JOURNAL OF ATHEROSCLEROSIS AND THROMBOSIS

Official Journal of the Japan Atherosclerosis Society and
The Asian-Pacific Society of Atherosclerosis and Vascular Diseases

Abstracts of the

9th Congress of the Asian-Pacific Society of Atherosclerosis and Vascular Diseases
and
16th Diabetes and Cardio Vascular Risk Factors – East Meets West Symposium

25-28 September 2014

Hong Kong Convention and Exhibition Centre

Contents

Oral Presentation (Clinical)

Ab11	The Prevalence of Coronary Artery Disease Risk Factors among A Sample of Human Immunodeficiency Virus-Infected Patients on Antiretroviral Therapy in India: Relationship with Clinical and Demographic Factors Pradnya Kulkarni, et al. (Hong Kong)	S1
Ab22	Association of The Neutrophil? – Lymphocyte Ratio (Nlr) with Outcomes in Patients Admitted for An Acute Coronary Syndrome Jaime Aherrera, et al. (Philippines)	S1
Ab24	Fasting Triglyceride is a Risk Factor for Cardiovascular Event in T-SPARCLE Registry in Taiwan Chun-Yen Chen, et al. (Taiwan)	S2
Ab27	Cost-Effectiveness Analysis of Pharmacogenetic-Guided Warfarin Dosing in Thailand Surasak Saokaew, et al. (Thailand)	S2
Ab28	Effect of Folic Acid Supplementation on HDL-Cholesterol and Other Lipid Profile: A Systematic Review and Meta-Analysis Surasak Saokaew, et al. (Thailand)	S3
Ab30	Postchallenge Hyperglycemia Potentiated the Lipoprotein Subclass Particles on The Risk of Arterial Stiffness in Healthy Adults Cheng Ding, et al. (China)	S3
Ab53	Long Sleep Duration is Associated with Resistance Resistance Independently of Obesity in Korean Non-Diabetic Adults Ki Dong Ko, et al. (South Korea)	S4
Ab61	The Role of C-Reactive Protein in Cardiovascular Diseases -- Lessons from The Experiments of Nature Yi Wu, et al. (China)	S4
Ab84	Young Chinese Adults' Attitudes towards Adopting A Mediterranean-Style Dietary Plan to Reduce Cardiovascular Disease Zann Ng, et al. (Singapore)	S5
Ab90	Mitochondrial Mutations and Atherosclerosis Igor Sobenin (Russian Federation)	S5
Ab98	Factors Associated with Health-Promoting Behavior of People with or at High Risk of Metabolic Syndrome: Based on The Health Belief Model Sally Wai-Sze Lo, et al. (Hong Kong)	S6
Ab100	Telmisartan Significantly Affected The Pharmacokinetics of Rosuvastatin in Healthy Subjects and in Patients with Hyperlipidaemia, in Vitro and in Vivo Experiments Teresa Hu, et al. (Hong Kong)	S6

Ab105	Predictors of The Extent of Carotid Atherosclerosis in Patients Treated with Radiotherapy for Nasopharyngeal Carcinoma Chuang Yuan, et al. (Hong Kong)	S7
Ab107	The Double-Blind Durable Effect of PCSK9 Antibody Compared with Placebo Study (DESCARTES): A 52 Week Phase 3 Double-Blind, Randomized, Placebo-Controlled Trial of Evolocumab (AMG 145) in Hyperlipidemic Patients Rani Somaratne, et al. (United States)	S7
Ab113	What are the Influencing Factors of Healthy Lifestyle Behaviors? A Qualitative Study in Adults with Metabolic Syndrome Qun Wang, et al. (Hong Kong)	S8
Ab115	Effects of Long-term, Monthly Administration of the Pcsk9 Inhibitor Evolocumab (Amg 145) in Patients with Dysglycemia or Metabolic Syndrome Rani Somaratne, et al. (United States)	S8
Ab118	The Effect of Bisoprolol on Central and Brachial Pressure in Chinese Hypertensive Patients Tanya T.W. Chu, et al. (Hong Kong)	S9
Ab120	Bisoprolol in Essential Hypertension: Effects on 24 Hour Ambulatory Blood Pressure and Metabolic Profile in Chinese Patients Tanya T.W. Chu, et al. (Hong Kong)	S9
Ab142	Bone and Mineral Metabolism and Incident Diabetes Mellitus: a Prospective Study Ching-lung Cheung, et al. (Hong Kong)	S10
Ab148	People with Peripheral Arterial Disease and Diabetes are Associated with Clinically Significant Weakness Ching-lung Cheung (Hong Kong)	S10

Poster Presentation (Clinical)

Ab07	Sesame Oil Exhibits Synergistic Effect With Anti-Diabetic Medication and Affects Glucose and Lipid Metabolism in Type 2 Diabetes Patients Devarajan Sankar (Japan)	S11
Ab19	The Utility of Fasting Capillary Blood Glucose in The Detection of Type 2 Diabetes Mellitus Among Patients at The Charity Out-Patient Section, Department of Internal Medicine at Chinese General Hospital And Medical Center Kristine Anne Melendres (Philippines)	S11
Ab23	A Comparison of 12 Lead Electrocardiogram and 2d-Echocardiography Derived Ejection Fraction among Patients with Depressed Ejection Fraction Jaime Aherrera, et al. (Philippines)	S12
Ab25	Quality of Life in Parents of Children with Type 1 Diabetes Receiving Insulin Treatment Anita Li, et al. (Hong Kong)	S12

Ab36	Association of Apolipoprotein E Gene Polymorphism with Cardiovascular Diseases in Patients on Long-Term Hemodialysis Hanaa Lahrach, et al. (Morocco)	S13
Ab46	Association of ECG Abnormalities with Metabolic Syndrome and Socio-Demographic Factors in The Philippine LIFECARE Cohort Alric Mondragon, et al. (Philippines)	S13
Ab49	Takayasu Arteritis in A Pregnant Patient Masquerading as Severe Pre-Eclampsia: a Case Report Antonio Jr Faltado, et al. (Philippines)	S14
Ab52	Apolipoprotein E Polymorphism and Risk of Coronary Artery Disease: A Moroccan Case-Control Study Hanaa Lahrach, et al. (Morocco)	S14
Ab54	Plasma Proprotein Convertase Subtilisin/Kexin Type 9 is Associated with Apolipoprotein B-48 Catabolism in Obese Subjects Dick C Chan, et al. (Australia)	S15
Ab70	Critical Limb Ischemia in The Setting of Polycythemia Vera in A Sixty-Three Year Old Male Edgar Wilson Timbol, et al. (Philippines)	S15
Ab71	Acquired Arteriovenous Fistula of The Right Common Iliac Artery and Left Common Iliac Vein and Bilateral Lower Extremity Deep Venous Thrombosis in A Woman Presenting as High Output Heart Failure Edgar Wilson Timbol, et al. (Philippines)	S16
Ab75	“When Stemi Is Not Stemi” HIV Myocarditis Mimicking St-Elevation Myocardial Infarction on Electrocardiogram: A Case Report Jaime Alfonso Aherrera, et al. (Philippines)	S16
Ab80	Clinical Characteristics of Large-Artery Atherosclerotic Stroke according to Age Seo Hyun Kim, et al. (South Korea)	S17
Ab81	Early Gene-Diet Interaction between Glucokinase Regulatory Protein (GCKR) Polymorphism, Vegetable and Fish Intakes in Modulating Triglyceride Levels in Healthy Adolescents. Claudia H.T. Tam, et al. (Hong Kong)	S17
Ab82	The Pre-Post Comparison of Patient Outcomes of A Structured Education Programme on Insulin Initiation among Patients with Type 2 Diabetes Attending General Out-Patient Clinics of New Territories East Cluster: Baseline Findings Wai Hing Caroline Chiu, et al. (China)	S18

Ab86	Pharmacokinetics of Fixed-Dose Combinations (FDC) of Enteric-Coated (EC) Acetylsalicylic Acid (ASA) and Enteric-Coated Pantoprazole (PP) Versus Concurrent Administration Of Individual Products: Two Comparative Bioavailability Studies (Fed And Fasted Conditions) - Randomized, Open-Label, Single-Dose, Three-Period, Three-Treatment, Six-Sequence, Crossover In Healthy Subjects Peng Kai Ong, et al. (Singapore)	S18
Ab94	“Double Trouble” Wolff Parkinson White Syndrome and Mitral Stenosis Presenting as a Stroke in the Young Jaime Alfonso Aherrera, et al. (Philippines)	S19
Ab101	Intake of Green Tea Extract Reduced Systemic Exposure to Rosuvastatin in Healthy Chinese Male Volunteers Teresa Hu, et al. (Hong Kong)	S19
Ab102	Effect of Green Tea Extract and Soy Isoflavones on The Pharmacokinetics of Simvastatin In Healthy Chinese Male Volunteers Teresa Hu, et al. (Hong Kong)	S20
Ab112	A Tale of Two Cities: Comparing the Knowledge of Metabolic Syndrome in the Risk Populations in Hong Kong and Xian, China Qun Wang, et al. (Hong Kong)	S20
Ab117	Serum Phospholipid Monounsaturated Fatty Acid Compositions and Delta-9-Desaturase Activity are Associated with Fasting Glycemic Status Seung Han Baek, et al. (South Korea)	S21
Ab121	Association between Myeloperoxidase, Serum Amyloid A Protein, and Secretory Phospholipase A2 Concentration with Proatherogenic High Density Lipoprotein in Acute Coronary Syndrome Marita Kaniawati, et al. (Indonesia)	S21
Ab122	Correlation between High Sensitivity C-Reactive Protein and Adiponectin Concentration with Oxidized LDL as A Marker Of Atherosclerosis in Metabolic Syndrome Marita Kaniawati, et al. (Indonesia)	S22
Ab124	Circulating Lp-PLA2 Activity Correlates with Oxidative Stress and Cytokines in Overweight/Obese Postmenopausal Women Not Using Hormone-replacement Therapy Minkyung Kim, et al. (South Korea)	S22
Ab125	Three-year Mild Caloric Restriction Partially Protects against Age-related Sphingomyelin Increase and Reduces Obesity-associated Amino Acids Minjoo Kim, et al. (South Korea)	S23
Ab126	The Effects of Chitosan Oligosaccharide (GO2KA1) Supplementation on Glucose Control in Subjects with Prediabetes Hyeon Yeong Ahn, et al. (South Korea)	S23

Ab127	Associations between Metabolomic-identified Changes of Biomarkers and Arterial Stiffness in Subjects Progressing to Impaired Fasting Glucose: a Nested Case-control Study Saem Jung, et al. (South Korea)	S24
Ab128	The Association between Retinal Information and Stroke Risk in Chinese Type 2 Diabetes Vivian Guo (Hong Kong)	S24
Ab129	Calcium Score is More Useful in Discriminating Coronary Artery Disease in Older but Not Younger Sudden Death Autopsy Cases Hapizah Mnohd Nawawi, et al. (Malaysia)	S25
Ab132	HDL-C is an Independent Predictor of Svcam-1 Concentration and Negatively Correlated with Endothelial Activation Nadzimah Mohd Nasir, et al. (Malaysia)	S25
Ab135	Serum Visfatin Concentration is Elevated in Centrally Obese Subjects with and without Metabolic Syndrome Nadzimah Mohd Masir, et al. (Malaysia)	S26
Ab139	Weight Loss is Accelerated by Legume Consumption through the Regulation of Adiponectin and 8-Epi-Prostaglandin F2alpha Minjoo Kim, et al. (South Korea)	S26
Ab141	The Socio-ecological View on the Barriers of Managing Childhood Obesity Sui Yu Yau (Hong Kong)	S27
Ab143	Multiple Infections in a Filipino with Polyangiitis Overlap Syndrome Lauro IV Abrahan, et al. (Philippines)	S27
Ab145	Bilateral Renal Artery Stenosis in a Young Filipino Male with Takayasu's Arteritis Lauro IV Abrahan (Philippines)	S28
Ab151	Homozygous Familial Hypercholesterolemia: a Case Report Noor Alicezah binti Mohd Kasim, et al. (Malaysia)	S28
Ab152	Low-Densitylipoprotein Particle Size Predicts Poor Outcome in Patients with Atherothrombotic Stroke Yong-Jae Kim (South Korea)	S29

Oral Presentation (Basic Science)

Ab05	Reactive Oxygen Species and Nitric Balance Determines The Artery Smooth Muscle Tension: Visualized By in Vivo Molecular Imaging Satoshi Nishimura (Japan)	S30
Ab29	Probucol Inhibits the Initiation of Atherosclerosis in Cholesterol-Fed Rabbits Niimi Manabu, et al. (Japan)	S30

Ab67	Induction of Dendritic Cell-Mediated T Cell Activation by Ldlx and Inhibition by Annexin A5 Anquan Liu, et al. (Sweden)	S31
Ab74	The effect of cow milk on the development of atherosclerosis and production of anti-bodies against oxidized LDL Alexandra Steinerova, et al. (Czech Republic)	S31
Ab83	Dipeptidyl Peptidase 4 (DPP4) Inhibitor Linagliptin Attenuates Neointima Formation after Vascular Injury Yuichi Terawaki, et al. (Japan)	S32
Ab87	Effect of Methanolic Fraction of Flax Lignan Concentrate against Experimental Diabetic Cardiomyopathy in Streptozotocin-Nicotinamide Induced Diabetic Rats Anand Zanwar, et al. (India)	S32
Ab136	Effect of High Glucose on Gene Expression in HCT116 Colorectal Cancer Cells Heung-man Lee, et al. (Hong Kong)	S33
Ab146	Role of SR-BI in Mononuclear Phagocytes in Atherosclerosis Development Lauriane Galle-Treger, et al. (France)	S33
Ab149	Bilirubin Increased by Heme Oxygenase-1 Induction Improves Endothelial Function in Diabetic Mice Jian Liu, et al. (Hong Kong)	S34
Ab153	Reduced Clusterin Contents Contribute to The Pro-Inflammatory and Pro-Senescent Activity of Low Density Lipoprotein Particles in Adiponectin Deficient Mice Han-bing Deng, et al. (Hong Kong)	S34

Poster Presentation (Basic Science)

Ab37	Effects of Edible Plants in Different solvents on Cholesterol Solubilization and Bile Acids Binding Acharaporn Duangjai, et al. (Thailand)	S35
Ab38	Leptin Attenuates Ethanol Induced Hepatic Hypercholesterolemia in Mice Balasubramanian Vairappan, et al. (India)	S35
Ab58	Involvement of Liver Oxidative Stress and Histopathological Changes in Type 2 Diabetes Rats Atcharaporn Ontawong, et al. (Thailand)	S36
Ab59	Effect of Pomelo Juice Extract on Vascular Dysfunction in Hypercholesterolemic Rats Sirinat Pengnet, et al. (Thailand)	S36
Ab63	A New Multimodal Contrast Agent for Molecular Imaging of Adhesion Molecules Expressed in Atherosclerosis Mona Ahmed, et al. (Sweden)	S37

Ab73	Fenugreek Extract is More Effective than Its Active Compound, Saponins in Reducing Interaction between Monocyte and Human Coronary Arterial Endothelial Cells Hapizah Mnohd Nawawi, et al. (Malaysia)	S37
Ab99	Diabetic Condition Exacerbates The Ischemic Brain Injury-Induced Damages Through The Changes Of Various Proteins Phil-ok Koh, et al. (South Korea)	S38
Ab116	Methylglyoxal Induced-astrocyte Dysfunction Mediated through JNK Pathway and Upregulation of Inflammatory Cytokines Kevin Yue, et al. (Hong Kong)	S38
Ab123	3 Days Modified Induction Protocol: Insulin-producing Cells Derived Human Bone Marrow for Human Insulin Replacement Therapy Sayid Ridho, et al. (Indonesia)	S39
Ab133	Citronellol a Major Component of Essential Oil Ameliorates Endothelial Dysfunction Induced by Diet Rich in Fat and Sucrose in Rats Rahul Kshirsagar, et al. (India)	S39
Ab137	Effective Dose of Total Body Irradiation for Streptozotocin-Induced Diabetic Rat as a Role Model for Xenotransplantation: a Challenge and Better Understanding Sayid Ridho, et al. (Indonesia)	S40
Ab138	Chemiluminescent Immunometric Assay for Insulin Measurement as a Marker of Insulin Producing Cells from Differentiation of Human Peripheral Blood Mononuclear Cells Sayid Ridho, et al. (Indonesia)	S40
Ab140	Anti-Inflammatory Effect of Saffron and Its Bioactive Compound, Crocin in Stimulated Human Coronary Artery Endothelial Cells (Hcaecs) Hapizah Mnohd Nawawi, et al. (Malaysia)	S41
Ab154	A Study of Anti-Helicobacter Pylori Effect of Mammalian Cathelicidins Jack Ho Wong, et al. (Hong Kong)	S41

Oral Presentation (Clinical)

Ab11 Theme: Cardiovascular

The Prevalence of Coronary Artery Disease Risk Factors among A Sample of Human Immunodeficiency Virus-Infected Patients on Antiretroviral Therapy in India: Relationship with Clinical and Demographic Factors

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Background: Human immunodeficiency virus (HIV)-related morbidity and mortality have declined since the widespread use of antiretroviral therapy (ART). However, cardiovascular disease (CVD) is an important emerging cause of mortality in HIV-infected patients on combination ART (cART).

Objectives: To evaluate the prevalence of coronary artery disease (CAD) risk factors in HIV-infected Indian patients on cART and examine their association with HIV and cART-related variables.

Methods: This cross-sectional non-comparative study used secondary data collected in routine outpatient care from HIV-infected patients attending the Institute of Infectious Diseases, Pune, India, from March 2012-October 2012. Patients aged > 18 years with confirmed HIV infection and on cART for > 1 year were included. Routine outpatient investigations including fasting lipid profile, fasting blood sugar level, and blood pressure estimations were performed.

Results: There was high prevalence of traditional CAD risk factors, particularly in adults aged 41-50 years. Overall, 97.5% ($n=389/399$) of the subjects had at least one risk factor. There was high prevalence of dyslipidaemia (62.9%) and hypertension (41.9%). The risk of dyslipidaemia was significantly increased in male (OR, 2.078; 95% CI, 1.035 to 2.638; $p=0.002$), obese (OR, 1.778; 95% CI, 1.106 to 2.857; $p=0.017$) and hypertensive subjects (OR, 1.653; 95% CI, 1.035 to 2.638; $p=0.035$). Risk of hypercholesterolaemia was significantly increased in subjects receiving protease inhibitor (PI)-based cART (OR, 2.275; 95% CI, 1.091 to 4.748; $p=0.028$), but decreased in those receiving tenofovir-based regimens (OR, 0.444; 95% CI, 0.247 to 0.798; $p=0.007$).

Conclusion: There was high prevalence of CAD risk factors in this cohort of HIV-infected Indian patients on cART. This warrants an urgent need for routine CAD risk factor screening in HIV-infected populations on cART, and timely institution of appropriate prevention and therapeutic strategies to decrease the morbidity and mortality associated with CAD. Risk of hypercholesterolaemia may be decreased by discouraging PI use and encouraging tenofovir use.

Ab22 Theme: Cardiovascular

Association of The Neutrophil-Lymphocyte Ratio (Nlr) with Outcomes in Patients Admitted for An Acute Coronary Syndrome

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Synopsis: Patients with documented acute coronary syndromes or ACS exhibit a wide spectrum of early risk of death, ranging from 1 to 10%. An elevated leukocyte count has been identified as an independent predictor of an increased risk for long-term mortality and myocardial infarction. An elevated neutrophil count predicts a worse outcome in ACS. In contrast, a low lymphocyte count is related to high risks of adverse outcomes and mechanical complications, low ejection fraction, high degree of myocardial necrosis and mortality in patients with ACS. The neutrophil-lymphocyte ratio (NLR), therefore, integrates for two WBC subtypes with opposite actions in terms of vascular inflammation.

Objectives: Among patients diagnosed with ACS in the Philippine General Hospital, we aim to determine if an elevated NLR taken within 24 hours of admission is associated with higher rates of cardiovascular morbidities & mortalities.

Methods: A prospective cohort of adult patients admitted with a diagnosis of ACS (unstable angina, NSTEMI, STEMI) was conducted. The participants were stratified into two groups: low to intermediate NLR ($NLR \leq 6.5$) and high NLR ($NLR > 6.5$). The primary outcome was in-hospital mortality. Secondary outcomes include development or worsening of congestive heart failure (CHF) and the development of cardiogenic shock, re-infarction, dialysis-requiring renal failure, high-risk pneumonia, and arrhythmias.

Results: 117 patients with a mean age of 60 ± 13 were included. Majority had 1-4 traditional risk factors for ACS. Diagnosis on admission was unstable angina (28%), NSTEMI (40%), and STEMI (37%). Analysis of data showed that the odds of in-hospital deaths among those with a high NLR is 5.71 times higher compared to those with low-intermediate NLR [OR 5.71 (1.53-21.23, $p=0.009$)]. Using linear regression, the NLR of patients who were non-survivors was computed at 9.91, while the NLR of those who survived was 5.47. A high NLR was also predictive of the development or worsening of CHF [OR 4.75 (1.47-15.3, $p=0.009$)], shock [OR 5.0 (1.97-12.67, $p=0.001$)], re-infarction [OR 6.26 (1.91-20.53, $p=0.002$)], development of significant arrhythmias [OR 4.12 (1.45-11.7, $p=0.008$)], and development of any adverse cardiovascular outcome [OR 6.46 (1.40-29.8, $p=0.017$)].

Conclusion: Among patients with ACS, an elevated NLR (>6.5) taken within 24 hours of presentation is a useful marker to predict in-hospital mortality, development or worsening of CHF, and development of shock, re-infarction, and arrhythmias.

Keywords: neutrophil-lymphocyte ratio, acute coronary syndrome

Ab24 Theme: Cardiovascular**Fasting Triglyceride is A Risk Factor for Cardiovascular Event in T-SPARCLE Registry in Taiwan**

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Background: The association between fasting triglyceride (TG) and the occurrence of major adverse cardiovascular event (MACE) remains elusive. The objectives of the present study were to analyze the magnitude of the association between TG and MACE in the Taiwanese Secondary Prevention for Patients with Atherosclerotic Disease (T- SPARCLE) registry.

Methods and Results: Two-year follow-up data from a nationwide cohort study of 3,434 patients with atherosclerotic cardiovascular disease (aged 65.6 years, 68.6% men) were used to identify risk factors for the occurrence of MACE, defined as cardiovascular death, nonfatal myocardial infarction (MI), and non-fatal stroke. Seventy cases of MACE occurred during the follow up. The Cox proportional hazard model was applied to detect the independent risk factors for MACE. Adjustment was made for variables including age, sex, history of stroke, heart failure, MI/coronary artery disease, hypertension, diabetes, lipid-lowering agents except statin, and statin. Compared with TG < 150mg/dL, multivariate-adjusted HRs for MACE ranged from 1.38 (95% confidence interval (CI): 0.73-2.59) for TG of 150-199 mg/dL, 1.69 (95%CI: 0.74-3.83) for TG of 200-249 mg/dL, to 2.43 (95%CI: 1.14-5.19) for TG ≥ 250 mg/dL.

Conclusions: By using the 2-year follow-up data of T- SPARCLE registry, we provide evidence that TG is an independent risk factor for MACE in subjects with higher TG levels (≥ 250 mg/dL).

Ab27 Theme: Cardiovascular**Cost-Effectiveness Analysis of Pharmacogenetic-Guided Warfarin Dosing in Thailand**

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Purpose: Pharmacogenetic (PGx) test is a useful tool for guiding physician on an initiation of an optimal warfarin dose. To implement of such strategy, the evidence on the economic value is needed. This study aimed to determine the cost-effectiveness of PGx-guided warfarin dosing compared with usual care (UC)

Methods: A decision analytic model was used to compare projected lifetime costs and quality-adjusted life years (QALYs) accrued to warfarin users through PGx or UC for a hypothetical cohort of 1,000 patients. The model was populated with relevant information from systematic review, and electronic hospital-database. Incremental cost-effectiveness ratios (ICERs) were calculated based on healthcare system and societal perspectives. All costs were presented at year 2013. A series of sensitivity analyses were performed to determine the robustness of the findings.

Results: From healthcare system perspective, PGx increases QALY by 0.002 and cost by 2,959 THB (99 USD) compared with UC. Thus, the ICER is 1,477,042 THB (49,234 USD) per QALY gained. From societal perspective, PGx results in 0.002 QALY gained, and increases costs by 2,953 THB (98 USD) compared with UC (ICER 1,473,852 THB [49,128 USD] per QALY gained). Results are sensitive to the risk ratio (RR) of major bleeding in *VKORC1* variant, the efficacy of PGx-guided dosing, and the cost of PGx test.

Conclusion: Our finding suggests that PGx-guided warfarin dosing is unlikely to be a cost-effective intervention in Thailand. This evidence assists policy makers and clinicians in efficiently allocating scarce resources.

Ab28 Theme: Obesity**Effect of Folic Acid Supplementation on HDL-Cholesterol and Other Lipid Profile: A Systematic Review and Meta-Analysis**

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Purpose: Obese patients with hypercholesterolemia are at high risk of cardiovascular disease. The evidences illustrating the effects of folic acid supplementation (FAS) on lipid profile remain controversy particularly on HDL-C levels. The aim of the study was to systematically search and quantitatively analyze the effect of FAS on lipid profiles compared with placebo.

Methods: The studies were identified by searching the electronic databases updated to March to 2014. We searched PubMed, Embase and Cochrane databases, used the Medical Subject Heading (MeSH) terms and explored the keywords “folic acid”, “lipid”, “lipid profile”, “cholesterol”, “homocysteine”, “dyslipidemia” and “monitor” with slight modifications based on the sources for search strategy were used. References of initially identified articles were examined to identify any other relevant studies. Two authors independently search, review, extract the information form the studies. Quality of included studies was assessed using Jadad scale. A random-effects model was used for estimation the pooled effect estimates (weighted mean different, WMD).

Results: Of 2,273 studies identified, 8 randomized controlled trials with 575 patients were included. Since there are various doses of FAS, we analyzed the pooled effect estimate based on the doses. We found that FAS had statistically significant effect on HDL-C levels (WMD, 2.53; 95% confidence interval (CI), 0.57 to 4.48). However, the effect on other lipid levels; total cholesterol levels (WMD, 1.48; 95% confidence interval (CI), -6.47 to 9.44); LDL-C levels (WMD, 3.52; 95% CI, -3.43 to 10.47); triglyceride levels (WMD, -5.32; 95% CI, -21.67 to 11.03) was not significant.

Conclusions: Folic acid supplementation may increase HDL-C levels in individuals either when <5 mg/day or 5 mg/day. To confirm such causal relation, further longitudinal studies on these intervention and outcomes are warranted.

Ab30 Theme: Atherosclerosis**Postchallenge Hyperglycemia Potentiated The Lipoprotein Subclass Particles on The Risk of Arterial Stiffness in Healthy Adults**

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Aim: To demonstrate the role of post-challenge hyperglycemia augmented the low-density lipoprotein cholesterol (LDL-C) subclass particles on the risk of arterial stiffness in middle-aged adults.

Methods: We recruited 592 middle-age healthy adults without history of clinical diabetes (fasting glucose <7.0 mmol/L or known coronary heart disease or stroke) since 2009 to 2011. All subjects were performed standard oral glucose tolerance test (OGTT) under fasting conditions; venous blood samples were obtained before and at 30, 60, 90, and 120 min after OGTT. The glucose area under curve (GluAUC) after OGTT was defined as the postchallenge glucose load. LDL-C and small dense LDL-C (sdLDL-C) levels and the brachial-ankle pulse wave velocity (baPWV) were measured.

Results: Postchallenge glucose levels at 1 h and baPWV in tertile distributions were significantly associated with all conventional cardiovascular risk factors, LDL-C, and sdLDL-C. Multivariate logistic regression analyses revealed that LDL-C (or sdLDL-C) combined with one of the seven glycemic indices (glucose levels at 0, 30, 60, 90, and 120 min; GluAUC; HbA1C) was associated with arterial stiffness after adjusting for age, male gender, BMI, hypertension, smoking, and alcohol consumption. At post-challenge hyperglycemic condition, GluAUC, sdLDL-C, and LDL-C were significant risk factors for increased baPWV. On the contrary, fasting glucose and HbA1C combined with LDL-C (or sdLDL-C) did not showed the potentiating effect.

Conclusions: Postchallenge hyperglycemia significantly potentiated and LDL-C subclass particles on the risk of arterial stiffness which indicated the important role of postchallenge hyperglycemia in the primary prevention of cardiovascular disease.

Ab53 Theme: Diabetes**Long Sleep Duration is Associated with Resistance Resistance Independently of Obesity in Korean Non-Diabetic Adults**

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Purpose of the Study: A close association has been known between sleep duration and cardiovascular diseases. **insulin resistance** is a major underlying cause driving **cardiovascular diseases**. We investigated whether sleep duration is associated with insulin resistance independent of obesity in Korean non-diabetic adults.

Methods: The data were collected from the KNHANES IV-2 2008, which is a part of the Fourth Korean National Health and Nutrition Examination Survey (2007-2009). A total of 5689 subjects (2375 males and 3314 females) with no diabetes were assessed in this study. After gender stratification, adjusted means of homeostasis model assessment of insulin resistance (HOMA-IR) were calculated according to sleep duration (≤ 5 hr, 6-7 hr, 8 hr, ≥ 9 hr). Furthermore, logistic regression analyses were conducted to examine the association between sleep duration and increased HOMA-IR (≥ 3.2).

Summary of the Results: Trends favoring a positive association between sleep duration and insulin resistance were demonstrated in women but not in men. In women, long sleep duration (≥ 9 hr/night) was associated with increased HOMA-IR (adjusted odds ratio 1.66, 95% CI 1.07-2.59) compared with normal sleep duration (6-7 hr/night), even after adjusting for body mass index (BMI) and other covariates.

Conclusions: This study shows the gender-specific association between sleep duration and insulin resistance. Women with long sleep duration are more likely to have increased insulin resistance, independently of obesity and other potential confounders.

Table. Association between sleep duration and increased insulin resistance by gender

HOMA-IR ≥ 3.2	Males			Females		
	<i>n</i> (%)	Adjusted OR*	95% CI	<i>n</i> (%)	Adjusted OR*	95% CI
Sleep duration [†] (hr)						
≤ 5	39 (12.3)	0.81	0.52-1.28	85(15.8)	1.25	0.86-1.81
6-7	172 (12.6)	1.0		197(11.2)	1.0	
8	68 (13.4)	1.26	0.92-1.74	101(13.6)	1.38	0.93-2.06
≥ 9	22 (12.1)	1.11	0.65-1.90	43(14.8)	1.66	1.07-2.59

*Adjusted for age, marital status, education level, monthly house income, smoking, binge drinking, exercise, BMI, WC

[†] Answering the question 'Usually, how many hours do you sleep a day?'**Ab61 Theme: Cardiocascular****The Role of C-Reactive Protein in Cardiovascular Diseases - Lessons from The Experiments of Nature**Ming-Yu Wang¹, Hai-Hong Zhou¹, Shi-Chao Zhang¹, Feng Hui¹, Jin Cheng¹, Hai-Xiang Su², Shang-Rong Ji¹ and Yi Wu¹¹School of Life Sciences, Lanzhou University, Lanzhou, 730000, PR China²Gansu Cancer Hospital, Lanzhou, Lanzhou, 730050, PR China

Purpose of the Study: Accumulating evidence indicates that the serum level of C-reactive protein (CRP) is closely associated with the risk and prognosis of cardiovascular disease and cancer. However, large-scale genetic epidemiological studies suggest that circulating CRP is not causally involved in these diseases. Moreover, contrasting findings have been obtained on the role of CRP in mouse models of atherosclerosis. Therefore, it remains elusive whether CRP contributes directly to the chronic inflammation underlying the diseases or simply represents a bystander marker. Our recent work thus aims to address this issue.

Methods: The mutation status of CRP in tumors were examined in over 450 tumor/normal sample pairs with the rationale that key inflammatory genes might be targeted for mutation to favor the development of cancer. The actions of CRP in vascular inflammation were studied by endothelial dysfunction-related experiments.

Summary of the Results: A recurrent somatic mutation at the SNP position -286 (rs3091244) in the promoter of CRP were identified with an average mutation frequency of over 20 % across 10 cancer types. This mutation enhanced the induction of CRP in tumors via disruption of the conserved CpG methylation site. Moreover, CRP was found to activate endothelial cells only after changing in its conformation triggered by local inflammatory conditions.

Conclusions: The prevalence and pervasiveness of CRP promoter mutations in cancers indicate that instead of circulating CRP, **LOCALLY PRODUCED CRP** is a potential driver of tumorigenesis, highlighting a role of CRP as a core component of the regulatory network of inflammation. As the full expression of the proinflammatory actions of CRP also depends on local inflammatory conditions, our results argue that the local abundance of CRP and its interactions with the stressful microenvironment should be the key to disease progression; while circulating CRP levels mainly mirror the underlying inflammatory status.

Ab84 Theme: Cardiovascular**Young Chinese Adults' Attitudes towards Adopting A Mediterranean-Style Dietary Plan to Reduce Cardiovascular Disease**

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Purpose of the Study: Once known as the disease of the Western world, cardiovascular disease (CVD) prevalence is rapidly increasing in many Asian countries. Changing the dietary intakes of populations living in Asia to a diet based on the Mediterranean Diet (MD) principles could possibly reduce CVD. The people living in Asia, like the Mediterraneans, are known to love their food and food has a major cultural-promotion role. It is only sensible to identify both culturally appropriate and readily available foods that have the same heart health-promoting effects as the ingredients of the MD. Therefore, (1) we designed a dietary Chinese menu plan based on the tenets of the MD and (2) examined young Chinese adults' attitudes towards adopting this dietary plan.

Methods: Eighty healthy volunteers (40 males and 40 females) aged 18-35 years old were asked to complete a 7-point Likert-scale questionnaire. The nutrient profile of the menu plan was analysed using WinDiets software. Cross tabulation analyses were used to compare the responses.

Summary of the Results: Most of the participants (75%) agreed that Mediterranean diet (MD) is relatively uncommon to them but more than half (51.25%) reported that they have some awareness of the health benefits of MD diet. Interestingly, 81.25% of the participants agreed that the food items in the proposed menu plan have beneficial effects on reducing risk of CVD. This suggests that although participants might not be aware of the term "MD", they are aware of the health benefits of key components of the MD (e.g. fruits, vegetables and olive oil). Generally, the proposed plan was well received and majority (60%) will adhere to it.

Conclusion: Our finding suggests that MD diet has potential to be implemented with the Chinese population. However, it is essential to consider convenience in food preparation and having a variety.

Ab90 Theme: Atherosclerosis**Mitochondrial Mutations and Atherosclerosis**

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Objectives: Mitochondrial mutations may be one of the causes of atherosclerosis development in human arteries. Recently we have found that at least ten mitochondrial mutations in eight genes (rRNA 12S, 2 genes tRNA-Leu (codons recognized UUR and CUN), cytochrome B, and subunits 1, 2, 5, and 6 NADH dehydrogenase) had different level of heteroplasmy in atherosclerotic plaques as compared to normal intima. The aim of present research was to reveal the association of the above mutations in mitochondrial genome with the extent of subclinical carotid atherosclerosis.

Methods: The level of heteroplasmy in human leucocytes was determined by pyrosequencing method adopted for conditions where both mutant and normal allele were present in the same specimen. The blood was taken from 156 apparently healthy persons in whom the extent of subclinical carotid atherosclerosis was determined by high-performance ultrasonography followed by quantitative measurement of common carotid artery intima-media thickness.

Results: According to the results of ultrasonographic evaluation, 51 participants were non-atherosclerotic (NA), 51 had diffuse intima-media thickening (DIT), and the rest 54 had at least one atherosclerotic plaque in common carotid artery (AP). The level of heteroplasmy for was significantly higher for C3256T, G12315A and G15059A mutations in DIT and further in AP as compared to NA. On the opposite, the level of heteroplasmy declined from NA to AP for G13513A and Ins652G mutations. There was a strict linear-linear relationship between the extent of subclinical carotid atherosclerosis and quartiles of heteroplasmy for all above mutations ($p < 0.001$).

Conclusion: These results demonstrate the evidence for genetic predisposition to atherosclerosis development on the level of mitochondrial genome.

Ab98 Theme: Cardiovascular**Factors Associated with Health-Promoting Behavior of People with or at High Risk of Metabolic Syndrome: Based on The Health Belief Model**

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Purpose of the Study: The purpose of this study is to identify the association between self-efficacy and health-promoting behaviors of people with or at high risk of metabolic syndrome (MS), guided by the Health Belief Model (HBM).

Methods: Participants with two or more MS components by the American Heart Association definition were invited to complete a questionnaire while attending a community health program. Health-promoting behavior was assessed using the exercise and diet management subscales of the Health promoting lifestyle profile II (HPLPII). Self-efficacy and the four-construct of HBM (perceived threat, cues, benefits, and barriers) were measured using validated tools. The contributions of each HBM factor towards the respective behavior were identified using a three-step hierarchical regression approach.

Summary of the Results: The final sample consisted of 132 adults (40.2% male) with the mean age of 49.3 years (SD 9.5). More than 1/3 had one or more chronic diseases. After controlling for age, gender, education level, income and knowledge of MS, HBM factors significantly increased the total variance of health-promoting behaviors by 9%. Beliefs about barriers was found to be a significant predictor of exercise ($\beta = -.28, p < .01$) and diet management ($\beta = -.24, p < .01$), which suggest higher level of perceived barrier was associated with less frequent of health-promoting behavior. In the final model, self-efficacy was added and explained an additional 31% of the variance in exercise behavior and 13% in diet management behavior.

Conclusions: Self-efficacy and perceived barriers made independent contributions to health-promoting behavior among people with or at high risk of MS. Community health program targeting this particular group should tailor strategies that can enhance individuals' self-efficacy and address barriers perceived.

Ab100 Theme: Cardiovascular**Telmisartan Significantly Affected The Pharmacokinetics of Rosuvastatin in Healthy Subjects and in Patients with Hyperlipidaemia, in Vitro and in Vivo Experiments**

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Purpose: The ATP-binding cassette G2 (ABCG2) transporter plays an important role in the disposition of rosuvastatin. Telmisartan, a selective angiotension-II AT₁ receptor blocker, inhibits the transport capacity of ABCG2. This study investigated the pharmacokinetic interaction between rosuvastatin and telmisartan.

Methods: In this two-phase fixed-order design study, healthy subjects received single doses of 10 mg rosuvastatin at baseline and after telmisartan 40 mg daily for 14 days. Patients with hyperlipidaemia who had been taking rosuvastatin 10 mg daily for at least 4 weeks were given telmisartan 40 mg daily for 14 days together with rosuvastatin. Plasma concentrations of rosuvastatin were measured over 24 hours before and after telmisartan. *In vitro* experiments using bidirectional transport assay were performed to investigate the involvement of ABCG2 in the drug-drug interaction between telmisartan and rosuvastatin.

Results: In all the 12 participants, rosuvastatin C_{max} was increased by 86% (from 12.1 ± 5.8 µg/L to 22.5 ± 14.2 µg/L, $P < 0.005$) and the AUC_{0-∞} was increased by 40% (from 124.0 ± 79.8 µg·h/L to 173.2 ± 130.0 µg·h/L, $P < 0.05$) after treatment with telmisartan. Patients receiving long-term rosuvastatin therapy ($n=4$, 2 males, weight 62.4 ± 9.3 kg) had significantly higher systemic exposure to rosuvastatin than healthy volunteers ($n=8$, all males, weight 74.2 ± 12.2 kg) both at baseline (212.1 ± 67.0 µg·h/L vs. 80.0 ± 37.7 µg·h/L, $P < 0.001$) and after telmisartan (310.0 ± 123.8 µg·h/L vs. 104.8 ± 62.7 µg·h/L, $P < 0.005$), but there was no difference in the pharmacokinetic interaction between the two groups of participants. The *in vitro* experiment indicated that telmisartan inhibited the transmembrane transport of rosuvastatin by nearly 24%.

Conclusion: This study demonstrated that telmisartan significantly increased the systemic exposure to single and multiple doses of rosuvastatin in healthy volunteers and in patients with hypercholesterolaemia. This interaction should be considered when the two drugs are used concomitantly to avoid excessive exposure to rosuvastatin.

Ab105 Theme: Cardiovascular**Predictors of The Extent of Carotid Atherosclerosis in Patients Treated with Radiotherapy for Nasopharyngeal Carcinoma**

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Purpose of the Study: to determine the predictors for carotid atherosclerosis in patients treated with radiotherapy (RT) for nasopharyngeal carcinoma (NPC).**Methods:** 129 post-RT NPC patients, who had completed a course of RT for at least 4 years, no history of carotid atherosclerosis prior to RT and no previous carotid endarterectomy and carotid stenting, were included in the present study. Carotid atherosclerotic parameters, such as carotid intima-media thickness, carotid arterial stiffness and carotid plaque burden (plaque score, the presence of plaque and $\geq 50\%$ stenosis) were assessed using ultrasonography. Association of carotid atherosclerosis and ten potential predictors, including age, gender, post-RT duration, radiation dose, chemotherapy, diabetes mellitus, hypertension, hypercholesterolemia, coronary heart disease and smoking, were determined using multiple regression. The cut-off values of age or post-RT duration for the presence of plaque or $\geq 50\%$ stenosis were analyzed using receiver operating characteristic (ROC) curve analysis.**Summary of the Results:** Age, post-RT duration and number of cardiovascular risk factors were positively associated with carotid plaque burden ($P < 0.01$). Age of 44.5 years old (Sensitivity=99.2% and Specificity=50%, AUC=0.757, $P < 0.01$) and post-RT duration of 8.5 years (Sensitivity=75.7% and Specificity=64.3%, AUC=0.772, $P < 0.001$) was the cut-off values for detecting carotid plaque, whilst post-RT duration of 13.5 years (Sensitivity=66.7% and Specificity=71.6%, AUC=0.709, $P < 0.001$) was the cut-off value for screening $\geq 50\%$ stenosis. Compared to patients with < 2 cardiovascular risk factors, those with ≥ 2 cardiovascular risk factors had significantly higher carotid plaque burden ($P < 0.001$).**Conclusions:** Age, post-RT duration and number of cardiovascular risk factors are significant predictors of carotid atherosclerosis in post-RT NPC patients. Post-RT NPC patients, who are aged 44 years old or above, with post-RT duration of 8 years or above, and/or with ≥ 2 cardiovascular risk factors, are more susceptible to carotid atherosclerosis.**Ab107 Theme: Cardiovascular****The Double-Blind Durable Effect of PCSK9 Antibody Compared with Placebo Study (DESCARTES): A 52 Week Phase 3 Double-Blind, Randomized, Placebo-Controlled Trial of Evolocumab (AMG 145) in Hyperlipidemic Patients**D Blom¹, T Hala², M Bolognese³, M J Lillestol⁴, P D Toth⁵, L Burgess⁶, R Ceska⁷, E Roth⁸, M J Koren⁹, M L Monsalvo¹⁰, K Tsirtsonis¹¹, J B Kim¹⁰, S M Wasserman¹⁰, R Scott¹⁰, C M Ballantyne¹², R Somaratne¹⁰ and E A Stein¹³¹Division of Lipidology, Department of Medicine, University of Cape Town, South Africa; ²Center for Clinical and Basic Research, Pardubice, Czech Republic; ³Bethesda Health Research Center, Bethesda, MD, USA; ⁴Lillestol Research, LLC, Fargo, ND, USA; ⁵Midwest Institute For Clinical Research, Indianapolis, IN, USA; ⁶Tread Research, Cardiology Unit, Tygerberg Hospital, Cape Town, South Africa; ⁷Center of Preventive Cardiology, 3rd. Dept. Internal Medicine, Charles University, Prague, Czech Republic; ⁸Sterling Research Group, Cincinnati, OH, USA; ⁹Jacksonville Center for Clinical Research, Jacksonville, FL, USA; ¹⁰Amgen, Thousand Oaks, CA, USA; ¹¹Amgen Ltd., Uxbridge, United Kingdom; ¹²Baylor College of Medicine, Houston, TX, USA; ¹³Metabolic and Atherosclerosis Research Center, Cincinnati, OH, USA**Purpose of the Study:** Evolocumab (AMG 145), a fully human monoclonal antibody to proprotein convertase subtilisin/kexin type 9 (PCSK9), markedly reduced low-density lipoprotein (LDL-C) in phase 2 studies of 12 week duration. We conducted a phase 3 trial (NCT01516879) to evaluate the safety and efficacy of 52 weeks of treatment with evolocumab.**Methods:** On the basis of the NCEP ATP III risk categories, patients were started on background lipid-lowering therapy with diet alone or diet plus atorvastatin at a dose of 10 mg daily, or 80 mg daily, or 80 mg daily plus ezetimibe 10 mg daily, for a run-in period of 4 to 12 weeks. Patients with a LDL-C level ≥ 75 mg/dL (1.9 mmol/L) were then randomized in a 2:1 ratio to receive either subcutaneous evolocumab (420 mg) or placebo every 4 weeks. The primary end point was percent change from baseline in LDL-C, as measured by ultracentrifugation, at week 52.**Summary of the Results:** 901 patients were randomized and dosed (48% male; mean [SD] age 56 [11] years; 26% high ATPIII risk). Evolocumab reduced LS mean (95% CI) LDL-C by 57% (53-61%) compared with placebo ($P < 0.001$) but responses varied, from 49-62%, among background therapies. LDL-C reduction at week 12 and week 52 were comparable. Significant improvements were observed in apolipoprotein B, non-high-density lipoprotein cholesterol, lipoprotein (a), triglycerides and HDL-C. The most common adverse events were nasopharyngitis, upper respiratory tract infection, influenza, and back pain. Treatment-emergent and muscle-related adverse events, and hepatic abnormalities were comparable across treatment groups.**Conclusions:** At 52 weeks, evolocumab added to diet alone, to low-dose atorvastatin, or to high dose atorvastatin with or without ezetimibe further reduced LDL-C by 57% in patients with a range of cardiovascular risk.

Ab113 Theme: Cardiovascular

What are the Influencing Factors of Healthy Lifestyle Behaviors? A Qualitative Study in Adults with Metabolic Syndrome

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Purpose of the Study: Lifestyle modification has been recommended as the primary intervention for metabolic syndrome (MetS). Since all lifestyle interventions involve behavior changes, it is necessary to understand the influencing factors of lifestyle behaviors comprehensively. This study was to explore the influencing factors of healthy lifestyle behaviors in adults with MetS.

Methods: The study was conducted in two medicine units of a general public hospital in Qingdao, China. Individual in-depth interviews were conducted among MetS patients by using a semi-structured interview guide. Purposive sampling was adopted to recruit a diverse group of participants. The interviews focused on exploring the facilitators and barriers during patients' lifestyle management experiences for MetS. Content analysis was used for data analysis and interpretation.

Summary of the Results: Thirty informants including 16 (53.3%) males, with the mean age of 56.6 years, participated in the study. Five themes were identified: motivations, health beliefs, social support, personal resistance to healthy lifestyles, and insufficient support from the society. The facilitators for healthy lifestyles included the following three aspects. Informants' motivations for healthy lifestyles were enhanced by their commitment for family responsibilities and eagerness for better health. Health beliefs gained from previous health experiences contributed to current healthy behaviors. Social support from family and friends facilitated the perseverance of healthy lifestyles. The barriers for lifestyle management came from two aspects: personal resistance to advices on exercise and healthy diet; lack of exercise facilities and limited education provided by health care professionals.

Conclusions: Understanding the influencing factors of healthy lifestyle behaviors will help the development of cultural sensitive interventions for Chinese MetS patients. Future lifestyle interventions should encourage the social support from family and friends, and provide comprehensive health education. The society should also provide more support and facilities for promoting healthy lifestyles.

Ab115 Theme: Diabetes

Effects of Long-term, Monthly Administration of the Pcsk9 Inhibitor Evolocumab (Amg 145) in Patients with Dysglycemia or Metabolic Syndrome

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Purpose of the Study: Patients with dysglycemia benefit from statin; however many are unable to achieve LDL target goals or have difficulty with side effects associated with statin use. We investigated the effects of evolocumab (AMG 145), a fully human monoclonal antibody against PCSK9 that effectively reduced LDL-C in phase 2 trials, in patients with dysglycemia or metabolic syndrome (MetS).

Methods and Summary of the Results: In the OSLER study, 1104 patients that participated in a parent study were randomized to evolocumab 420 mg monthly with standard of care (SOC) or SOC alone. Of the OSLER patients with type 2 diabetes mellitus (T2DM; $n=109$), impaired fasting glucose (IFG; $n=134$), or MetS, $n=(425)$, 91, 119 and 369, respectively, had an observed week 52 LDL-C value. Observed mean (SE) LDL-C changes from parent-study baseline at week 52 in OSLER patients on Evolocumab + SOC were -47 (3)% (T2DM); -51 (2)% (IFG); and -52 (1)% (MetS). In the SOC arm, LDL-C changes were -1 (4)% (T2DM); 1 (5)% (IFG); and -1 (2)% (MetS). Adverse event (AE) rates for patients with T2DM, IFG, or MetS were 78% (Evolocumab + SOC in OSLER) and 72% (SOC); serious AEs occurred in 8% and 6% of patients, respectively. Evolocumab + SOC patients did not demonstrate notable changes in FPG or HbA1C at week 52.

Conclusions: Monthly evolocumab reduced LDL-C in patients with dysglycemia or MetS and was well tolerated without notable changes in glycemic control.

Ab118 Theme: Cardiovascular**The Effect of Bisoprolol on Central and Brachial Pressure in Chinese Hypertensive Patients**Ww Zeng, Ttw Chu, Bsp Fok, M Hu and B Tomlinson

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Purpose of the Study: Central aortic pressure differs from brachial blood pressure (BP) and may be a superior predictor of cardiovascular events. Recent studies have suggested that compared with other antihypertensive treatments, beta-blockers are less effective in reducing central aortic pressures despite similar effects on brachial BP. The present study compared the effects of bisoprolol, a highly selective beta1-blocker, on central aortic and brachial BP in Chinese patients with essential hypertension.

Methods: This was an open-label study in 48 hypertensive patients. Central systolic pressure (C-SBP), pulse pressure (C-PP), radial augmentation index (rAI), radial augmentation pressure (rAP), brachial SBP (Br-SBP), pulse pressure (Br-PP) and heart rate (HR) were derived from the radial artery waveform obtained by pulse wave analysis using the BPro radial pulse wave acquisition device with A-PULSE software at baseline, 24 hours after the first dose and after 6 weeks treatment with bisoprolol 2.5 mg daily.

Results: Forty-six patients (age 55 ± 11 years, 57% male) completed a single dose of bisoprolol and 6 weeks treatment. At 24 hours after the first dose, the changes in C-SBP, Br-SBP, C-PP, Br-PP, HR, rAI and rAP were -9.4 ± 10.4 mmHg ($p < 0.01$), -10.4 ± 11.0 mmHg ($p < 0.01$), -2.7 ± 10.3 mmHg ($p = 0.09$), -3.7 ± 11.3 mmHg ($p = 0.04$), -3.6 ± 5.7 beats/min ($p < 0.01$), $+3.0 \pm 13.4\%$ ($p = 0.14$) and -1.0 ± 4.7 mmHg ($p = 0.25$), respectively. After 6 weeks of treatment, the pre-dose changes in C-SBP, Br-SBP, C-PP, Br-PP, HR, rAI and rAP were -13.6 ± 13.1 mmHg ($p < 0.01$), -14.4 ± 13.3 mmHg ($p < 0.01$), -4.1 ± 9.1 mmHg ($p = 0.004$), -5.1 ± 9.4 mmHg ($p = 0.001$), -3.7 ± 5.1 beats/min ($p < 0.01$), $1.0 \pm 14.0\%$ ($p = 0.64$) and -0.6 ± 4.6 mmHg ($p = 0.48$). There were significantly greater reductions in Br-SBP than in C-SBP (-1.0 ± 2.8 mmHg, $p = 0.02$) after the first dose but no significant difference (-0.8 ± 3.5 mmHg, $p = 0.13$) after 6 weeks of treatment. Significantly greater reductions were observed in Br-PP than C-PP after the first dose (-1.0 ± 2.8 mmHg, $p = 0.02$) and after 6 weeks of treatment (-1.0 ± 2.6 mmHg, $p = 0.009$).

Conclusions: These findings suggest that low dose bisoprolol has similar effects on central and brachial SBP with long-term treatment.

Ab120 Theme: Cardiovascular**Bisoprolol in Essential Hypertension: Effects on 24 Hour Ambulatory Blood Pressure and Metabolic Profile in Chinese Patients**Ww Zeng¹, Hb Deng², Ttw Chu¹, Bsp Fok¹, M Hu¹ and B Tomlinson¹¹Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Shatin, Hong Kong²Department of Pharmacology and Pharmacy, The University of Hong Kong, Pokfulam, Hong Kong

Purpose of the Study: Some studies have found beta-blockers (BBs) inferior to other antihypertensive treatments in reducing stroke incidence and overall mortality possibly because of adverse effects on glucose and lipid profiles. The aim of this study was to investigate the genetic and phenotypic factors which influence the metabolic profile and ambulatory blood pressure (BP)-lowering effects of bisoprolol in Chinese patients with essential hypertension.

Methods: This was an open-label trial in patients with mild to moderate essential hypertension. Patients received bisoprolol 2.5 mg once daily for 6 weeks after a placebo run-in period. Clinic and 24 hour ambulatory BPs were measured before and after 6-weeks of bisoprolol treatment. Changes in lipids and glucose were evaluated after 6 weeks treatment.

Results: 98 patients (54 ± 10 years, 59% male) completed this study. After 6 weeks of treatment, there were significant reductions in clinic systolic BP (SBP), clinic diastolic BP (DBP), and clinic heart rate (HR) of -14.1 ± 10.8 mmHg ($p < 0.001$), -8.2 ± 6.4 mmHg ($p < 0.001$) and -6.5 ± 7.6 beats/min ($p < 0.001$), respectively. 24 hour ambulatory SBP, DBP and HR were reduced significantly by -13.5 ± 12.7 mmHg, -8.2 ± 7.4 mmHg, and -9.7 ± 4.9 beats/min (all $p < 0.001$), respectively. Small but significant increases of 0.3 ± 1.0 mmol/L ($p = 0.002$), 1.8 ± 6.2 μ mol/L ($p = 0.005$) and 0.01 ± 0.04 mmol/L ($p = 0.003$) were observed in plasma urea, creatinine and urate, respectively. The changes in total cholesterol, HDL-C, triglycerides, LDL-C and non-HDL-C were not significant at -0.05 ± 0.5 mmol/L ($p = 0.36$), -0.03 ± 0.1 mmol/L ($p = 0.05$), -0.01 ± 0.5 mmol/L ($p = 0.85$), -0.03 ± 0.5 mmol/L ($p = 0.56$), -0.01 ± 0.5 mmol/L ($p = 0.79$), respectively. There was no significant change in fasting plasma glucose, -0.02 ± 0.5 mmol/L ($p = 0.74$).

Conclusions: The administration of low-dose bisoprolol significantly reduced clinic BP and effectively reduced ambulatory BP over 24 hours. There was no adverse effect on lipids and glucose metabolism in these hypertensive patients. Reduction in heart rate may be an additional benefit in some patients.

Ab142 Theme: Diabetes

Bone and Mineral Metabolism and Incident Diabetes Mellitus: a Prospective Study

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Purpose of the Study: Bone and mineral metabolism plays an important role in glucose metabolism, whether markers of bone and mineral metabolism can predict diabetes mellitus remains largely unknown. In this study, we aimed to evaluate the association of markers of bone and mineral metabolism with incident diabetes.

Methods: A total of 1702 male and 4394 female Southern Chinese aged 20 or above, who were free of diabetes at baseline, participated in this prospective cohort study with a median follow-up of 10.2 years. Markers of bone and mineral metabolism (bone mineral density [BMD], serum alkaline phosphatase [ALP], parathyroid hormone, albumin-adjusted calcium, total calcium, and phosphate) were measured at baseline. Dietary calcium intake was estimated from a validated food frequency questionnaire. Data on incident diabetes were retrieved from the electronic medical record system.

Summary of the Results: In 59130 person-years of follow-up, 631 participants developed diabetes. Serum ALP (highest quartile, hazard ratio [HR] 1.41; 95% confidence interval [CI] 1.06-1.88; as compared to the lowest quartile) and total calcium (third quartile, HR 1.42; 95% CI 1.12-1.8; highest quartile, HR 1.42; 95% CI 1.11-1.79; as compared to the lowest quartile) were significantly associated with incident diabetes. Addition of serum ALP and total calcium to age, sex and BMI significantly improved integrated discrimination and category-less net reclassification index. Significant interactions with BMI and age were observed. Greater total calcium intake was significantly associated with lower incident diabetes (comparing extreme quartile, hazard ratio 0.78; 95% confidence interval 0.61-0.98).

Conclusions: In this prospective study, elevated serum ALP, total calcium, and lower total calcium intake were associated with incident diabetes. Adding serum ALP and total calcium to basic clinical risk factors significantly improved risk prediction. Bone and mineral metabolism may play a role in diabetes development and risk prediction.

Ab148 Theme: Atherosclerosis

People with Peripheral Arterial Disease and Diabetes are Associated with Clinically Significant Weakness

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Purpose of the Study: Low lean mass is associated with weakness, limited mobility, and increased risk of mortality. In the recent effort of the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project, an appendicular lean mass (ALM) cut-points for clinically significant weakness were derived. Peripheral arterial diseases (PAD) and diabetes have been shown to be associated with reduced lean mass. However, whether these diseases are associated with clinically significant weakness remain unknown. We aimed to investigate whether PAD and diabetes are associated with clinically significant weakness as defined by the FNIH Sarcopenia Project.

Methods: Data on 4841 participants aged ≥ 40 years of the National Health and Nutrition Examination Survey 1999-2004 were examined. ALM was measured using Dual Energy X-ray Absorptiometry. Logistic regression was used to assess the association of diabetes and PAD with low lean mass. Low lean mass was defined as ALM < 19.75 kg in men and ALM < 15.02 kg in women.

Summary of the Results: In the simple model adjusted for age, sex, BMI, and race/ethnicity, participants with PAD alone and both PAD and diabetes were associated with low lean mass with an odds ratio (OR) of 1.65 (95% confidence interval [CI]: 1.07-2.56) and 2.07 (95% CI: 1.10-3.89), respectively. No association was observed between diabetes and low lean mass. After further adjustment for smoking, drinking, exercise, hypertension, estimated glomerular filtration rate, microalbuminuria, serum biomarkers of liver function, and cardiometabolic biomarkers, participants with both PAD and diabetes remained significantly associated with low lean mass (OR: 2.08; 95% CI: 1.03-4.19). The association with PAD became insignificant.

Conclusion: People with both diabetes and PAD had a higher likelihood of low lean mass and hence clinically significant weakness. Intervention to improve muscle mass and strength may be useful to improve mobility and reduce risk of mortality in these people.

Poster Presentation (Clinical)

Ab07 Theme: Diabetes**Sesame Oil Exhibits Synergistic Effect With Anti-Diabetic Medication and Affects Glucose and Lipid Metabolism in Type 2 Diabetes Patients**

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Background and Aims: Studies have reported that sesame oil lowered blood pressure and improved antioxidant status in hypertensive and diabetic-hypertensive patients. The aim of this study was to evaluate the effectiveness of sesame oil with antidiabetic (glibenclamide) medication as combination therapy in mild-to moderate diabetic patients.

Methods: This open label study consists of sixty type II diabetes mellitus patients divided into 3 groups, receiving sesame oil ($n=18$), 5 mg/d (single dose) of glibenclamide ($n=20$), or their combination ($n=22$). The patients were supplied with sesame oil except glibenclamide group, and instructed to use ~30 g of oil/day/person for cooking, or salad preparation for 60 days. Overnight fasting blood samples were collected at baseline (0 day) and after 60 days of the experiment for various biochemical analysis.

Results: As compared with sesame oil and glibenclamide alone, combination therapy showed an improved antihyperglycemic effect with 36% reduction of glucose ($P<0.001$ vs before treatment, $P<0.01$ vs sesame oil monotherapy, $P<0.05$ vs glibenclamide monotherapy) and 43% reduction of HbA_{1c} ($P<0.001$ vs before treatment, $P<0.01$ vs sesame oil monotherapy, $P<0.05$ vs glibenclamide monotherapy) at the end point. Significant reductions in the plasma TC, LDL-C and TG levels were noted in sesame oil (20%, 33.8% and 14% respectively vs before treatment) or combination therapies (22%, 38% and 15% respectively vs before treatment). Plasma HDL-C was significantly improved in sesame oil (15.7% vs before treatment) or combination therapies (17% before treatment). Significant ($P<0.05$) improvement was observed in the activities of enzymatic and non-enzymatic antioxidants in patients treated with sesame oil alone or combination with glibenclamide.

Conclusions: Sesame oil exhibits synergistic effect with glibenclamide and provides a safe and effective option for the drug combination may be very useful in clinical practice for the effective improvement of blood glucose and lipid.

Ab19 Theme: Diabetes**The Utility of Fasting Capillary Blood Glucose in The Detection of Type 2 Diabetes Mellitus Among Patients at The Charity Out-Patient Section, Department of Internal Medicine at Chinese General Hospital And Medical Center**

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Venous fasting blood sugar (vFBS) is the method of choice used to screen for type 2 diabetes mellitus (T2DM). Nonetheless, capillary fasting blood glucose (cFBS) measurements may constitute an alternative to venous blood glucose measurements, specifically during the screening phase, because they are easier, less expensive, and less invasive to obtain. This research explored the use of the cFBS to screen for T2DM.

From August until September 2013, after informed consent was obtained, 117 male and female charity OPD patients were included in the study. The subjects were asked to undergo an overnight fast of 8-12 hours. In the laboratory, on the next day, 0.5 µL of blood for cFBS was drawn from the fingertip. After which, 3-5 ml of blood was drawn from the antecubital vein of the same patient to determine the vFBS. Results were divided into normal, impaired fasting glucose, and type 2 diabetes according to the cut-offs set by the American Diabetes Association. Data processing and analyses were done in SPSS v18.

The results showed that the sensitivity and specificity of the cFBS in the screening of T2DM was 100% and 91%, respectively. At a prevalence rate of 8.22%, a patient has 67% chances of being diagnosed with T2DM (PPV=67%) using this screening method.

This study showed that cFBS can be utilized to screen for T2DM because of its high accuracy (97%). It is a suitable alternative for patients because it is convenient, less invasive, and cost-effective.

Ab23 Theme: Cardiovascular**A Comparison of 12 Lead Electrocardiogram and 2d-Echocardiography Derived Ejection Fraction among Patients with Depressed Ejection Fraction**

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Introduction: A 12 lead electrocardiogram continues to be one of the most frequently ordered test in the practice of cardiology. In third world countries where access to 2D echocardiogram is limited, the value of the ECG as a tool in determining patients with depressed ejection fraction should be investigated. We aim to compare the computed ejection fraction by electrocardiogram with the ejection fraction taken from a transthoracic 2D echocardiogram via Simpsons method in patients with an echocardiogram derived EF $\leq 50\%$.

Methods: Patients with an echocardiographically derived ejection fraction (taken by Simpson's method) of $\leq 50\%$ will be included. The ejection fraction by ECG will be computed by another cardiologist investigator using the formula $(2.264 \times \text{aVR QRS amplitude}) + (\text{age} \times 0.645)$. The mean difference in ejection fraction derived by ECG and 2D echo will be computed. The sensitivity and specificity of ECG compared to 2D echo to detect a severely depressed ejection fraction ($<35\%$) will also be computed. Since age of the patient is used to derive the EF by ECG, data would be further stratified by age group

Results: A total of 129 participants were included in the analysis. Among the participants, the ejection fraction computed by ECG using aVR was less than 50% in 71%. The mean ejection fraction taken by 2D echocardiography was 37% (SD: 8%), while the mean ejection fraction computed using ECG was 44.5% (SD: 10%). The sensitivity and specificity of ECG to detect a severely depressed ejection fraction ($<35\%$) was also determined at 39% and 86%, respectively. Among those 40 years old and below, the sensitivity and specificity of an ECG to predict an EF $\leq 35\%$ is 100% and 20%, respectively. Among those older than 40 years old, the sensitivity and specificity was 20% and 96%, respectively.

Conclusion: Previous studies have repeatedly demonstrated the importance of LVEF. A rapid and readily available estimation method of EF is crucial in the management of the vast majority of cardiac patients, especially in third world countries.

Ab25 Theme: Diabetes**Quality of Life in Parents of Children with Type 1 Diabetes Receiving Insulin Treatment**

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Purpose of the Study: To examine quality of life (QoL) in parents of children with type 1 diabetes (T1D) receiving insulin treatment, and to identify factors that might affect parental QoL.

Methods: The study used descriptive cross-sectional design. A convenience sample of 46 parents of patients aged 18 years or below with T1D was recruited from a specialist outpatient clinic of a teaching hospital and a diabetes association. A self-report questionnaire consisted of World Health Organization QoL-BREF(HK) and demographics was used to assess parental QoL.

Results: Data were collected from 46 eligible parents between September 2013 and January 2014. Parents perceived relatively good QoL compared with parents of children with developmental disabilities. Parents with part-time/full-time employment reported better QoL in psychological ($B=9.869$, 95% CI=2.615-17.123, $\beta=0.370$, $t=2.744$, $p=0.009$) and environment domains ($B=10.497$, 95% CI=1.527-19.467, $\beta=0.325$, $t=2.360$, $p=0.023$); parents whose child had no hospitalisation due to severe hypoglycaemia reported better physical health ($B=-21.775$, 95% CI=-41.382--2.167, $\beta=-0.300$, $t=-2.241$, $p=0.030$); parents whose child had no hospitalisation due to diabetic ketoacidosis reported better psychological health ($B=-17.401$, 95% CI=-34.762--0.041, $\beta=-0.272$, $t=-2.021$, $p=0.049$); and parents whose monthly household income was HK\$20,000 or above reported better overall QoL ($B=0.739$, 95% CI=0.382-1.096, $\beta=0.571$, $t=4.179$, $p<0.001$).

Conclusions: The study contributes to knowledge on parental QoL among children with T1D receiving insulin treatment. Findings suggest that it is important to attend to the unmet healthcare needs of parents caring for children with T1D and to develop supportive interventions to best meet their needs in order to improve QoL, and ultimately, health outcomes of children with T1D in Hong Kong.

Ab36 Theme: Cardiovascular**Association of Apolipoprotein E Gene Polymorphism with Cardiovascular Diseases in Patients on Long-Term Hemodialysis**

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Background: Cardiovascular diseases (CVDs) are the leading cause of death of patients with chronic renal failure. Apolipoprotein E plays an important role in the homeostasis of cholesterol and triglycerides.

Objective: We aimed to investigate the possible link(s) between apoE gene polymorphism and cardiovascular diseases in hemodialysis patients.

Methods: We studied 109 end-stage renal disease (ESRD) patients and 97 controls. The serum lipids, apolipoproteins (apo), lipoprotein particles, high-sensitivity C-reactive protein (hs-CRP), and total homocysteine (t-Hcy) levels and paraoxonase (PON) activity were determined in our patients. We also analyzed apoE gene polymorphism in the patients and controls.

Results: The analysis of the apoE genotype and allele frequencies showed significantly higher e4 allele and E3E4 genotype frequencies and decreased e3 allele and E3E3 genotype frequencies in the patients compared with the controls. The e2, e4, and E3E4 carriers within the ESRD patient population presented an atherogenic lipid profile. 38.53% had cardiovascular diseases, especially the left ventricular hypertrophy (22.94%), angor (7.34%) and the myocardial infarction (5.50%). When compared with the controls, ESRD patients with cardiovascular diseases had lower frequency of e3 allele (OR=2.23, $p=0.025$) and higher frequency of e4 allele (OR=0.244, $p<0.001$). These ESRD patients also showed lower frequency of E3E3 genotype (OR=2.128, $p=0.033$) and higher frequency of E3E4 genotype (OR=0.338, $p=0.006$).

Conclusions: Our findings suggest an association between the e4 allele, E3E4 genotype and cardiovascular diseases. The apoE polymorphism affects the serum lipoprotein levels and the ESRD patients who are e4 and e2 allele carriers are more likely to present an atherogenic lipoprotein profile that may be a major factor associated with increased risk of CVD.

Ab46 Theme: Cardiovascular**Association of ECG Abnormalities with Metabolic Syndrome and Socio-Demographic Factors in The Philippine LIFECARE Cohort**

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Purpose of the Study: To determine the prevalence of various electrocardiogram (ECG) abnormalities among apparently healthy adult Filipinos in the Life Course Study in Cardiovascular Disease Epidemiology (LIFECARE) Study and correlate it to metabolic syndrome, its components, and socio-demographic factors

Methods: ECG of the 3072 participants in the LIFECARE cohort recruited from both rural and urban areas in Metro Manila and four provinces were read by a cardiologist. ECG abnormalities were interpreted and correlated with metabolic syndrome, its components, and socio-demographic factors. Quantitative and qualitative data are presented as mean, standard deviation, and proportion. Two-tailed hypothesis testing with alpha of 0.05 and 95% confidence interval was performed.

Summary of the Results: Overall, ECG abnormalities were seen in 54.04% of the study participants. Most of these abnormalities were ST-T wave abnormalities (31.90%), rhythm abnormalities (16.18%), and morphological abnormalities (9.77%).

The five most common specific ECG abnormalities are (i) non-specific ST-T wave changes (29.26%), (ii) sinus bradycardia (12.96%), (iii) left ventricular hypertrophy or LVH (8.59 %), (iv) intraventricular conduction delay (3.91%), and (v) sinus tachycardia (1.86%).

ECG abnormalities were more prevalent among males (67.27%, $p<0.0001$). Rhythm (25.21%, $p<.0001$), conduction (10.08%, $p<.0001$), morphological (18%, $p<.0001$), axis abnormalities (2.71%, $p<.05$), LVH (17%, $p<.0001$), and ischemic ECG changes (2.86%, $p<.0001$) were likewise more prevalent in males.

Furthermore, ECG abnormalities were significantly associated with current smokers (66.08%, $p<.0001$), metabolic syndrome (57.56%, $p<.05$), impaired fasting glucose (58.35%, $p<.01$), high blood pressure (69.57%, $p<.0001$), hypertriglyceridemia (58.07%, $p<.01$), and optimal waist circumference (55.03%, $p<.05$). No significant correlation was seen between ECG abnormalities and age, family history of heart disease, place of residence, total cholesterol, LDL, HDL, and BMI.

Conclusion: ECG abnormalities are common among males and current smokers in the Philippine LIFECARE cohort. It is significantly associated with metabolic syndrome, impaired fasting glucose, high blood pressure, hypertriglyceridemia, and optimal waist circumference.

Ab49 Theme: Cardiovascular**Takayasu Arteritis in A Pregnant Patient Masquerading as Severe Pre-Eclampsia: a Case Report**

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Synopsis: Takayasu arteritis is a rare inflammatory vasculitis that commonly affects women of childbearing age. Most patients are pulseless, but hypertension has been reported in previous series especially if there is concomitant renal artery stenosis. We present a case of a young pregnant patient manifesting as a hypertensive emergency initially managed as severe pre-eclampsia. Post-caesarean delivery, worsening blood pressure control and overall clinical status led to a diagnosis of Takayasu arteritis. She was discharged improved with anti-hypertensives and immunosuppressants.

The Case: A 29 year old G1P0 on her 35th week of pregnancy sought consult for headache. Blood pressure on her right arm was 200/100 mmHg. Initially managed as pre-eclampsia and an emergency cesarean section was done. Post delivery, blood pressure did not improve and symptoms worsened. Another secondary cause of hypertension was suspected. Further examination revealed a blood pressure of 190-210/120 on her right upper extremity, 150-160 / 80-90 on her left upper extremity and both lower extremities. Pulses on her left brachial and radial pulse were diminished. Electrocardiogram was suggestive of an old septal wall infarction. Echocardiogram showed concentric left ventricular hypertrophy with good systolic function. Cranial CT showed chronic lacunar infarcts. Takayasu arteritis was confirmed by a CT aortogram which revealed multiple areas of stenosis (left sub-clavian, superior mesenteric, and both renal arteries). She was started on prednisone and intravenous then oral antihypertensives. She was discharged improved on the 16th hospital day.

Significance and Conclusion: This case highlights that clinical history and physical examination are still the best tools in diagnosis, supported by ancillary tests. Because of the rarity of this combination, management was a challenge. Early recognition, a multidisciplinary team, and optimal medical management were the keys to a successful outcome.

Ab52 Theme: Atherosclerosis**Apolipoprotein E Polymorphism and Risk of Coronary Artery Disease: A Moroccan Case-Control Study**

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Background: Coronary artery disease (CAD) is the most common cardiovascular disorder in the general population. The association between ApoE gene polymorphism and the risk of CAD remains inconsistent.

Objective: We investigated for the first time in the Moroccan population the relationship between lipids, lipoproteins, apolipoprotein E genotyping, and the progression of coronary atherosclerosis.

Methods: Plasma total cholesterol, triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol, apolipoproteins AI and B were measured in 58 Moroccan adults aged of 54 ± 9 years, who suffered from myocardial infarction. The results were compared with the healthy controls (n=50) matched for age and sex. In parallel, apolipoprotein E genotypes were determined in both groups.

Results: Plasma total cholesterol and triglycerides levels of patients did not differ significantly from those of control subjects. Patients had higher plasma LDL-cholesterol ($p < 0.05$) and apolipoprotein B ($p < 0.005$). However, Plasma HDL-cholesterol ($p < 0.05$) and apolipoprotein AI ($p < 0.001$) were decreased in the patients compared with the controls. E2, E3 and E4 allele frequencies were 10.7%, 71.3% and 18% respectively in the coronary artery disease patients and were 11%, 83% and 6% in the healthy subjects respectively. The allele frequency of apolipoprotein E4 in the patient group was significantly higher than that in the control group (18% vs. 6%; $P = 0.007$), odds ratio = 4.614 (95% CI: 1.263-16.863; $P = 0.021$).

Conclusions: The present study demonstrate the relationship between apolipoprotein E polymorphism and coronary artery disease. E4/E4 genotype is associated with disturbed lipid profile in coronary artery disease patients. Our findings demonstrate that ApoE4 is a risk factor associated with myocardial infarction among the Moroccan population.

Ab54 Theme: Obesity**Plasma Proprotein Convertase Subtilisin/Kexin Type 9 is Associated with Apolipoprotein B-48 Catabolism in Obese Subjects**

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Purpose of the Study: Postprandial lipemia, due to elevated plasma apolipoprotein (apo) B-48 concentrations, contributes to increased risk of cardiovascular disease in obesity. Proprotein convertase subtilisin/kexin type 9 (PCSK9) may play a role in regulating chylomicron metabolism. We investigated the association between plasma PCSK9 concentration and apoB-48 metabolism in obese subjects.

Methods: Seventeen subjects (9 men and 8 women, age 59 ± 6 yrs, waist circumference ≥ 94 cm for men and ≥ 80 cm for women) were given an oral fat load. ApoB-48 tracer/tracee ratios were measured after intravenous d_3 -leucine administration using gas chromatography-mass spectrometry. Kinetic parameters, including fractional catabolic rate (FCR) and secretion rate (SR), were derived using a multi-compartmental model. Fasting and postprandial plasma apoB-48 and PCSK9 concentrations were determined using immunoassays. Plasma total and incremental triglyceride and apoB-48 area-under-the-curves (0-24 hr AUCs) were also determined.

Summary of the Results: Plasma PCSK9 concentration was significantly correlated ($P < 0.05$ in all) with AUCs for plasma triglycerides and apoB-48 ($r = 0.577$ and $r = 0.587$, respectively), incremental AUC for plasma apoB-48 ($r = 0.668$), and inversely correlated with apoB-48 FCR ($r = -0.589$). Plasma PCSK9 was not significantly correlated with basal apoB-48 secretion rate or number of apoB-48-containing particles secreted over the postprandial period. Plasma apoC-III concentration was inversely correlated apoB-48 FCR ($r = -0.597$, $P < 0.05$). The association between plasma PCSK9 and apoB-48 FCR remained significant ($P < 0.05$ in all) after adjusting for age ($r = -0.567$), HOMA score ($r = -0.575$) or energy intake ($r = -0.583$). However, the significant correlation between apoB-48 FCR and plasma PCSK9 concentrations was lost after adjusting for apoC-III concentration ($r = -0.217$, $P > 0.05$).

Conclusions: In obese individuals, variation in plasma PCSK9 concentration may influence the catabolism of apoB-48. Inhibition of PCSK9 offers a new therapy for regulating postprandial dyslipidemia in obesity.

Ab70 Theme: Atherosclerosis**Critical Limb Ischemia in The Setting of Polycythemia Vera in A Sixty-Three Year Old Male**

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We present a case of a 63 year old male with a non-healing wound of the right foot. He presented with a two-month history of claudication and progressive swelling, pain, cyanosis of 4th toe of the right foot which eventually progressed to gangrene and spread to involve the second to the fifth. This prompted consult to our institution.

The patient came in with stable vital signs and unremarkable physical exam findings of the head, neck, chest and lungs. Examination of the extremities revealed atrophy of bilateral calf and thigh muscles with dry gangrene of the second to fifth toes in the right foot. Pulses of in the brachial, radial, femoral and popliteal arteries were full and equal; however there was no appreciable pulse in the dorsalis pedis and posterior tibial artery areas of the right lower extremity. Ankle brachial index (ABI) of the left was 0.9. There was no Doppler signal detected on the right lower extremity.

Peripheral angiography was done revealing 70% focal stenosis of the common iliac and 70% tubular stenosis of the common iliac to external iliac artery right with totally occluded distal third of anterior tibial and posterior tibial artery. Serial complete blood count revealed consistently elevated counts of three cell lines (erythrocytosis, leucocytosis, thrombocytosis). Holoabdominal ultrasound showed splenomegaly with prominent portal vein and splenic vein. Erythropoietin level was low at 2.35 mIU/mL and JAK 2 was positive.

Patient was diagnosed with critical limb ischemia of the right lower extremity and chronic myeloproliferative disorder and polycythemia vera. Recommendation for this patient was revascularization via PTCA of the bilateral common iliac artery. Peripheral arterial disease (PAD) is a disorder that obstructs the blood supply to the lower or upper extremities and is most commonly caused by traditional risk factors such as atherosclerosis. In rare cases it may occur without the identified well-known risk factors and result from abnormal rheology and accelerated atherosclerosis in patients with hematologic disorders.

Ab71 Theme: Cardiovascular**Acquired Arteriovenous Fistula of The Right Common Iliac Artery and Left Common Iliac Vein and Bilateral Lower Extremity Deep Venous Thrombosis in A Woman Presenting as High Output Heart Failure**

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Clinical Presentation: A 36-year old female presented with complaints of shortness of breath. Eighteen years prior to consult, she sustained a gunshot wound through the abdomen for which she underwent surgery. Over the years, she had been experiencing progressive exertional dyspnea, abdominal enlargement and lower extremity edema with decreasing functional capacity. She came in cardiorespiratory distress, with neck vein engorgement and crackles with an enlarged abdomen associated continuous abdominal bruit.

Labs: Echocardiogram showed left ventricular hypertrophy with preserved ejection fraction, dilated right atrium and ventricle, tricuspid regurgitation, severe pulmonary hypertension. CT-aortogram showed arteriovenous fistula of the right common iliac artery and left common iliac vein with extensive collateralization, aneurysmal dilatation of the right common iliac artery and severe fusiform ectasia of the left common iliac vein. A metallic structure was lodged at the left sacroiliac joint suggesting a post-traumatic etiology probably a bullet slug. Bilateral lower extremity venous duplex showed right lower extremity DVT of common and superficial femoral vein, and left lower extremity DVT Iliac vein.

Diagnosis: The final diagnosis was congestive heart failure functional class III from high output heart failure secondary to ilioiliac fistula, right common iliac artery aneurysm and bilateral lower extremity DVT.

Treatment And Outcome: CHF was treated with diuretics, and beta blockers which remarkably resolved the symptoms. Anticoagulation was also given for DVT. Surgical repair was advised however the patient declined and was discharged with maximal heart failure medications and oral anticoagulation.

Significance And Recommendations: The case described here is an example of progressively deteriorating hyperdynamic heart failure due to the chronic, sustained volume overload caused by a traumatic AVF with associated DVT. It is a testament on how effectively the body can adapt to unusual stresses and function to a degree, before eventually succumbing to the complications and hemodynamic strain.

Ab75 Theme: Cardiovascular**When Stemi Is Not Stemi HIV Myocarditis Mimicking St-Elevation Myocardial Infarction on Electrocardiogram: A Case Report**

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Synopsis: Myocarditis is a common occurrence among human immunodeficiency virus (HIV) infected patients, which either resolves spontaneously or results in death. Anecdotal reports have shown that myocarditis can mimic acute myocardial infarction with chest pain and electrocardiographic (ECG) abnormalities. We present a case of HIV myocarditis unusually presenting with transient ST-segment elevations and cardiogenic shock.

Case Presentation: A 42 year old male sought consult for dyspnea and recurrent pneumonia for 4 months associated with weight loss and febrile episodes. HIV testing on admission was positive and he was managed as a case of pneumocystis pneumonia. Electrocardiogram (ECG) suggested left ventricular hypertrophy (LVH) with Q-waves in lead V1-V3. Troponin-I at this time was normal. Co- On the fourth hospital day, he was referred for worsening dyspnea and desaturations. He had a blood pressure of 170/100 mmHg, crackles all over, distended neck veins, and an S3 gallop. Electrocardiogram showed ST segment elevations on the anteroapical wall. Assessment at this time was an ST elevation myocardial infarction (STEMI), but management was limited due to gastrointestinal bleeding. Serial troponin-I was taken at baseline, at 12 hours, and at 24 hours after the onset of ST elevation, and none were significantly elevated. Echocardiogram showed a depressed ejection fraction with global hypokinesia. Because of the fulminant heart failure, transient ST elevation on ECG, troponin-I values that were not significantly elevated, and typical echocardiogram findings, an assessment of HIV myocarditis was made. He was managed supportively for the fulminant heart failure. Coronary angiography with possible revascularization was offered to rule out an MI, but no consent was given. Three days after, he went into sudden cardiac arrest leading to his demise.

Significance and Recommendation: This report highlights that not all ST elevations are due to an ACS. In a relatively young male with paucity of risk factors, fulminant myocarditis must be considered, especially if acute heart failure occurs on a background of a viral infection, such as HIV. Judicious work up and a high index of suspicion for this entity will avoid unnecessary treatment that may even be detrimental to the patient.

Ab80 Theme: Atherosclerosis**Clinical Characteristics of Large-Artery Atherosclerotic Stroke according to Age**

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Purpose: Atherosclerosis is the most common mechanism of ischemic stroke. The aim of our study was investigate the clinical characteristics of large-artery atherosclerotic stroke according to age.**Methods:** Among 1118 consecutive patients with acute ischemic stroke, who were admitted within 7 days of the onset, 413 patients, belonged to large-artery atherosclerosis according to the Trial of Org 10172 in Acute Stroke Treatment classification, were enrolled. Demographics, atherosclerosis patterns, and stroke patterns were analyzed according to the age groups of <50, 50-59, 60-69, 70-79, and ≥80.**Results:** Twenty six patients belonged to the age group of <50, 74 to the age group of 50-59, 135 to the age group of 60-69, 148 to the age group of 70-79, and 30 to the age group of ≥80. Hypertension and current non-smokers were more prevalent in older age groups ($p<0.05$). In baseline blood laboratories, white blood cell count was lower and erythrocyte sedimentation rate was higher in older age groups ($p<0.05$). More than 80% of the youngest and oldest age group had atherosclerotic stenotic lesions in only intracranial arteries. In comparison, more than 40% of the other groups had atherosclerotic stenotic lesions in extracranial arteries.**Conclusions:** There were several distinctions of large-artery atherosclerotic stroke among the different age groups.**Ab81 Theme: Diabetes****Early Gene-Diet Interaction between Glucokinase Regulatory Protein (GCKR) Polymorphism, Vegetable and Fish Intakes in Modulating Triglyceride Levels in Healthy Adolescents**Claudia H.T. Tam¹, Ying Wang¹, Heung Man Lee¹, Andrea O.Y. Luk^{1,4}, Peter C.Y. Tong^{1,3,4}, Michael H.M. Chan⁵, Risa Ozaki^{1,4}, Alice P.S. Kong^{1,4}, Wing Yee So^{1,3,4}, Juliana C.N. Chan^{1,4} and Ronald C.W. Ma^{1,4}¹Department of Medicine and Therapeutics, The Chinese University of Hong Kong (CUHK), Prince of Wales Hospital (PWH), Hong Kong²Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong³Hong Kong Institute of Diabetes and Obesity, The Chinese University of Hong Kong⁴CUHK-PWH International Diabetes Federation (IDF) Centre of Education, Hong Kong⁵Department of Chemical Pathology, Prince of Wales Hospital, The Chinese University of Hong Kong**Background:** The benefits of dietary vegetable and fish consumptions on improving glucose and lipid metabolism have been well established. Recently, the T-allele of a common genetic variant rs780094 at glucokinase regulatory protein (GCKR) was reported to be associated with elevated triglyceride (TG) levels but reduced fasting plasma glucose (FPG) and type 2 diabetes (T2D) risk.**Objectives:** In this study, we aimed to investigate the role of habitual dietary intakes of vegetable and fish in modulating the genetic effects of the rs780094 polymorphism on cardiometabolic traits.**Design:** A cohort of 2,095 Chinese adolescents (mean age 15.6 ± 2.0 years, 45.3% male) recruited from a population-based school survey for cardiovascular risk factor assessment, with dietary data including weekly vegetable and fish consumptions as well as clinical data were genotyped for the GCKR rs780094 polymorphism.**Results:** In the linear regression analysis with adjustment for sex, age, body mass index, and socioeconomic status (school banding, paternal and maternal education levels), the frequency of vegetable intake per week was inversely associated with FPG ($P=0.044$). Individuals with low fish intake generally had elevated TG levels but reduced TC, HDL-C and LDL-C ($0.006 < P < 0.029$). We also observed significant associations of the minor T-allele of GCKR rs780094 with decreased FPG ($P=0.013$) and increased TG levels ($P=2.7 \times 10^{-8}$). There were significant gene-diet interaction effects in elevating TG levels, with TT carriers who took ≤ 3 fish meals weekly having the highest TG level ($P=0.031$) while CC carriers with ≥ 7 vegetable meals weekly having the lowest TG level ($P=0.009$).**Conclusions:** In summary, we noted early beneficial effects of vegetable and fish intakes on triglyceride levels, particularly in genetically predisposed individuals.

Ab82 Theme: Diabetes**The Pre-Post Comparison of Patient Outcomes of A Structured Education Programme on Insulin Initiation among Patients with Type 2 Diabetes Attending General Out-Patient Clinics of New Territories East Cluster: Baseline Findings**

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Purpose of the Study: This paper presents baseline findings of a pilot study that examines the impact of a structured education programme on insulin initiation on patient outcomes.

Methods: The study adopts a one-group pretest-posttest design, with the 14-week education programme (4 sessions) as the test. The programme took place in four General Out-Patient Clinics (GOPCs) of New-Territories East Cluster. Adult Chinese patients with type 2 diabetes who required insulin initiation were recruited using convenience sampling method. The following patient outcomes were assessed using a self-administered pre-posttest questionnaire.

1. Diabetes knowledge, measured by the Diabetes Knowledge Scale (range, 0-18).
2. Engagement to diabetes-related self-management activities, measured by the Summary of Diabetes Self Care Activities Questionnaire (SDSCA).
3. Quality of life, measured by the EQ-5D.
4. Self-perceived anxiety level (range, 0-50) related to insulin therapy: mastering injection technique, injection, inconvenience, social stigma, and feelings of failure in the past effort in glycemic control.
5. Glycaemic control, measured by glycated haemoglobin (HbA_{1c}) retrieved from patient record.

Summary of the Results: The sample's (n=39) characteristics included: mean age, 58 years (SD, 8.6); mean diabetes history, 10.9 years (SD, 5.8); 51.3% had achieved secondary or above education. The baseline (pretest) data included: mean Diabetes Knowledge, 13 (SD, 3); mean EQ-5D-VAS, 67 (SD, 15.6); mean HbA_{1c}, 8.9% (SD, 1.5); 44% of the sample obtained self-perceived anxiety level related to insulin therapy ≥ 25 ; SDSCA -23% (diet and exercise), 31% (SMBG) and 56% (hypo-glycemic management) of the sample did not engage in self-care activities.

Conclusion: The education programme was well received and collection of posttest data is in progress. It is envisaged that the pre-post comparison findings will provide empirical information to further refine the programme with a view to strengthening the support to GOPC patients requiring insulin initiation and in turn better patient outcomes.

Ab86 Theme: Cardiovascular**Pharmacokinetics of Fixed-Dose Combinations (FDC) of Enteric-Coated (EC) Acetylsalicylic Acid (ASA) and Enteric-Coated Pantoprazole (PP) Versus Concurrent Administration Of Individual Products: Two Comparative Bioavailability Studies (Fed And Fasted Conditions) - Randomized, Open-Label, Single-Dose, Three-Period, Three-Treatment, Six-Sequence, Crossover In Healthy Subjects**

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Background/Purpose of The Study: Clinical guidelines recommend daily use of low-dose ASA to reduce the risks of cardiovascular (CV) events in patients with CV disease. However, long-term daily ASA is associated with an increased risk of bleeding, especially in the gastrointestinal (GI) tract. Clinical guidelines recommend pantoprazole (PP) and other proton pump inhibitors (PPIs) for the treatment and prevention of ASA-associated GI injury. Combining both drugs in a FDC would increase patient compliance, and reduce prescriptions and co-payer fees. The purpose of the GSK-sponsored studies was to identify a bioequivalent ASA EC 100 mg/PP EC 20 mg FDC formulation.

Methods: Two comparative bioavailability single-dose crossover studies in healthy subjects (n=24/study) under fed [NCT01847417] and fasted [NCT01847404] conditions. The treatments were EC ASA tablet /EC PP pellets in a capsule (FDC1), EC ASA/EC PP tablets in a capsule (FDC 2), and individual reference drugs administered simultaneously. The safety and tolerability of each treatment were also evaluated.

Results and Discussion: The bioequivalence acceptance criterion was 90% confidence interval (CI) for the ratio of the geometric means for C_{max} and AUC_{0-t} to lie within 80%-125%. Neither ASA formulation met the criteria under fed or fasted conditions. The PP pellet formulation also failed to meet the criteria and the PP tablet formulation met the criteria only under fasted conditions. Significant intra subject variability for ASA with RSD >90% for C_{max} and >60% for AUC. The ASA 90% CI (C_{max} & AUC_{0-t}) ranged from 93%-321% under fasted conditions and 67%-190% under fed conditions. This high variability could be attributable to i) differences in gastric emptying time, ii) short half life of ASA and iii) lack of IVIVC. No adverse events were reported by subjects participating in either study.

Conclusion: Test FDC formulations failed to meet bioequivalency criteria under fed and fasted conditions. Formulation modifications, along with study design improvement, need to be taken into consideration to develop a bioequivalent FDC product.

Ab94 Theme: Cardiovascular**“Double Trouble” Wolff Parkinson White Syndrome and Mitral Stenosis Presenting as a Stroke in the Young**

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Synopsis: The Wolff Parkinson White syndrome and mitral stenosis (MS) is a rare combination, with less than 15 patients reported in literature. They are individually associated with supraventricular arrhythmias and their combination may have profound hemodynamic consequences. Our case is a young male presenting with neurologic deficits who was newly diagnosed with the WPW syndrome and mitral stenosis.

Case: A 25 year old male sought consult syncope. He manifested with occasional palpitations and dizziness in the past. On the day of admission, he experienced persistent palpitations then subsequently lost consciousness. On examination, he had right sided hemiparesis and dysarthria. A cranial CT scan revealed an infarct at the left basal ganglia. Because of an early diastolic murmur, he was referred to our service for co-management. Electrocardiogram showed sinus rhythm and left atrial enlargement, a short PR interval, wide QRS complexes, and delta waves. Holter monitoring showed episodes of atrial flutter with rapid ventricular rates. QRS complexes were narrow during other episodes of tachycardia. Echocardiogram revealed moderate mitral stenosis and a dilated LA with no evidence of thrombus formation. Diagnosis was WPW syndrome and rheumatic MS manifesting as a stroke in the young.

Management and Outcome: Percutaneous transvenous mitral commissurotomy (PTMC) was done for the MS and amiodarone was given for the WPW syndrome, with consideration for radiofrequency ablation. He is now on regular follow up at our clinics on chronic anticoagulation and medical therapy for the WPW syndrome.

Conclusion: To our knowledge, this is the first case of a WPW syndrome with rheumatic MS presenting as a stroke in the young who was successfully managed with PTMC for MS and anti-arrhythmics for the WPW syndrome. This unfortunate combination may have potentiated the risk for cardioembolic events which emphasizes that detection of these entities is of paramount importance. Though either of the two entities may have caused the stroke, treatment is warranted for both entities as to avoid future episodes of cardioembolic phenomena.

Ab101 Theme: Cardiovascular**Intake of Green Tea Extract Reduced Systemic Exposure to Rosuvastatin in Healthy Chinese Male Volunteers**

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Background: Recent studies have shown that the green tea catechins and soy flavonoids may modulate various drug metabolizing enzymes and drug transporters. The present study examined whether green tea extract and soy isoflavones affect the pharmacokinetics of rosuvastatin, a substrate for the ATP-binding cassette G2 (ABCG2) transporter, in healthy subjects and whether these interactions are influenced by the ABCG2 421C>A polymorphism.

Methods: In this open-label, single-dose, three-phase fixed-order design study, 20 healthy male volunteers, who were selected based on their ABCG2 421 C>A genotype (6 CC, 8 CA, 6 AA), were given rosuvastatin 10 mg on 3 occasions: 1. without herbs; 2. with green tea extract; 3. with soy isoflavone extract with a washout period of at least 4 weeks between phases. The green tea and soy isoflavone extract were given at doses containing epigallocatechin gallate (EGCG) 800 mg once daily or isoflavones 120 mg once daily for 14 days before statin dosing. Plasma concentrations of rosuvastatin were measured up to 24 hours after the dose.

Results: Intake of green tea extract significantly reduced the systemic exposure to rosuvastatin by nearly one third (mean AUC_{0-24h} reduced from 120.2 µg·h/L to 85.0 µg·h/L; mean C_{max} from 14.8 µg/L to 9.3 µg/L, $P < 0.001$ for both) without affecting the elimination half-life ($t_{1/2}$) in the 20 healthy subjects. Reduction in systemic exposure to rosuvastatin with EGCG was observed in 17 out of 20 subjects. The soy isoflavones had no significant effect on the pharmacokinetics of rosuvastatin. This pharmacokinetic interaction between the green tea extract and rosuvastatin was not affected by the ABCG2 421C>A polymorphism.

Conclusion: This study showed that green tea extract reduces the systemic exposure and the peak plasma concentration of rosuvastatin by approximately 30% in healthy volunteers. This may be related to an inhibitory effect of EGCG on the intestinal uptake transporters and this mechanism and the overall effects warrant further investigation.

Ab102 Theme: Cardiovascular**Effect of Green Tea Extract and Soy Isoflavones on The Pharmacokinetics of Simvastatin In Healthy Chinese Male Volunteers**

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Background: Certain herbs/foods which interfere with statin metabolism or transport may be associated with increased risk of myopathy or altered statin efficacy. A recent case report revealed that consumption of green tea was associated with increased plasma simvastatin concentration and simvastatin-induced myopathy. The present study examined whether green tea extract and soy isoflavones affect the pharmacokinetics of simvastatin in healthy subjects.

Methods: In this open-label, single-dose, three-phase fixed-order design study, 18 healthy male volunteers, who were selected based on their *SLCO1B1* 521 T>C genotype (6 TT, 8 TC, 4 CC), were given simvastatin 10 mg on 3 occasions: 1. without herbs; 2. with green tea extract; 3. with soy isoflavone extract with a washout period of at least 4 weeks between phases. The green tea and soy isoflavone extract were given at doses containing epigallocatechin gallate (EGCG) 800 mg once daily or isoflavones 120 mg once daily for 14 days before statin dosing. Plasma concentrations of simvastatin acid and lactone were measured up to 24 hours after the dose.

Results: In the 18 healthy Chinese male volunteers (mean ($\pm$ SD) age: 26.6 $\pm$ 6.0 years; body weight: 61.7 $\pm$ 6.3 kg), intake of green tea extract had no effect on the average pharmacokinetic parameters for simvastatin or simvastatin acid. However, intake of soy isoflavones significantly reduced the systemic exposure to simvastatin acid, but not the lactone, by 25%. Further analysis showed that the green tea extract and soy isoflavones reduced the systemic exposure to simvastatin only in subjects with the 521TT genotype but not in those with the 521C variant allele.

Conclusion: This study showed that green tea and soy isoflavones may reduce the systemic exposure of simvastatin in subjects with the *SLCO1B1* 521 TT genotype. Future studies with large sample size are warranted to verify this result and to investigate the underlying mechanisms.

Ab112 Theme: Cardiovascular Disease**A Tale of Two Cities: Comparing the Knowledge of Metabolic Syndrome in the Risk Populations in Hong Kong and Xian, China**

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Purpose of the Study: This study aimed to understand and compare the knowledge level of metabolic syndrome (MetS) among risk populations in Hong Kong (HK) and China.

Methods: A cross-sectional comparison study was conducted. Adults aged ≤ 65 years and with $\geq$ one MetS risk factor were recruited from HK and Xian, China. The knowledge level was assessed by the 10-item Metabolic Syndrome Knowledge Scale (MSKS). Demographic information, anthropometric data and clinical indicators of MetS were collected.

Summary of the Results: The study recruited 167 participants from HK and 158 participants from Xian, China, with the mean age of 49.4 (SD=9.4) years and 54.5 (SD=7.6) years respectively. Most participants (HK: 88.6% and China: 84.9%) had secondary or above education. Participants' mean body mass index were 25.6 (SD=3.6) and 24.4 (SD=3.3) for HK and China, respectively. A total of 175 participants met the criteria of MetS, including 90 (53.89%) in HK and 85 (53.80%) in China. The total score of MSKS in HK was higher than that in China (44.4 vs. 35.8, out of 100, $p < 0.001$). Though HK had a higher score in the subscale of definition and diagnostic criteria (15.4 vs 4.9, out of 50, $p < 0.001$), both cohorts performed poorly in this subscale. HK had higher scores in the subscale of complications (12.7 vs 8.7, out of 20, $p < 0.001$), but lower in prevention and management (16.3 vs. 22.2, out of 30, $p < 0.001$). People with higher educational levels had higher scores in MSKS ($p < 0.001$).

Conclusions: Though the knowledge level of MetS was consistently low in both cities, participants in HK performed better than those in China. Health education on MetS is urgently needed in both cities, especially in Xian, China. Future MetS education for the risk populations should focus on definition and diagnostic criteria, especially in those less educated.

Ab117 Theme: Diabetes**Serum Phospholipid Monounsaturated Fatty Acid Compositions and Delta-9-Desaturase Activity are Associated with Fasting Glycemic Status**Seung Han Baek¹, So Ra Yoon², Jae Hyang Lee² and Oh Yoen Kim²¹Department of Systems Biology, College of Life Science and Biotechnology, Yonsei University, Seoul, Republic of Korea²Departement of Food Science and Nutrition, Dong-A University, Brain Busan 21 project, Busan, Republic of Korea

Purpose of the Study: Blood and dietary fatty acid (FA) compositions are associated with insulin resistance and related metabolic disorder. However, few studies reported the association of serum phospholipid FA compositions with the early alteration of fasting glycemic status. Therefore, we investigated if serum phospholipid FA composition would reflect the early alteration of fasting glycemic status even in people without metabolic syndrome (MetS).

Methods: Serum phospholipid FAs, desaturase activities, fasting glycemic status and cardiometabolic parameters were measured in study participants ($n=1022$, 30-69yrs, male: $n=527$, female: $n=495$; non-diabetic, without disease), stratified into normal fasting glucose (NFG) and impaired fasting glucose (IFG) groups.

Summary of the Results: Total monounsaturated FAs (MUFAs), oleic acid (OA;18:1n-9), dihomo- γ -linolenic acid (DGLA;20:3n-6), delta-9-desaturase activity (D9D;18:1n-9/18:0) and DGLA/linoleic acid (LA) (20:3n-6/18:2n-6) in serum phospholipids were significantly higher in IFG subjects than NFG controls. Study subjects were subdivided into four groups based on fasting glucose levels and MetS status. Palmitoleic acid (16:1n-7) was highest in IFG-MetS and lowest in NFG-non-MetS subjects. OA and D9D were higher in IFG-MetS than in the other three groups. DGLA and DGLA/LA were higher in MetS than in nonMetS regardless of fasting glucose levels. The hs-CRPs and 8-epi-PFG_{2a} were higher in IFG than in NFG regardless of MetS status. Oxidized-LDLs were higher in IFG-MetS than in the other three groups. Total MUFAs, OA and D9D were positively correlated with HOMA-IR, fasting glucose, TG, hs-CRP and 8-epi-PFG_{2a}. Palmitoleic acid was positively correlated with TG and hs-CRP.

Conclusion: Total MUFAs, OA, palmitoleic acid and D9D were associated with early alteration of fasting glycemic status, suggesting these may be useful markers for predicting risk of type 2 diabetes and cardiometabolic diseases.

Ab121 Theme: Cardiovascular**Association between Myeloperoxidase, Serum Amyloid A Protein, and Secretory Phospholipase A2 Concentration with Proatherogenic High Density Lipoprotein in Acute Coronary Syndrome**Marita Kaniawati¹, Anwar Santoso², Irawan Yusuf³ and Syakib Bakri⁴¹Post Graduate Program Faculty of Medicine, University of Hasanuddin, Indonesia²Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Indonesia³Department of Physiology, Faculty of Medicine, University of Hasanuddin, Indonesia⁴Department of Internal Medicine, Faculty of Medicine, University of Hasanuddin, Indonesia

Purpose of the Study: High density lipoprotein (HDL) have atheroprotective effect by several mechanisms, including its role in reverse cholesterol transport and through its antiinflammatory properties. However, not all HDL is functionally similar. HDL become dysfunctional or even proinflammatory and thus promote atherosclerosis. One possibility to have HDL dysfunction or become proatherogenic is alteration in lipid and protein composition of HDL. Association between Myeloperoxidase (MPO), serum amyloid A (SAA) protein, and secretory phospholipase A2 (sPLA2) with proatherogenic HDL is not clearly understood and need further investigations.

Methods: The study recruited 52 male subjects with Acute Coronary Syndrome (ACS) and 30 healthy subjects. Concentrations of MPO, sPLA2 and SAA were measured by ELISA method. Proatherogenic HDL criteria was made by case-control study, based on ApoA-1, PON-1, Neopterin and HDL-cholesterol concentration. Levels of Apo A-1, PON-1, HDL-C and Neopterin were determined by immunoturbidimetry, EIA, homogenous and ELISA, respectively. Multiple logistic regression analysis was done using atherogenic status of HDL as dependent variables and levels of MPO, SAA, and sPLA2 as independent variables.

Summary of the Results: Patient's age was 50.89 ± 12.63 year. Univariate logistic regression analysis showed the odd ratios (OR) for ApoA-1, PON-1, Neopterin and HDL-cholesterol towards ACS respectively were 29.759 (95% CI: 4.074-217.382), 1.647 (95% CI: 0.412-6.586), 4.317 (95% CI: 1.098-16.977), 13.286 (95% CI: 3.566-49.493). In defining HDL type, ApoA-1 and HDL-cholesterol were defined as major criteria, whereas PON-1 and Neopterin were defined as minor criteria. Proatherogenic HDL type can be determined by combination of 2 major criteria, or 1 major criteria and 2 minor criteria, or 1 major criteria and 1 minor criteria. Association between MPO, SAA, and sPLA2 with proatherogenic HDL type was made by cross-sectional study. Based on multivariate logistic regression analysis using all combination of criteria, the study found that sPLA2 had the biggest OR.

Conclusions: Secretory Phospholipase A2 (sPLA2) was the best independent predictor for having proatherogenic HDL type.

Ab122 Theme: Atherosclerosis

Correlation between High Sensitivity C-Reactive Protein and Adiponectin Concentration with Oxidized LDL as A Marker Of Atherosclerosis in Metabolic Syndrome

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Purpose of the Study: The metabolic syndrome consists of a collection of risk factors or metabolic abnormalities in individual associated with insulin resistance and increase of cardiovascular risk factor and diabetes. Oxidized LDL in plasma is a biochemical marker for determining cardiovascular disease associated with atherosclerosis process of the arteries as a result of the obstruction by cholesterol deposit involving endothelial dysfunction, lipid disorder, platelet activation, thrombosis, oxidative stress, activation of vascular smooth muscle and genetic factors. The aim of the study is to determine the correlation between high sensitivity C Reactive Protein (hs-CRP) and adiponectin with oxidized LDL as marker of atherosclerosis in metabolic syndrome.

Methods: This was a cross-sectional study recruited 52 male subjects with metabolic syndrome. The hs-CRP level was measured by the sensitive immunometric assay method, and adiponectin and oxidized LDL were measured by ELISA method.

Summary of the Results: Patient's age was 44 ± 8 year, hs-CRP was 2.16 ± 1.74 mg/L, adiponectin was 3.49 ± 1.33 ng/mL, and oxidized LDL was 98 ± 28 U/L. This study showed significant positive correlation between hs-CRP and oxidized LDL ($r=0.316$; $p=0.022$), and negative correlation between adiponectin and oxidized LDL ($r=-0.177$; $p=0.046$).

Conclusions: There was significant positive correlation between hs-CRP and oxidized LDL, and negative correlation between adiponectin and oxidized LDL as a marker of atherosclerosis in male metabolic syndrome.

Ab124 Theme: Obesity

Circulating Lp-PLA2 Activity Correlates with Oxidative Stress and Cytokines in Overweight/Obese Postmenopausal Women Not Using Hormone-replacement Therapy

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Purpose: Controversy remains regarding whether there is an association between circulating lipoprotein-associated phospholipase A₂ (Lp-PLA₂), cytokines, and oxidative stress in healthy postmenopausal women.

Methods: We investigated the influence of age on Lp-PLA₂ activity in postmenopausal women not using hormone therapy, and the relationship of Lp-PLA₂ enzyme activity to serum cytokine levels and oxidative stress indices. Normal weight ($n=1284$) and overweight/obese ($n=707$) postmenopausal women not using hormone therapy were categorized into five age groups: 50-54, 55-59, 60-64, 65-69, and 70-89 years.

Results: Overweight-obese women showed higher plasma Lp-PLA₂ activity, urinary 8-epi-prostaglandin F_{2a} (8-epi-PGF_{2a}), serum interleukin (IL)-6, and smaller LDL particles than normal-weight women after adjusting for age, years post-menopause, smoking, drinking, blood pressure, glucose, insulin, lipid profiles, BMI, and waist circumference. Overweight/obese women 70-89 years old showed higher Lp-PLA₂ activity than those aged 50-54 years, whereas no significant difference in Lp-PLA₂ activity existed across normal-weight female age-groups. Overweight/obese women aged ≥ 65 years showed higher Lp-PLA₂, oxidized LDL (ox-LDL), IL-6, and 8-epi-PGF_{2a} than age-matched normal-weight controls. Overweight/obese women aged ≥ 70 years had higher ox-LDL levels than those aged 50-59, and overweight/obese women aged 65-89 showed higher IL-6 and 8-epi-PGF_{2a}. There were strong positive correlations between Lp-PLA₂ and ox-LDL ($r=0.385$, $P<0.001$), Lp-PLA₂ and IL-6 ($r=0.293$, $P<0.001$), and ox-LDL and IL-6 ($r=0.303$, $P<0.001$) in overweight/obese women; however, these relationships were weak in normal-weight women.

Conclusions: These results demonstrate enhanced oxidative- and inflammatory mediator-associated Lp-PLA₂ activity in overweight/obese postmenopausal women not using hormone therapy.

Ab125 Theme: Obesity**Three-year Mild Caloric Restriction Partially Protects against Age-related Sphingomyelin Increase and Reduces Obesity-associated Amino Acids**M Kim^{1,2}, S Jung^{1,2}, S-H Lee³ and JH Lee^{1,2,4}¹National Leading Research Laboratory of Clinical Nutrigenetics/Nutrigenomics, Department of Food and Nutrition, College of Human Ecology, Yonsei University, Seoul, Korea²Department of Food and Nutrition, Brain Korea 21 PLUS Project, College of Human Ecology, Yonsei University, Seoul, Korea³Department of Family Practice, National Health Insurance Corporation, Ilsan Hospital, Goyang, Korea⁴Yonsei University, Research Institute of Science for Aging, Yonsei University, Seoul, Korea**Purpose:** The effect of weight loss from long-term low-calorie diet (LCD) on plasma metabolites is unknown. The aim of this study was to examine whether LCD-induced weight reduction caused changes in the extended plasma metabolites.**Methods:** Overweight/obese subjects [$25 \leq$ body-mass index (BMI) $< 33 \text{ kg/m}^2$] aged 40-59 years consumed LCD (approximately 100 kcal/day deficit) or weight-maintenance diet (control) in a randomized, controlled design with three-year clinical intervention period. Plasma samples of the LCD group ($n=47$) and the control group ($n=47$) were analyzed using ultra-performance liquid chromatography—linear trap quadrupole (UPLC-LTQ)-Orbitrap mass spectrometry.**Results:** The three-year LCD intervention resulted in weight loss (-8.87%) and significant decreases in homeostasis-model assessment insulin resistance (HOMA-IR) and serum triglyceride. The three-year follow-up of the LCD group identified reductions in the following thirteen metabolites: L-leucine; L-phenylalanine; lysophosphatidylcholines (lysoPCs) containing C16:1, C16:0, C17:0, C18:2, C18:1, C18:0, C20:4, C20:3, and C22:6; phosphatidylcholine (PC) 18:0/20:4; and sphingomyelin (SM) d18:0/16:1. The three-year LCD-group follow-up identified increases in palmitic amide, oleamide, and PC (18:2/18:2). Considering age-related alterations of the identified metabolites, the LCD group showed a greater decrease in L-leucine ($q=0.008$), L-phenylalanine ($q=0.041$), and SM (d18:0/16:1) ($q=0.008$) compared to those of the control group. Overall, the change (Δ) in BMI positively correlated with Δ triglyceride, Δ HOMA-IR, Δ L-leucine ($r=0.559$, $P<0.001$), and Δ SM (d18:0/16:1) ($r=0.602$, $P<0.001$). The Δ HOMA-IR positively correlated with Δ triglyceride, Δ L-leucine ($r=0.460$, $P<0.001$), Δ L-phenylalanine ($r=0.305$, $P=0.003$), and Δ SM (d18:0/16:1).**Conclusions:** Weight loss resulting from three-year mild caloric restriction conferred protection against age-related increases in sphingomyelin and reduced the levels of obesity-associated amino acids. These changes were coupled with improved insulin resistance. (ClinicalTrials.gov: NCT02081898)**Ab126 Theme: Diabetes****The Effects of Chitosan Oligosaccharide (GO2KA1) Supplementation on Glucose Control in Subjects with Prediabetes**HY Ahn¹, HJ Kim¹, JH Kwak², DY Shin³, Y-I Kwon⁴, C-G Oh⁵ and JH Lee^{2,3,6,7}¹Interdisciplinary Course of Science for Aging, Graduate School, Yonsei University, 134 Shinchon-Dong, Seodaemun-Gu, Seoul, Republic of Korea²Research Institute of Science for Aging, Yonsei University, 134 Shinchon-Dong, Seodaemun-Gu, Seoul, Republic of Korea³Endocrinology, Department of Internal Medicine, College of Medicine, Yonsei University, 134 Shinchon-Dong, Seodaemun-Gu, Seoul, Republic of Korea⁴Department of Food and Nutrition, Hannam University, Ojeong-dong, Daedeok-gu, Daejeon, Republic of Korea⁵Kunpoong Bio Co., Ltd., Gumnung-ri, 407-11, Hallim-eup, Jeju Special Self Governing Province, Jeju, Republic of Korea⁶National Research Laboratory for Clinical Nutrigenetics/Nutrigenomics, Department of Food and Nutrition, Yonsei University, 134 Shinchon-Dong, Seodaemun-Gu, Seoul, Republic of Korea⁷Department of Food and Nutrition, Brain Korea 21 PLUS Project, College of Human Ecology, Yonsei University, Seoul, Republic of Korea**Purpose:** We aimed to evaluate the effect of GO2KA1 supplementation on glucose control in subjects with prediabetes.**Methods:** This study was randomized, double-blind, placebo-controlled clinical trial. Subjects with prediabetes were randomly assigned to the GO2KA1 intervention group or the placebo group for 12-weeks. We assessed the serum levels of glucose, insulin, and C-peptide by 2-hour value in the 75 g oral glucose tolerance test (OGTT), HbA1c, pro-inflammatory cytokines, and plasma adiponectin at baseline and after the 12-week intervention.**Results:** The treatment group showed a significant decrease in serum glucose level at 30 min ($p=0.013$) and at 60min ($p=0.028$). The change of serum glucose level at 60min was significant in the treatment group compared with the placebo group ($p=0.030$). Also, the plasma level of HbA1c ($p=0.023$) and the pro-inflammatory cytokines (IL-6 and TNF- α) were reduced and plasma adiponectin was increased in the GO2KA1 intervention group after the 12-week treatment. However, the placebo group did not show any significant changes in these biomarkers.**Conclusions:** In conclusion, the GO2KA1 supplementation may be effective for controlling serum glucose levels and postprandial glycemic response in prediabetes.

Ab127 Theme: Atherosclerosis**Associations between Metabolomic-identified Changes of Biomarkers and Arterial Stiffness in Subjects Progressing to Impaired Fasting Glucose: a Nested Case-control Study**

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Purpose: We investigated correlations between age-related changes in circulating metabolites and arterial stiffness in impaired fasting glucose.

Methods: This prospective cohort study included 602 healthy, normal fasting glucose (NFG) subjects (30-65 years old) who underwent triennial medical evaluation. After three years, 9.3% of subjects developed impaired fasting glucose (IFG group, $n=56$). Age, gender, BMI, and fasting glucose were used to match the remaining NFG subjects ($n=546$) that were included for the control group (NFG group, $n=80$).

Results: After three years, levels of fasting glucose, insulin, malondialdehyde, and brachial-ankle pulse wave velocity (baPWV), were significantly greater in the IFG group than the NFG group after adjusting for baseline values. The IFG group had a greater increase in lactosylceramide ($P=0.001$) and a greater reduction in phosphatidylcholine (PC) (18:0/20:4) than those in the NFG group. Multiple linear regression analysis showed that the change in baPWV was independently and positively associated with changes in fasting glucose and lactosylceramide. In all subjects, lactosylceramide levels positively correlated with changes in baPWV and fasting glucose, and negatively correlated with changes in PC and LDL particle size.

Conclusion: This study indicates that age-related increase in circulating lactosylceramide is an independent predictor of increased arterial stiffness in subjects with impaired fasting glucose.

Ab128 Theme: Cardiovascular**The Association between Retinal Information and Stroke Risk in Chinese Type 2 Diabetes**

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Aims: We assessed the association between retinal information (including diabetic retinopathy [DR] and retinal vascular characteristics), with the probability of first stroke attack in 5 years in a Chinese type 2 diabetes population.

Methods: In 540 individuals (239 women and 301 men) participating, we graded the presence of DR and quantified retinal vascular diameter, fractal dimension, tortuosity and bifurcation-related characteristics using a reliable semi-automatic program. The 5-year probability of stroke for Chinese type 2 diabetes was calculated using age, HbA1c, urine albumin to creatinine ratio (ACR) and history of coronary heart disease (CHD). The association between retinal information and 5-year probability of stroke was examined using stepwise multivariate linear regression.

Results: Chinese type 2 diabetes patients with DR, larger venular standard deviation of vessel widths (BSTDv) and vascular attenuation (length diameter ratio for arterioles [LDRa]) had higher risk of getting first stroke attack in 5 years. Furthermore, reduced complexity of the branching pattern (fractal dimension) and reduced optimality of the branching geometry (junctional exponent deviation for venules [JEv], asymmetry factor for arterioles [AAa]) were inversely associated with 5-year probability of stroke after multivariate adjustment. The predicted values of the model using retinal information fitted well with logarithmic 5-year probability of stroke ($r=0.525$).

Conclusion: Retinal information may provide an opportunity to evaluate the risk of stroke and identify patients with high risk of stroke in type 2 diabetes.

Ab129 Theme: Atherosclerosis**Calcium Score is More Useful in Discriminating Coronary Artery Disease in Older but Not Younger Sudden Death Autopsy Cases**

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Purpose Of Study: Coronary artery disease is the main cause of death in Malaysia. Data on the prevalence of CAD in sudden death autopsy cases in Malaysia is still lacking, as well as prevalence of young CAD in this population. Calcium scoring on Computed Tomography [CT] has been suggested to be a predictive tool for CAD evaluation; however the data on this has been conflicting. The objectives of this study are [i] to investigate the prevalence of CAD in sudden death autopsy cases as well as prevalence of young CAD cases in this population and [ii] to investigate the association between CT calcium score and presence of CAD in sudden death autopsy cases and correlating with age of CAD cases.

Methods: A total of 110 autopsy cases were recruited. The presence or absence of CAD was obtained from autopsy finding. The cases were divided into young [<40 years old] and old [≥ 40 years old] CAD groups. CT images of the heart were acquired using a multislice CT machine (Toshiba Aquilion 64 TSX-101A, Japan) and the total calcium score was measured using the Cardio Scoring software (CSCS -001A-Agatson's, Korea) on the Infinitt Monitor (PACS version 3091, Korea). The calcium scoring of the groups were compared and analyzed for statistically difference.

Results: Twenty six [23.6%] deaths were due to CAD; of these, 12 [46.2% of CAD cases; 10.9% of total cases] were young individuals. Overall, calcium score was higher in CAD than non-CAD subjects [294.8 ± 498.7 vs 30.4 ± 95.7 , $p=0.013$]. Calcium score in young CAD was lower than that of old CAD subjects [29.8 ± 67.4 vs 520.7 ± 595.7 , $p=0.009$]. In the older subjects, the calcium score is higher in those with CAD than those without [520.7 ± 595.7 vs 85.7 ± 157.2 , $p=0.018$]. In the young subjects, there was no difference in calcium score between CAD compared to non-CAD cases [29.8 ± 67.5 vs 7.0 ± 31.5 , $p=0.276$].

Conclusion: Calcium score is greater in CAD compared to non-CAD sudden death subjects. Calcium score appears to be more useful in discriminating CAD in older but not younger SD subjects.

Ab132 Theme: Atherosclerosis**HDL-C is an Independent Predictor of Svcam-1 Concentration and Negatively Correlated with Endothelial Activation**

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Purpose of Study: Soluble vascular cell adhesion molecule 1 (sVCAM-1), intercellular cell adhesion molecule 1 (sICAM-1), and E-selectin are biomarkers reflecting endothelial activation, a key event in the initiation and progression of atherosclerosis. High-density lipoprotein cholesterol (HDL-c) is protective against atherosclerosis by reverse cholesterol transport but its association with endothelial activation is not well established. This study aims to determine (a) the correlation between concentrations of HDL-c and biomarkers of endothelial activation (sVCAM-1, sICAM-1 and E-selectin), and (b) whether HDL-c concentration is an independent predictor of these biomarkers.

Methods: 422 subjects (mean age $\pm$ SD = 43.2 ± 11.9 years, 157 males and 265 females), of whom 207 had low HDL-c concentration (HDL-c <1.0 mmol/L and <1.3 mmol/L for males and females respectively) and 215 were normal HDL-c subjects (HDL-c ≥ 1.0 and ≥ 1.3 mmol/L for males and females respectively). The two groups were matched for age, gender, ethnicity, smoking status, diabetes and hypertension. Fasting blood samples were collected for biomarkers of endothelial activation (sVCAM-1, sICAM-1 and E-selectin). Pearson's correlation and multiple linear regression analyses were performed to determine the correlation between HDL-c concentration and these biomarkers and whether HDL-c is an independent predictor of the biomarkers, respectively.

Results: HDL-c concentration was negatively correlated with E-selectin and sVCAM-1 ($r = -0.15$ $p < 0.03$ and $r = -0.11$, $p < 0.005$, respectively). Multiple linear regression analysis revealed that HDL-c was an independent predictor of sVCAM-1 ($p < 0.03$) after correcting for gender, age, ethnicity, smoking status, triglyceride and low density lipoprotein cholesterol (LDL-c) concentrations, diabetes, hypertension and central obesity.

Conclusion: The negative correlation between HDL-c and biomarkers of endothelial activation, as well as being an independent predictor of sVCAM-1 suggest that low HDL-c enhances atherogenesis through endothelial activation.

Ab135 Theme: Obesity**Serum Visfatin Concentration is Elevated in Centrally Obese Subjects with and without Metabolic Syndrome**

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Purpose of Study: Metabolic syndrome (MS) encompasses multiple risk factors that increase the risk of developing atherosclerosis. Adiponectin is an atheroprotective adipokine produced exclusively by adipocytes. Visfatin, on the other hand is postulated to be an atherogenic adipokine, in which its relationship with MS is unclear. The objective of this study is to compare adiponectin and visfatin concentration in centrally obese subjects with and without MS, and normal controls.

Methods: A total of 471 subjects (157 males and 314 females, age (mean $\pm$ SD): 47.5 $\pm$ 8.3 years) were divided into 3 groups; MS, central obesity without MS (COBXMS) and normal lean controls (NC). Based on the International Diabetes Federation (IDF) 2006, MS was defined as central obesity (waist circumference $\geq$ 90 cm and $\geq$ 80 cm for males and females, respectively) plus at least 2 of 4 MS components. Fasting plasma and serum samples were collected to measure adiponectin and visfatin concentrations using enzyme-linked immunosorbent assay (e-Bioscience, Austria and Adipogen, Korea, respectively).

Results: Concentrations of adiponectin were significantly lower in MS and COBXMS groups compared to NC (mean $\pm$ SEM: 10.3 $\pm$ 0.5 mg/l and 10.5 $\pm$ 0.4 mg/l vs. 13.3 $\pm$ 0.9 mg/l, respectively, $p < 0.05$). In contrast, serum visfatin concentrations were significantly higher in both MS and COBXMS groups when compared to NC (mean $\pm$ SEM: 4.6 $\pm$ 0.3 ng/ml vs. 3.3 $\pm$ 0.3 ng/ml, $p < 0.05$; 6.2 $\pm$ 0.3 ng/ml vs. 3.3 $\pm$ 0.3 ng/ml, $p < 0.0001$, respectively).

Conclusion: Centrally obese subjects with and without MS have lower serum concentration of atheroprotective adiponectin but higher atherogenic visfatin compared to normal lean controls, suggesting that central obesity is pivotal in the pathogenesis of atherogenesis. This may contribute in part to the increased coronary risk in subjects with central obesity.

Ab139 Theme: Obesity**Weight Loss is Accelerated by Legume Consumption through the Regulation of Adiponectin and 8-Epi-Prostaglandin F₂alpha**

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Purpose of the Study: Legume consumption has shown an inverse relationship with obesity and related metabolic disorder (i.e. metabolic syndrome, diabetes and cardiovascular disease). Legumes are nutritionally recognized for their high proteins, soluble-fibers and other bioactive compounds. Particularly, bioactive components therein are of great interest, because their antioxidant capacities are involved in the regulation of oxidative stress thereby attributing to the improvement of metabolic disorder and cardiovascular risk. Therefore, we aimed to investigate if weight loss accelerated by legumes-enriched diet is accompanied by regulating oxidative stress.

Methods: Study participants [$n=383$, body mass index (BMI) ≥ 25 kg/m²] were randomly assigned to the high-fat diet (HFD) or the low-fat diet (LFD) group for 12 weeks. The HFD group was educated to replace 1/3 of refined rice with legumes as a carbohydrate source in every meals of the day (3 times/day), while the LFD group maintained their usual diet.

Summary of the Results: For 12 weeks, the HFD group consumed less amount of energy and carbohydrate and higher amount of fat and protein. However, LFD group did not show any significant differences. Mean weight loss after the intervention was 2.87 $\pm$ 0.21kg in the HFD group and 0.17 $\pm$ 0.11kg in the LFD group, which was significantly different between the groups ($P < 0.001$). The levels of HDL-cholesterol and adiponectin were increased, but those of glucose, insulin, triglyceride, homeostasis-model assessment of insulin resistance (HOMA-IR), and 8-epi-prostaglandin F₂alpha were decreased in the HFD, however, no significant changes were shown in the LFD group. In addition, BMI change was negatively correlated with the changes of HDL-cholesterol and adiponectin and positively with that of HOMA-IR.

Conclusions: Legume consumption may accelerate weight loss accompanied by regulating adiponectin and 8-epi-prostaglandin F₂alpha in obese subjects. Also, increases in plasma adiponectin induced by larger amount of weight loss may be related to greater activation of insulin.

Ab141 Theme: Obesity**The Socio-ecological View on the Barriers of Managing Childhood Obesity**

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Purpose of the Study: Childhood obesity is an epidemic health problem and becoming more prevalent. World Health Organization reports that childhood obesity has increased from 31 million to 44 million globally within twenty years. This health problem is associated with a variety of adulthood cardiovascular morbidity and mortality such as hypertension, dyslipidemia, Type 2 diabetes mellitus, and carotid artery atherosclerosis. The purpose of this study is to explore the barriers of managing childhood obesity based on socio-ecological view.

Methods: A systematic review was adopted in this study. Literature related to the topic was searched using the following databases: PubMed, ProQuest, Medline, Cinahl and Embase. Results were retrieved and analysed based on socio-ecological view.

Summary of the Results: Socio-ecological influences impacted childhood obesity. The personal level influence of lack of time was one of the major barriers on healthy eating and physical activity participation in managing childhood obesity. The childhood obesity problem was common in lower income groups reporting economic barrier in buying healthy diet. Also, children preference, habits, motivation were also highlighted. At the socio-cultural level, unhealthy family lifestyle, lack of family support with poor parent motivation and initiatives, physical inactivity lifestyle, lower educational level, and resistance in discussing the issues were reported to be the barriers on managing the children obesity problems. At the physical environmental level, the safety concerns and poor conditions around the neighbourhood environment for physical activity such as graffiti and dense residential areas were recognized as the barriers.

Conclusions: With strong evidences supporting childhood obesity leading to cardiovascular dysfunction in adulthood, effort is needed in minimizing childhood obesity. The present study reviewed the barriers in managing childhood obesity based on the socio-ecological view. Intervention programmes should consider overcoming the barriers for obesity prevention and education.

Ab143 Theme: Cardiovascular**Multiple Infections in a Filipino with Polyangiitis Overlap Syndrome**Racaza GZ, Abraham LL IV, Reyes KA and Penserga EG

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Purpose: Polyangiitis overlap syndrome (POS), a systemic vasculitis not classifiable into well-defined syndromes, is usually diagnosed from combinations of two or more vasculitides, such as Takayasu's arteritis and an ANCA-associated vasculitis (AAV), but not two AAVs. Recognizing POS is important as management delays and morbidity may result from inability to classify patients into distinct syndromes.

Method: We present a unique case of POS with features of two AAVs, aggravated by multiple infections.

Summary: A 25-year-old Filipino female presented with a six-year history of dyspnea, recurrent purpuric skin lesions and joint pains, rhinorrhea with epistaxis and hemoptysis, eye redness, and abdominal cramps. She had multiple oral ulcers, clear nasal discharge, fine bibasal crackles and polyarthrititis.

Blood tests showed anemia, eosinophilia, elevated ESR and CRP, and high c-ANCA and anti-proteinase-3 antibody titers. Radiographs exhibited mid-to-lower lung interstitial infiltrates. High-resolution CT demonstrated lower lobe ground-glass opacities, thickened dilated bronchi, and nodular densities, consistent with pulmonary vasculitis. 2D-echocardiography revealed adequate LV contractility with moderate pulmonary hypertension and mild pulmonary and tricuspid regurgitation. Rigid rhinoscopy showed chronic sinusitis. Skin biopsy revealed leukocytoclastic vasculitis without necrotizing granulomas. She had increased anti-streptolysin O titers, chronic hepatitis B serology, and grew *Pseudomonas aeruginosa* from bronchial washings and MRSA from nasal swabs.

She had characteristics of two AAVs - limited granulomatosis with polyangiitis (oronasal inflammation, pulmonary vasculitis) and Churg Strauss Syndrome (peripheral blood eosinophilia) with multiple infections. She was given NSAIDs, culture-guided antibiotics, and lamivudine for hepatitis B reactivation prophylaxis prior to low-dose prednisone, resulting in resolution of symptoms and inflammatory marker improvement after twelve weeks. Her disease remains controlled with prednisone 5 mg OD.

Conclusion: This is the first case of POS involving two AAVs. As cardiovascular specialists, we should broaden our familiarity beyond the more common larger-vessel vasculitides and realize the role infections play in perpetuating the process.

Ab145 Theme: Cardiovascular**Bilateral Renal Artery Stenosis in a Young Filipino Male with Takayasu's Arteritis**

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Purpose of the Study: Renal artery stenosis (RAS) is among the most common causes of secondary hypertension. In the younger population, the top etiologies for RAS are fibromuscular dysplasia (FMD) and Takayasu's arteritis. It is essential to arrive at the correct diagnosis, as the two entities differ in terms of management.

Methods: We present a unique case of Takayasu's arteritis in a male patient with secondary hypertension from bilateral renal artery stenosis.

Summary: A 29-year-old Filipino presented with a 2-year history of hypertension, with BP ranging from 140-160/80-90. There were nape pains and occipital headaches, but no note of fever, weight loss, night sweats, joint pains or arm/leg claudication. Physical examination was normal except for bruits in the periumbilical area.

Blood exams such as CBC, creatinine, electrolytes, thyroid function tests, and a urinalysis were all within normal limits. ESR and CRP were also normal. Left ventricular hypertrophy was noted on ECG and 2D echocardiography, with preserved overall systolic function. Renal ultrasound with Doppler studies was normal, but a magnetic resonance angiogram revealed high-grade stenosis at the ostia of bilateral renal arteries. There were two areas of aneurysmal dilatation involving the suprarenal abdominal aorta. Adrenals were normal.

The initial consideration was FMD, but the lesions' ostial location and aortic dilatation gave us a higher index of suspicion for Takayasu's arteritis. A subsequent CT aortogram clinched the diagnosis, demonstrating significant stenosis in the celiac trunk, superior mesenteric arteries and bilateral renal arteries, as well as dilatation of the inferior mesenteric artery.

His blood pressure is currently controlled with amlodipine 5 mg BID and carvedilol 25 mg BID. Steroids will be given in case of flares of activity.

Conclusions: In a young patient with renal artery stenosis, ostial lesions always warrant further investigation for Takayasu's arteritis even with a paucity of clinical symptoms.

Ab151 Theme: Cardiovascular**Homozygous Familial Hypercholesterolemia: a Case Report**

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Purposes of Study: Familial hypercholesterolemia (FH) is genetic disorder of lipid metabolism characterized by significant elevation of LDL-C level leading patient at risk to develop premature coronary artery disease (CAD). The prevalence of homozygous FH (HoFH) is rare, 1: 1000000 while heterozygous FH (HeFH) is 1:500. In Malaysia, many of them still remain undiagnosed. Thus, we report a very rare case of HoFH.

Methods: A 20 years old lady had hypercholesterolemia at 12 years old. She was relatively asymptomatic until recently when she developed dyspnea, poor effort tolerance and chest pain on exertion. She was hospitalized and diagnosed to have CAD with left main stenosis, severe triple vessel coronary artery. There is marital consanguinity between both parents. Her father and one older sister have hypercholesterolemia and premature CAD. Her mother and brother have hypercholesterolemia and on lipid-lowering medications. She is euglycemic and non-smoker.

Results: Clinically, there were bilateral corneal arcus bilateral (grade 2), tendon xanthomata at both hand, elbows, dorsum of both feet and archilles tendons. There were systolic murmur, bilateral carotid and abdominal bruit. All peripheral pulses were present. Her baseline total cholesterol, LDL, HDL and Triglycerides were 16.83, 15.46, 1.0, 0.82 mmol/L respectively. The renal profile, creatinine kinase, glucose and liver function test were normal except for mild elevation ALT 45.2 (normal <33 IU/L). Thus, based on Simon Broome Criteria, the patients diagnosed as having HoFH. She was further referred to cardiologist where she was planned for coronary artery bypass grafting (CABG). She was the started on Rosuvastatin 40 mg ON, Ezetimibe 10 mg OD, Cholestyramine 8 mg day and planned for lipid apheresis.

Conclusions: FH is the most common genetic disease in the world but is also treatable. Thus, early diagnosis and proper management are important for the optimal care to lower the risk for premature CAD and prevent or delay the incidence of CAD-related events.

Ab152 Theme: Atherosclerosis**Low-Densitylipoprotein Particle Size Predicts Poor Outcome in Patients with Atherothrombotic Stroke**

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Background and Purpose: Lowdensity lipoprotein (LDL) particle size is considered to be one of the important cardiovascular risk factors, and small LDL particle has atherogenic potential. This study was conducted to investigate whether LDL particle size is associated with stroke severity and functional outcome in patients with atherothrombotic stroke.

Methods: Between January 2009 and May 2011, we prospectively enrolled 248 patients with first episode cerebral infarction who were admitted to our hospital within 7 days after symptom onset. LDL particle size was measured by nondenaturing polyacrylamide gradient gel electrophoresis assay. Severity of stroke was assessed using National Institutes of Health Stroke Scale (NIHSS) at admission. Functional outcome was investigated at three months after the index stroke using modified Rankin scale (mRS), and poor functional outcome was defined as an mRS ≥ 3 .

Results: In the 248 patients, the mean LDL particle size was 25.99 ± 0.86 nm. The LDL particle size showed an inverse correlation with the degree of cerebral artery stenosis ($p=0.010$). In multinomial multivariate logistic analysis, after adjustment for age, sex, and variables with $p<0.1$ in univariate analysis, LDL particle size was independently and inversely associated with stroke severity (NIHSS ≥ 5 , reference with NIHSS 0-2) (odds ratio: 0.38, $p=0.028$) and poor functional outcome (odds ratio: 0.40, $p=0.038$).

Conclusions: Our results demonstrate the pleiotropic roles of small LDL particle in mediating atherosclerosis and ischemic brain injury. The LDL particle size is potential biomarkers for prognosis of atherothrombotic stroke patients

Oral Presentation (Basic Science)

Ab05 Theme: Cardiovascular Disease**Reactive Oxygen Species and Nitric Balance Determines The Artery Smooth Muscle Tension: Visualized By in Vivo Molecular Imaging**Satoshi Nishimura¹⁻³¹Jichi Medical University, Center for Molecular Medicine, The University of Tokyo, Japan²Department of Cardiovascular Medicine, The University of Tokyo, Japan³Translational Systems Biology and Medicine Initiative, The University of Tokyo, Japan

The dynamic regulation of smooth muscle tension against blood pressure is not well known due to the absence of direct visualization technique. Thus, we developed in vivo imaging technique and revealed the dynamic regulation in living mice. We identified smooth muscle cells in femoral artery in mice using two-photon microscopy, and induced transient artery contractions in living animals by ROS produced by photo-chemical reactions. Using this models, we elucidated that cellular mechanisms of hypertensive responses in femoral arteries, .

Notably, ROS induced transient relaxation, and following contractions. Against our speculations, NO and ROS productions is increased in the late phase of contractions, and NO is counterbalanced for ROS during artery contractions. The both relaxation and contraction phases were inhibited by Ca blockers, ARB, nitrated, and sildenafil. In eNOS knockout mice, the relaxation phase was diminished, and contraction was decreased in early phase, without changing in later phase. These results indicated the eNOS contribution in early phase of contractions.

In addition, thrombus formation was observed in contracted arteries in mice treated with CaCl₂ solutions in arteries, which induced local inflammation. Aneurysm formation was also observed in chronic phase.

In sum, we evaluated smooth muscle function in living animals by direct visualization technique, which was useful for development of new therapeutic approaches against hypertensive disease.

Ab29 Theme: Atherosclerosis**Probucol Inhibits the Initiation of Atherosclerosis in Cholesterol-Fed Rabbits**Niimi M¹, Keyamura Y², Nozako M², Koyama T², Kohashi M², Yasufuku R², Yoshikawa T² and Fan J¹¹Department of Molecular Pathology, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Yamanashi, Japan²Free Radical Research Project, Otsuka Pharmaceutical Co., Ltd., Tokushima, Japan

Background: Probucol and statin are often prescribed for treating hypercholesterolemia and atherosclerosis. These two drugs exhibit different mechanisms but it is unknown whether they have the same anti-atherogenic properties. In the current study, we made a side-to-side comparison of these two drugs in terms of inhibitory effects on the initiation of atherosclerosis in cholesterol-fed rabbits.

Methods: New Zealand White rabbits were fed a cholesterol-rich diet for 5 weeks to produce the early-stage lesions of atherosclerosis. Drug-treated rabbits were administered either probucol or atorvastatin and serum lipids and aortic atherosclerotic lesions were compared with control group.

Results: Atorvastatin treatment significantly reduced serum total cholesterol levels while probucol treatment led to significant reduction of high-density lipoprotein cholesterol levels without changing total cholesterol levels compared with those in the control group. Compared with the control, probucol treatment led to 65% ($p < 0.01$) reduction while atorvastatin treatment led to 23% ($p = 0.426$) reduction of the aortic lesions. Histological and immunohistochemical analyses revealed that the lesions of the probucol-treated group were characterized by remarkable reduction of monocyte number adhered to endothelial cells and macrophage accumulation in the subintima compared with those of both atorvastatin and control groups. Furthermore, low-density lipoprotein (LDL) isolated from the probucol group exhibited prominent anti-oxidative reaction, which was not present in LDL isolated from either the atorvastatin-treated or the control group.

Conclusions: This study suggests that probucol inhibits the initiation of atherosclerosis by reducing monocyte adherence and infiltration into the subintima. Anti-oxidation of LDL by probucol protects more effectively against early-stage lesion formation than statin-mediated lipid-lowering effects.

Ab67 Theme: Atherosclerosis**Induction of Dendritic Cell-Mediated T Cell Activation by Ldlx and Inhibition by Annexin A5**

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Purpose of the Study: Atherosclerosis is an chronic inflammatory disease, where activated immune competent cells including dendritic cells (DCs) and T cells are abundant in plaques. Low- density lipoprotein modified either by oxidation (oxLDL) or by human group X-secreted phospholipase A2 (LDLx) and heat shock proteins (HSP), especially HSP60 and 90, have been implicated as antigens in atherosclerosis. We reported that Annexin A5 (ANXA5) inhibits inflammatory effects of phospholipids, decreases vascular inflammation and improves vascular function in apolipoprotein E^{-/-} mice. Here we focus on the LDLx effects on human DCs and T cells.

Methods and Results: Human DCs were differentiated from peripheral blood monocytes, stimulated by oxLDL or LDLx. Naïve T cells were co-cultured with pre-treated DCs. oxLDL and LDLx, but not LDL, induced DC-activation and T-cell proliferation. T-cells exposed to LDLx-treated DCs produced IFN- γ and/or IL-17 but not IL-4 and IL-10. ANXA5 abrogated LDLx effects on DCs and T cells but increased production of TGF- β and IL-10. Furthermore, IL-10 producing T cells suppressed primary T cell activation via soluble IL-10, TGF- β . Lentiviral-mediated shRNA knock-down HSP60 and HSP90 in DCs attenuated the effect of LDLx on DCs and subsequent T cell proliferation. Experiments on DC and T cells derived from carotid atherosclerotic plaques gave similar results.

Conclusion: Our data show that modified forms of LDL like LDLx but not native LDL activate human T cells through DCs. HSP60 and/or 90 are involved in this T cell activation. ANXA5 promotes induction of regulatory T cells and is potentially interesting as a therapeutic agent.

Ab74 Theme: Cardiovascular**The effect of cow milk on the development of atherosclerosis and production of antibodies against oxidized LDL**

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Purpose of the Study: Oxidative stress is one of risk factors of atherosclerosis. Since 2009, we had been studying oxidative stress as one of the atherosclerosis risk factors. We observed high concentration of antibodies against oxidized LDL (AboxLDL) in serum of infants fed with formula milk based on cow milk. The aim of the study was to explain the effects of beta casein variant A1 on production of antibodies against oxidized LDL as well as on atherosclerosis.

Methods: Blood serum with high titer of AboxLDL was saturated with different antigens: breast milk, formula milk, casein A1/A2 variants, and beta casomorphin. After precipitation of immunocomplexes, residual titer of AboxLDL was measured.

Results: Both casomorphin and beta-casein A1 caused a decrease in concentration of AboxLDL after incubation in serum with high titer of aboxLDL. Breast milk on the contrary had no effect. That is why we presumed that mainly casein A1 and beta-casomorphin are responsible for AboxLDL increase in blood serum of 3 month old infants. It is supposed that AboxLDL rise after oxidative modification of apolipoprotein B via casomorphin (part of casein A1 produced during its hydrolysis) and thus oxidized LDL could trigger atherosclerosis and other autoimmune diseases.

Conclusion: We can conclude that high concentration of AboxLDL is present only in children fed by milk formula based on cow milk. Up to 80% of these antibodies are formed by antibodies against beta casein A1 and against its elastase-released peptide beta casomorphin.

Since fatty streaks in vascular walls develop even in children as a precursor of more advanced lesions later in life, the type of casein ingested in childhood may be considered critical for the development of atherosclerosis. It is a crucial problem to be solved with respect to the epidemic of atherosclerosis in western a middle Europe.

Ab83 Theme: Cardiovascular**Dipeptidyl Peptidase 4 (DPP4) Inhibitor Linagliptin Attenuates Neointima Formation after Vascular Injury**

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The aim of glycemic control is not only lowering blood glucose level but also improving quality of life and mortality through preventing occurrence and progression of vascular complications. According to this opinion, to investigate direct vascular protective effect of antidiabetic agents might be able to provide important information for the choice of antidiabetic agents. We previously reported that GLP-1 receptor agonist Exendin-4 directly decreases atheroma formation (Arakawa M, Diabetes 2010), neointima formation (Goto H, BBRC 2011) and cancer cell growth (Nomiyama T, Diabetes 2014) independent on glucose lowering effect. In the present study, we examined whether DPP-4 inhibitor linagliptin could reduce vascular smooth muscle cell proliferation in vitro and in vivo model. Six-week-old male C57BL/6 mice were divided into the control ($n=19$) and linagliptin (3 mg/kg/day) ($n=20$) treated groups. Endothelial denudation injuries were induced in the femoral artery at the age of 8 weeks, followed by evaluation of neointimal formation at the age of 12 weeks. Blood samples were collected at euthanasia. To evaluate cell proliferation of Rat Aortic smooth muscle cells, the bromodeoxyuridine (BrdU) incorporation assay was performed. Linagliptin reduced neointima formation after vascular injury significantly ($p<0.05$), while linagliptin did not change body weight and blood glucose in mice. Linagliptin increased serum active GLP-1 concentration significantly ($p<0.05$). However, linagliptin did not change serum SDF-1 α and PDGF concentration. Further, linagliptin reduced PDGF-induced vascular smooth muscle proliferation in vitro. These data suggest that linagliptin attenuates neointima formation after vascular injury beyond glucose lowering effect.

Ab87 Theme: Diabetes**Effect of Methanolic Fraction of Flax Lignan Concentrate against Experimental Diabetic Cardiomyopathy in Streptozotocin-Nicotinamide Induced Diabetic Rats**

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Purpose of the Study: The objective of the present study was to investigate the effect of methanolic fraction of flax lignan concentrate (MF-FLC) on cardiomyopathy in streptozotocin-nicotinamide induced diabetes in rats.

Methods: MF-FLC fraction was subjected for high performance liquid chromatographic analysis for bioactive secoisolariciresinol diglucoside (SDG) content. Diabetes was induced in overnight fasted male Wistar rats pre-treated with nicotinamide (100 mg/kg, i.p.) followed by administration of streptozotocin (65 mg/kg, i.p.) 20 min after. The rats were divided into; 1- non-diabetic (vehicle control), 2- diabetic control, 3- MF-FLC (200 mg/kg, p.o.), 4- MF-FLC (400 mg/kg, p.o.). The pretreatment of MF-FLC was started from beginning of 4th week and continued till the end of 12th week. Serum glucose was determined every week. Hemodynamic parameters, oxidative stress parameter, serum biochemical parameter, lipid profile and histopathology of heart were performed on the last day of experiment.

Summary of the Results: The content of secoisolariciresinol diglucoside in methanolic fraction of flax lignan concentrate was found to be 9.97% by high performance liquid chromatography. MF-FLC (400 mg/kg) administration significantly ($p<0.001$) reduced serum glucose, AST, LDH, CK-MB and oxidative stress parameters compared to diabetic control groups. MF-FLC (400 mg/kg) normalized ST, QT, QTc and MABP, elevated GSH and MDA, SOD was lowered and able to controlled lipid profile. Histopathology of heart of MF-FLC (200 mg/kg) treated diabetic animals showed mild and MF-FLC showed moderate reduction of myocardial necrosis, vascular congestion, cellular infiltration and hyperemia as compared to diabetic control group.

Conclusion: Present investigation orchestrates the cardioprotective effect of MF-FLC in diabetic rats via modulation of endogenous antioxidant defence system along with control over hyperglycemia and hyperlipidemia. Thus antidiabetic, antioxidant and antihyperlipidemic activities of MF-FLC appear to contribute to cardioprotective effect in streptozotocin-nicotinamide induced diabetic cardiomyopathy mainly due to bioactive secoisolariciresinol diglucoside content.

Ab136 Theme: Diabetes**Effect of High Glucose on Gene Expression in HCT116 Colorectal Cancer Cells**

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Purpose of the Study: Although it is well recognized that diabetes confers a higher risk for cancer, the cellular mechanisms underlying cancer development in diabetes remain to be explored. We used the microarray approach to study the effect of high glucose on gene expression changes of the HCT116 colorectal cancer cells.

Methods: The HCT116 colorectal cells were treated with high glucose (25 mM). Total RNA was extracted and gene expression change was tested using the Affymetrix Human Gene 1.0 ST array that covered over 28,000 genes. Changes in gene expression were validated with real-time PCR.

Results: Expressions of 25,917 genes were detected, with 100 genes showing higher than 50% changes in expression after high glucose treatment. Bioinformatic analysis using DAVID (<http://david.abcc.ncifcrf.gov/home.jsp>) of the genes showing changes in high glucose medium revealed that the activated genes were enriched in pathways promoting cell proliferation and progression of cell cycle and the suppressed genes were enriched in pathways in promoting apoptosis, including genes expressed in the endoplasmic reticulum (ER) in response to ER stress. Quantitative real-time PCR was used to validate the gene expression changes in HCT116 cells after high glucose treatment. Two microRNAs, miR-181b-1 and miR-222, showed decreased expression in HCT116 cells under high glucose treatment. Both miR-181b-1 and miR-222 have target genes involved in cell proliferation and cell cycle control. The suppression of miR-181b-1 and miR-222 were confirmed in HCT116 cells by quantitative PCR.

Conclusions: Our results suggested that hyperglycemia promoted cancer cell growth by increasing expression of key regulatory genes controlling cell proliferation and cell cycle progression as well as suppressing expression of genes promoting apoptosis. Expression of microRNAs were also changed in concert to promote cell cycle progression and reduce apoptosis under high glucose treatment.

Ab146 Theme: Atherosclerosis**Role of SR-BI in Mononuclear Phagocytes in Atherosclerosis Development**

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SR-BI is a physiological HDL receptor whose role in mediating selective uptake of cholesterol ester from HDL in liver has been largely demonstrated to provide atheroprotection. However, Bone Marrow Transfer studies (BMT) using SR-BI deficient-bone marrow cells have also suggested that this receptor could exert a protective function in hematopoietic cells. Notably, SR-BI is considered as a pattern recognition receptor with anti-inflammatory activities in macrophages, but it also contributes to platelet activation and lymphocyte homeostasis.

To fully evaluate the role of SR-BI in mononuclear phagocytes in atherosclerosis development, we generated mouse models specifically deleted for SR-BI in Monocytes/Macrophages or Dendritic Cells (DC).

BMT of SR-BI KOMono/Macro (SR-BI^{flox/flox}; LysM-Cre) or SR-BI KODC (SR-BI^{flox/flox}; CD11c-Cre) were conducted in an atherogenic mouse model (SR-BI KOLiver; CETP-Tg) fed a 1.25% cholesterol diet for 20 weeks. At sacrifice, plasma cholesterol levels were not different between groups. However, Oil-Red-O revealed a small increase in atherosclerosis in both SR-BI KOMono/Macro and SR-BI KODC models as compared to controls. Moreover this increase in the size of lipid lesions was associated with a two-fold increase in macrophage accumulation in atherosclerotic lesions in SR-BI KOMono/Macro and SR-BI mice. Plasma cytokine profiling revealed a significant reduction in systemic inflammation, with specific cytokine changes for SR-BI KOMono/Macro or SR-BI KODC. Finally, compared to controls, SR-BI KOMono/Macro mice exhibited higher anti-MDA-LDL IgG (1.7-fold, $p < 0.05$) and IgM (2.5-fold; $p < 0.01$) auto-antibody titers, whereas only a small increase in anti-MDA-LDL IgM was observed in SR-BI KODC.

This study identifies a potential atheroprotective role for SR-BI in both monocytes/macrophages and DC. Complementary experiments in other atherogenic mouse models are being performed to decipher the differential impact of SR-BI deletion in these cell types.

Ab149 Theme: Cardiovascular**Bilirubin Increased by Heme Oxygenase-1 Induction Improves Endothelial Function in Diabetic Mice**

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Purpose of the Study: Cardiovascular disease is the leading cause of death and disability in patients with diabetes. And emerging evidence indicates heme oxygenase-1 (HO-1) induction benefits metabolic disease. However, no studies have investigated the possible role of HO-1 in diabetic vasculopathy. The present study aims to illustrate the impact of HO-1 induction on endothelial dysfunction in diabetes and we hypothesize that bilirubin mediates the vascular benefit of HO-1 induction in diabetes.

Methods: Diabetic *db/db* mice were treated with hemin, HO-1 inducer, for two weeks, and aortas were isolated for functional and molecular assays. Nitric oxide (NO) production was measured in cultured endothelial cells.

Results: Hemin increased HO-1 expression and augmented endothelium-dependent relaxations in aortas of *db/db* mice. This effect was inhibited by co-treatment with HO-1 inhibitor Sn(IV) Mesoporphyrin IX dichloride (SnMP) or HO-1 shRNA virus transduction. Improved relaxations were accompanied by elevated phosphorylation of Akt and endothelial nitric oxide synthase (eNOS). Hemin treatment also increased serum bilirubin and chronic bilirubin treatment improved relaxations in diabetic mouse aortas. Furthermore, silencing biliverdin reductase by shRNA *in vivo* reduced serum bilirubin level and attenuated the vascular benefit of chronic hemin treatment. In addition, high glucose-induced reductions in phosphorylation of Akt and eNOS, and NO production in human endothelial cells were reversed by hemin and bilirubin. Importantly, the effect of hemin but not bilirubin was inhibited by SnMP or biliverdin reductase shRNA. Finally, bilirubin augmented endothelium-dependent relaxations in renal arteries from diabetic patients.

Conclusions: HO-1 restores endothelial function in diabetic mice. The effect is most likely mediated by bilirubin, which activates Akt/eNOS cascade and preserves NO bioavailability. The present study suggests bilirubin as a potential therapeutic target for clinical intervention of diabetic vasculopathy.

Ab153 Theme: Cardiovascular**Reduced Clusterin Contents Contribute to The Pro-Inflammatory and Pro-Senescent Activity of Low Density Lipoprotein Particles in Adiponectin Deficient Mice**

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Purpose of the Study: Low adiponectin level is associated with highly oxidized low density lipoprotein (LDL) in patients with coronary heart disease. Clusterin inhibits LDL-induced monocyte chemotactic activity in artery wall. In the present study, we aim to investigate the relationship between adiponectin and clusterin in regulating the pathophysiological function of LDL.

Methods: Cholesterol and protein levels in LDL, HDL2 and HDL3 fractions were measured in serum from wild type and adiponectin-deficient mice after separation of these fractions by density gradient ultracentrifugation. Clusterin was detected in each lipoprotein fraction by Western blotting using specific antibody. LDL-induced endothelial cell senescence were determined by senescence-associated beta-galactosidase staining. Vascular functions were assessed in wild type and adiponectin-deficient mice using wire myography.

Summary of the Results: Circulating levels of total, LDL- and HDL2-cholesterols were significantly increased in adiponectin-deficient mice by 64.7%, 32.5%, 36.1% compared with wild type control mice (All $P < 0.05$). Protein concentrations of these lipoprotein particles were similar between adiponectin-deficient and wild type mice. However, the clusterin levels were significantly decreased in LDL particles from adiponectin-deficient mice (fold change in protein expression: 0.2). Cellular senescence was significantly higher in primary porcine endothelial cells treated with the clusterin-poor LDL from adiponectin-deficient mice than that with the control LDL from wild type mice. In mice with dietary obesity, the endothelium-dependent contractions were significantly enhanced in arteries from the adiponectin-deficient mice compared to their wild type controls. Endothelium dependent relaxation were significantly attenuated by adiponectin deficiency.

Conclusions: Adiponectin exerts its anti-inflammatory and anti-atherogenic effects via regulating the function of LDL particles through its interactions with clusterin.

Poster Presentation (Basic Science)

Ab37 Theme: Obesity

Effects of Edible Plants in Different solvents on Cholesterol Solubilization and Bile Acids Binding

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Purpose: Many plants have been shown to prevent obesity and cardiovascular diseases by decreasing cholesterol absorption. In this study, we investigated the effects of three extracting solvents (methanol, ethanol and aqueous) of pollen of *Bombax ceiba* Linn, fruits of *Solanum torvum* Sw, flowers of *Azadirachta indica* A. Juss. var. *siamensis* Valetton, leaves of *Citrus hystrix* DC, and leaves of *Polygonum odoratum* Lour on interference with cholesterol absorption through micellar cholesterol solubilization and bile acids binding.

Methods: Cholesterol mixed micelles were prepared for cholesterol solubilization study. The mixture of mixed micelles and extracts (1 mg/mL) was incubated and determined the amount of cholesterol contents. Bile acid binding study, plant extracts (1 mg/mL) were incubated with bile acids (Taurocholic acid or glycodeoxycholic acid or taurodeoxycholic acid). The mixtures were filtered and measured spectrophotometrically at 540nm. Cholestyramine was used as a positive control.

Results: The results showed that edible plants have a potential difference in reduced solubility of cholesterol micellization and bound with bile acids in different solvents. Aqueous extract of *Polygonum odoratum* Lour showed highly effective to reduce cholesterol solubility by approximately 85%, whereas residues edible plants of three solvents extraction reduced the solubility of cholesterol micellization in range of 27-83%. Furthermore, all extracts bound to bile acids. Ethanolic extract of *Solanum torvum* Sw had the highest to bind taurodeoxycholic acid 97%, while cholestyramine (1 mg/mL) bound 30%. *Ethanolic and Methanolic* extracts of *Polygonum odoratum* Lour showed most effectively to bind taurocholic acid 57% and glycodeoxycholic acid 40%, respectively. Cholestyramine bound to taurocholic acid and glycodeoxycholic acid was 81% and 15%, respectively.

Conclusions: These findings suggest that these edible plant extracts may be useful for treatment or decreased a risk factor in hypercholesterolemia, obesity, and cardiovascular disease by reducing cholesterol solubility and binding with bile acids.

Ab38 Theme: Atherosclerosis

Leptin Attenuates Ethanol Induced Hepatic Hypercholesterolemia in Mice

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Purpose of the Study: Alcohol induced fatty liver disease is the most common and earliest response to the progression of fibrosis, cirrhosis and/or hepatocellular carcinoma. The mechanism by which ethanol causes fatty liver disease is complex and not fully understood, however, enhanced hepatic lipogenesis has been proposed as an important biochemical mechanism. We have previously noted that the potential preventive effect of leptin on alcohol elicited toxicity in invitro. The purpose of this study was to evaluate the effect of leptin on ethanol induced elevated hepatic cholesterol synthesis and fatty acid composition in mice.

Methods: CD-1 mice ($n=12$ /group) were studied for 45 days. Four groups were studied. 1) control, 2) leptin + control (230 μ g/kg intraperitoneal every alternate day from day 15), 3) alcohol (6.32 g/kg daily by gastric lavage, for 45 days) and 4) alcohol + leptin (as prior dosing). Summary of the results: Compared to control, ethanol supplementation significantly ($p<0.05$) increased % of palmitic acid (16:0), stearic acid (18:0), oleic acid (18:1) and docosapentaenoic acid (22:5) levels, whereas palmitoleic acid (16:1) concentration was decreased significantly ($p<0.05$). Leptin treatment to ethanol fed mice significantly corrects the above indices. Furthermore, leptin administration significantly down regulates ethanol induced plasma total and ester cholesterol and hepatic HMG CoA reductase, cholesterol ester synthase and sterol regulatory element binding protein 2 protein expression. The activities of hepatic lipoprotein lipase, plasma lecithin cholesterol acyl transferase and hepatic cholesterol ester hydrolase were significantly ($p<0.05$) lowered following ethanol supplementation compared to control mice. These features were significantly ($p<0.05$) increased by addition of leptin. Liver histology showed that mice given ethanol had macro and micro vesicular steatosis. However, ethanol + leptin treated liver showed sinusoidal dilatation and no fatty change.

Conclusion: Thus, administration of exogenous leptin to alcohol fed mice significantly decreased hepatic cholesterol accumulation and also regulates fatty acid composition; warranting population based further mechanistic studies.

Ab58 Theme: Diabetes**Involvement of Liver Oxidative Stress and Histopathological Changes in Type 2 Diabetes Rats**

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Purpose: Type 2 Diabetes mellitus (T2DM) is characterized by a decreased of insulin secretion, a presence of insulin resistance and excessive hepatic glucose production. Liver is the major target organs of insulin action and plays a crucial role in the development of insulin resistance and T2DM. Thus, the present study aimed to investigate the involvement of liver oxidative stress and morphology in the development of insulin resistance in T2DM rats.

Methods: Type 2 diabetes (T2DM) rats were induced by high-fat diet (60% fat of total energy) and low single-dose streptozotocin injection. Plasma biochemical parameters were measured to determine general characteristics of T2DM while malondialdehyde levels was analysed to identify liver oxidative stress condition. The liver morphological change was also identified using bright-field microscopic evaluation.

Results: Marked hyperglycemia, hypertriglyceridemia and decreased insulin sensitivity were observed in T2DM rats. Moreover, a significantly high level of malondialdehyde which reflects a production of liver lipid peroxidation was also observed in T2DM rats. In addition histopathological change revealed microlipid droplet accumulation enclosed to portal triad in the cytoplasm of hepatocytes in T2DM rats.

Conclusions: These findings indicate that high-fat diet with a single dose of STZ induced liver lipid peroxidation and microlipid droplet in rats. This consequence could partially contribute in the development of insulin resistance in T2DM.

Ab59 Theme: Atherosclerosis**Effect of Pomelo Juice Extract on Vascular Dysfunction in Hypercholesterolemic Rats**

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Aims of this Study: Hypercholesterolemia is a major risk factor for atherosclerosis. The aim of the present study was to investigate the effect of pomelo juice extract (PJE) on serum lipid levels, aortic superoxide generation, and vascular function in hypercholesterolemic rats.

Method: Male Sprague-Dawley rats were fed normal diet, high-cholesterol diet or high-cholesterol diet supplemented with PJE (1 and 10 mg/kg body weight per day) for 8 weeks. At the end of experiment, serum total cholesterol (TC), triglyceride, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels were determined. In addition vascular reactivity and superoxide generation were assessed in aortic rings using standard organ bath techniques and lucigenin-enhanced chemiluminescence, respectively.

Results: Eight weeks after high cholesterol diet consumption, serum TC, triglyceride and LDL levels were elevated compared to normal diet treated control rats and there was an increased aortic generation of superoxide anion. In aortic rings from hypercholesterolemic rats, endothelium-dependent relaxation to acetylcholine was impaired whereas endothelium-independent relaxation to sodium nitroprusside was unaffected. Chronic oral administration of PJE (1 and 10 mg/kg body weight per day) lowered the elevated blood TC and LDL levels and significantly reduced the increased aortic superoxide generation in hypercholesterolemic rats. In addition the endothelium-mediated aortic relaxation in rats fed with high cholesterol diet was partially restored after PJE consumption.

Conclusions: These results show that the oral administration of PJE decreases TC and LDL levels reduces oxidative stress and preserves endothelium-dependent relaxation in aortae from hypercholesterolemic rats.

Ab63 Theme: Atherosclerosis**A New Multimodal Contrast Agent for Molecular Imaging of Adhesion Molecules Expressed in Atherosclerosis**

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Background: Inflammation is an important component of atherosclerosis and early detection of inflammation might improve clinical management. Most existing contrast agents on the market are non-specific and single-modal. We studied an innovative new multimodal contrast agent, a polyvinyl alcohol based microbubble, targeting adhesion molecules and putatively opening a new scenario for biomedicine.

Objective: to evaluate a contrast agent with different surface modifications and their adhesion to inflammatory *in vitro* models as a proof of concept, by imaging inflamed endothelium, which is involved in the pathogenesis of atherosclerosis.

Methods: Microbubbles were antibody (Ab) or peptide conjugated to the adhesion molecule of interest. To evaluate attachment between MBs and an inflamed murine cell line, endothelial cells (EC), fluorescence microscopy, confocal laser scanning microscopy (CLSM) and Flow cytometry (FACS) were used. To verify expression of cell adhesion molecules we used FACS. Stimulated and non-stimulated cells were incubated with MBs conjugated with active ligands (1 of 4), or a negative control (1 of 2).

Results: In endothelial cells FACS and CLSM showed an increased uptake, or adherence, of Abs or Ab-conjugated microbubbles compared to non-stimulated control. MBs tagged with Abs (ICAM-1, VCAM-1, Selectin) or with cRGD-peptide showed stronger adherence to EC as compared to non-targeted control. *Anti-VCAM-1* and *anti-ICAM1* monoclonal Ab labeled MB was shown to be the most prominent, indicating a specific interaction.

Conclusions: Adhesion molecules expressed in atherosclerosis may be targeted by our labeled multimodal contrast agent *in vitro*, with potential for disease specific diagnostics *in vivo*.

Ab73 Theme: Atherosclerosis**Fenugreek Extract is More Effective than Its Active Compound, Saponins in Reducing Interaction between Monocyte and Human Coronary Arterial Endothelial Cells**Ahmad R^{1,2}, Rahman T¹, Froemming GRA², Osman MT¹ and Nawawi H¹¹The Centre for Pathology Diagnostic and Research Laboratories (CPDRL), Universiti Teknologi MARA, Sungai Buloh, Malaysia²Institute of Medical Molecular Biotechnology (IMMB), Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh, Malaysia

Purpose of Study: There has been a shift towards utilizing natural products as an adjunct therapy to the standard treatment as a preventive measure of coronary artery disease (CAD), and *Trigonella foenum graecum*, also known as fenugreek, is one of the potent natural products of interest. Fenugreek contains about 4-8% of saponins which may have beneficial effects on human health. However, to date, there have been few studies on the potential atheroprotective properties of fenugreek and saponin. Thus, the objective of this study is to determine the effects of fenugreek crude extract and its saponins on monocyte-endothelial cell interaction *in-vitro*.

Methods: Cytotoxicity was assessed by methyl-thiazol-tetrazolium assay using varying concentrations of fenugreek (Sigma, USA) and its total saponin (Shaanxi Sciphar, China). HCAECs (Lonza, USA) were seeded into 96-well culture plate, stimulated with LPS and treated with different concentrations of fenugreek (0.73-375.00 µg/ml) and saponins (0.05-25.00 µg/ml). After 16 hours of incubation, U937 cell line (ATCC, USA) was added into each well and incubated for an hour. The unbound cells were then removed prior to adding 0.25% rose bengal and the reaction was stop using 1:1 ethanol:PBS solution. The absorbance was read at 570 nm.

Results: Fenugreek and saponins concentrations of up to 375.00 µg/ml and 25.00 µg/ml respectively gave >85% cell viability. Treatment with fenugreek reduced monocyte-endothelial cell interaction at all doses with the highest significance at doses 46.88, 93.75 and 187.50 µg/ml ($p < 0.001$) of fenugreek while saponins treatment reduced monocyte-endothelial cell interaction only at doses 0.20, 0.39, 1.56, 6.25, 12.50 and 25.00 µg/ml ($p < 0.03$) with highest significance in reduction at doses 12.50 and 25.00 µg/ml ($p < 0.001$).

Conclusion: Fenugreek crude extract is more effective than its bioactive compound saponins in reducing monocyte-endothelial cell interaction *in-vitro* suggesting that fenugreek in its natural form has better potential as anti-atherosclerotic agent.

Ab99 Theme: Diabetes**Diabetic Condition Exacerbates The Ischemic Brain Injury-Induced Damages Through The Changes Of Various Proteins**Sang-Ah Gim, Jin-Hee Sung, Fawad-Ali Shah and Phil-Ok Koh

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Diabetes is a metabolic disorder that has a major risk factor of ischemic cerebrovascular disease. Diabetic patients have at least two fold higher dangerousness of stroke than non-diabetic counterparts, and also have high mortality and morbidity after stroke. The aim of this study was to identify that are differentially expressed in the cerebral cortex of diabetic and non-diabetic animals during ischemic injury. Adult male rats (210–250 g) were treated with streptozotocin (40 mg/kg) to induce diabetes. After one month, diabetic and non diabetic rats were induced cerebral ischemic injury by middle cerebral artery occlusion (MCAO). The cerebral cortex tissues were collected 24 hr after MCAO and cerebral cortex proteins were identified by two-dimensional gel electrophoresis and mass spectrometry. Several proteins were identified as differentially expressed between non-diabetic and diabetic animals during ischemic injury. Among these proteins, expression of adenosylhomocysteinase, albumin, peroxiredoxin-2, neuroleukin, pyruvate kinase, α -synuclein, carboxy terminal hydrolase L1, 14-3-3, hippocalcin, parvalbumin, and isocitrate dehydrogenase was decreased in the diabetic animals during MCAO. However, diabetic condition leads to up-regulation of C3 and annexin A3 in brain ischemia. These results suggest that diabetes may exacerbate ischemic brain injury through mediating up- and down- regulation of various proteins. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (NRF-2013R1A1A2007300).

Ab116 Theme: Diabetes**Methylglyoxal Induced-astrocyte Dysfunction Mediated through JNK Pathway and Upregulation of Inflammatory Cytokines**KM Lee, MT Chu, KK Fong and KKM Yue

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Purpose of the Study: Methylglyoxal (MG) is one of the most reactive advanced glycation end-product precursors in which its abnormal accumulation is found in the serum of diabetic patients. MG is reported to induce neuronal cell death in the central nervous system (CNS). Astrocytes, which form the blood-brain-barrier and regulate the homeostasis of the internal environment of CNS, are severely affected by MG. Hence the effect of MG leading to subsequent astrocytic dysfunction is investigated.

Methods: Astrocytes (cell line DiTNC1) were treated with different concentrations and exposure time of MG. The expressions of p-JNK and its downstream effects p-c Jun (Ser63), p-c Jun (Ser73), and GFAP (marker of astrocyte activation), together with the mRNA expression of pro-inflammatory markers $\text{TNF-}\alpha$, $\text{TGF-}\beta$, $\text{IL-1}\beta$ and IL-6 were measured using western blotting and PCR respectively.

Summary of the results: There was a significant increase in protein levels of p-JNK, p-c-Jun (Ser63) and p-c-Jun (Ser73) after exposure of 400 μM MG for 1 hour, indicating activation of JNK pathway. RT-PCR was performed to further confirm the activation of JNK pathway. The inflammatory reactions in astrocytes were demonstrated by increased mRNA expression of $\text{TNF-}\alpha$, $\text{TGF-}\beta$, $\text{IL-1}\beta$, IL-6 . The presence of astrogliosis was shown by an increase in GFAP level though the increase was found at 24 hours.

Conclusions: MG activates the JNK pathway, leading to increased expression of inflammatory cytokines and subsequent astrogliosis. Astrocytic dysfunction may be an important event leading to dysfunction of neural cells resulting in neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease.

Ab123 Theme: Diabetes**3 Days Modified Induction Protocol: Insulin-producing Cells Derived Human Bone Marrow for Human Insulin Replacement Therapy**Sayid Ridho^{1,2}, Norrulhuda Ibrahim¹, Fazlina Nordin¹ and Fadilah S Abdul Wahid¹¹Cell Therapy Centre & Department of Medicine, Faculty of Medicine, UKM Medical Centre, National University of Malaysia, Kuala Lumpur, Malaysia²Internal Medicine Department, Faculty of Medicine, Syarif Hidayatullah Islamic State University, Jakarta, Indonesia

Introduction/Objective: There is no curative treatment for diabetic patients to date, and the global incidence of diabetes mellitus continues to increase. Moreover, uncontrolled diabetes mellitus may result in serious long-term implications. Efforts to reverse the insulin dependency in diabetes mellitus are focused on the possibility of promoting islet-cells replacement and/or regeneration. This study described the 3 days modified protocol for generation of insulin producing cells (IPC) from human bone marrow (BM) mesenchymal (MSC) stem cells as a candidate cells for human insulin replacement therapy.

Methods: Human mononuclear cells were isolated from BM aspirations. The cells were cultured in Mesencult conditioning medium, and the MSC-derived BM cells were further confirmed by flow cytometry. MSC-derived BM cells were induced into IPC using serum-free DMEM/F12 medium containing specific growth factors for 3 days. The morphology of IPC was confirmed by microscopy analysis using dithizone staining method, following expression of Pdx1 gene by PCR analysis. The secretion of Insulin was further analysed by ELISA.

Results: The MSC-derived human BM was confirmed at day 14 of culture (D105⁺, CD90⁺, Cd44⁺, CD29⁺, CD45^{low/-}, and CD34^{low/-}). Following, expression of Pdx-1 gene at Day 1, 2 and 3 of induction. Furthermore, the Pdx-1 gene was able to secrete Insulin into culture medium.

Conclusions: These results demonstrated the differentiation of human MSC-derived BM cells into IPC using a 3 days modified protocol. The IPC-derived human BM will be transplanted in Sprague Dawley induced STZ Rat for further investigation of its functional ability.

Ab133 Theme: Cardiovascular**Citronellol a Major Component of Essential Oil Ameliorates Endothelial Dysfunction Induced by Diet Rich in Fat and Sucrose in Rats**

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Purpose of the Study: Modernization of lifestyle leads towards frequent consumption of diet rich in fat and sucrose contributes to metabolic disorders like diabetes, obesity and cardiovascular complications. Citronellol a major component of geranium oil and also it is found in essential oils of various spices and aromatic herbs (e.g., ginger, nutmeg, coriander, lemon, lemon-grass, orange, lavender, etc.). Citronellol a monoterpene is known for potent anti-inflammatory, antihypertensive, hypoglycemic and antioxidant activity. Hence, the present study was aimed to explore the vasorelaxant and cardioprotective property of citronellol by determining the activity of nitrous oxide synthase (NOS) in endothelial dysfunction caused by diet rich in fat and sucrose in rats.

Methods: Metabolic complications were induced by feeding high fat - high sucrose (HFS) diet containing 20% fat and 30% sucrose for 12 weeks. Male Wistar rats were divided in five groups as control group fed with standard chow diet, HFS group and three treatment groups administered with citronellol (100, 200, 400 mg/kg p.o) for last 6 weeks along with HFS diet. Body weight, food intake were determined during the study and at the end of study plasma glucose, insulin, lipid profile, HOMA-IR, glucose tolerance, antioxidants levels, lipid peroxidation, serum NO level, NOS activity in aorta, ECG changes, mean arterial pressure (MAP) and endothelial dependent and independent vascular function in aorta were assessed.

Summary and Results: Administration of citronellol in HFS diet fed rats exhibited a significant decline in body weight, glucose ($p < 0.01$), insulin ($p < 0.01$), triglyceride ($p < 0.001$), total cholesterol ($p < 0.01$), LDL levels and increase in HDL levels ($p < 0.01$) and insulin resistance. Decreased serum NO level ($p < 0.01$) along with decrease NOS activity ($p < 0.01$), increased oxidative stress (as estimated by the attenuated levels of anti-oxidant enzymes and increased MDA levels) and impaired glucose tolerance associated with HFS diet were attenuated by citronellol in dose dependent manner. Also decreased MAP and ECG changes were normalized ($p < 0.01$) and reduced acetylcholine-induced, endothelium-dependent relaxation was improved significantly in citronellol treated rats ($90.16 \pm 0.17\%$).

Conclusions: Citronellol ameliorates endothelial dysfunction and metabolic complications in HFS diet fed rats by repressing insulin resistance, oxidative stress, lipid lowering effect and normalizing NO production.

Ab137 Theme: Diabetes**Effective Dose of Total Body Irradiation for Streptozotocin-Induced Diabetic Rat as a Role Model for Xenotransplantation: a Challenge and Better Understanding**

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Purpose of the Study: There are many diabetic in vivo studies using immunocompetence rats as a recipient to evaluate the engraftment of human stem cells. Most of those studies did not use an irradiation exposure for the rat. Principally, the human immune system differs significantly from rodent immune system. This study described to assess the effective dose of Total Body Irradiation (TBI) for immunocompetence Streptozotocin(STZ)-induced diabetic rats before xenotransplantation.

Methods: A total of 18 Sprague Dawley male rats aged 6 to 8 weeks are prepared in ABSL II animal house. Rats were injected with 50 mg/kg STZ of body weight for 2 days. Diabetic rats then were divided into 2 groups with different sublethally (middle and high) dose and control group of TBI using a Cesium source. After TBI, diabetic rats then were transplanted with human bone marrow mononuclear cells as prepared before TBI into liver via laparotomy. The engraftment were then analysed through detection by using immunohistochemistry (IHC) study after rats were sacrificed at day 14.

Summary of the Results: All rats become diabetic. All group of different sublethally dose of TBI showed an engraftment after transplantation. IHC study revealed that the sublethally high dose group rats have more showed of the engraftment than the middle dose group. Control group have less showed of engraftment.

Conclusions: Sublethally high dose group of TBI rat have more detection of the engraftment than middle dose and control group. These results demonstrate the needy of TBI for immunocompetence STZ-induced diabetic rats as a recipient for xenotransplantation.

Ab138 Theme: Diabetes**Chemiluminescent Immunometric Assay for Insulin Measurement as a Marker of Insulin Producing Cells from Differentiation of Human Peripheral Blood Mononuclear Cells**

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Purpose of the Study: Diabetes is an endocrine disease and it is emerging at alarming rates around the globe and there is no curative treatment for diabetic patients to date. Efforts to reverse the insulin dependency in diabetes mellitus are focused on the possibility of promoting islet-cells replacement and/or regeneration. It has been very rare using of human peripheral blood mononuclear cells as a source of stem cells without molecular engineering in diabetic in vitro study. Most diabetic invitro study were used other method for measurement secreted insulin of Insulin Producing Cells (IPC). This study described the measurement of insulin with chemiluminescent immunometric assay for insulin producing cells originated from human peripheral blood mononuclear cells differentiation.

Methods: Human mononuclear cells were isolated from the peripheral blood. The cells were proliferated for 5 days in normal glucose DMEM medium on gelatin-coated culture dishes. Cells were then induced to differentiate into IPC using high glucose DMEM medium supplemented with a potent inducer for 25 days. IPC were observed by dithizone staining. Furthermore, the titers of secreted insulin were determined using chemiluminescent immunometric assay.

Summary of the Results: Insulin-producing cells were observed morphologically by dithizone staining and were shown to contain human insulin. The secreted insulin titers were 80.1 μ IU/mL.

Conclusions: These results demonstrate the ability of the human peripheral blood mononuclear cells to differentiate into insulin-producing cells without molecular engineering and the insulin productions have determined by chemiluminescent immunometric assay.

Ab140 Theme: Atherosclerosis**Anti-Inflammatory Effect of Saffron and Its Bioactive Compound, Crocin in Stimulated Human Coronary Artery Endothelial Cells (Hcaecs)**Alicezah M.K¹, Ahmad R¹, Rahman T¹, Froemming G.R.A² and Nawawi H¹¹The Centre for Pathology Diagnostic and Research Laboratories (CPDRL), Universiti Teknologi MARA, Sungai Buloh, Malaysia²Institute of Medical Molecular Biotechnology (IMMB), Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh, Malaysia

Purposes of Study: Saffron is derived from dried stigma of *Crocus sativus* L flower, whereas crocin is its bioactive compound. Animal studies suggest that crocin has potential anti-atherosclerosis properties. To date, there is scarce information on the cellular effect of crocin at the cellular level. Thus, we aim to investigate the potential effects of anti-inflammatory saffron and crocin on protein and gene expression of inflammatory biomarkers IL-6, IL-8 and NF-KB in stimulated human coronary artery endothelial cells (HCAECs).

Methods: LPS stimulated confluent HCAECs (Lonza, USA) were treated with saffron and crocin [concentration range: 25.0-3.1 g/ml; 0.2-1.6 g/ml]. IL-6 and IL-8 were analyzed on Procartaassay (Affymetrix, USA) while NF-KB p50 and p65 on ELISA (Cayman, USA) to measure protein expression. The RNA extraction was performed on the 16 hours post-incubated cells for gene expression.

Results: Saffron and crocin reduced protein expression of IL-6 across all concentrations [3.1-25.0 µg/ml, $p < 0.05$; 0.2-1.6 µg/ml, $p < 0.05$]. Gene expression of IL-6 was suppressed at high saffron concentration [25.0 µg/ml, $p = 0.01$] while crocin at all concentrations [0.2, 0.4, 0.8, 1.6 µg/ml, $p < 0.05$]. Similarly, IL-8 protein expression was suppressed at high saffron concentration [25.0 µg/ml, $p < 0.029$] while crocin at 0.8 and 1.6 µg/ml [$p < 0.01$]. The gene expression of IL-8 was not suppressed by both compounds [$p > 0.01$]. The protein and gene expression of p 50 NF-KB were also suppressed at higher concentration of saffron [25.0 µg/ml, $p = 0.01$; 12.5 and 25.0 µg/ml, $p < 0.03$] while crocin at 0.4, 0.8 and 1.6 µg/ml, $p < 0.01$; 0.4, 0.8 and 1.6 µg/ml, $p < 0.04$. Both compounds also suppressed NF-KB p65 protein and gene expression at high concentration [(25.0 µg/ml, $p = 0.04$; 1.6 µg/ml, $p = 0.05$), (25.0 µg/ml, $p = 0.03$; 1.6 µg/ml, $p = 0.04$) respectively].

Conclusion: Although both saffron crude extract and its bioactive compound, crocin exert anti-inflammatory effects, crocin appears to be a more potent anti-inflammatory agent.

Ab154 Theme: Diabetes**A Study of Anti-Helicobacter Pylori Effect of Mammalian Cathelicidins**Jack Ho WONG¹, Yau Sang CHAN¹, Ching Ching LEE², Thomas LING², Chi Hin CHO¹ and Tzi Bun NG¹¹School of Biomedical Sciences, CUHK²Department of Microbiology, CUHK

Diabetes has been identified as a risk factor for *Helicobacter pylori* (*H. pylori*) infection. Compared to subjects without diabetes, the eradication rate of *H. pylori* using standard regimens is less than satisfactory in patients with type 2 diabetes mellitus (T2DM). Moreover, a recent meta-analysis disclosed that HP infection is 1.3-fold more prevalent in people with diabetes than in those without diabetes. Improvement in T2DM patients with eradication of insulin resistance has been reported after successful treatment of *H. pylori* infection. Thus, a relationship may exist between *H. pylori* infection and diabetes.

In this study, six mammalian cathelicidins (including one each from horse, guinea pig, snake, and chicken, and two from cow) were tested for antibacterial effect against two *H. pylori* strains, SS1 and 43504. Our preliminary data showed that after treatment with cathelicidin for 72 hours, guinea pig cathelicidin inhibited the growth of 50% of *H. pylori* cells at a concentration below 100 micrograms/ml, and snake and chicken cathelicidins did so at a concentration below 200 micrograms/ml. However, cow cathelicidins and horse cathelicidin could not inhibit the growth of 50% of *H. pylori* cells even at 500 micrograms/ml.

We gratefully acknowledge the award of an HMRF research grant (reference no.12110282) from Food and Health Bureau, The Government of Hong Kong Special Administrative Region.

Edited and published by
The Japan Atherosclerosis Society
Vol.21, Supplement 3
September 2014

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