Affiliated to Shandong University, China; ²Jinan Central Hospital Affiliated to Shandong University, China

OBJECTIVE: We examined whether glycosylated hemoglobin of Chinese showed seasonal variation.

METHODS: A total of 11,799 HbA1c measurements, as well as sex and age were extracted from Hospital Information System (HIS) in Jinan Central Hospital from 2008 to 2011. The mean HbA1c by month and by the sex and age was calculated for a maximum of four years for HbA1c data.

RESULTS: The seasonal variation of HbA1c is significant, higher in winter (December, January and February), lower in summer (June, July and August) ($P < 0.01$). No significant sex difference existed for HbA1c, except for the group over 60 years of age, in which men had lower levels than women ($P < 0.01$). In both sexes, HbA1c was significantly lower in the elderly than in the youth and the middle age ($P < 0.05$). There was no significant difference between the youth and the middle age ($P > 0.05$). Multiple linear regression analysis showed that season, age and gender had negative correlation with HbA1c (standardized regression coefficients = -0.050, -0.06, -0.040 respectively; $P < 0.01$).

CONCLUSIONS: There was significant seasonal variation in HbA1c, higher in the cooler season, lower in the warmer season. Physiological and metabolic factors related to temperature may be the main cause of seasonal variation in HbA1c levels. Age, season and gender appeared as risk factors influencing HbA1c independently.