

ABSTRACTS

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THE COMPARATIVE ROLES OF INSULIN AND LEPTIN AS PRIMARY REGULATORS OF HUMAN FETAL GROWTH. A CORRELATION STUDY ON THE RELATIONSHIP OF CORD BLOOD HORMONES WITH BIRTH WEIGHT AND GESTATIONAL AGE

Abdel Fattah Alhader

Jordan University of Science & Technology

Objective: To investigate the relationship between the levels of various cord blood hormones (leptin, insulin, human placental lactogen (hpl), free estriol (f-E₃), free triiodothyronine (f-T₃), free thyroxin (f-T₄), TSH, free testosterone (f-test), sex hormone binding globulin (SHBG), cortisol and GH) with birth weight and gestational age (GA) of Jordanian newborns.

Methods: 113 full term newborns and 33 preterm newborns were included in this study. Full term newborns were classified into 40 appropriate for gestational age (AGA), 39 large for gestational age (LGA) and 34 small for gestational age (SGA) newborns. Cord blood samples were collected and newborn anthropometry was measured at time of delivery. Cord blood hormones were measured by RIA or IRMA.

Results: In full term group cord blood leptin was 46% higher in LGA and 36.2% lower in SGA compared with AGA newborns, while insulin was 18.8 % higher (p<0.01) in LGA compared with AGA newborns. Cord blood f-T₄ was 9.4% lower (p<0.05) in SGA compared with AGA newborns. Levels of leptin, f-T₄, f-E₃, f-test, SHBG and cortisol were significantly lower in preterm group compared to their levels in full term group. While the levels of hpl, TSH and GH were significantly higher in preterm group compared their levels in full term group. Insulin and f-T₃ were comparable in both groups. Leptin concentration in cord blood correlated positively with birth weight, Ponderal index, gestational age and newborn's length in the whole study group.

Conclusion: Our results suggest that level of leptin is a useful index for fetal growth and may be an important regulator of fetal growth. Comparable level of insulin in SGA and preterm groups with full term AGA group suggests that insulin might not be a primary regulator of fetal growth. Results regarding levels of hormones in preterm newborns should be viewed as endocrinopathy of prematurity.

CLINICAL STUDY ON TREATMENT OF DIABETIC FOOT BY IMPROVING BLOOD SUPPLY THROUGH TWO DIFFERENT WAYS

Xiao-yan Li¹; Kun Lu²; Shilong Han²

¹The Department of Endocrinology and medical imaging, Hospital Affiliated to Shanghai Ligong University, 200092, China. ²Tongji University School of Medicine, No. 1299 Siping Road, Shanghai 200072, China

Objective: To analysis the clinical value on treatment of diabetic foot by improving blood supply by different methods, and summary our experience of diagnosis and treatment.

Methods: 85 patients with diabetic foot disease was graded according to classification and divided into surgical and conservative treatment group respectively, compared the efficacy between the two groups.

Results: 85 cases of patients were in therapy longest up to a year, the shortest 3 months, the average 6 months. 42 patients were in conservative treatment group: 26 patients were cured, 8 cases were markedly effective, 5 cases were effective, 3 cases were invalid, death 0 cases, and the total effective rate was 92.9%. 43 patients were in surgical treatment group: 28 cases, 9 cases, 4 cases, 2 cases, 0 cases separately, the total effective rate 95.3%. The curative effect of difference was statistically significant (P>0.05).

Conclusion: The treatment of vascular disease by improving the blood supply is the key to diabetic foot treatment. Clinically surgical or conservative treatment method is selected individually, the two ways are quite and curative effects on anticoagulation, thrombolysis and enlarging vessels.

Key words: *Diabetic foot; Peripheral artery disease; Surgery; Conservative treatment.*

TELOMERASE ACTIVITY IN DIABETIC PATIENTS WITH ANGIOPATHY

Ayman El Badawy¹; Mohamed Shawky¹; Amr M. El Hammady¹, Mohamed Elassal¹; Ashraf Talaat¹; Khalid Belal²

¹Internal Medicine, and ²Clinical Pathology Departments, Banha University, Egypt

Abstract Background: Diabetes mellitus (DM) is associated with damage to target organs and premature aging and

telomeres serve as a mitotic clock and biological marker of senescence.

Aim of Study: was to A) evaluate telomerase activity in both type 1 and type 2 diabetic patients with microangiopathy and macroangiopathy, B) to study the possible factors that affect the activity of this enzyme in these patients.

Subjects and Methods: Study was carried out on 40 patients from those attending diabetes clinics of Banha University Hospital, they were divided into three groups:

Group I: 10 type 1 diabetic patients with angiopathy (4males & 6 females).

Group II: 10 type 2 diabetic patients with angiopathy (3males & 7females)

Group III: 20 apparently healthy age & sex matched volunteers serving as a control group. The following laboratory investigations were performed to all patients: Plasma glucose (fasting and post prandial), Glycated hemoglobin, Lipogram (Total cholesterol, LDLc, HDLc and Triglycerides), Serum creatinine, Urinary microalbumin and Study of telomerase activity in whole blood.

Results: Our results showed: that (HbA1C, microalbumin, creatinine, LDL, TG, TCH, PPBS and FBS) are significantly higher in diabetic patients compared to control group where (telomerase and HDL) are significantly lower in diabetic patients compared to control group. Also, Telomerase activity was significantly low in diabetic patients with HbA1C ($\geq 7\%$), LDL-c ($>100\text{mg/dl}$), HDL-c ($<45\text{mg/dl}$), TG ($>150\text{mg/dl}$), TCH ($>200\text{mg/dl}$), microalbuminuria ($>30\text{mg/ml}$) respectively compared to diabetic patients with HbA1C ($<7\%$), LDL-c ($<100\text{mg/dl}$), HDL-c ($>45\text{mg/dl}$), TG ($<150\text{mg/dl}$), TCH ($<200\text{mg/dl}$), and normoalbuminuria ($<30\text{mg/ml}$). There was significant relation between telomerase activity and macroangiopathic complications, There was nonsignificant correlation between telomerase activity and each of creatinine level and age in the case group. Statistical analysis showed that 80% of diabetic patients (16 patients) were telomerase negative (lower than cut off value ≤ 49.20), whereas 20% of diabetic patients (4 patients) were telomerase positive (higher than cut off value >49.20).

Conclusion: it was concluded that telomerase enzyme activity decreased in both type 1 and type 2 diabetic patients with angiopathy, There was a relation between telomerase activity and both micro & macroangiopathic complications.

Key words: telomerase, diabetic patients, angiopathy (micro- or macroangiopathy)

PREVALENCE OF METABOLIC SYNDROME AND INSULIN RESISTANCE IN NEWLY DIAGNOSED TYPE 2 DIABETIC PATIENTS

Kelmendi Matilda¹; Husi Gerond²; Ylli Agron²; Ylli Zamira³; Thanas Furera²

¹Policlinic of specialty Tirana, ²Endocrinology Service UHC Mother Teresa, ³Imunology service UHC Mother Teresa

In our study we try to evaluate the prevalence of insulin resistance and MS in newly diagnosed with T2D, correlations of insulin resistance with elements of MS.

Materials and Methods: 100 patients newly diagnosed with T2D, 49 men 50 ± 29.1 years and 51 women 47.01 ± 1.10 years. The control group with 100 healthy subjects: 54 men 48.01 ± 1.21 years and 46 women 46.96 ± 1.24 years. Depending on the value of HOMA - IR and fasting insulinemia, were divided in three groups; control group and Group A where HOMA - IR <3.5 and fasting insulinemia $<20 \mu\text{IU/ml}$ (insulin deficiency) and Group B where HOMA - IR >3.5 and fasting insulinemia $>20 \mu\text{IU/ml}$ (insulin resistance). Subjects were classified according to the MS NCEP ATP III criteria.

Results: In our study we find that 30% of patients newly diagnosed with T2D resulted with insulin deficiency while 70% resulted with insulin resistance. HOMA - IR in the three groups presented a linear relationship with TG and abdominal circumference. Weight, BMI and abdominal circumference resulted significantly higher in Group B (insulin resistance) Based on the criteria of NCEP ATP III showed that the prevalence of MS in our population was 80%, while in the control group 21%. MS distribution by groups in the diabetic population resulted in 46.66% in Group A and 94.28% in Group B.

Conclusions: MS our study resulted in 4 of 5 people newly diagnosed with type 2 diabetes. High prevalence of insulin resistances and MS in our study confirms that hyperinsulinemia, deterioration of HOMA - IR resulting in loss of compensator insulin secretion, are the key factor in the pathogenesis of T2D.

EFFECT OF DAIRY MILK POWDER ON HEPATIC MALONDIALDEHYDE (MDA) LEVELS IN WHITE MALE RATS (RATTUS NOVERGICUS WISTAR STRAIN) TYPE 2 DIABETES MELLITUS MODELS

Adi Lukas Kurniawan

Final Assignment, Nutrition Program, Faculty of Medicine, Brawijaya University. Supervisors: (1) drg. Prasetyo Adi, MS (2) Fajar Ari Nugroho, S.Gz., M.Kes.

Background: dairy milk powder contains of various components such as whey protein, calcium, and vitamin D. These components are thought to be able to prevent an increasement levels of hepatic Malondialdehyde (MDA) in diabetes mellitus type II. The aim of this study is to determine the effect of powdered milk in hepatic tissue MDA levels on Wistar rat model of diabetes mellitus type II.

Methods: This is an experimental study using Post Test Only Control Group Design. Thirty Wistar rats were randomly divided into five groups. Group K (-) is the negative control group with normal diet without induction treatment of streptozotocin. Group K (+) is the positive control group treated with high fat diet and streptozotocin induction. While the groups P1, P2, and P3 are given a high fat diet, streptozotocin induction and milk powder 0.9, 1.8, and 2.7 grams/day. All of Wistar rats were adapted to a normal diet in 1 week then continued with high fat diet for 4 weeks. On 91th day rat hepatic tissue MDA levels were measured with a spectrophotometer.

Results: There is an effect of dairy milk powder with various doses in rat hepatic tissue MDA levels. Kruskal-Wallis test showed a difference between groups ($p = 0.003$). Mann-Whitney test showed that all of three doses milk powder could prevent hepatic tissue MDA levels significantly compared to the positive control group. The most effective doses are 1.8g/day and 2.7g/day because it can prevent the increasement of hepatic tissue MDA levels closer to the negative group.

Conclusion: Giving a dairy milk powder with some doses such as 0.9, 1.8, and 2.7g/day for 8 weeks were able to prevent the increasement of MDA levels in hepatic tissue in rats with diabetes mellitus was significant and the most effective doses are 1.8 and 2.7 grams/day.

Key words: *milk powder, hepatic tissue of Malondialdehyde, streptozotocin, high fat diet.*

ROLE OF PATHOGEN PATTERN RECOGNITION RECEPTORS AND INFLAMMATORY MEDIATORS FOLLOWING GUT MICROBIOTA ALTERATION IN HIGH SUGAR DIET MEDIATED TYPE 2 DIABETES

Bhumika Prajapati; Prasant Kumar Jena; Parth Rajput; Sriram Seshadri

Institute of Science, Nirma University, Sarkhej Gandhinagar Highway, Chharodi, Gujarat, India

Obesity and Type 2 Diabetes are leading health problems around the world due to high consumption of dietary sucrose via gut microbiota alteration. Manipulation of the gut microbiota using antibiotics can prevent the progression of metabolic disorders by affecting the gut dominant bacterial communities and their metabolites like short chain fatty Acids (SCFAs). This investigation was aimed to study the effect of altering gut microbiota by oral administration of Moxifloxacin microspheres in high Sucrose diet (HSD) rats in context with insulin sensitivity.

Simultaneous administration of HSD and antibiotics microspheres had showed increased insulin sensitivity with reduced hyperglycemia, hyperinsulinemia, hypertriglyceridemia as compared to HSD group. Antibiotics co-administered group had showed relatively less histopathological symptoms in small intestine, colon and liver compared to HSD group. Quantitative PCR study of fecal bacteria from treated group had showed marked increase in *Lactobacillus*, while decrease in *Enterobacteriaceae* and *E. coli* as compared to HSD group, which further can be correlated with decrease in gut derived Lipopolysaccharide (LPS). Gas chromatographic study indicated the increased levels of the SCFAs in antibiotic treated group as compared with HSD, which indicated the gut manipulation towards increasing the insulin sensitivity. Reduced TLR4 and NLR1 expression were observed in treated group which decreased inflammatory mediator, NF-kB activity to reduced the expression of proinflammatory cytokines such as TNF- α , IL-1 β and IL-6 as compared with HSD, indicating the decreased inflammation via gut microflora manipulation. Such manipulation needs to be further explored for its therapeutic applications to treat the metabolic complications.

Key words: *Type 2 Diabetes, Toll like Receptors, Gut Microbiota, Inflammation, Short Chain fatty Acids and Antibiotics.*

A CROSS SECTIONAL STUDY TO FIND THE ASSOCIATION BETWEEN PROLONGED QTc INTERVAL AND MICROALBUMINURIA IN PATIENTS OF TYPE 2 DIABETES MELLITUS

Shekhar Bhise

Kle University In Medical College Belgaum Karnataka, India

The link between microalbuminuria and premature death in type 2 diabetes is not completely explained by conventional cardiovascular risk factors. Cardiac autonomic neuropathy can be detected in at least one third of type 2 diabetic patients. CAN is associated with a high mortality which is attributed not only to sudden death but also to diabetic nephropathy. Prolonged QT_c interval is found to be a specific indicator for CAN. The present study was undertaken to find the association between prolonged QT_c interval and microalbuminuria in type 2 diabetes patients.

The present one year cross-sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 86 (43 with normoalbuminuria and 43 with microalbuminuria) patients with type 2 DM during the period of January 2009 to December 2009. Investigations like complete blood count, erythrocyte sedimentation rate, urine routine and microscopy, fasting blood sugar or post prandial blood sugar or random blood sugar were done. Urine albumin excretion test (Microalbumin to creatinine ratio) was done. Electrocardiogram was done to calculate the QT_c interval. QTc interval was calculated using Bazett's formula.

In the present study, 60.47% and 69.77% were males in normoalbuminuric and microalbuminuric groups respectively. The mean age in normoalbuminuric group was 54.51 ± 10.15 years and it was 55.93 ± 11.73 years in microalbuminuric group. Most of subjects had duration of diabetes less than 10 years (44.19% in normoalbuminuric and 34.88% in microalbuminuric groups respectively). QTc interval was significantly prolonged in 25.58% of patients in normoalbuminuric and 69.77% in microalbuminuric group (p=0.001). Mean QTc interval was significantly more (454.73 ± 29.33 ms) in microalbuminuric group compared to normoalbuminuric group (418.13 ± 27.44 ms) (p=0.001). Mean duration of diabetes was less (14.93 ± 3.81 years) in microalbuminuric group compared to (16.00 ± 4.87 years) normoalbuminuric group.

The study showed that, prevalence of CAN as diagnosed by prolonged QTc interval was more in Type 2 DM patients with microalbuminuria and type 2 diabetic patients with microalbuminuria can develop CAN with short duration of diabetes.

IN VITRO ANTI-HYPERGLYCEMIA AND BIOCHEMICAL EVALUATION OF THE AQUEOUS EXTRACT FROM *STRYCHNOS HENNINGSII* GILG IN DIABETIC ANIMAL MODEL

Sunday Oyedemi¹; Trevor Koekemoer²;
Graeme Bradley¹; Maryna van de Venter²;
Anthony Afolayan¹

¹Department of Biochemistry and Microbiology, University of Fort Hare, ²Department of Biochemistry and Microbiology, Nelson Mandela Metropolitan University

Strychnos henningsii Gilg (SH) is a plant commonly used in southern African traditional medicine for the management of diabetes mellitus. The present study investigated beneficial effect of the herbal extract on some biochemical and haematological parameters in streptozotocin-nicotinamide induced diabetic animal model. Diverse in vitro models known to target glucose homeostasis and its direct complications were also evaluated to elucidate its mechanism of action. Significant decrease of blood glucose levels between 6 and 10 mmolL⁻¹ was observed after oral administration of the extract at the tested dose. The level of triglyceride, urea, calcium, AST and ALP was drastically reduced whereas the level of Hb, PCV, MCV, RBC, MCH and ALT was significantly improved. Moreover, the folklore medicine appreciably increased the white blood count and its differentials but had no significant effect on the cholesterol and uric acid. The plant extract was found to stimulate both basal and insulin stimulated glucose uptake in differentiated 3T3-L1 cells but not in Chang liver cells. The effect on 3T3-L1 cells appears independent of PPAR γ as the extract did not stimulate adipogenesis. Although, SH extract was inhibitory toward intestinal alpha glucosidase, the physiological relevance is doubtful based on the recommended dosages. The extract strongly inhibited protein glycation which, at least in part, may be explained by the antioxidant and phenolic content of this plant. Cytotoxicity in Chang liver cells yielded an IC₅₀ value of 130.0 μ g/mL raising concern that continual exposure to this herbal remedy may initiate hepatotoxicity. The finding from this study suggests that SH extract may attenuate hyperglycemia through enhanced peripheral tissue glucose utilization. The extract also has the capability of regularising some abnormalities associated with pathophysiological condition of diabetes mellitus.

Key words: *Strychnos henningsii*; Hyperglycemia; Hepatotoxicity; Glucose uptake; Adipocyte; Haematology; Biochemical

INCIDENCE OF LACTOSE INTOLERANCE AMONG DIABETIC PATIENTS WITH AND WITHOUT HYPERTENSION FROM NORTH INDIA

Rana SV; Malik A; Bhadada S; Morya RK

Department of Gastroenterology, Endocrinology, Post graduate Institute of Medical Education and Research, Chandigarh, India

Background: Individuals who have lactose intolerance tend to avoid dairy foods. Avoidance of dairy foods may lead to nutrient shortcomings that could predispose them to adverse health outcomes, including poor bone health, higher blood pressure, higher body weight and a higher risk of developing diabetes. Thus, the present study was planned to study the incidence of lactose intolerance in diabetic patients with and without hypertension.

Material and Methods: 71 diabetic patients, 43 diabetic with hypertension patients (who had GI symptoms) and 82 healthy controls were enrolled for this study. Lactose intolerance was measured by non-invasive lactose breath test with Quintron Microlyser.

Results: Out of 43 diabetic patients with hypertension, 26 (60.4%) were males with age range 43-80 years. While in diabetes, out of 71 patients, 42 (59.1%) were males and 29 were females with age range 43-84 years. Out of 82 healthy controls, 51 were males and 31 were females with age range 40-81 years. Lactose intolerance was significantly higher in diabetic patients with hypertension (56/71; 78.8%) as compared to without hypertension (25/43; 58.1%) and controls (30/82; 40.2%). It was also significantly higher ($p < 0.05$) in diabetic patients as compared to controls.

Conclusion: The results of this study indicate that diabetic patients with and without hypertension should be advised to consume less amount of milk at one time so that GI symptoms in these patients can be avoided.

CYTOKINE PATTERN OF GESTATIONAL DIABETES

Ahia Garshasbi

Shahed University, Tehran, Iran

Objectives: Compare the cytokine pattern dependent on Thelper1 / Thelper2 (Th1 and Th2) and vital activity of peripheral blood mononuclear cells (PBMC) of healthy pregnant women and women with gestational diabetes.

Methods: In a case - control study, 37 women with GDM (case group) and 37 healthy pregnant women (control group) in 28-36 weeks of gestation were recruited.

Peripheral blood mononuclear cells in presence and absence of mitogen (PHA) were cultured for 48 hours. IFN γ and Interleukin-4 (IL-4) concentration in the cell culture supernatant was measured by ELISA technique. Vital activity of PMN cells measured by MTT technique and stimulation index was calculated.

Results: Stimulation index of PBMC cells was not different between the two groups. Mean concentrations IFN γ in women with GDM were significantly higher than in healthy pregnant women $692 \pm 362/27$ vs $312/65 \pm 313/68$ ($p < 0.001$).

There was no significant difference in the level of IL-4 ($87/72 \pm 47/91$ vs $85/37 \pm 47/12$) ($p = 0.835$)

Conclusion: These results show that Gestational diabetes is associated with TH1 shift. This suggests a pathogenic role for Th1 profile in GDM.

Key words: *Interleukin-4, Gestational diabetes mellitus, T helper1 T helper 2, cell viability.*

OVER EXPRESSION OF SUPEROXIDE DISMUTASE 3 GENE BLOCKS HIGH FAT DIET-INDUCED OBESITY, FATTY LIVER AND INSULIN RESISTANCE

Ran Cui^{1,2}; Mingming Gao²; Shen Qu¹; Dexi Liu²

¹Shanghai Tenth People's Hospital of Tongji University, School of Medicine, Shanghai, P. R. China. ²Department of Pharmaceutical and Biomedical Sciences, University of Georgia College of Pharmacy, Athens, GA

Oxidative stress plays an important role in the development of obesity and obesity-associated metabolic disorders. As an endogenous antioxidant enzyme, superoxide dismutase 3 (SOD3) has the potential to affect diet-induced obesity and obesity associated complications. In the current work, we overexpressed SOD3 in C57BL/6 mice fed a high fat diet to study its effect on high fat diet-induced obesity, fatty liver and insulin resistance. We demonstrated that the *Sod3* gene transfer blocked high fat diet induced obesity, fatty liver and insulin resistance. Real Time-PCR analysis of adipose and liver tissues revealed that overexpression of the *Sod3* gene suppressed expression of pro-inflammatory genes in adipose tissue including *Tnfa*, *Mcp1*, *Il6*, *F4/80* and *Cd11c*, and increased expression of anti-inflammatory genes such as *Adiponectin* and *Il4*. In the liver, high levels of SOD3 activity in animals enhanced expression of the

genes responsible for energy expenditure including *Cpt1 α* , *Cpt1 β* , *Pgc1 α* , *Pgc1 β* and *Ucp2*. These results suggest that overexpression of the *Sod3* gene through gene transfer is an effective approach in preventing diet induced obesity and obesity-associated complications.

Key words: Obesity, fatty liver, superoxide dismutase 3, insulin resistance.

CHARACTERISTICS OF RISK STRATIFICATION OF PATIENTS WITH ISCHEMIC HEART DISEASE (IHD) ASSOCIATED WITH DIABETES MELLITUS TYPE 2

B.G. Hojakuliyev; M. Elyasov; M.B. Muhammedov

Turkmen State Medical University, Ashgabat, Turkmenistan

The purpose of the study was to compare frequency of occurrence of risk factors (RF) influencing the prognosis in patients with ischemic heart disease and concurrent diabetes mellitus type 2.

Data from 224 patients with ischemic heart disease and diabetes mellitus type 2 were analyzed, where 20,1% of the patients died during the year of observation. The cause of death was myocardial infarction (MI). Comparison group comprised 150 surviving patients.

The main risk factors were: Old myocardial infarction ($p<0,02$), Diabetes mellitus type 2 duration over 5 years ($p<0,004$), Obesity ($p<0,05$), Left ventricular hypertrophy ($p<0,03$); Heart failure ($p<0,04$). In patients with a poor prognosis, negative $T_{V4,6}$ was associated: any one or more ($p<0,02$) or any two or more ($p<0,03$). In patients who died, the first indicator was 33,3% versus 6,8% cases of survivors ($p<0,02$); the second indicator was, respectively, 22,2% versus 6,8% ($p<0,03$). ST depression revealed a number of features that were more common in those who died: any one or more ($p<0,002$), any one or more of $V_{1,6}$ ($p<0,01$), any one of $V_{4,6}$ ($p<0,0001$), +/-t in any lead ($p<0,0001$). LVEF was lower in patients who died ($p<0,001$). Reliable differences of SDNN, SDANN, RMSSD, TI were not disclosed. Thus, SDNN <68 msec² was disclosed in only 33,3% ($p<0,04$) of patients who died. The frequency and duration of painful and painless myocardial ischemia were observed more often in survivors ($p<0,05$).

ANTIPROTEINURIC EFFECT OF RASILEZ (ALISKIREN) IN HYPERTENSIVE/NORMOTENSIVE TYPE 2 DIABETES ADDED ON TO ACEI BASE TREATMENT

Sudzilla Nordin¹; Wan Mohamad Izani WM¹; Wan Mohamad WB¹; Kamaliah D¹; Wan Mohd Zahiruddin WM²

¹Medical department Universiti Sains Malaysia Kubang Kerian Kelantan Malaysia, ²Department of Community Medicine Universiti Sains Malaysia Kubang Kerian Kelantan Malaysia

Introduction: Diabetic nephropathy is the leading cause of end stage renal disease in developed countries. Microalbuminuria is one of the markers of early diabetic nephropathy with the presence of diabetic retinopathy. We evaluated the renoprotective effects of dual blockade of the renin-angiotensin-aldosterone system by adding treatment with aliskiren, an oral renin inhibitor to treatment with the optimal and stable dose of an ACE-I, while patient on optimal antihypertensive therapy in patients who had hypertension and type 2 diabetes with nephropathy.

Objectives: The aims of this study were to evaluate anti-proteinuric and antihypertensive effects of direct renin inhibitor (aliskiren) when added on to ACE-I in type 2 diabetic patients with microalbuminuria.

Patients and Methods: A randomized, open labeled trial, 2 arm parallel group study was done on diabetic nephropathy with microalbuminuria patients at KPP and KRK, HUSM. A total of 89 patients were successfully randomized into two arms, Aliskiren and control group. After 2 weeks of screening period, patients were randomly assigned to receive 6 month of treatment with aliskiren(150mg daily for 3 months, followed by an increase in dosage to 300mg daily for another 3 months) or in a control group, in addition to an ACE-i. The primary outcome was a reduction in the ratio of albumin to creatinine, as measured in an early morning urine sample, at 6 months.

Results: The baseline characteristics of the two groups were similar. Treatment with 300mg of aliskiren daily, as compared with control group, had reduced the mean urinary albumin to creatinine ratio from baseline by 40%, with mean UACR 12.18mg/mmol (95% CI, 7.80 to 16.56; $p=0.006$). A difference in blood pressure was seen between the groups by the end of the study period (systolic, 12.05mmHg lower [<0.001] and diastolic, 5mmHg lower [0.001] in the aliskiren group). Both groups had declining of eGFR, however the decline rate were slower in the aliskiren group when compared to control group ($p=0.039$).

The total number of adverse events were not significant between the two groups.

Conclusions: Aliskiren may have renoprotective effects that are independent of its blood-pressure lowering effect in patient with hypertension, type 2 diabetes mellitus and nephropathy who receiving the maximum dose of aliskiren 300mg as added on to an ACE-I at stable dose.

METABOLIC PROFILE OF PATIENTS WITH TYPE 1 DIABETES FROM AN OUTPATIENTS CLINIC OF SISTEMA UNICO DE SAUDE (SUS)

Veronica Freitas

Escola Bahiana de Medicina e Saúde Pública, Salvador, Brazil

Diabetes Mellitus type 1 is a group of metabolic disorders characterized by hyperglycemic and associated a complications, dysfunction and insufficiency of many organs. The adequate control glycemic reduces these complications and the treatment intensification is a procedure that occasions a better clinic control of the disease.

Objective: To describe the metabolic profile of patients with type 1 from an outpatients clinic of Sistema Único de Saúde (SUS) and test the association between demographic, clinical and laboratory and the nice and bad control of Diabetes.

Methodology: It's a describe study of morbidity in patients with diabetes treatment in endocrinology ambulatory of SUS at the General Hospital Roberto Santos in Salvador ,Bahia,Brasil. Data collection was performed by a questionnaire applied by the researchers during the medical treatment. Been evaluated demographic, anthropometric, socioeconomic, comorbidities, complications of type 1 diabetes, drug treatment and adequacy glycemic control or not.

Results: Of 21 patients, 57, 1% were female and 42, 9% were male with a mean age of 9,6 + 50 years. In relation to comorbidities dyslipidemia was observed in 14, 3%, hypertension in 9,5%, overweight in 10%. Ophthalmology complications was observed in 23, 8%, as peripheral neuropathy in 19% Finally, satisfactory glycemic control glycosated hemoglobin was observed in 5,6%, fasting plasma glucose in 15,8% and postprandial glycemic in 35,3%.

Conclusion: This study shows that only a minority of patients achieved satisfactory glycemic control. Therefore it's necessary investments in the care of diabetic patients by multidisciplinary team.

Key words: *Diabetes mellitus type 1. Metabolic profile. Glycemic control.*

EFFECT OF N-3 POLYUNSATURATED FATTY ACIDS ON ADIPOKINES AND BIOMARKERS OF ENDOTHELIAL DYSFUNCTION IN OBESE ASTHMATIC ADOLESCENTS WITH HYPERTRIGLYCERIDEMIA

Fengyang Huang¹; Blanca Estela del Río Navarro²; Omar Josué Saucedo Ramírez²; Margareth Sharon Hall Mondragón²; José Alfredo Pérez Ontiveros¹; Saúl Torres Alcántara¹

¹Laboratory of Pharmacology and Toxicology, Hospital Infantil de México Federico Gómez; ²Department of Allergy, Hospital Infantil de México Federico Gómez, Mexico

Topics: Clinical-Obesity

Background: Obesity and asthma prevalence have been increasing over the past decade. Epidemiological evidence demonstrates that obesity results in an increased risk of developing incident asthma. Recently published data suggest that obese asthmatic patients may represent a distinct phenotype of asthma. Evidences demonstrate that deficiency in omega-3 fatty acids could promote both obesity and excessive inflammation, resulting in greater asthma severity.

Objective: To evaluate the effect of supplemental omega-3 fatty acid daily (2.0 g eicosapentaenoic acid (EPA) and 1.0 g docosahexaenoic acid (DHA)) for 12 weeks on adipokines and biomarkers of endothelial dysfunction in obese asthmatic adolescents with hypertriglyceridemia.

Methods: The study was controlled, 12-week parallel group intervention trial involving 86 obese asthmatic adolescents with hypertriglyceridemia (the level of triglyceride is higher than 150 mg/dl) randomized to either omega-3 fatty acid treatment (n=45) or placebo (n=41). Fasting glucose, insulin, lipid profile, leptin, adiponectin, selectin E (sE) and asymmetrical dimethylarginine (ADMA) were measured at baseline and endpoint.

Results: Compared with placebo, the supplement of omega-3 for 12 weeks reduced weight, triglycerides, sE and ADMA in obese asthmatic adolescents with hypertriglyceridemia. Also, Omega-3 fatty acid demonstrated tendency to improve insulin resistance and decrease leptin. However, no changes were observed in glucose and adiponectin after treatment.

Conclusion: These results suggest that supplement treatment with omega-3 may be useful as an adjuvant therapy in obese asthmatic adolescents with hypertriglyceridemia. (HIM/2011/004)

ANTIHYPERGLYCAEMIC POTENTIAL OF PSIDIUM GUAJAVA LEAF IN STREPTOZOTOCIN INDUCED DIABETIC RATS

Toluwani Tella¹; Samson Mukaratirwa²;
Bubuya Masola¹

¹Department of Biochemistry, ²Department of Biological Sciences University of KwaZulu-Natal, Westville Campus

Introduction: *Psidium guajava* (PG) leaf is known to have a blood-glucose lowering effect in diabetic rats. The aim of the present study was to carry out a phytochemical study of PG leaf extract; investigate its protective effect on pancreas and also its effect on muscle glycogen synthase and phosphorylase activities in streptozotocin induced diabetic male Sprague-Dawley rats.

Methods: Diabetes was induced in male Sprague-Dawley rats with a single dose of 40 mg/kg body weight streptozotocin. The aqueous extract of *Psidium guajava* leaves was used to treat both normal and diabetic animals (400 mg/kg body weight) for 2 weeks while control animals were treated with the vehicle.

Results: After 2 weeks of treatment, PG lowered blood glucose and protected pancreatic tissue from diabetic damage. The treatment restored glycogen synthase activity depressed by diabetes and decreased glycogen phosphorylase activity in skeletal muscle. GC-MS analysis of the aqueous extract of PG indicated the presence of phenolic compound and triterpenoids.

Conclusions: We conclude that PG has a significant antihyperglycaemic effect, and that this effect may be associated with the presence of phenolic compound and triterpenoids. PG also protects the pancreas against diabetic damage and modulates the activity of enzymes in the insulin signalling pathway.

IMPACT OF SILENT CORONARY ARTERY DISEASE ON INCIDENCE OF CARDIOVASCULAR AND ALL-CAUSE MORTALITY EVENTS AT DIFFERENT STAGES OF GLUCOSE TOLERANCE

Ehteshami-Afshar S; Hajebrahimi MA; Hadaegh F

Prevention of Metabolic Disorders Research Center, Research Institute for Endocrine Sciences (RIES), Shahid Beheshti University of Metabolic Sciences, Tehran, Iran

To determine the impact of silent coronary artery disease (CAD), in different glucose tolerance status at baseline, i.e. those with normal fasting glucose/ normal glucose tolerance (NFG/NGT), pre diabetic and new diagnosed diabetes (NDM) for cardiovascular disease (CVD) and total mortality in Iranian population.

Study population included 1809 individuals, aged ≥ 50 years; free of CVD at baseline with a median follow-up of 9.1 years. To explore the risk of CVD and mortality associated with adding silent CAD (as defined using Minnesota coding criteria on baseline electrocardiogram in the absence of a history of CVD) into each of the glucose tolerance categories, we calculated multivariate adjusted Hazard ratios (HRs) for different glycemic status in the presence of silent CAD, compared to the corresponding non-silent CAD counterpart, as references.

During follow-up 277 CVD (234 coronary heart disease) and 168 deaths occurred. The presence of silent CAD, independent of traditional risk factor, among female population, significantly increased the risk of CVD for population with NFG/NGT [2.49 (1.22-5.07)] or pre-diabetes [HR: 2.52 (1.29-4.88) at baseline; among men population, however, the risk was significant for NFG/NGT population for mortality events [2.11 (1.05-4.27)] and for NDM for CVD [2.59 (1.23-5.44)] as well as mortality events [3.09 (1.39-6.87)].

Different strategies should be considered for males and females with silent CAD in different level of glucose tolerance. It might be justified that screening ECG for prevention of CVD events should be considered mainly among non-diabetic women and men with NDM.

INHIBITION OF MMP-2 AND MMP-9: A NOVEL APPROACH TO PREVENT CARDIOVASCULAR DYSFUNCTIONS IN TYPE 2 DIABETES

Bhatt L. K.¹; Addepalli V.²

¹Dr. Bhanuben Nanavati College of Pharmacy, Vile Parle (W), Mumbai, India, ²SPP School of Pharmacy and Technology Management, Vile Parle (W), Mumbai, India

Background: Upregulation of matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) in type 2 diabetic patients causes ECM remodelling thus resulted cardiovascular dysfunction. We hypothesized that inhibition of MMP-2 and MMP-9 may prevent cardiovascular dysfunction of type 2 diabetes.

Method: Type 2 diabetes in male wistar rats was induced by nicotinamide (100mg/kg, i.p.) and streptozotocin (55mg/kg, i.p. 15 min later). Type 2 diabetes and insulin resistance was confirmed by calculating HOMA-index. Four weeks after the inductions of diabetes rats were treated with MMP-2 and MMP-9 inhibitor Minocycline (25 mg/kg and 50 mg/kg) for next four weeks. At the end of the treatment protocol hemodynamic parameters, vascular reactivity and cardiac hypertrophy were measured. Histopathology and gelatin zymography were performed.

Results: The concentrations of fasting blood glucose, plasma insulin, and the HOMA-index of the diabetic rats confirmed induction of type 2 diabetes. Diabetes resulted in significant reduction in heart rate, mean arterial pressure, + dp/dt max and -dp/dt max compared to normoglycemic group. Treatment with minocycline (50 mg/kg) significantly ameliorated these parameters. Vascular reactivity was attenuated significantly in treated group (% relaxation 53.7 ± 2.31) compared to diabetic rats (% relaxation 41.7 ± 2.26). Treatment also attenuated cardiac hypertrophy, collagen, MMP-2 and MMP-9 levels significantly.

Conclusion: Results of his study suggest that inhibition of MMP-2 and MMP-9 ameliorates cardiovascular dysfunctions in type 2 diabetic rats.

AMELIORATION OF CARDIAC AUTONOMIC NEUROPATHY BY NOBILETIN IN DIABETIC RATS

Parkar Nishad^{1,2}; Veeranjanyulu Addepalli²

¹Dr. B. N. College of Pharmacy, Mumbai, India, ²SPP School of Pharmacy and Technology Management, NMIMS, Mumbai, India

Background: Cardiovascular autonomic neuropathy is one of the serious complications of diabetes. We hypothesized that nobiletin, a citrus flavonoid, due to its antioxidant and MMP-2 and MMP-9 inhibitory activity may attenuate cardiovascular autonomic neuropathy in diabetes.

Methods: We investigated effect of nobiletin on cardiac autonomic neuropathy and left ventricular function in streptozotocin-induced (50 mg/kg i.p.) diabetic rats by analysis of heart rate variability (HRV) and left ventricular functions. Four weeks after induction of diabetes, rats were administered nobiletin (10mg/kg and 25mg/kg) over a four-week period.

Results: Diabetes resulted in bradycardia (223 ± 26 vs. 344 ± 22** bpm; P<0.01). Time- and frequency-domain parameters of HRV were reduced significantly in diabetic rats. Spectral power was reduced around 33% at high frequencies and about 59% at low frequencies in diabetic rats, suggested a decrease of parasympathetic activity. Treatment with 25 mg/kg nobiletin attenuated bradycardia (296 ± 27** bpm; P<0.01 vs. diabetic control). Further the treatment resulted in significant increase in standard deviation of heart rate compared to untreated diabetic rats (P<0.05). Significant attenuation (P<0.05) was also observed in power spectrum analysis of treated animals. Left ventricular functions were also ameliorated significantly compared to diabetic control. Treatment also showed decreased MMP-2 and MMP-9 levels compared to diabetic control.

Conclusion: In conclusion, inhibition of MMP-2 and MMP-9 by nobiletin prevented development of cardiovascular autonomic neuropathy and ameliorated left ventricular function in streptozotocin-induced diabetes in rats.

RECEIVER OPERATING CHARACTERISTIC CURVE ANALYSIS OF ANTHROPOMETRIC INDICES AND A COMPARISON BETWEEN THREE INTERNATIONAL DEFINITIONS ATP-III, IDF AND MATP-III FOR SCREENING METABOLIC SYNDROME AMONG PRE- AND POSTMENOPAUSAL RURAL FEMALES OF AMRITSAR (PUNJAB)

Randhawa Ramanpreet;
Kaur Jaspreet and Sidhu Sharda

Department of Human Genetics, Guru Nanak Dev University, Amritsar -143005, Punjab, India

Background: Metabolic Syndrome (MS) is one of the major cause of morbidity and mortality across the globe. Limited data is available on the prevalence of MS in India especially among rural females in context to their

menopausal status. Therefore, this study was undertaken to determine the prevalence of MS and its components using three international diagnostic criteria in the premenopausal and postmenopausal rural females of Amritsar (Punjab).

Methods: This cross-sectional study was conducted among 300 rural females (186 premenopausal and 114 postmenopausal) of Amritsar (Punjab) during the period from June 2013 to June 2014. The age range of females was 25-55 years. Two anthropometric measurements (height and weight) were taken on each subject. From height and weight measurements, Body Mass Index (BMI) was calculated. Waist circumference was measured for the assessment of abdominal obesity. Waist-to-Height ratio (WHtR) was calculated. Percent Body Fat (PBF) was estimated using body fat analyser (Bodystat-1500) with the help of Bioelectrical Impedance Analysis. Moreover, Fat Mass Index (FMI) was calculated. Blood pressure of each participant was also measured. Fasting blood samples were taken and analysed for the estimation of Total Serum Cholesterol (TC), Triglycerides (TGL), High Density Lipoproteins-Cholesterol (HDL-C) and Fasting Blood Glucose (FBG). Low Density Lipoproteins-Cholesterol (LDL-C) and Very Low Density Lipoproteins-Cholesterol (VLDL-C) were also calculated. The prevalence of MS was assessed using three international criteria namely National Cholesterol Education Program Adult Treatment Panel-III, International Diabetes Federation and modified National Cholesterol Education Program Adult Treatment Panel-III criteria. SPSS-15 package was used for data analysis and the mean and standard deviation were calculated. Further Student's t-test, chi-square test and kappa statistic were also applied. Receiver Operating Characteristic (ROC) curve analysis was used to determine optimal cut off values for WC, WHtR, BMI, PBF and FMI among Punjabi rural females.

Results: In the pooled sample, the postmenopausal women had significantly higher values of waist circumference, systolic blood pressure and diastolic blood pressure than their premenopausal counterparts. In context to lipid profile variables, the values were again significantly higher among postmenopausal females as compared to premenopausal females except LDL-C. The prevalence of MS was 21.66%, 24.33% and 25.66 % using NCEP ATP-III, IDF and modified NCEP ATP-III criteria, respectively. The postmenopausal females were observed to have significantly higher prevalence of MS than premenopausal females. When these criteria were applied in the pooled sample, the degree of agreement (kappa statistic) was more (0.87) between mATP-III and IDF criteria as compared to between ATP-III and IDF (0.85) criteria and between mATP-III and ATP-III (0.76) criteria which shows that mATP-III has more concordance with IDF and less concordance with ATP-III criterion. It can be concluded from

the present results that we can use mATP-III or IDF criterion in future studies for detection of MS even though all these criteria have significant agreement but the maximum agreement was observed between mATP-III and IDF criteria. Among 300 rural females, 18.3% (55) females were screened positive for MS by all the three criteria. The most prevalent component of MS was reduced levels of HDL-C whereas the least common component was elevated levels of FBG. According to ROC curve analysis, WC, PBF and FMI showed the greatest area under the ROC curve in premenopausal as well as postmenopausal females.

Conclusion: This preliminary study concludes that MS is quite prevalent in rural women of Amritsar using all the three criteria. This high prevalence in this study suggests that primary prevention should be initiated in rural population.

ASSOCIATION BETWEEN METABOLIC SYNDROME AND MICROALBUMINURIA IN KOREAN ADULTS

Hyun-Ok Lee

Department of Family Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: We conducted a population-based sectional study of Korean adults to evaluate the association between metabolic syndrome (MetS) and microalbuminuria as a marker for early stage of chronic kidney disease.

Methods: A total of 8,497 adults (3,625 men and 4,872 women) who participated in the Korea National Health and Nutrition Examination Survey between 2011 and 2012 were included. MetS was defined according to recommendation from a joint interim statement of international organizations published in 2009. Microalbuminuria was defined as a urinary albumin-to-creatinine ratio of 30 to 300 mg/g. The association between MetS and microalbuminuria was evaluated using logistic regression analysis with adjustment for covariates while considering sampling weights and the complex survey design.

Results: The prevalence of microalbuminuria in subjects with MetS was 11% for men and 14.4% for women, whereas the prevalence in subjects without MetS was 3.1% for men and 6.7% for women. MetS was significantly associated with an increased risk of microalbuminuria in both women (odds ratio [OR]: 2.79; 95% confidence interval [CI]: 2.01-3.88) and men (OR: 3.00; 95% CI: 2.11-4.27). All components of MetS were associated with a significantly increased risk of microalbuminuria with the strongest association for high blood pressure. The risk of

microalbuminuria increased in a dose-dependent manner (P value for the trend <0.001) with the number of MetS components observed for both sexes.

Conclusion: These findings suggest that MetS is a risk factor for chronic kidney disease from early stage.

Key words: *Metabolic Syndrome X; Albuminuria; Hypertension; Obesity; Dyslipidemias*

ASPALATHIN ENHANCES INSULIN SENSITIVITY IN PALMITATE-INDUCED INSULIN RESISTANT 3T3-L1 ADIPOCYTES

S.E. Mazibuko^{1,2,*}; C.J.F. Muller¹; E. Joubert^{3,4}; R. Johnson¹; A.R. Opoku²; J. Louw¹

¹Diabetes Discovery Platform, South African Medical Research Council, South Africa, ²Department of Biochemistry and Microbiology, University of Zululand, South Africa, ³Post-Harvest and Wine Technology Division, Agricultural Research Council (ARC), Infruitec-Nietvoorbij, South Africa, and ⁴Department of Food Science, Stellenbosch University, South Africa.

High levels of saturated free fatty acids (FFAs), such as palmitate, are associated with insulin resistance of muscle, fat and liver tissues. Recently we demonstrated that an aqueous extract of Rooibos (*Aspalathus linearis*), well-known as herbal tea, inhibits adipogenesis and stimulates glucose metabolism in 3T3-L1 adipocytes. This study aims to establish whether aspalathin, the major flavonoid and a dihydrochalcone, present in Rooibos can contribute significantly to the amelioration of experimentally induced insulin resistance in 3T3-L1 adipocytes.

3T3-L1 adipocytes were made insulin resistant by culturing in DMEM containing 0.75 mM palmitate for 16 h. Thereafter the cells were cultured for 3 h in DMEM with or without 0.75 mM palmitate, and insulin (1 μ M) supplemented with aspalathin (10 μ M). Glucose uptake, cell viability and mitochondrial activity were measured using 2-deoxy-[3H]-D-glucose, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and ATP assays, respectively, and protein expression by Western blot analysis.

Insulin resistance in 3T3-L1 adipocytes was confirmed by a reduction in insulin-stimulated glucose uptake, MTT activity and ATP content, after 16 h of culture with palmitate. Aspalathin reversed these effects. At a protein level aspalathin increased the activation of threonine kinase B (AKT) and AMPK, as well as the expression of glucose

transporter 4 (GLUT4). Peroxisome proliferator-activated receptor gamma (PPAR γ) and carnitine palmitoyltransferase one (CPT1), regulators of lipid metabolism in 3T3-L1 adipocytes were also increased. Malonyl CoA, the rate-limiting substrate for lipid oxidation, was reduced. The activation of nuclear factor kappa beta (NF- κ B) was also suppressed. At mechanistic level the activation of AKT and AMPK, increased levels of GLUT4, PPAR γ and CPT1, together with malonyl CoA suppression, will enhance glucose uptake and lipid oxidation. Inhibition of NF- κ B activation by aspalathin will also suppress palmitate-induced activation of the inflammatory pathway. This offers a plausible explanation for the ameliorative effect of aspalathin on insulin-resistance, an underlying cause for obesity.

ASSOCIATION BETWEEN LOW DIETARY SODIUM INTAKE AND INSULIN RESISTANCE IN THE KOREAN POPULATION: THE KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (KNHANES), 2009-2010

Seong-Hoon Kwon

Samsung Medical Center Seoul, South Korea

Background: There has been controversial evidence for relation between sodium intake and insulin resistance, and little research has been conducted on the Korean population. Therefore, we investigated an association between sodium intake and insulin resistance in Korean.

Methods: This is a cross-sectional study. Of those aged more than 10 years who participated in the 4th and 5th KNHANES (2009-2010), a total of 11549 participants were included. Subjects were excluded if they reported implausible daily total energy intake, were pregnant, or were diagnosed with diabetes, renal failure, liver cirrhosis, or thyroid disease. Sodium intake was calculated from 24-h recall and categorized into quartiles. Subjects with the homeostasis model assessment of insulin resistance (HOMA-IR) scores >2.0 or the quantitative insulin sensitivity check index (QUICKI) <0.35 were classified as insulin resistance. Multivariate linear and logistic regression analyses were used to identify the association between sodium intake and insulin resistance.

Results: After adjusting for confounding factors, multivariate linear regression analyses revealed that sodium intake was inversely associated with insulin resistance. This result was confirmed by multivariate logistic regression analyses after adjusting for confounding factors. Compared to subjects in the 1st quartile, subjects in the 4th quartile had a lower prevalence of insulin resistance with

odds ratios of 0.83 (HOMA-IR, 95% confidence intervals [CIs], 0.70–0.98) and 1.22 (QUICKI, 95% CIs, 1.03–1.45), respectively.

Conclusion: There was a significant association between low dietary sodium intake and insulin resistance in the Korean population.

Key words: Sodium, Insulin resistance, Korean.

SYNERGETIC EFFECTS OF L-CARNITINE AND α -LIPIC ACID ON VIABILITY OF HCT 116 CELL LINE

Aktan, F¹, Karabay, A.Z¹., Koc, A²

¹Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey, ²Ankara University, Faculty of Pharmacy, Ankara, Turkey

L-carnitine is an important molecule in fat metabolism, it participates in the transport of long-chain fatty acids into mitochondrial matrix. It is an effective antioxidant molecule that exhibits free radical scavenging activity and it enhances antioxidant status in rats and exhibited anticancer properties. It has been shown that α -Lipoic acid is a very effective molecule against type 2 diabetes, atherosclerosis, inflammatory skin diseases, reperfusion arrhythmias and Parkinson's disease and serves apoptotic action in different cancer cells. These molecules can display important roles in treatment of colon cancer. In this study, we examined the synergetic effects of α -lipoic acid and L-carnitine on HCT 116 +/+ colon cancer cell line. For this purpose, HCT 116 +/+ colon cancer cells were treated with L-carnitine and α -Lipoic acid for 24 hours and MTT assay was conducted. Insoluble formazan product was dissolved in dimethyl sulfoxide (DMSO). The extent of MTT reduction was quantified by measuring the absorbance at 550 and 690 nm. Survival (%) was calculated relative to control. α -Lipoic acid and L-carnitine alone or in combination decreased cell viability in HCT 116 +/+ colon cancer cells and exhibited synergetic effect on the cell viability. Further studies must be conducted to find out the mechanism of their effects in cancer therapy.

ASSOCIATIONS OF IRON INDICES WITH IMPAIRED FASTING GLUCOSE AND DIABETES AMONG KOREAN ADULTS; THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2010–2012

Hyun-ju Bak

Department of Family Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: Previous studies indicated that excessive iron stores induce organ damage, leading to diabetes. This study evaluated the relationship between iron indices-serum ferritin and transferrin saturation (TSAT)-and impaired fasting glucose (IFG) and diabetes.

Methods: We performed a cross-sectional study of a representative sample of South Korean adults aged ≥ 19 years using data from the Korean National Health and Nutrition Examination Survey 2010–2012. Totally, 14,468 participants were included after excluding those who were pregnant and those with chronic liver disease, chronic kidney disease, or anemia. The subjects were classified into the following three groups: normal fasting glucose, IFG (defined as fasting glucose, 100–125 mg/dL), and diabetes. We also measured glycated hemoglobin, serum ferritin, and TSAT (percentage of iron-saturated transferrin).

Results: IFG and diabetes prevalence were related to increasing ferritin quartiles and decreasing TSAT quartiles. After adjusting for age, education level, smoking, drinking, and body mass index, IFG and diabetes were significantly elevated in the highest ferritin quartile compared with the lowest quartile; IFG (adjusted odds ratio: 2.12, 95% CI: 1.66–2.71) in men and (1.37, 1.05–1.78) in women; Diabetes (2.08, 1.55–2.79) in men and (1.88, 1.32–2.69) in women. In contrast, IFG and diabetes were less prevalent in the highest TSAT quartile; IFG (0.87, 0.70–1.08) in men and (0.66, 0.52–0.84) in women; Diabetes (0.67, 0.49–0.92) in men and (0.44, 0.32–0.61) in women.

Conclusion: Increased serum ferritin and decreased TSAT levels are independently associated with IFG and diabetes among Korean men and women.

Key words: Serum ferritin; Transferrin saturation; impaired fasting glucose; Diabetes

A 6-MONTHS STUDY OF TWO DIFFERENT DIETS IN TYPE 2 DIABETES

Andreea Soare¹; Yeganeh M. Khazrai¹;
Rossella Del Toro¹; Elena Roncella¹; Sara Fallucca¹;
Silvia Angeletti¹; Valeria Formisano¹;
Francesca Capata¹; Silvia Manfrini¹;
Francesco Fallucca²; Mario Pianesi³; Paolo Pozzilli^{1,4}

¹Department of Endocrinology and Diabetes, University Campus Bio-Medico, Rome, Italy; ²International Center for the Study of Diabetes (CISD) Rome, Italy; ³International Study Center for Environment, Agriculture, Food, Health and Economics, Rome, Italy; ⁴Centre of Diabetes, St. Bartholomew's and the London School of Medicine, Queen Mary, University of London, UK

Background and Aims: The original MADIAB trial (randomized controlled trial of 21 days in type 2 diabetic patients who were admitted and followed-up in hotel settings for such period) comparing the macrobiotic Ma-Pi2 diet with the diet recommended by scientific medical societies for the treatment of type 2 diabetes (control diet) showed the beneficial effects of the former on HbA1c, weight loss and lipid profile. In order to investigate whether these achievements are maintained and, most importantly, to assess the acceptance and compliance of these two diets in the real-life on the long-term, a 6-months follow-up study was carried out in patients who participated in the MADIAB trial.

Materials and Methods: The follow-up study included 43 type 2 diabetes patients (n = 18 in the Ma-Pi2 group, mean age 64.4 years ± 10 and n = 25 in the control group, mean age 63.6 years ± 9) who continued their respective diets for a 6-month period. Anthropometric measurements and blood samples for biochemical parameters were assessed at the end of the MADIAB trial and after 3 and 6 months of the follow-up period.

Results: At the end of the 21 days MADIAB trial, which coincided with the beginning of follow-up, HbA1c values were 6.4% ± 0.9% in the Ma-Pi2 group and 6.6% ± 0.8% in the control group. At 3-months follow-up HbA1c levels dropped in the Ma-Pi2 group to 5.9% ± 0.7% and were 5.9% ± 0.9% after 6 months; in the control group HbA1c levels dropped to 6.2% ± 0.7% at 3 months and were 6.3% ± 0.6% at 6 months. The percentage reduction in HbA1c within groups was significantly lower compared to the beginning of follow-up (p<0.001) but the reduction was not significant between groups (p = 0.2). However after multivariate analysis adjusted for age and gender a significantly greater reduction in HbA1c values was observed in the Ma-Pi2 group compared to the control group (p = 0.03). A major weight loss with the Ma-Pi2 diet (mean body weight 77.1 kg ± 17.6 vs. 85.6 kg ± 15.8 in the control group)

was maintained up to 6-months follow-up (p<0.001). Both groups maintained their lipid profile in the recommended range for age and gender during follow-up.

Conclusion: Both diet treated groups (although the Ma-Pi2 group showed higher weight loss and a tendency for greater reduction in HbA1c) maintained an excellent metabolic control underling the important role of an intensive initial short period of closely monitored diet in the therapy of type 2 diabetes. This study emphasizes the concept that, beyond the type of diet, a close follow-up and a continuous reinforced diet program helps maintaining metabolic control in type 2 diabetes patients on the long term.

RELATION OF PLASMA NITRIC OXIDE (NO) AND *IN VITRO* NO PRODUCED BY VAT/SAT ISOLATED ADIPOCYTES WITH ENDOTHELIAL DYSFUNCTION, SUBCLINICAL ATHEROGENESIS AND METABOLIC RISK IN MORBID OBESE PATIENTS.

Melchor-López A¹; Martínez-Hernández JE²;
Gómez-Cortés E²; Ortíz-Fernández M³;
Montoya-Ramírez J³; Gaytán-Fuentes OF³;
Brito-Munive RH³; Urbina León D³;
Villanueva-Canelo JP³; Blas-Azotla R³;
Rodríguez-Trejo JM⁴; González-deLeo S⁴;
Rizo-García Y⁴; Orozco-Vázquez J⁵; Toríz-Ortíz A⁵;
Osorio-Valero M⁵; Moreno-delValle TR²;
Pérez-Cabeza de Vaca R²; Mondragón-Terán P²;
Suárez-Cuenca JA²

¹Posgraduate Program in Medical Science, National University of Mexico; ²Divisions of Biomedical Research, ³Bariatric Surgery, ⁴Vascular Surgery and Angiology and ⁵Diagnostic and Therapeutic Imaging, National Medical Centre, "20 de Noviembre", ISSSTE, Mexico City, Mexico

Aim: Metabolic and endothelial dysfunction leading to progressive atherogenesis are considered cardiovascular risk factors in obese patients; whereas visceral adipose tissue (VAT) shows significant metabolic differences compared with subcutaneous adipose tissue (SAT), their association with Nitric Oxide (NO) bioavailability is yet not clear. The aim of this research was to estimate whether plasma NO, and *in vitro* NO from VAT/SAT isolated adipocytes, are related to endothelial dysfunction, subclinical atherogenesis and metabolic risk in morbid obese patients.

Methods: This research was performed as a cross-sectional study. Morbid obese patients programmed for bariatric surgery were included. Metabolically Unhealthy Obese (MUO) group was defined according to metabolic syndrome, using NCEP-ATPIII criteria, and compared with

Metabolically Healthy Obese (MHO). Adipocyte isolation was performed according to a standard protocol and further stained with oil red as a marker for adipocytes. NO was measured through nitrite levels, reflecting nitric oxide production, determined either in plasma or in 2-weeks culture media of adipocytes isolated from VAT and SAT. Endothelial dysfunction and subclinical atherogenesis were measured through ultrasonographic determination of brachial artery Flow Mediated Dilatation (FMD) and Carotid Intima Media Thickness (CIMT), respectively.

Results: Seven patients were eligible for this study, aged 40 ± 9 years-old, gender male 2, female 5; whereas 4 obese patients were classified as MUO. Plasma concentration of NO directly correlated with NO from cultured adipocytes isolated from VAT, and inversely correlated with NO from SAT isolated adipocytes. In order to include both NO determinations *in vitro*, the ratio of NO from VAT adipocytes / NO from SAT adipocytes was used for further analysis. Plasma NO levels showed correlation with Body Mass Index (BMI) ($p=-0.6$, $p=0.4$) and higher values were observed in UHO patients; while NO produced by cultured VAT/SAT adipocytes showed particular correlation with FMD and CIMT.

Conclusion: Results from our study suggest early evidence that plasma NO levels and NO produced by VAT/SAT cultured adipocytes are related with metabolic risk, endothelial dysfunction and/or subclinical atherogenesis in morbid obese patients.

INSULIN RESISTANCE IN LIVERS OF OBESE AND TYPE 2 DIABETIC HUMANS

Robert V. Farese; Mini P. Sajan

Research and Internal Medicine Sections of the James A. Haley VA Medical Center, and Department of Internal Medicine, University of South Florida College of Medicine, Tampa, FL

In high-fat-fed (HFF) and ob/ob mice, initiation of insulin resistance involves increases in hepatic ceramide, subsequent activation of atypical protein kinase C (aPKC), aPKC accumulation on scaffolding protein WD40/ProF, selective impairment of Akt-dependent FoxO1 phosphorylation on the WD40/ProF scaffold by co-localized aPKC, and increased gluconeogenic enzyme expression. Resulting hyperinsulinemia hyperactivates hepatic Akt and aPKC, which together increase hepatic lipogenesis, and metabolic syndrome features develop. As insulin resistance progresses, hepatic Akt activation diminishes, but hepatic aPKC remains elevated. Fortunately, selective inhibition of hepatic aPKC improves hepatic and clinical

abnormalities. To see if a similar situation exists in obese and type 2 diabetic (T2D) humans, we examined flash-frozen livers of transplant donors. As in HFF and ob/ob mice, hepatic ceramide levels and aPKC activity of both obese (BMI, 34-44) non-diabetic and T2D humans were increased, relative to controls (BMI, <25). Hepatic aPKC activity increases in obese and T2D humans were maximal (unresponsive to PIP_3) and accompanied by: increased aPKC and decreased Akt association with WD40/ProF; decreased FoxO1 phosphorylation; and increased expression/abundance of gluconeogenic (and lipogenic) enzymes. As expected, hepatic Akt activity was diminished in T2D humans; but, unexpectedly, hepatic Akt was similarly diminished in markedly obese humans, indicating advanced hepatic insulin resistance. We conclude that the inordinate elevation of hepatic aPKC activity, its excessive presence on the WD40/ProF platform, and the resultant impairment of Akt-dependent hepatic FoxO1 phosphorylation, is a consistent mechanism underlying the pathogenesis of insulin resistance in humans and mice. Therapeutic measures that directly target this basic abnormality are needed.

3,5-DIODO-L-THYRONINE REDUCES BLOOD GLUCOSE IN MICE BY INCREASING METABOLIC RATE AND DECREASING GLUCOSE PRODUCTION BY THE LIVER

Teixeira SS¹; Minze LJ²; Filgueira CS²; Zhang A²; Webb P²; Nunes MT¹

¹*Department of Physiology and Biophysics, University of Sao Paulo (USP), Sao Paulo, Sao Paulo, Brazil.* ²*Center for Genomic Medicine, The Methodist Hospital Research Institute, Houston, Texas, United States.*

Introduction: Thyroid hormones have an important function in a number of physiological events. The thyroid gland synthesizes and releases mainly T4 and T3; although the majority of circulating thyroid hormone is T4, which is later converted to the more bioactive form, T3. T3 is further metabolized by type 3 deiodinase to T2, which has been considered an inactive metabolite. However, there are multiple and recent reports of T2 biological activity both *in vivo* and *in vitro*.

Material and Methods: The aim of this study was to investigate the effects of T2 treatment on glucose metabolism. Male C57BL/6 mice were treated with high fat diet (HFD) for 8 weeks to induce insulin resistance. After this period, the animals were divided into groups receiving daily intraperitoneal injections of vehicle (saline), T3, or T2 for 4 weeks. Tail blood glucose, body temperature, body weight, and body fat were measured weekly. For the calculation of

the food intake, food was weighed daily for 7-8 days. The intravenous glucose tolerance test (IGTT) was performed 4 days before the end of the experimental period. At the end of the experimental period, the production of glucose by the liver was evaluated using a perfused rat liver model.

Results: We observed that T2 decreased body weight, body fat, and blood glucose. Moreover, hepatic glucose production, after liver perfusion with lactate, was decreased in HFD animals treated with T2.

Conclusion: Our results suggest that T2 increases metabolic rate and decreases hepatic glucose output, thereby lowering plasma glucose levels. *Fapesp* 2010/18151-7.

THYROID HORMONE TREATMENT REDUCES INFLAMMATORY CYTOKINES AND INFLAMMATORY CELLS INFILTRATION IN WHITE ADIPOSE TISSUE IMPROVING INSULIN SENSITIVITY OF DIABETIC RATS

Panveloski-Costa AC; Teixeira SS; Poyares LL; Nunes MT

Department of Physiology and Biophysics, Institute of Biomedical Sciences, University of São Paulo

Background: Abnormal macrophage infiltration is typical in adipose tissue and pancreatic islets from both type 1 and type 2 diabetes (DM1 or 2) in human and animal models, and it is accompanied by expression of some cytokines which are correlated to dysfunction of insulin secretion and signaling in the islet and peripheral tissues. Hypothyroidism has been linked to low insulin-induced glucose uptake in both skeletal muscle and adipose tissue, and patients with subclinical hypothyroidism have signs of low-grade inflammation. In this context, we hypothesize that thyroid hormone treatment could decrease inflammation grade and improve glycemia and insulin sensitivity in rats.

Methods: Male Wistar rats were assorted in control (C), diabetic (D) and T3-treated (1.5 $\mu\text{g}/100\text{g BW}$, for 28 days) diabetic group (DT₃). The diabetes was induced by alloxan injection and after 15 days, rats with glycemia higher than 250 mg/dL were included in the study. After the experimental period, rats were anesthetized for glycemia and insulin sensitivity measurement. The epididymal white adipose tissue (eWAT) was removed for analysis of TNF- α and IL-6 content, as well as inflammatory cells infiltration by western blotting and light microscopy, respectively.

Results: T3 treatment reduced glycemia in 50% and restored insulin sensitivity to control values. These

alterations were accompanied by a decrease in TNF- α and IL-6 content and inflammatory cells infiltration.

Conclusion: The present data provide evidence that, at least part of the benefits of T3 treatment on insulin sensitivity of diabetic rats occurs by its negative modulation of inflammatory status of WAT.

HETEROGENEITY IN 1-HOUR PLASMA GLUCOSE IN PATIENTS WITH PREDIABETES DIAGNOSED BY HEMOGLOBIN A1C

Aidar R. Gosmanov, MD, PhD; Jim Wan, PhD

University of Tennessee HSC, Memphis, TN

Purpose: One-hour plasma glucose (PG) above 155mg/dL during oral glucose tolerance test (OGTT) may identify subjects with increased risk for cardiovascular disease. Here we studied 1-hour PG in patients with prediabetes diagnosed by HbA1c.

Methods: We identified 66 subjects with newly diagnosed prediabetes by HbA1c criterion (values of 5.7-6.4%) in general endocrinology clinic. All subjects subsequently underwent confirmatory 2-hr OGTT. PG and insulin at 0, 60, and 120mins and other biochemical characteristics were analyzed in all subjects using Mann-Whitney or chi-square tests.

Results: In the cohort of subjects (54 females, 41 blacks/25 whites), 32 had normal glucose tolerance (NGT), 26 had true prediabetes, and 8 people had diabetes. Compared with true prediabetes group, the NGT patients had lower fasting PG (86.3 ± 7.7 vs $95.1 \pm 10.4\text{mg/dL}$, $P = 0.0009$), 1-hour PG (118.1 ± 28.8 vs $183.0 \pm 19.3\text{mg/dL}$, $P < 0.0001$), and 2-hour PG (102.3 ± 24.3 vs $154.9 \pm 21.6\text{mg/dL}$, $P < 0.0001$). All patients with the NGT had 1-hour PG $< 155\text{mg/dL}$ and all subjects with true prediabetes had 1-hour PG $> 155\text{mg/dL}$. These differences in plasma PG persisted after adjustment for personal history of hypertension, sex, body mass index, hematocrit, vitamin D level, statin use and family history of diabetes in multivariate logistic regression analysis. Indices of homeostatic model of assessment of insulin resistance (HOMA-IR) and beta cell function (HOMA-B) were not different between the NGT and prediabetes patients.

Conclusions: Our data demonstrates that all NGT patients with HbA1c of 5.7-6.4% had 1-hour PG below 155mg/dL. These results suggest that patients with HbA1c of 5.7-6.4% are heterogeneous in their metabolic and potentially cardiovascular characteristics.

A STUDY ASSOCIATION OF INSULIN RESISTANCE AND CIRCULATING PCSK9 LEVELS IN HYPOTHYROID CASES

Amit Jain, Promod Lali; Dinesh K. Dhanwal; Lal Chandra

Department of Biochemistry and Department of Medicine, Maulana Azad Medical College and Associated Hospitals, NewDelhi-110 002 INDIA

Objective: PCSK9 (Proprotein convertase subtilisin/kexin type 9) promotes the degradation of the Low-density lipoprotein receptor in hepatocytes, leading to an increase in plasma LDL-C (LDL cholesterol). Previous studies have shown that insulin stimulates PCSK9 transcription and showed a positive correlation between plasma PCSK9 concentration and fasting insulinemia. Hypothyroidism is also associated with insulin resistance and high LDL levels. The purpose of this study was to investigate the relationship of PCSK9 levels and insulin resistance in hypothyroid patients.

Methods: One hundred eighteen patients with the diagnosis of hypothyroidism based on their clinical and thyroid function test profile were included in this cross sectional hospital based descriptive study with their informed consent. HOMA-IR (Homeostatic model assessment of insulin resistance) as an index of insulin resistance was calculated for each subject from their fasting plasma glucose and serum insulin levels. PCSK9 levels measured by sandwich ELISA.

Results: Baseline PCSK9 concentration was significantly higher (18.0% $p=0.019$) in patients in the highest tertile (90-260 pmol/L) of baseline insulin concentration compared to the lowest tertile (20-50 pmol/L). Similarly, PCSK9 concentrations were 15.0% higher ($p=0.038$) in the high tertile (8.6-14.2) group of HOMA-IR compared to the lower tertile (1.8-4.4) group. Insulin resistance in these patients was independent of thyroid hormones levels. PCSK9 levels are correlated significantly ($r=0.030$, $P=0.018$) with TSH levels.

Conclusions: Our results suggest that patient with higher hepatic insulin resistance have higher baseline PCSK9 concentration. It is therefore likely that hepatic insulin resistance impairs the inhibitory action of insulin on PCSK9. Also PCSK9 levels correlated significantly with TSH levels.

MOLECULES REGULATING SYSTEMIC TRAFFICKING AND/OR HOMING OF (CANCER) STEM CELLS – ANALYSIS IN HUMAN ADIPOSE TISSUE.

Blogowski W^{1,4}; Budkowska M²; Salata D²; Lokaj M³; Prowans P³; Dolegowska B²; Starzynska T⁴

¹Department of Public Health, University of Zielona Gora, Poland, ²Departments of Medical Analytics, ³Plastic, Endocrine and General Surgery, ⁴Gastroenterology, Pomeranian Medical University in Szczecin, Poland

Introduction: Recent experimental studies demonstrated that adipose tissue (AT) may offer a “vivifying” environment for cancer stem cells (SCs). However, little is known about the composition of human AT in terms of crucial molecules regulating trafficking and/or homing of (cancer) SCs.

Material and Methods: In this study we comprehensively examined plasma and AT (subcutaneous and visceral/omental) levels of stromal-derived factor-1 (SDF-1), sphingosine-1-phosphate (S1P), stem cell factor (SCF), hepatocyte/vascular-endothelial growth factors (HGF/VEGF) and/or granulocyte-colony stimulating factor (G-CSF) in lean, overweight and obese individuals. Moreover, we verified their associations with values of anthropometric features characterizing our patients, such as BMI or body adiposity index (BAI). Blood and AT samples (subcutaneous and visceral/omental) were obtained from 35 individuals undergoing elective surgery.

Results: AT levels of SDF-1, SCF and G-CSF were significantly lower than in plasma (all $p<0.0001$), whereas AT concentrations of other molecules were comparable (VEGF, S1P) or even much higher (HGF) than the corresponding levels in the peripheral blood, particularly in overweight/obese subjects. Depot-specific differences in SDF-1, SCF, G-CSF and VEGF concentrations were found in all examined groups revealing that visceral/omental AT in obese individuals, is particularly “rich” in these substances. Moreover, several correlations were established between analyzed molecular substances and BMI or BAI values.

Conclusions: Human AT seems to possess relatively high levels of all cardinal molecules that are necessary to create suitable niches for (cancer) SCs. In humans, the exact composition of AT environment seems to be related to the amount of body mass/adiposity. Supported by TANITA Healthy Weight Community Trust.

EFFECTS OF OBSTRUCTIVE SLEEP APNEA ON INSULIN SENSITIVITY AND INSULIN RESISTANCE IN OBESE AND LEAN PERSONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Sikarin Upala, MD, MS^{1,2}; Anawin Sanguankeo, MD^{1,2}

¹Department of Internal Medicine, Bassett Medical Center and Columbia University College of Physicians and Surgeons, Cooperstown, NY; ²Department of Preventive and Social Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

Background: Many studies have found that obstructive sleep apnea (OSA) is associated with insulin resistance. However, there is still controversy whether such association is influenced by obesity. This is a systematic review and meta-analysis of available studies on association between OSA and insulin resistance. Our primary objective is to explore whether there is difference of such association in the obese compared with non-obese groups.

Methods: We comprehensively searched the databases of PubMed/MEDLINE, EMBASE, and CENTRAL. The inclusion criterion was observational or interventional studies in adults that examined association between OSA versus control and insulin resistance or insulin sensitivity. Studies that were indifferent in body mass index (BMI) in OSA and control group were included in a quantitative data analysis comparing the homeostasis model assessment-estimated insulin resistance (HOMA-IR) and insulin sensitivity index (ISI) between the two groups.

Results: From 126 full-text articles, 51 studies met our inclusion criterion and 18 studies involving 2,847 participants were included in the meta-analysis based on the random effects model. In obese participants with OSA, there was lower ISI compared with the obese control with mean difference (MD) of -0.54 (95% CI: -1.01 to -0.06). Also, OSA group has higher insulin resistance measured by HOMA-IR in both obese (MD = 0.91, 95% CI: 0.23 to 1.59) and non-obese (MD = 0.94, 95% CI: 0.35 to 1.53) subgroups.

Conclusions: Overall, subjects with OSA were found to have higher insulin resistance and lower insulin sensitivity compared to those without OSA. This association were found in both obese and non-obese individuals.

FAILURE TO SUPPRESS POSTPRANDIAL NON-ESTERIFIED FATTY ACIDS FOLLOWING HIGH FRUCTOSE FEEDING IN MEN OF BLACK-AFRICAN ORIGIN BUT NOT IN MEN OF WHITE-EUROPEAN ORIGIN

Louise M. Goff; Miriam Samuel; Scott V. Harding

Division of Diabetes & Nutritional Sciences, School of Medicine, King's College London, London, SE1 9NH

Background: Black-African (BA) populations have historically had cardioprotective lipid profiles⁽¹⁾ but more recent North American data indicates this protection has been for the most part lost⁽²⁾. Epidemiological studies have demonstrated concurrent increases in fructose consumption and cardiovascular risk in the United States⁽³⁾. Fructose has lipogenic potential because of its insulin-independent hepatic metabolism however there have been no studies of its effect in BA people. The present study investigated the hypothesis that high fructose feeding would potentiate greater post-prandial hypertriglyceridemia in BA compared to White-European (WE) men.

Methods: We conducted a double-blinded pilot study in healthy BA (n=7) and WE (n=8) men in which 25% of total 24hr energy intake was provided as fructose. Blood sampling was performed throughout the postprandial period to determine serum triglyceride (TG), glucose, non-esterified fatty acid (NEFA) and insulin concentrations. The iAUC for each outcome was calculated and compared between ethnic groups by t-test and multivariate ANOVA.

Results: The serum glucose, insulin and NEFA iAUC did not differ between ethnic groups, but a trend towards significance was observed for TG iAUC ($p=0.07$) (Figure 1A-1D). Multivariate ANOVA demonstrated multiple significant time-point differences showing a lack of suppression of NEFA in BA men ($p<0.05$) (Figure 1C).

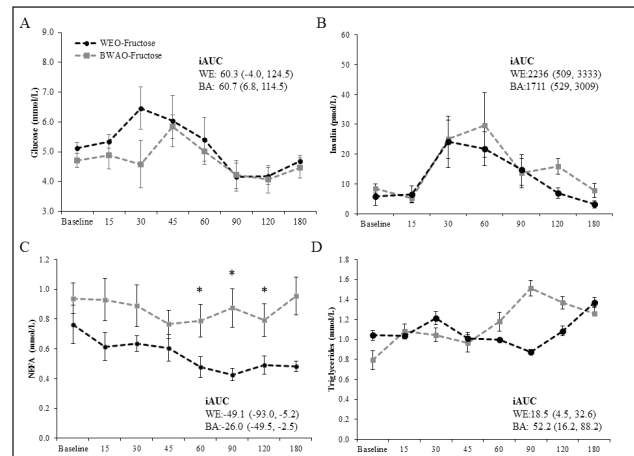


Figure 1. Postprandial glucose (panel A), insulin (panel B), NEFA (panel C) and TG (panel D) in men of BA and WE origin following a mixed-meal feeding study with fructose intakes at 25% of total energy. Values are means \pm SEM; n=15. * denotes significantly different values at same time point with $p<0.05$.

Conclusions: These data show a trend towards raised post-prandial TG and a failure to suppress NEFA production in BA compared to WE men following acute high fructose feeding. Excessive fructose consumption could drive metabolic changes, similar to those reported here, and may be particularly relevant to cardiometabolic risk development in BA populations.

1. Chaturvedi N, McKeigue PM, Marmot MG. (1994) *Diabetologia* 37(8), 765.
2. Jolly S, Vittinghoff E, Chattopadhyay A *et al.* (2010) *Am J Med* 123, 811.
3. Tappy L and Lê K (2010) *Physiol Rev* 90, 23.

INCREASED INCRETIN RELEASE COMPENSATES FOR EARLY INSULIN SECRETORY DEFICITS IN TYPE 2 DIABETES IN MEN OF BLACK WEST AFRICAN ORIGIN

Louise M. Goff¹; Cynthia Mohandas¹; Stephanie A. Amiel¹; Janet Peacock²; Margot Umpleby³

¹Division of Diabetes & Nutritional Sciences; ²Division of Health & Social Care Research, King's College London, School of Medicine, Franklin-Wilkins Building, Stamford Street, London, SE1 9NH, UK; ³Division of Diabetes & Metabolic Medicine, University of Surrey, Postgraduate Medical School, Guildford, UK

Hypothesis: Compared to men of White-European origin (WEO), men of Black West African origin (BWAO) with early type 2 diabetes (T2D) will have markedly greater insulin secretory deficits in response to intravenous and oral glucose.

Methods: Beta-cell function was assessed in 15 BWAO and 17 WEO men, matched for age and BMI, using a hyperglycaemic clamp (HC; plasma glucose = basal + 6.9 mmol/l) and mixed meal tolerance test (MMTT; 6kcal/kg 'Ensure Plus™, milkshake). Plasma insulin and c-peptide were assessed following both procedures, and GLP-1 and GIP following the MMTT. Total (AUC) and incremental area under the curve (iAUC), and 1st and 2nd phase insulin and c-peptide responses (1) were calculated and compared between groups using independent samples t-tests.

Results: There were no differences in age, BMI, diabetes duration or HbA1c between the two ethnic groups (table 1). BWAO men demonstrated significant insulin secretory deficits, measured through c-peptide, in response to both intravenous (HC) and oral glucose (MMTT) (Table 1). However circulating insulin responses were not different

between the groups suggesting reduced hepatic insulin clearance in BWAO participants. The BWAO participants demonstrated significantly greater GIP secretion in the MMTT (table 1).

Conclusion: These data support the hypothesis that men of BWAO with early T2D have significantly greater insulin secretory deficits compared to men of WEO, matched for age, BMI and clinical status. These data indicate a role of reduced hepatic insulin clearance in maintaining peripheral insulin concentrations and increased incretin responses compensating for reduced glucose stimulated insulin secretion in T2D in men of BWAO.

1. DeFronzo R.A., Tobin J.D. and Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol* 1979; 6(3): E214-E223.

Table 1. Clinical characteristics of study participants and insulin, c-peptide and incretin responses in the hyperglycaemic clamp and mixed meal tolerance test.

	BWAO (n=15)	WEO (n=17)	p
Age (years)	53 ± 7.8	57 ± 5.0	0.10
BMI (kg/m ²)	30.5 ± 3.8	32.7 ± 4.6	0.17
Waist circumference (cm)	106 ± 10.9	114 ± 13.4	0.07
Duration of diabetes (years)	2.9 ± 1.2	3.2 ± 0.8	0.35
HbA1c (%)	6.8 ± 0.7	6.7 ± 0.8	0.70
Hyperglycaemic clamp			
*1 st phase insulin response (pmol/l)	102.1 ± 64.1	168.8 ± 119.3	0.07
#2 nd phase insulin response (pmol/l)	222.9 ± 153.0	379.9 ± 312.4	0.09
*1 st phase c-peptide response (nmol/l)	0.59 ± 0.18	0.92 ± 0.28	0.009
#2 nd phase c-peptide response (nmol/l)	1.06 ± 0.45	1.70 ± 0.50	0.010
Mixed meal tolerance test			
Glucose iAUC (mmol/l min ⁻¹)	558.3 ± 361.5	544.4 ± 248.0	0.91
Insulin iAUC (pmol/l min ⁻¹)	90234 ± 46727	91963 ± 63172	0.93
c-peptide iAUC (nmol/l min ⁻¹)	171.7 ± 54.2	254.8 ± 72.4	0.016
GLP-1 iAUC (pmol/l min ⁻¹)	462.9 ± 653.2	259.2 ± 285.5	0.29
GIP iAUC (ng/l min ⁻¹)	37063 ± 9674	27247 ± 10567	0.016

Data are mean ± SD. AUC = area under the curve; iAUC = incremental area under the curve. *1st phase response calculated as mean concentration in the first 10 minutes; #2nd phase response calculated as mean concentration in the last 10-120 minutes according to the methods of DeFronzo *et al.* 1979⁽¹⁾.

ANTIHYPERGLYCEMIC EFFECT OF AQUEOUS EXTRACT OF FOENICULUM VULGARE MILLER IN DIABETIC MICE

Baljinder Singh¹; Navneet Sharma²

¹GTB Khalsa College of Pharmacy, Chhapianwali, malout, Punjab, India, ²GTB Khalsa College of Pharmacy, Chhapianwali, malout, Punjab, India

Introduction: *Foeniculum vulgare* Mill. is a biennial medicinal and aromatic plant belonging to the family Apiaceae (Umbelliferae). It is a hardy, perennial–umbelliferous herb with yellow flowers and feathery leaves.

Objective: To study the control of blood glucose in alloxan induced diabetic mice.

Methods: Method used for extraction was continuous hot percolation method in which Soxhlet apparatus was used. 95% ethanol was used as solvent. Male albino mice weighing about 20–25 g obtained from Guru Angad Dev University of Veterinary Science, Ludhiana were used for the study. Diabetes was induced by a single i.p. injection of 125 mg/kg of alloxan monohydrate in sterile saline (11). After 48 h, animals with serum glucose level above 200 mg/dl (diabetic) were selected for the study. Blood samples from mice were collected by retro-orbital puncture (ROP) technique. Serum glucose levels were determined by glucose oxidase and peroxidase method.

Results: Single administration (single dose) of aqueous extract of fennel (25, 50, and 100 mg/kg, p.o.) in diabetic Swiss albino mice, showed reduction in serum glucose level after 45 min. Maximum reduction in serum glucose level was seen at doses of 100 mg/kg. Aqueous extract of fennel in all doses except 25 mg/kg did not cause any significant decrease in blood glucose.

Conclusion: It may be said that the aqueous extract of fennel decreased the serum glucose level and improved glucose tolerance owing to the presence of aldehyde moiety. The aqueous extract of fennel has antihyperglycemic activity as it lowers serum glucose level in diabetic mice.

WITHANIA COAGULANS FRUIT EXTRACT AMELIORATES THE ACTIVITY OF TYROSINE KINASE AND STIMULATES THE RELEASE OF INSULIN FROM PANCREATIC B-CELL ISLETS

Kirtikar Shukla*; Jasvinder K. Gambhir; Piyush Dikshit; Rimi Shukla

*Department of Biochemistry - Laboratory Medicine, Medanta The Medicity, Gurgaon, India, Departments of Biochemistry, University College of Medical Sciences (University of Delhi) and GTB Hospital, Delhi, India

Objectives: *Withania coagulans* fruit is widely used for its anti-hyperglycemic effect in the traditional health care system in India. The aim of this study was to evaluate insulinotropic effects of aqueous extract of *Withania coagulans* (aqWC) from pancreatic β -cell islets.

Materials and Methods: Diabetic animals were treated with aqWC extract for 30 days. Tyrosine kinase activity was assayed in RBC and hepatocytes. At the end of treatment, pancreatic islets were isolated, suspended in culture medium with glucose at 3 mM (normoglycemic concentration) and 11 mM (hyperglycemic concentration) and studied the insulinotropic effect of aqWC.

Results: Diabetic animals treated with aqWC at a dose of 250 mg/kg showed significantly decreased fasting and postprandial plasma glucose level and increased circulating insulin and C-peptide levels as compared to diabetic-untreated animals ($p < 0.001$). Similarly, tyrosine kinase activity in RBCs and hepatocytes were significantly increased in diabetic treated with aqWC for 30 days as compared to diabetic untreated animals ($p < 0.01$). Release of insulin from pancreatic β -cells islets isolated from healthy controls and diabetic-untreated animals was studied using two different concentrations of glucose, i.e. 3mM and 11mM in the medium. The release of insulin from islets was increased in 11 mM of glucose as compared to 3mM glucose. Further addition of aqWC to the incubation mixture showed more release of insulin from pancreatic islets ($p < 0.05$). However, the release of insulin from islets isolated from healthy animals was higher as compared to diabetic animals.

Conclusions: These results suggest that aqWC has effective glucose lowering potential which might be due to increased tyrosine kinase activity as well as the insulinotropic effect leading to increased insulin secretion from pancreatic β -cells.

MYOCARDIAL BRIDGING OF CORONARY ARTERY MAY REPLACE THE DIAGNOSIS OF CARDIAC SYNDROME X

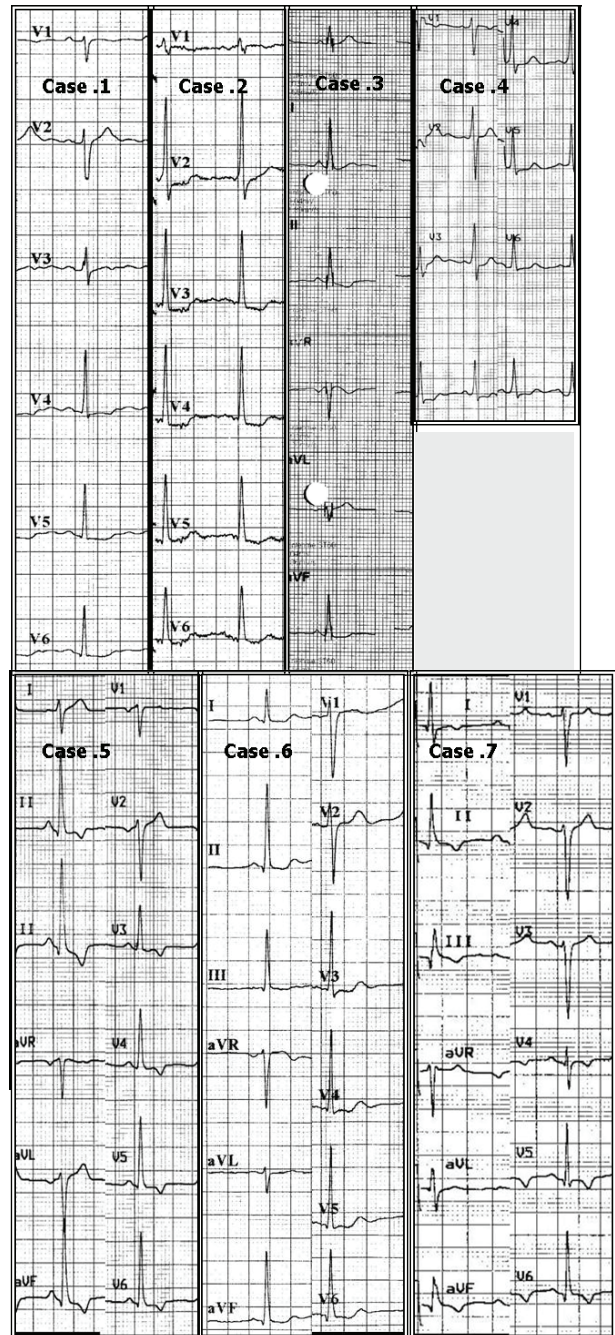
Mustafa Aparcı¹; Cengiz Ozturk²; Şevket Balta³;
Ugur Bozlar⁴; Zafer Isilak⁵; Turgay Çelik²

¹Etimesgut Military Hospital, Dept. of Cardiology, Ankara, Turkey, ²Gulhane Military Medical Academy, Dept. of Cardiology, Ankara, Turkey, ³Eskisehir Military Hospital, Dept. of Cardiology, Eskisehir, Turkey, ⁴Gulhane Military Medical Academy, Dept. of Cardiology, Ankara, Turkey, ⁵Haydarpaşa Training Hospital, Dept. of Cardiology, Ankara, Turkey

Aim: Cardiac Syndrome X is used to define a clinical state which was composed of repetitive angina pectoris accompanied with dynamic or silent ST segment depression or T wave inversion either at rest or stress test, reversible perfusion defect on SPECT, and generally normal coronary angiogram. Myocardial bridging (MB) of coronary artery is mainly associated with the anatomically and physiologically restriction of coronary flow especially at systolic and diastolic period. Since myocardial blood flow is generally augmented by mechanically dilatation of coronary artery mainly during diastolic period and also increasing heart rate. However MB will be an obstacle which restricts the coronary vasodilatation when the myocardial oxygen demand exponentially increased.

We presented ECGs of seven cases, who similarly presented with angina pectoris, ECG changes, positive treadmill test, and normal coronary angiogram. However those patients were diagnosed as having myocardial bridging on coronary arteries via MSCT angiography (320 sliced). All of those subjects had normal findings on echocardiographical examination and were far away from any myocardial disease associated with thickening of myocardium or dilatation of left ventricle which could potentially induce those ECG changes.

Conclusion: In current clinical practice MSCT coronary angiography is able to image the intra- and extraluminal pathologies of coronary artery wall e.g. atherosclerotic plaque, myocardial bridging, etc. which may potentially disturb the coronary flow and myocardial perfusion. Those cases who had been previously diagnosed as cardiac syndrome X are probably suffering those signs and symptoms due to myocardial bridging compressing on the coronary artery. Myocardial bridging should sought and also stated on the assessment of MSCT angiography imaging if the patients had the diagnosis of cardiac syndrome X. Myocardial bridging may replace the diagnosis of cardiac syndrome X in the future.



Case 1: A 24 years old male who has MB on mid portion of LAD coronary artery. *Case 2:* A 28 years old male who has MB on mid portion of LAD coronary artery. *Case 3:* A 25 years old male who has MB on mid portion of CX coronary artery. *Case 4:* A 26 years old male who has MB on mid portion of LAD and CX coronary artery. *Case 5:* A 32 years old male who has MB on mid portion of LAD and CX coronary artery. *Case 6:* A 34 years old male who has MB on mid portion of LAD coronary artery. *Case 7:* A 35 years old male who has MB on mid portion of LAD and OM1 branch of CX coronary artery.

Key words: coronary, myocardial bridging, angina, ischemia, syndrome X.

NORMAL VALUES OF AORTIC INDICES IN HEALTHY YOUNG ADOLESCENTS

Mustafa Aparci¹; Cengiz Ozturk²; Sevket Balta³; Zafer Isilak⁴; Turgay Çelik²; Ejder Kardesoglu⁴

¹Etimesgut Military Hospital, Dept. of Cardiology, Ankara, Turkey, ²Gulhane Military Medical Academy, Dept. of Cardiology, Ankara, Turkey, ³Eskisehir Military Hospital, Dept. of Cardiology, Eskisehir, Turkey, ⁴Haydarpaşa Training Hospital, Dept. of Cardiology, Istanbul, Turkey

Aim: Rupture or dissection of aortic aneurysm is of high mortality and morbidity rates. Recently cardiologists have been focused on the prevention or management of adults with aortic aneurysm. We evaluated the normal ranges of aortic diameters in a large young population at 19 years old. So cardiologist may easily identify the adolescents with aortic indices larger than upper normal limits and get him to avoid isometric type exercise.

Material and Method: Totally 499 young healthy adolescents were examined by echocardiography. Minimum and maximum, Mean±SD, Median values of aortic root(AoR), aortic sinus (AoS) and ascending aorta(AoAsc), and also values those indexed to BSA and height were calculated.

Results: Min-Max of AoR, AoS, and AoAsc were varied between 19-28, 25-36, and 21-34 mm, respectively. We also found that Height(m) was significantly correlated with BSA (R=0,746, R²=0,557, p<0,001). Similarly AoS/Height (R=0,845, R²=0,714, p<0,001) and AoAsc/Height (R=0,850, R²=0,722, p<0,001) were significantly correlated with AoS/BSA and AoAsc/Height.

Conclusion: Measurements aortic sinus and ascending aorta higher than abovementioned maximum values could indicate adolescents with the potential to progress aortic aneurysm in his further life. He should be warned to avoid from strenuous isometric type exercise or weight lifting sports. Presence of family history of aortic aneurysm and dissection will increase the risk of that adolescent with aortic diameters higher than we found. Additionally Height in meter for indexing could be used in daily clinical practice and also follow up instead of BSA which requires using a complex formula on a digital device.

Table 1. Normal ranges aortic diameters and indexed values

	AoR	AoS	AoAsc	AoR/BSA	AoS/BSA	AoAsc/BSA	AoR/H	AoS/H	AoAsc/H
Mean	22,36	29,97	25,62	12,29	16,48	14,09	12,81	17,18	14,68
SD	1,635	2,351	1,926	1,00	1,45	1,218	0,93	1,346	1,126
Median	22,00	30,00	26,00	12,22	16,43	13,97	12,71	17,14	14,62
Min	19	24	21	9,56	12,67	11,27	10,61	13,71	12,17
Max	28	36	34	15,39	20,95	19,70	15,91	21,18	19,88
25 th	21,00	28,00	24,00	11,56	15,46	13,23	12,08	16,20	13,87
50 th	22,00	30,00	26,00	12,22	16,43	13,97	12,71	17,14	14,62
75 th	24,00	32,00	27,00	12,96	17,43	14,88	13,45	18,07	15,34
95 th	25,00	34,00	29,00	14,05	19,07	16,16	14,45	19,52	16,66

BSA = Body Surface Area calculated by Dubois Formula; H = height in meter

ASSOCIATION OF THE β_3 -ADRENERGIC RECEPTOR TRP64ARG POLYMORPHISM WITH OBESITY DISORDER IN SAUDI SUBJECTS

Maha H. Daghestani¹; Nadia A. Aleisa¹; Mazin H. Daghestani²

¹Department of Zoology, College of Science, King Saud University, Riyadh 11495, Saudi Arabia, ²Department of Obstetrics and Gynecology, Faculty of Medicine, Umm-Al-Qura University, Makkah 21955, Saudi Arabia

Background: Obesity and body weight related disorders have a very strong correlation with polymorphism in three subtypes of beta adrenoceptor (β_1 , β_2 , and β_3) genes. We scanned for the polymorphism of Trp64/Arg in β_3 adrenoceptors in Saudi population to determine any association of such polymorphism with obesity and related disorders among Saudi population.

Methods: We studied 329 non-related adults (33.1% men and 66.9% women), aged 18-36 years. Body mass index (BMI), anthropometric measurements were calculated, leptin, insulin, lipid profile and glucose concentrations were determined. Beta3 adrenoceptor polymorphism (Trp64/Arg) were screened. The subjects were divided into three groups according to BMI: 115 lean (BMI <25 kg/m²), 68 overweight (BMI ≥25 kg/m²), and 146 obese (≥30 kg/m²).

Results: In the matched age groups of the control, obese and overweight male and female subjects, all anthropometric parameters were found to be significantly higher and all biochemical parameters were also significantly elevated in the obese and overweight groups as compared to the controls. The allelic frequency of Arg64 of ADRB3 gene among overweight and obese subjects had a significantly higher frequency compared with normal weight subjects In

addition, subjects carrying Arg64 allele regardless of their BMI had greater waist and hip circumference, W/H ratio, plasma cholesterol, triglyceride, LDL, leptin, insulin and glucose level compared to those with the wild type allele.

Conclusion: The present study show a significant association between the Trp64/Arg polymorphism in ADRB3 gene and the development of overweight and obesity in Saudi populations with an influence on the levels of lipid, insulin, leptin and glucose.

SOFT TYPE ATHEROSCLEROTIC PLAQUE IS ACCOMPANIED WITH INCREASED MEAN PLATELET VOLUME AND ALSO INCREASED WHITE BLOOD CELL, BASOPHIL AND MONOCYTES COUNT

Turgay Çelik¹; Mustafa Aparci²; Cengiz Ozturk¹; Sevket Balta³; Zafer Isilak⁴; Atilla İyisoy¹

¹Gulhane Military Medical Academy, Dept. of Cardiology, Ankara, Turkey, ²Etimesgut Military Hospital, Dept. of Cardiology, Ankara, Turkey, ³Eskisehir Military Hospital, Dept. of Cardiology, Eskisehir, Turkey, ⁴Haydarpasa Training Hospital, Dept. of Cardiology, Istanbul, Turkey,

Purpose: A vulnerable atherosclerotic plaque (AP) may potentially progress to acute coronary syndrome (ACS) by causing thrombotic occlusion of a coronary artery. We evaluated whether the complete blood count (CBC) varied according to the coronary artery lesion type.

Material and Method: We retrospectively analyzed the medical recordings of 50 patients with CAD diagnosed by MSCTA. Coronary artery lesions were defined as mixed type AP or soft type AP, and myocardial bridging (MB) on the LAD artery. WBC, Hgb, and Hct, neutrophil, lymphocyte, and monocyte, eosinophil, basophil percentages and mean platelet volume (MPV) derived from CBC were compared among those study groups.

Results: Patients with MAP and SAP were older compared to MB group. WBC was significantly increased in patients with SAP whereas neutrophil and lymphocytes percentages were not different among groups. Additionally patients with SAP and MAP had significantly elevated basophil ($0,4 \pm 0,2$, $0,7 \pm 0,2$, and $0,8 \pm 0,3$, $p=0.001$) and monocyte ($5,2 \pm 2,2$, $7,7 \pm 2,1$, and $7,1 \pm 2,8$, $p=0.007$) percentages compared to MB group. Moreover MPV ($9,2 \pm 0,9$, $8,9 \pm 0,8$, and $10,1 \pm 0,2$, $p=0.005$) was significantly increased in patients with SAP. Platelet distribution width ($15,9 \pm 1,4$, $15,6 \pm 1,8$, $17,7 \pm 1,3$, $p=0.005$) was also increased in patients with SAP.

Conclusion: While the Patients with SAP and MAP had significantly higher basophil and monocytes percent, patients with SAP had additionally higher WBC, MPV, and PDW. Those findings may suggest that while SAP and MAP had a chronic inflammatory state Higher leukocyte count, MPV, and PDW may support the potential of SAP to cause thrombosis.

Table 1. Comparison of complete blood count components among patients with myocardial bridging, mixed and soft type atherosclerotic plaque

	patients with MB (n = 28)	patients with mixed type plaque (n = 12)	patients with soft plaque (n = 10)	p
Age (years)	33,8 ± 7,2	45,1 ± 5,7	47,1 ± 4,4	0.001
White Blood Cell (×1000/mm ³)	6,5 ± 1,3	6,8 ± 1,6	9,2 ± 2,1	0.001
Hemoglobin (gr/dL)	15,9 ± 0,7	15,5 ± 0,6	16,1 ± 1,4	0.257
Hematocrit	48,1 ± 2,2	47,1 ± 1,7	48,2 ± 2,8	0.407
Platelet (×1000/mm ³)	239,1 ± 41,4	223,6 ± 40,8	232,6 ± 37,2	0.545
Mean Platelet Volume	9,2 ± 0,9	8,9 ± 0,8	10,1 ± 0,2	0.005
Neutrophil Percentage (%)	60,3 ± 3,8	57,9 ± 5,3	59,2 ± 16,1	0.678
Lymphocyte Percentage (%)	31,1 ± 4,1	31,4 ± 5,7	30,1 ± 12,2	0.888
Eosinophil Percentage (%)	2,1 ± 1,2	1,5 ± 0,4	2,4 ± 1,1	0.191
Basophil percentage (%)	0,4 ± 0,2	0,7 ± 0,2	0,8 ± 0,3	0.001
Monocyte Percentage (%)	5,2 ± 2,2	7,7 ± 2,1	7,1 ± 2,8	0.007
Platelet Distribution Width (PDW)	15,9 ± 1,4	15,6 ± 1,8	17,7 ± 1,3	0.005

*One Way ANOVA Test

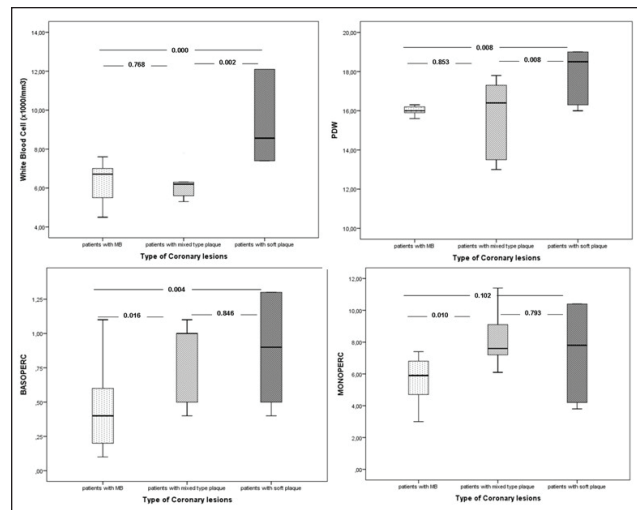


Fig. 1. Comparison of CBC parameters in respect with coronary plaque type.

PREVALENCE OF OVERWEIGHT, PREHYPERTENSION AND HYPERTENSION IN TURKISH YOUNG POPULATION

Mehmet Karaduman, MD¹, Associate Professor of Internal Medicine; Mustafa Aparci, MD², Associate Professor of Cardiology; Cengiz Ozturk, MD³, Associate Professor of Cardiology; Sevket Balta, MD⁴, Specialist of Cardiology; Turgay Çelik, MD³, Professor of Cardiology

¹*Etimesgut Military Hospital, Department of Internal Mecine, Ankara, Turkey,* ²*Etimesgut Military Hospital, Department of Cardiology, Ankara, Turkey,* ³*Gulhane Military Medical Faculty, Department of Cardiology, Ankara, Turkey,* ⁴*Eskisehir Military Hospital, Department of Cardiology, Ankara, Turkey,*

Objective: Hypertension is one of the most leading causes of mortality and morbidity in adult and elderly population. Although a global strategy against the hypertension is being conducted throughout the world and focused on the adult population, the fact of prehypertension and hypertension among adolescent and young population is generally ignored and overlooked. So we aimed to determine the blood pressure and body mass abnormalities in such a young population.

Material method: We retrospectively evaluated and recorded the systolic (SBP) and diastolic blood pressures (DBP), weight and height of 571 young healthy subjects from the medical recordings. We analyzed the prevalence of normotension, prehypertension, and hypertension, and also overweight and obesity among the young subjects.

Results: Prevalence of normotension (n=149), prehypertension (n=314), and hypertension (n=108) was as 22.97%, 55.79%, and 21.24%, respectively (Figure 1). Overweight was about 23.8% in the study population (Figure 2) and was slightly correlated with only SBP but not the DBP. We observed that SBP was significantly higher in overweight group compared to group with BMI <20 kg/m² while normoweighted group tended to be higher compared to ones with lower BMI (Figure 3).

Conclusion: Higher prevalence of prehypertension and hypertension in such a young aged population should alert us. Higher dietary salt consumption of Turkish population which was previously documented may be accounted for the higher levels of prehypertension and hypertension among young population. Increasing prevalence of prehypertension and hypertension inevitably burst the hypertension related cardiovascular and cerebrovascular morbidity and mortality in the further ages.

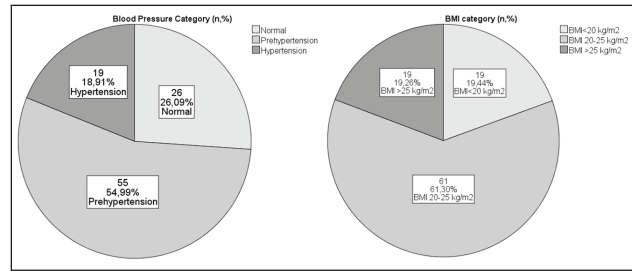


Fig. 1. Prevalence of Blood pressure and BMI abnormalities among young population.

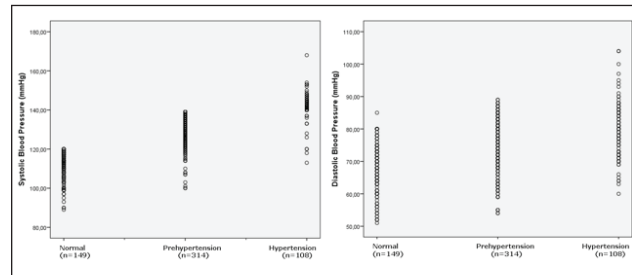


Fig. 2. Distribution of SBP and DBP values according to Blood pressure category.

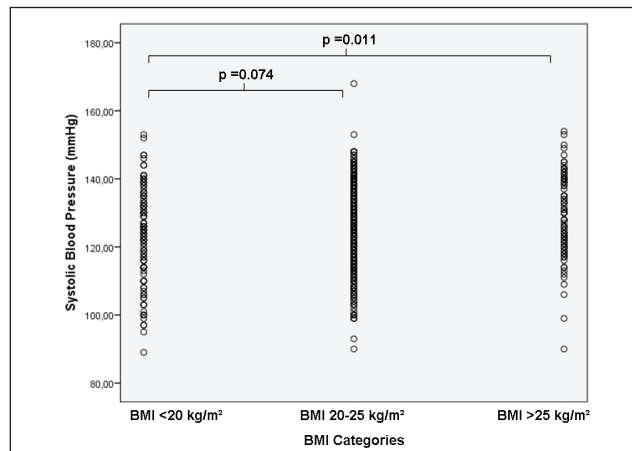


Fig. 3. Comparison of SBP of groups according to the BMI category.

RELATIONSHIP OF HYPERTENSION AND OVERWEIGHT WITH LEFT VENTRICULAR MASS AND MASS INDEXES IN ADOLESCENTS

Mustafa Aparci¹; Cengiz Ozturk²; Mehmet Karaduman³; Sevket Balta⁴; Turgay Çelik²; Atilla İyisoy²

¹*Etimesgut Military Hospital, Department of Cardiology, Ankara, Turkey,* ²*Etimesgut Military Hospital, Department of Internal Mecine, Ankara, Turkey;* ³*Gulhane Military Medical Faculty, Department of Cardiology, Ankara, Turkey;* ⁴*Eskisehir Military Hospital, Department of Cardiology, Ankara, Turkey*

Abstract: Aim: Prevalence of Hypertension is growing among children and adolescents. It is commonly ignored and not emphasized in adolescents as if it does not produce any end-organ damage (EOD) at such an earlier age. We evaluated the relationship of hypertension and overweight with LV mass (LVM) and LV mass indexed to BSA (LVMBSA) and height (LVMIHeight); an earlier representative of hypertension; among adolescents.

Material and Method: We evaluated the demographic features and echocardiographic parameters of 520 young male subjects. We compared the LVM, LVMBSA and LVMIHeight among the normotensive (n=123), pre-hypertensive (n=256), and hypertensive (n=141) young groups and also their correlation with the demographic features.

Results: We observed that heart rate, BMI, LV IVS, LVM, LVMBSA, LVMIHeight significantly increased as the category of BP increased (Figure 1). We observed that the SBP, DBP, and BMI were significantly correlated with the LVM, LVMBSA and LVMIHeight (Table 1). Linear Regression analysis revealed a significant relationship between SBP, BMI and LVM, LVMBSA and LVMIHeight (Figure 2, 3). **Conclusion:** Hypertension is not a public health problem which is limited to adults and elderly patients. Hypertension even among children and adolescents may cause myocardial hypertrophy at such a young age. Indexing LVM to height in adolescents may be an effective way of determining the LVMI in clinical practice alternative to BSA. BMI is still a clinically important confounding factor related with LVM and LVMI in addition to Hypertension. It reminds the necessity of improvement of overweight or obesity in the management of hypertension among young population.

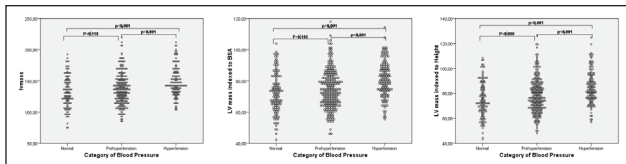


Fig. 1. Comparison of LVM, LVMBSA, LVMIHeight among the young subjects with normotension, prehypertension, and hypertension.

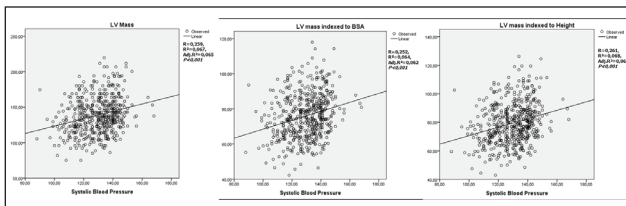


Fig. 2. Linear regression analysis of SBP and LVM, LVMBSA, LVMIHeight.

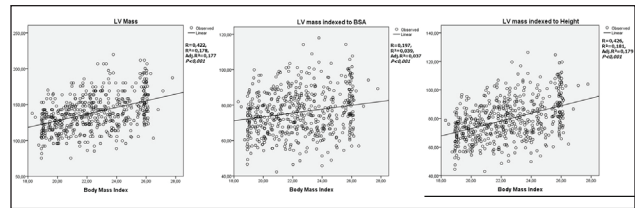


Fig. 3. Linear regression analysis of BMI and LVM, LVMBSA, LVMIHeight.

A NOVEL PARAMETER; SYMPATHETIC ACITIVITY INDEX; MAY IDENTIFY THE YOUNG SUBJECTS AT RISK FOR HYPERTENSION AND RELATED ORGAN DAMAGES

Mustafa Aparci¹; Cengiz Ozturk²; Sevket Balta³; Mehmet Karaduman⁴; Turgay Celik²; Atilla Iyisoy²

¹*Etimesgut Military Hospital, Department of Cardiology, Ankara Turkey,* ²*Gulhane Military Medical Academy, Department of Cardiology, Ankara Turkey,* ³*Eskisehir Military Hospital, Department of Cardiology, Eskisehir, Turkey,* ⁴*Etimesgut Military Hospital, Department of Internal Medicine, Ankara Turkey,*

Aim: Hypertension, metabolic and hemodynamic abnormalities have a complex interaction. We proposed a novel scoring system to determine sympathetic activity level derived from heart rate, BMI, and blood pressure category.

Material and Method: A Novel index “Sympathetic Activity Index” is composed of 1, 2, and 3 points for HR<69, 70-89, and >90 bpm; -1, 1, and 2 points for BMI <20, 20-24,9, and ≥25 kg/m²; 1, 2, and 3 points for the BP category; normal, prehypertension, and hypertension, respectively. Demographic and echocardiographic features (LV parameters, LVMass, LVMBSA and LVMIHeight) were compared among groups with SAI 1 to 8. Medical recordings of 545 young male subjects with age 19 were performed a pre-test screening as a routine procedure for professional training.

Results: We found that weight, BMI, HR, SBP, DBP, LAD, LVM, LVMBSA and LVMIHeight were significantly increased in parallel with the SAI of groups (p<0.001). SAI was correlated with LVM (R=0,314, p<0.001), LVMBSA (R=0,193, R²=0,37, p<0.001), and LVMIHeight (R=0,316, R²=0,100, p<0.001). We observed that SAI ≥5,5 could determine the LVH with sensitivity and specificity of %57 and %70, respectively (AUC=682, 95% CI 0,610-0,753, p<0,001).

Conclusion: SAI may be a novel index which globally represents the actual sympathetic activity. It may provide a quantitative score to identify and follow up the young subjects at risk for hypertension and related abnormalities.

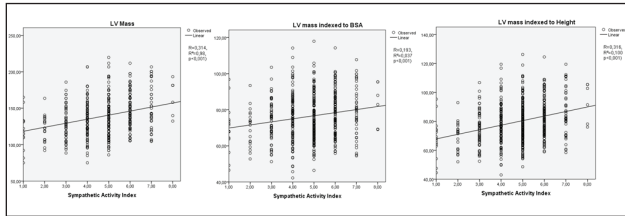


Fig. 1. Linear Regression Analysis of SAI and LVM, LVMBSA, LVMHeight.

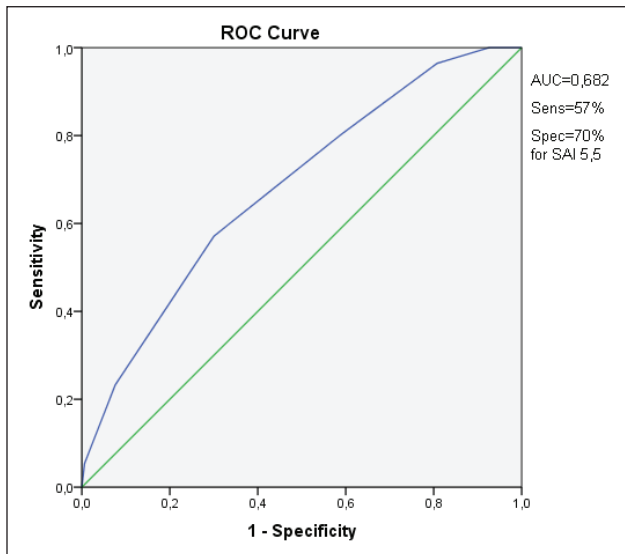


Fig. 2. ROC Curve analysis of SAI in determining the presence of LVH in young subjects.

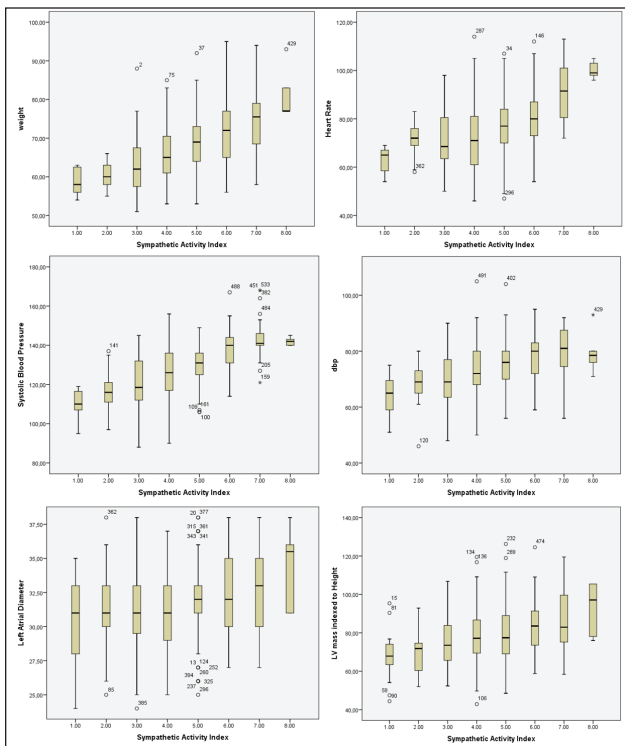


Fig. 3. Comparison of variables among the groups with SAI 0 to 8.

ETHNIC PREDISPOSITION TO DIABETES AMONG THE ASIAN INDIANS IS ASSOCIATED WITH FAMILY HISTORY OF DIABETES AND INFLAMMATION: CALCUTTA BIRTH OUTCOME STUDY

Mithun Das¹; Riddhi Goswami²; Indrani Lodh³; Arnab Ghosh⁴

¹Sree Chaitanya College, Habra 743268, West Bengal, India; ²Heritage Institute of Technology, Kolkata 700107, India; ³Urvaraa IVF, Kolkata 700019, India; Kolkata, India; ⁴Visva Bharati University, Santiniketan 731235, West Bengal, India.

Elevated high sensitivity C-reactive protein (hsCRP) is a marker of low-grade systematic inflammation and involved in the etiology of diabetes. Asian Indians are ethnically predisposed to diabetes and tend to develop the disease much earlier, and have an underlying pro-inflammatory state that may contribute to their increased risk. The present study was conducted on 160 healthy (non-diabetic, normotensive) adult Asian Indian women [including 90 with and 70 without family history of diabetes (FHD)] living in and around Kolkata (*erstwhile* Calcutta), India. During the gestation period they were studied twice, first within 12 weeks and second by 32 weeks. They were then followed up till delivery. During delivery both mothers' venous blood and cord blood were collected to find out the serum hsCRP of the respective mothers and their new born babies. It was found that: a) The odds of being elevated hsCRP (>1.0 mg/L) were 2.2802 (95% C.I. 1.2032 - 4.3214, p = 0.0115) in women with FHD than their counterparts; b) Similarly, the odds of being elevated hsCRP (>1.0 mg/L) were 3.1552 (95% C.I. 1.6451 - 6.0514, p = 0.0005) in babies born of women with FHD than their counterparts. It is therefore reasonable to argue that these factors are linking early life events to disease in late life making Asian Indians ethnically predisposed to diabetes. Hence, intervention and life-style management should therefore be implemented from early childhood in order to curb this epidemic among the people of Indian origin.

SEX DIFFERENCES IN THE RELATIONSHIP BETWEEN SARCOPENIA AND HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN KOREAN OBESE ADULTS

Yun A Kim

Samsung Medical Center (135-710) 81 Irwon-Ro Gangnam-gu. Seoul, Korea

Background: This study aims at elucidation of a relationship between sarcopenia and HRQoL in Korean obese adults.

Methods: In the 2010 and 2011 Korean National Health and Nutrition Examination Surveys, 2,605 obese subjects (BMI \geq 25 kg/m²) aged 19 and older were divided into three groups; men, premenopausal women, and postmenopausal women. Based on skeletal muscle index (SMI), sarcopenia was classified into two classes in each group; higher-SMI Class I and lower-SMI Class II. The SMI was calculated as appendicular skeletal muscle mass divided by body weight. HRQoL was evaluated using both EuroQoL-5 dimension (EQ-5D) and EuroQoL-visual analog scale (EQ-VAS). To evaluate a relationship between sarcopenia and HRQoL, we conducted the multivariate logistic regression analysis.

Results: There was no significant difference in mean of EQ-VAS among groups. However, the odds ratios (OR) for the least quartile of EQ-VAS were significantly higher in Class II sarcopenia in men (OR = 2.28, 95 % confidence interval [CI] = 1.30-4.00) and premenopausal women (OR = 5.52, 95 % CI = 1.85-16.44) than Class I sarcopenia (OR = 1.27, 95 % CI : 0.85-1.90 in men and OR = 1.06, 95 % CI = 0.52-2.20 in premenopausal women). The likelihood of reporting problems for the mobility dimension was significantly higher in men with Class II sarcopenia than men with normal SMI. (OR = 2.45, 95 % CI = 1.01-5.98).

Conclusion: In men and premenopausal women, sarcopenia was independently associated with low EQ-VAS in obese adults. Further studies are needed to investigate the impact of sarcopenia on menopausal related HRQoL using specific measurement tools.

EFFECTS OF LONG-TERM, MONTHLY ADMINISTRATION OF THE PCSK9 INHIBITOR EVOLOCUMAB (AMG 145) IN PATIENTS WITH DYSGLYCEMIA OR METABOLIC SYNDROME

Robert R. Henry¹; Rury R. Holman²;
Robert P. Giugliano³; Frederick J. Raal⁴;
David Sullivan⁵; Narimon Honarpour⁶;
Patric Nelson⁶; Mary Elliott⁷; Thomas Liu⁶;
Scott M. Wasserman⁶; Michael J. Koren⁸

¹Center for Metabolic Research, VA San Diego Healthcare System and University of California San Diego, CA, USA; ²Diabetes Trials Unit, OCDEM, University of Oxford, UK; ³TIMI Study Group, Brigham and Women's Hospital, Boston, MA, USA; ⁴Carbohydrate & Lipid Metabolism Research Unit, University of Witwatersrand, Johannesburg, South Africa; ⁵Department of Clinical Biochemistry, Royal Prince Alfred Hospital, Camperdown, Australia; ⁶Amgen Inc., Thousand Oaks, CA, USA; ⁷Amgen Ltd., Cambridge, UK; ⁸Jacksonville Center for Clinical Research, Jacksonville, FL, USA

Background: Patients with dysglycemia benefit from statin therapy; however, they may either fail to achieve LDL-C target goals or experience statin related side-effects. Evolocumab (AMG 145) is a fully human monoclonal antibody against PCSK9 that effectively reduced LDL-C in phase 2 and 3 trials.

Objective: To assess the safety and efficacy of evolocumab in patients with dysglycemia or metabolic syndrome (MetS).

Methods: In the OSLER study, 1104 patients who participated in a parent study were randomized to evolocumab 420 mg monthly with standard of care (SOC) or to SOC alone.

Results: Of the OSLER patients with type 2 diabetes mellitus (T2DM; n=109), impaired fasting glucose (IFG; n=134), or MetS (n=425), 86%, 66% and 61%, respectively, were on a statin at baseline. In total, 91 (T2DM), 119 (IFG) and 369 (MetS) had an observed week 52 LDL-C value. Monthly evolocumab (420 mg) reduced mean (SE) LDL-C by 47(3)%, 51(2)% and 52(1)% (all P<0.001) in patients with T2DM, IFG, or MetS, respectively; reductions were comparable to that observed in patients without T2DM, IFG, or MetS. Adverse event (AE) and serious AE rates were comparable across treatment groups (evolocumab + SOC vs SOC alone). In the evolocumab + SOC group, no notable changes were observed at week 52 in fasting plasma glucose (FPG), HbA_{1c} blood pressure, weight, or estimated glomerular filtration rate.

Conclusion: Monthly evolocumab reduced LDL-C in patients with dysglycemia or MetS and was well tolerated with no notable changes in glycemia or key safety parameters.

Study Funding: Amgen, Inc.

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

Dirk Blom¹; Tomas Hala²; Michael Bolognese³; Michael J. Lillstol⁴; Phillip D. Toth⁵; Lesley Burgess⁶; Richard Ceska⁷; Eli Roth⁸; Michael J. Koren⁹; Maria Laura Monsalvo¹⁰; Kate Tsirtsonis¹¹; Jae B. Kim¹⁰; Scott M. Wasserman¹⁰; Rob Scott¹⁰; Christie M. Ballantyne¹²; Evan A. Stein¹³

¹Division 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; ⁴Lillstol 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, IIIrd. Dept. Internal Medicine, Charles University, Prague, Czech Republic; ⁸Sterling Research Group, Cincinnati, OH, USA; ⁹Jacksonville Center for Clinical Research, Jacksonville, FL, USA; ¹⁰Amgen, Inc., Thousand Oaks, CA, USA; ¹¹Amgen Ltd., Uxbridge, United Kingdom; ¹²Baylor College of Medicine, Houston, TX, USA; ¹³Metabolic and Atherosclerosis Research Center, Cincinnati, OH, USA

Background: Evolocumab (AMG 145), a fully human monoclonal antibody to proprotein convertase subtilisin/kexin type 9 (PCSK9), markedly reduced low-density lipoprotein cholesterol (LDL-C) in phase 2 studies of 12 week duration.

Objective: To evaluate the safety and efficacy of 52 weeks of treatment with evolocumab in a phase 3 trial (NCT01516879).

Methods: Based on NCEP ATP III risk categories, patients received background lipid-lowering therapy with diet alone or diet plus atorvastatin (10 mg daily, 80 mg daily, or 80 mg daily plus ezetimibe 10 mg daily) for a run-in period of 4–12 weeks. Patients with LDL-C \geq 75 mg/dL (1.9 mmol/L) were then randomized 2:1 to subcutaneous evolocumab (420 mg) or placebo every 4 weeks. The primary end point was percent change from baseline in LDL-C, measured by ultracentrifugation, at week 52.

Results: 901 patients were randomized and dosed (48% male; mean [SD] age 56 [11] years; 26% high ATP III risk). Evolocumab reduced LS mean (95% CI) LDL-C by 57% (53–61%) vs placebo ($P<0.001$); responses varied from

49–62% among background therapies. LDL-C reduction at weeks 12 and 52 were comparable. Significant improvements were observed in other lipids. The most common AEs were nasopharyngitis, upper respiratory tract infection, influenza, and back pain. Treatment-emergent and muscle-related AEs, and hepatic abnormalities, were comparable across treatment groups.

Conclusion: At 52 weeks, evolocumab added to diet alone, low-dose atorvastatin, or high-dose atorvastatin with or without ezetimibe further reduced LDL-C by 57% in patients with a range of cardiovascular risk.

Study funding: Amgen, Inc.

HOUSSAY REVISITED: THE ESSENTIAL ROLE OF THE GH ACTION PATHWAY IN INSULIN RESISTANCE: DISSOCIATION OF OBESITY AND INSULIN SENSITIVITY IN TWO RARE SHORT STATURE SYNDROMES

Arlan Rosenbloom

University of Florida College of Medicine Gainesville, Florida

An Ecuadorian cohort with GH receptor deficiency (GHRD) provides a unique human model to study the role of GH signaling in metabolism. Among 100 adults there is no diabetes compared to a 5% prevalence among relatives. We report insulin, IGFBP-1, lipid and adipocytokine concentrations in affected adults and matched relative controls, metabolomics, metabolic responses to a high caloric meal, and oral glucose tolerance tests (OGTT). The indicator of insulin sensitivity, HOMA2%S, was 2.5 times greater ($P<0.0001$) and that of insulin resistance, HOMA2-IR, 1/3 that of controls in GHRD ($P<0.01$). Marked insulin sensitivity, absence of leptin resistance, and elevated total and high molecular weight adiponectin, despite high percent body fat in GHRD, are inconsistent with obesity. Because GHRD eliminates direct metabolic effects of GH, the explanation for the dissociation of obesity and insulin resistance in subjects with GHRD is the lack of the counterregulatory effect of GH.

Insulin sensitivity in GHRD contrasts with a recently described consanguineous population isolate in Ecuador with intrauterine growth retardation (IUGR), failure of catch up growth, and absence of an adolescent growth spurt resulting in adult short stature with insulin resistance (Guevara syndrome). The condition is transmitted in a paternally imprinted pattern; a *CDKN1C* gain of function mutation apparently results in inhibition of critical growth promoting proteins. The intrauterine inhibition of cellular

growth would likely include pancreatic beta cell mass. Subsequent insulin resistance in this population, which contrasts with the GHRD cohort in having intact GH counterregulation, would be consistent with the thrifty phenotype hypothesis.

ARTERIAL HYPERTENSION IN ASTANA CITY, KAZAKHSTAN A PILOT STUDY

A. Supiyev; M. Khamzina; A. Kossumov; L. Utepova; T. Nurgozhin; Zh. Zhumadilov; M. Bobak

Center for Life Sciences, Nazarbayev University, and Department of Epidemiology and Public Health, University College London

Objective: To assess the prevalence, awareness, treatment, and control of arterial hypertension and factors associated with these indices in a population sample of Astana, the new capital city of Kazakhstan.

Design: Cross-sectional study

Setting: Subjects registered in 8 outpatient polyclinics in Astana, Kazakhstan.

Participants: A total of 497 adults (response rate 56%) aged 50-75 years randomly selected from registers of the polyclinics.

Outcome Measures: Hypertension was defined as a mean systolic and/or diastolic blood pressure of $\geq 140/90$ mmHg and/or anti-hypertensive medication use during the last 2 weeks. Awareness and treatment were based on self-report. Hypertension control was defined as blood pressure $< 140/90$ mmHg among hypertensive subjects.

Results: The overall prevalence of hypertension was 70%. Among hypertensive subjects, 91% were aware of their condition, 77% took anti hypertensive medications, and 34% had blood pressure controlled ($< 140/90$ mm Hg). The prevalence of hypertension and its awareness, treatment and control was more common in women, among persons aged 60 years of more and (except control) among those with high body mass index. None of several available socioeconomic measures was associated with any of hypertension indices.

Conclusions: The levels of awareness, treatment and control of hypertension were higher than in most Eastern European and Central Asian populations with available data, most likely reflecting high education and

large proportion of civil servants in the new capital city. However, even in this relatively privileged population the rates of successful control of hypertension were modest.

THE FATTY ACID COMPOSITION OF ERYTHROCYTES IN CHRONIC COMPLICATIONS OF TYPE 1 DIABETES MELLITUS

Alexander N. Osipenko¹; Denis A. Orlov²

¹Resource Center, A.A. Kuleshov Mogilev State University, Mogilev, Belarus; ²Consultative Clinic, Mogilev Regional Children's Hospital, Mogilev, Belarus

The aim of study was to elucidate the effects of diabetes mellitus type 1 (DM-1) complicated by neuropathy and microangiopathy on fatty acid (FA) composition in erythrocytes.

The object of research were 16 teenagers (14.5 ± 1.28 years) suffering from diabetic polyneuropathy and microangiopathy (retinopathy, nephropathy, etc.). The control group included 10 healthy schoolchildren (16.8 ± 1.1 year). The analysis of FA composition was made by capillary gas-liquid chromatography. Statistical analysis was performed using the Mann-Whitney U test ($p < 0.05$).

Analysis of erythrocytes FA composition showed that complicated DM-1 is characterized by increased content of saturated palmitic FA and decreased amounts of saturated stearic acid. These shifts, in our opinion, can be explained by specificity of developed dyslipidemia (the increase of oleic and palmitic FA normalized contents, and the decrease of stearic and polyunsaturated linoleic FA levels in blood plasma, caused by lipolysis). On the other hand, we observed a higher amount of polyunsaturated linoleic FA in erythrocytes of the patients. At the same time, the sum of polyunsaturated dihomo- γ -linolenic and polyunsaturated docosahexaenoic FA amounts of was reduced. These changes in FA composition of erythrocytes can be explained by decreased activity of $\Delta 6$ - and $\Delta 5$ -desaturases under insulin deficiency conditions. We should also mention that we found no changes in the level of polyunsaturated arachidonic FA in erythrocytes. This fact can be explained by a sufficient dietary intake of this FA; and may indicate a proinflammatory pattern of changes related to the examined pathology.

Revealed shifts indicate that complicated DM-1 results in development of systemic membranopathy.

ABROGATION OF ADENOSINE A₁ RECEPTOR SIGNALING IMPROVES METABOLIC REGULATION IN AGING AND OBESITY BY MODULATING OXIDATIVE STRESS AND INFLAMMATORY RESPONSES

Xiang Gao^{1*}; Ting Yang^{2*}; Monica Sandberg¹; Christa Zollbrecht²; Xing-Mei Zhang³; Michael Hezel²; Ming Liu²; Maria Peleli²; En Yin Lai⁴; Robert A. Harris³; Bertil B. Fredholm²; A. Erik G. Persson¹; Leif Jansson¹; Mattias Carlström^{2,4}

¹*Department of Medical Cell Biology, Uppsala University, Sweden;* ²*Department of Physiology and Pharmacology, Karolinska Institutet, Sweden;* ³*Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden* ⁴*Division of Nephrology & Hypertension, and Hypertension, Kidney & Vascular Research Center, Georgetown University, Washington DC*
**shared 1st authors*

Adenosine is an important regulator of glucose and lipid metabolism, but the role of A₁ receptor signaling during aging and obesity is unclear. We investigated the role of A₁ receptors in metabolic regulation, islet endocrine and arteriolar function during aging and increased visceral adipose tissue (VAT) using age-matched young (3-5 months) and aged (14-16 months) A₁-knockout (A₁^{-/-}) and wild-type (A₁^{+/+}) mice. Advanced age was associated with reduced glucose clearance and insulin sensitivity, and increased VAT in A₁^{+/+} compared to A₁^{-/-} mice. Islet morphology and insulin content were similar between genotypes, but relative changes in *in vitro* insulin release following glucose stimulation were reduced in aged A₁^{+/+} compared with A₁^{-/-} mice. Islet arteriolar responses to angiotensin II were stronger in aged A₁^{+/+} mice, this being associated with increased NADPH oxidase activity. Aging resulted in multiple changes in A₁^{+/+} compared with A₁^{-/-} mice, including enhanced superoxide formation in pancreas and VAT, elevated levels of circulating insulin, leptin and pro-inflammatory cytokines (TNF- α , IL- β , IL-6 & IL-12) and accumulation of CD4⁺ T-cells in VAT. These studies emphasize that A₁ receptors regulate metabolism and islet endocrine and vascular functions during aging by modulating oxidative stress and inflammatory responses.

ADENOSINE A1 RECEPTORS IN METABOLIC CONTROL

Xiang Gao

Department of Medical Cell Biology, Uppsala University, Sweden

Adenosine is an important regulator of glucose and lipid metabolism, but the role of A₁ receptor signaling during aging and obesity is unclear. We investigated the role of A₁ receptors in metabolic regulation, islet endocrine and arteriolar function during aging and increased visceral adipose tissue (VAT) using age-matched young (3-5 months) and aged (14-16 months) A₁-knockout (A₁^{-/-}) and wild-type (A₁^{+/+}) mice. Advanced age was associated with reduced glucose clearance and insulin sensitivity, and increased VAT in A₁^{+/+} compared to A₁^{-/-} mice. Islet morphology and insulin content were similar between genotypes, but relative changes in *in vitro* insulin release following glucose stimulation were reduced in aged A₁^{+/+} compared with A₁^{-/-} mice. Islet arteriolar responses to angiotensin II were stronger in aged A₁^{+/+} mice, this being associated with increased NADPH oxidase activity. Aging resulted in multiple changes in A₁^{+/+} compared with A₁^{-/-} mice, including enhanced superoxide formation in pancreas and VAT, elevated levels of circulating insulin, leptin and pro-inflammatory cytokines (TNF- α , IL- β , IL-6 & IL-12) and accumulation of CD4⁺ T-cells in VAT. These studies emphasize that A₁ receptors regulate metabolism and islet endocrine and vascular functions during aging by modulating oxidative stress and inflammatory responses.

SAXAGLIPTIN RESPONDER ANALYSIS: A POOLED ANALYSIS OF 5 CLINICAL TRIALS

Boaz Hirshberg¹; Gil Leibowitz²; William Cook¹; Cheryl Wei¹; Mikaela Sjöstrand³

¹*AstraZeneca, Wilmington, DE, USA;* ²*Hadassah Medical Center, Jerusalem, Israel;* ³*AstraZeneca, Mölndal, Sweden*

Type 2 diabetes mellitus (T2DM) treatment should be individualized to maximize patients' benefits. We analyzed the treatment response of patients with T2DM based on their initial response to saxagliptin. Data were pooled from five, 24-week, randomized, placebo-controlled trials of saxagliptin. Patients (N = 1994) were categorized by HbA1c change after 12 weeks of saxagliptin treatment as nonresponders (NR, HbA1c decrease <0.2%; 25% of saxagliptin-treated patients), intermediate responders (IR, HbA1c decrease \geq 0.2% and <0.5%; 14% of patients), and responders (R, HbA1c decrease \geq 0.5%; 61% of patients).

The mean change (95% CI) from baseline to week 24 in HbA1c with saxagliptin was greatest in the R (-1.11% [-1.16%, -1.06%]) followed by IR (-0.33% [-0.41%, -0.25%]) and NR (0.09% [0%, 0.18%]) groups. The proportion of patients achieving HbA1c <7% after 24 weeks was greater in the R (48%) and IR (41%) vs NR group (22%, $P<0.0001$ for each). The mean increase from baseline to week 24 in HOMA2 was greatest in the R group (18.2% [15.5%, 20.9%]) compared with the other groups (IR, 10.2% [4.7%, 15.6%]; NR, 6.7% [2.6%, 10.7%]). Baseline characteristics that were associated with glycemic response to saxagliptin included higher baseline HbA1c ($P<0.001$), lower fasting ($P<0.001$) and postprandial plasma glucose ($P=0.01$), and higher HOMA2 β ($P=0.04$). Responders, who comprised 61% of saxagliptin-treated patients analyzed, derived significant benefit from saxagliptin treatment, with an ~1% decline in HbA1c and increased β -cell function at 24 weeks compared with nonresponders.

ASSOCIATIONS BETWEEN C - REACTIVE PROTEIN AND SLEEP DURATION IN U.S ADULTS: NHANES 2007-2010

Michael R. Richardson MSH;
James R. Churilla PhD, MPH, FACSM

University of North Florida, Department of Clinical and Applied Movement Sciences, Jacksonville FL 32224

C - reactive protein (CRP), a non-specific marker of inflammation, has proven useful in predicting cardio-metabolic risk. Short and long sleeping duration has also been shown to be positively associated with cardio-metabolic risk.

Purpose: To examine the associations between elevated CRP and sleep duration in a nationally representative sample of U.S. adults.

Methods: Study sample included male (n = 5033) and female (n = 4917) adult (≥ 20 years of age) participants in the 2007-2010 National Health and Nutrition Examination Survey. Sleep duration was categorized as short (≤ 6 h), adequate (7-8 h) or long (≥ 9 h). Gender stratified logistic regression analysis was used to examine the associations between elevated CRP (>3 to 10 mg/L) and sleep duration. Logistic regression models were adjusted for age, race, smoking status, physical activity, and waist circumference.

Results: Analysis revealed significantly ($p=0.0151$) higher odds of elevated CRP in men reporting ≤ 6 h of sleep (OR 1.26; 95% CI 1.05-1.52) when compared to a referent group of men reporting 7-8 h of sleep. In contrast, similar associations were not revealed in women.

Conclusion: Sleep duration was significantly associated with elevated serum concentrations of CRP independent of waist circumference and moderate physical activity in men but not women.

HOW CARDIAC EJECTION FRACTION AND HBA1C LEVELS CONSTITUTE A PREDICTOR OF DIABETIC NEPHROPATHY IN T2DM PATIENTS WHO SURVIVED AFTER THEIR FIRST EPISODE OF MYOCARDIAL INFARCTION?

S. Papazoglou; M. Aslam; D. Richter; C. Stefanadis; N. Standfield

Cardiac Dept. Euroclinic, Athens, Cardiology Dept. Hippokraton University Hospital, Faculty of Medicine, University of Athens, Greece, Vascular Surgery Dept. Hammersmith Hospital, NHS Trust, Imperial College, London, UK.

Purpose: The association of diabetes mellitus and coronary artery disease is one of the cornerstones of evidence-based medical practice in our days. Diabetes Mellitus is also associated most commonly with renal impairment attributed to renal ischemia as a result of systemic arteriosclerosis. The aim of this study was to investigate any association between the levels of glycosylated hemoglobin HbA1c and Cardiac Ejection Fraction with different degrees of renal impairment in T2DM patients after their first incidence of myocardial infarction followed by limited cardiac function.

Methods: 551 (309 male, 242 female) post-MI T2DM patients participated on this study. Age range of the patients was between 48-76 years of age. All patients were assessed for cardiac functioning and their Cardiac Ejection Fraction was estimated after MI. Renal impairment was considered significant, when GFR <90 ml/min. Data were analyzed using ANOVA and logistic regression analysis. Ejection Fraction and HbA1c levels were analyzed as independent risk factors. Data is presented as mean \pm standard deviation and level of significance was accepted when $p<0.05$.

Results: Data were analyzed on 551 (309 male, 242 female) post-MI T2DM patients, 154 (28%) presented with Ejection Fraction of $32.7 \pm 4.1\%$, HbA1c levels of $7.98 \pm 0.91\%$ and a GFR of 89 ± 8.4 ml/min. 129 patients (23%) with Ejection Fraction of $30.9 \pm 2.2\%$ had HbA1c levels of $8.27 \pm 0.87\%$ and a GFR of 81 ± 7.2 ml/min. 203 (37%) Ejection Fraction of $29.8 \pm 3.7\%$ had HbA1c levels of $8.69 \pm 0.74\%$ and a GFR of 68 ± 7.9 ml/min and 142 (25%) patients with Ejection Fraction of $27.7 \pm 2.9\%$ had HbA1c levels of $8.27 \pm 0.81\%$ and a GFR of 82 ± 7.2 ml/min. Considering the cardiovascular burden that

follows a diminished cardiac function after Myocardial Infarction and the severity of diabetic nephropathy, renal impairment was more acute in post- MI T2DM diabetic patients $p < 0.001$ with increased levels of HbA1c were associated with increased renal impairment $p < 0.001$.

Conclusion: Evaluating limited cardiac function and renal impairment considering the severity of diabetic nephropathy in post- MI type 2 Diabetes Mellitus patients, a diminished cardiac ejection fraction and increased HbA1c levels are independent risk factors of acute renal damage.

THE HOSPITALIZED PATIENT WITH MEDICALLY COMPLICATED OBESITY: ARE WE MISSING AN OPPORTUNITY TO ENCOURAGE WEIGHT LOSS?

Oscar L. Morey-Vargas, MD¹;
Benjamin Mba, MD, FACP, FHM, MRCP²

¹Mayo Clinic, Rochester, MN, USA. Division of Endocrinology, Diabetes, Metabolism, and Nutrition;
²John H. Stroger, Jr. Hospital, Chicago, IL, Division of Hospital Medicine.

Objectives: Identify the frequency of medically complicated overweight and obesity among adults hospitalized in the General Medicine Ward of a large urban community hospital.

Identify the reasons for admission, rate of obesity documentation, and implementation of weight loss strategies by internal medicine residents and supervising physicians.

Methods: Prospective review of the electronic medical records of patients hospitalized in the General Medicine Ward of John H. Stroger Hospital of Cook County between February and March 2012. Body mass indexes (BMI) were calculated and the clinical notes reviewed. Internal medicine team members completed a survey where they reported if obesity was routinely targeted for management in their hospitalized patients.

Results: Six-hundred patients were included in the study, 41% were obese (BMI ≥ 30 kg/m²) and 25% were overweight (BMI 25–29.9 kg/m²). Nine percent had obesity class III (BMI ≥ 40 kg/m²). Heart failure was the most common cause of hospitalization in obese patients (9.7%), and also in those with obesity class III (16.3%). Other frequent causes of hospitalization in the obesity class III group were non-cardiac chest pain, chronic obstructive pulmonary disease exacerbations, asthma exacerbations, cellulitis, acute coronary syndromes, ischemic stroke and gallstone disease. In contrast, non-obese individuals were hospitalized

more commonly for malignancy-related complications and pneumonia. Among obese patients, obesity was documented in the past medical history (PMH) in 10% of cases and in the assessment and plan (AP) section of the admission notes in only 3% of cases. Among class III obesity patients, obesity was documented in the PMH in 36% of cases and in the AP just in 11% of cases. Sixty-six percent of physicians (27/41) reported not routinely discussing weight reduction strategies with their hospitalized patients.

Discussion: We found that the majority of hospitalized adult patients in the General Medicine Ward of a large urban community hospital were either obese or overweight. Almost one in ten had obesity class III. Obesity was not documented in the clinical notes in the vast majority of patients, and interventions targeting obesity management were rarely planned during the hospitalization. Similar findings have been reported in a university-affiliated hospital, where documentation of obesity by hospitalist providers was scarce (1). Many of the diseases associated with obesity have complications that require frequent hospitalizations. It is therefore important to develop and test strategies that could be started in the hospital aiming to encourage patients to lose weight after an acute illness.

Conclusion: Medically complicated overweight and obesity are highly prevalent in the General Medicine Ward. Despite obesity being an important underlying etiologic factor for several illnesses associated with frequent admissions, this problem is commonly ignored in the inpatient setting.

References:

1. Addressing obesity in the hospitalized patient: a needs assessment. Howe EE, Wright SM, Landis R, Kisuule F. *South Med J* 2010; 103(6):500-4.

RECOGNITION OF REVERSIBLE LIVER DISEASE: A WINDOW OF OPPORTUNITY IN THE METABOLIC SYNDROME EPIDEMIC

Harold T. Pretorius, MD, PhD¹;
Alexander K. Antony, BA²; Dennis E. Menke, AA¹;
Nichole M. Bodnar, CNMT¹; Betsy A. Budke, CNMT¹

Blue Ash Nuclear Medicine, LLC Cincinnati, Ohio

Background: Fatty liver (FL) is a fundamental aspect of visceral adiposity and the metabolic syndrome. Potentially reversible liver disease (RELD) includes FL, hepatic steatosis (FL with hepatocellular damage) and alcoholic or viral hepatitis.

Methods: Diagnostic tests included SPECT liver-spleen scans with modified fractal (Sn) analysis and blood tests. FL was confirmed by ultrasound, CT or biopsy. Untreated insulin resistant (IR) patients had HbA1c (5.7-6.1)% and diabetics (DM), HbA1c >6.1%.

Results: Near normal (27) patients had Sn 0.822 ± 0.133. RELD patients had Sn >1.09 (95% CL of normals). Sn 3.0 ± 0.21 was higher (p<0.001) in 16 hepatic steatosis patients than Sn 2.15 ± 0.12 in 42 with FL. Sn 2.44 ± 1.33 in DM was higher (p<0.04) than Sn 2.15 ± 0.98 in IR. Severely hyperglycemic diabetics (HbA1c 10.8 ± 1.5%; n = 21) had Sn 3.22 ± 1.98, similar (p=0.65) to Sn 3.68 ± 1.43 for 60 patients with splenomegaly and (p = 0.11) to Sn 2.56 ± 0.34 in 14 patients with hepatoxin exposure. RELD included cases of cirrhosis, severe diabetes, acute cholecystitis, splenomegaly, Cushing's syndrome and viral hepatitis. Abnormal Sn>1.09 (RELD) detected liver disease in 87.0% (315/362) of all patients, including 90.6% (145/160) with DM and 87.7% (136/155) with IR, more sensitively than abnormal liver enzymes 14.1% (51/362). Sn was stable or improved in 71% (25/35) of cases 2 to 24 months after therapies including mifepristone, Qsymia, omega 3 fish oil, vitamin E, pioglitazone and GLP-1 agonists.

Conclusions: Recognition of FL and RELD facilitates multiple, specific liver disease therapies which have potential to reduce the devastating impact of the metabolic syndrome epidemic.

ANTI-INFLAMMATORY, HYPO-LIPIDEMIC AND HYPO-INSULINEMIC EFFECTS OF HIGH COMPLEX CARBOHYDRATE DIET IN APPARENTLY HEALTHY VOLUNTEERS

Olga Raz, Tovit Rozenzveig; Ori Rogovsky; Itzhak Shapira; Shlomo Berliner

Departments of Dietetics and Nutrition, Ward D and Cardiology, Tel-Aviv Sourasky Medical Center and Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, and Departments of Nutritional Sciences, Ariel University, Ariel, Israel.

Aims: To evaluate the effect of high complex-carbohydrate diet on weight reduction, metabolic and inflammatory profile in a group of apparently healthy individuals, as well as to establish its effect of the diet on hyper-insulinemic individuals.

Methods: 72 women and men (age 50 ± 9 years, BMI 31.5 ± 5.6 kg/m²) were given high complex carbohydrate diet

for 8 weeks. The diet composition was: 1200-1600 Kcal, 60-62% carbohydrates, 30% fats, 10% proteins.

Results: The high complex carbohydrate diet significantly reduced BMI (31.5 ± 5.6 vs. 30.2 ± 5.5, p<0.001), waist (101 ± 16.7, vs. 96 ± 16.3, p<0.001) and hip (113 ± 12.8, vs. 110 ± 11, p<0.001) circumferences, insulin concentration (26.9 ± 11.1 vs. 20.5 ± 6.7, p<0.001) and insulin resistance index HOMA-R (6.2 ± 3.6 vs. 4.4 ± 2.3, p<0.001), fasting triglycerides (130 ± 61 vs. 114 ± 44, p=0.001), total (224.5 ± 38.7 vs. 199.5 ± 30.2, p<0.001) and LDL cholesterol (143.7 ± 32.8 vs. 126.3 ± 24.3, p<0.001), as well as the inflammatory profile, including the ESR (22.5 ± 14.5 vs. 17.9 ± 11.5, p<0.001), high sensitivity CRP (5.5 ± 4.2 vs. 3.6 ± 2.9, p<0.001), fibrinogen (308.6 ± 56.6 vs. 298.5 ± 51.5, p=0.005), the white blood cell count (7.4 ± 2.2 vs. 20.5 ± 6.7, p<0.001), and ICAM (258.5 ± 13.4 vs. 233.2 ± 12.4, p<0.0001).

Conclusions: A high complex-carbohydrate based diet is effective in improving the individuals' anthropometric measurements, metabolic and inflammatory markers and in improving insulin resistance.

COMPLEMENTARY MECHANISMS OF ACTION OF DAPAGLIFLOZIN AND METFORMIN

Arie Katz; Janelle M. Hardisty; Vicky W. Osborn

AstraZeneca, Fort Washington, Pennsylvania

Metformin (MET) is recommended by major diabetes organizations as initial pharmacotherapy for patients with type 2 diabetes mellitus (T2DM). For those patients not adequately controlled with MET alone, addition of 1 or more agents is recommended. Available agents vary in their mechanism of action, effects on body weight, and risk of hypoglycemia. MET noncompetitively inhibits mitochondrial glycerophosphate dehydrogenase, resulting in altered hepatocellular redox state and decreased lactate and glycerol conversion to glucose, contributing to reduced hepatic gluconeogenesis. Dapagliflozin (DAPA) is an oral, highly selective sodium-glucose cotransporter 2 inhibitor that improves glycemic control and produces body weight loss in patients with T2DM by increasing glucose excretion in the urine independently of insulin secretion or action. MET has been shown to increase glucagon-like peptide-1, potentially mitigating, at least in part, the increase in plasma glucagon seen with DAPA. We analyzed the results of 4 clinical trials of DAPA as add-on therapy to MET (NCT00528879, NCT00660907, NCT00855166, NCT01606007) and 2 clinical trials of DAPA+MET as initial therapy in treatment-naïve patients (NCT00643851,

NCT00859898). The combination of DAPA+MET provided sustained glycemic control and reductions in body weight for up to 102 weeks, without increasing the risk of hypoglycemia. Thus, complementary mechanisms of action, proven efficacy, lack of weight gain, and low risk of hypoglycemia support the use of DAPA+MET therapy in patients with T2DM.

POSTPRANDIAL DYNAMICS OF PLASMA GLUCOSE, INSULIN, AND GLUCAGON IN PATIENTS WITH TYPE 2 DIABETES TREATED WITH SAXAGLIPTIN PLUS DAPAGLIFLOZIN ADD-ON TO METFORMIN THERAPY

Lars Hansen, MD, PhD¹; Nayyar Iqbal, MD¹; Ella Elkhohm, MD, PhD²; William Cook, PhD³; Boaz Hirshberg, MD³

¹Bristol-Myers Squibb, Princeton, NJ, USA;

²AstraZeneca, Mölndal, Sweden; ³AstraZeneca, Wilmington, DE, USA

We recently reported results of a randomized, phase 3 clinical trial demonstrating that addition of saxagliptin (SAXA) plus dapagliflozin (DAPA) to metformin (MET) in patients with type 2 diabetes mellitus (T2DM) poorly controlled with MET resulted in greater reductions in HbA1c than addition of each component alone. In this study we analyzed changes in plasma glucose, insulin, and glucagon in relation to glycemic response. Adults with HbA1c $\geq 8.0\%$ – $\leq 12.0\%$ were randomized to SAXA 5 mg/d plus DAPA 10 mg/d (n=179), or SAXA 5 mg/d and placebo (n=176), or DAPA 10 mg/d and placebo (n=179) added to background MET XR ≥ 1500 mg/d. Mean change from baseline in area under the curve (AUC) from 0 to 180 minutes was calculated for glucose, insulin, and glucagon during a liquid meal tolerance test. Glucose AUC was reduced more from baseline with SAXA + DAPA + MET (–12940 mg/dL) compared with SAXA + MET (–6309 mg/dL) and DAPA + MET (–11247 mg/dL). Insulin AUC decreased with SAXA + DAPA + MET (–1120 μ U/mL) and DAPA + MET (–1019 μ U/mL) and increased with SAXA + MET (661 μ U/mL). Glucagon AUC increased only with DAPA + MET (2346 pg/mL). Change in glucose ($P < 0.0001$) and insulin ($P = 0.0003$) AUC correlated with change in HbA1c whereas change in glucagon AUC did not ($P = 0.27$). When added to background MET, the combination of SAXA + DAPA provided additional reduction in glucose AUC and HbA1c without the increase in insulin seen with SAXA and without the increase in glucagon seen with DAPA. Change in insulin and glucose but not glucagon AUC correlated with change in HbA1c.

TOO SHORT, BUT NOT TOO LONG SLEEP DURATION WORSENS INSULIN RESISTANCE IN NON-APNEA INDIVIDUALS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Sikarin Upala, MD MS^{1,2}; Anawin Sanguaneko, MD^{1,2}

¹Department of Internal Medicine, Bassett Medical Center and Columbia University College of Physicians and Surgeons, Cooperstown, N.Y., USA; ²Department of Preventive and Social Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

Background: Many sleep disorders have been linked to abnormal glucose metabolism and increase risk of diabetes. However, there is still controversy whether short or long sleep duration effect insulin resistance independent of apnea status. This is a systematic review and meta-analysis of available studies on association between abnormal sleep duration and insulin resistance. Our primary objective is to explore whether too short or too long sleep worsens insulin resistance in non-apnea participants.

Methods: We comprehensively searched the databases of PubMed/MEDLINE, EMBASE, and CENTRAL. The inclusion criterion was observational or interventional studies in non-apnea adults that examined association between short, long or normal sleep duration and insulin resistance. Included studies were quantitatively analyzed by comparing the homeostasis model assessment-estimated insulin resistance (HOMA-IR) between short versus normal, long versus normal, and short versus long sleep duration.

Results: From 126 full-text articles, 11 studies involving 4,962 participants were included in the meta-analysis based on the random effects model. In non-apnea individuals, there was higher insulin resistance measured by HOMA-IR in short sleep compared with normal sleep with mean difference (MD) of 0.14 (95% CI: 0.04 to 0.25). In contrast, long sleep was not significantly associated with higher HOMA-IR compared with normal sleep (MD = 0.12, 95% CI: –0.03 to 0.27).

Conclusions: Overall, non-apnea participants who had sleep deprivation were found to have higher insulin resistance compared to those with normal sleep duration. This association was not found in those who slept too long.

DIFFERENTIAL UTILIZATION OF GLUCOSE AND FRUCTOSE FOR DE NOVO LIPOGENESIS (DNL) IN INTESTINAL EPITHELIAL CELLS AND LIVER CELLS

Károly Mészáros¹; Grace Marie Jones¹;
Ewan Sinclair¹; Peter Scherp²; Jean-Marc Schwarz^{1,3}

¹Touro University CA, ²Pennington Biomedical Research Center, LSU, LA, ³University of California San Francisco, CA

Dietary glucose and fructose (ingredients of sugar-sweetened beverages) cause hypertriglyceridemia, and probably contribute to obesity and insulin resistance. While the liver is the primary producer of triglycerides (TG), we have recently demonstrated DNL in the intestines in humans.⁴ However, little is known about the substrate(s) of DNL in the gut.

For hepatocytes, human-derived HepG2 cells were used. For gut cells, human-derived Caco-2 cells differentiated into intestinal epithelial cells were employed; substrates were added to the apical (luminal) side of the cell layer. To approximate postprandial conditions, cells were incubated with a mixture of glucose and fructose (10 mmol/L each), where either glucose or fructose was labeled with ¹³C. In the intestinal cells, the contribution to DNL⁴ of 2-¹³C-glucose was 2.2 ± 0.7% per 6 h (mean ± S.D, n=5), while the contribution of 2-¹³C-fructose was undetectable. In contrast, preliminary results with HepG2 cells showed that fructose was slightly preferred to glucose as a DNL substrate, as expected.

In conclusion, fructose is not supporting intestinal DNL, provided that the Caco-2 culture is an adequate model of intestinal epithelium. Though fructose is well absorbed when ingested with glucose, it is uncertain whether it is phosphorylated and metabolized in the gut.

⁴Jones et al., 2014. <http://ada.scientificposters.com/epsAbstractADA.cfm?id=1>

LIPOCALIN-2 INDUCES INSULIN RESISTANCE IN CARDIOMYOCYTES VIA REGULATION OF OXIDATIVE STRESS AND AUTOPHAGY

Hye Kyoung Sung; Yee Kwan Chan; Gary Sweeney

Department of Biology, York University, Toronto

Lipocalin-2 (Lcn2; also termed neutrophil gelatinase-associated lipocalin (NGAL)) is a small, secreted adipokine that belongs to a diverse family of lipocalins. Lcn2 is a

proinflammatory marker associated with insulin resistance and obesity-related metabolic disorders. However, the precise mechanisms via which Lcn2 alters cardiac function are not fully known. Here we aimed to elucidate the effects of Lcn2 on cardiomyocyte insulin sensitivity with a focus on autophagy and oxidative stress as regulatory cellular mechanisms. In H9c2 cells derived from rat ventricle, Lcn2 (1µg/ml) induced insulin resistance as determined by Western blotting for stimulation of insulin receptor substrate and Akt phosphorylation. Using CellROX assay we observed that Lcn2 increased generation of reactive oxygen species (ROS). Our data also suggested that Lcn2 reduced autophagy; indicated by decreased phospho-mTOR, phospho-ULK1, Beclin1 and LC3II protein levels. This was confirmed by indication of fewer autophagosomal structures using transmission electron microscope, which also showed clear evidence of increased endoplasmic reticulum stress in cells treated with Lcn2. We are now generating cells stably expressing tandem fluorescent LC3 (tf-RFP/GFP-LC3) to carefully investigate Lcn2-induced changes in autophagic flux and autophagy-deficient cell lines to examine the functional significance of changes in autophagy. In summary, Lcn2 induced insulin resistance in cardiomyocytes and this involved regulation of the crosstalk between autophagy, endoplasmic reticulum stress and oxidative stress.

MCP-1 SERUM LEVELS AND INFLAMMATION MARKERS ASSOCIATED WITH THE PHENOTYPE G- OF POLYMORPHISM -2518G >A OF MCP-1 IN A MEXICAN POPULATION WITH INSULIN RESISTANCE

Navarro-Hernández Rosa Elena^{1,2,3};
Corona-Meraz María Fernanda;
Vázquez-Del Mercado Mónica²;
Ruiz-Quezada Sandra Luz³;
Ríos-Ibarra Clara-Patricia²; Petri Marcelo-Herón¹;
Guzmán-Ornelas Milton Omar²

¹IIRSME, Departamento de Biología Molecular y Genómica, Centro Universitario de Ciencias de la Salud; UDG-CA-701, Grupo de Investigación Inmunometabolismo en Enfermedades Emergentes (GIIEE). Universidad de Guadalajara; ³Laboratorio de Biología Molecular, Departamento de Farmacobiología, Centro Universitario de Ciencias Exactas e Ingenierías, Universidad de Guadalajara. This work was supported by grant No. PS-2009-552 to RENH of the State Council of Science and Technology (COECyTJal-Universidad de Guadalajara).

Introduction: In insulin resistance (IR), the major pathological mechanism is a chronic low grade inflammatory

response. MCP-1 (secreted by white adipose tissue) promotes the inflammatory process, the polymorphism -2518G>A has been suggested regulates expression of the MCP-1 gene and associated with obesity comorbidities.

Objective: To determine the association of levels of sMCP-1 and inflammatory markers with polymorphism -2518G>A *MCP-1* in Mexican-Mestizos with RI.

Material and Methods: In a cross-sectional study with ethical considerations, 380 Mexican-Mestizos, classified by RI were included. Were measured by routine methods inflammatory markers, metabolic and adiposity, sMCP-1 by ELISA and polymorphism -2518G>A by PCR-RFLP.

Results: The following differences ($P<0.05$) were observed: between individuals without and with IR genotype frequencies were (GG: 17.4%, 29%; GA: 50%, 46.4%; AA: 32.6%, 24.6%), with higher contribution of the A+ phenotype. While in individuals with A+ phenotype (GA plus AA genotypes) versus A- phenotype (genotype GG) in sLeptin ($x = 49.1 \pm 3.51$; $x = 68.5 \pm 7.89$ ng/mL) and sAdiponectin ($x = 4,850 \pm 330$, $x = 3,722 \pm 430$ ng/mL), sInsulin ($x = 16.6 \pm 1.2$, 20.50 ± 3.1 UI/mL); and, in individuals with G- phenotype (AA genotype) versus G+ (GG plus GA genotypes) in sMCP-1 ($x = 280 \pm 21.6$, $x = 191 \pm 14.9$ ng/mL) and C-reactive protein ($x = 2.8 \pm 2.98$, $x = 2.2 \pm 2.29$ mg/L). sMCP-1 correlated with inflammation markers, metabolic and hip circumference ($r = 0.190$ to 0.350).

Conclusions: sMCP-1 levels and A+ phenotype are associated with low-grade inflammatory process, adipokine profile and abnormal body fat distribution in Mexican-Mestizo population with insulin-resistance.

ASSOCIATION OF CD36 T188G POLYMORPHISM WITH ATHEROGENIC INDEX IN MEXICAN PATIENTS WITH RHEUMATOID ARTHRITIS

Sandoval García Flavio; Rocha Muñoz Alberto Daniel; Sánchez Hernández Pedro Ernesto; Huerta Viera Miguel; Trujillo Trujillo Xochitl; Petri Marcelo Herón; Pizano Martínez Oscar; Arreola Ramírez Guillermo Alberto; Madrigal Ruiz Perla Monserrat; Navarro Hernández Rosa Elena; Vázquez Del Mercado Mónica; Martín Márquez Beatriz Teresita

Universidad de Guadalajara, Guadalajara, Jalisco, Mexico

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects synovial joints. CD36, a

type B scavenger receptor, is postulated as a key molecule in the development of atherosclerosis. A T188G polymorphism in exon 10 results in decrease of CD36 and increase of total cholesterol (TC) and atherogenic index. The aim of this study was analyze the association of CD36 T188G polymorphism with atherogenic index, cytokines and CD36 membrane expression on monocytes in mexican RA patients.

Methods: Transversal analytical study. We included 62 mexican RA patients who underwent lipid profile, quantifying TNF- α and IL-6 and monocyte CD36 expression. The polymorphism was performed by PCR-RFLP. Comparisons between means were performed using T test and was considered significant $p<0.05$.

Results: CD36 T188G polymorphism was in Hardy-Weinberg equilibrium. Genotype frequencies for TT, TG and GG were 62.9%, 37.1% and 0%. Significant differences between TG and TT genotypes were found in TC mg/dL (180.84 ± 53.50 vs. 246.12 ± 42.82 $p = 0.01$), HDL mg/dL (54.16 ± 12.81 vs. 43.84 ± 5.95 $p<0.001$), atherogenic index TC/HDL (3.92 ± 1.09 vs. 5.48 ± 2.20 $p<0.001$), TNF- α pg/mL (26.03 ± 5.38 vs. 32.77 ± 12.30 $p=0.04$), IL-6 pg/mL (18.54 ± 14.09 vs. 45.07 ± 34.95 $p=0.01$) and mean fluorescence index for CD36 (89.56 ± 65.62 vs. 68.53 ± 68.53 $p=0.05$).

Conclusions: Mexican RA patients carriers of TG genotype of CD36 T188G polymorphism exhibit high atherogenic index that may be associated with decreased of CD36 expression on monocytes and increase levels of TNF- α and IL-6.

CORRELATION OF INTERARM SYSTOLIC BLOOD PRESSURE DIFFERENCE TO ANKLE BRACHIAL INDEX (ABI) IN DETECTING PERIPHERAL VASCULAR DISEASE IN TYPE TWO DIABETES MELLITUS PATIENTS – A ONE YEAR CROSS SECTIONAL STUDY

Shekhar Bhise

Kle University jn Medical College Belgaum, Karnataka, India

Peripheral vascular disease is a major macrovascular complication of diabetes mellitus. The ABI is useful in the diagnosis of both symptomatic and asymptomatic PAD. Interarm systolic blood pressure differences have been studied in patients with various manifestations of vascular disease. The present study was attempt to examine whether interarm differences in SBP and ABI correlate in diagnosing PVD among the patients with type 2 diabetes mellitus.

The present cross-sectional study was conducted for a period of one year from January 2013 to December 2013 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 45 patients with type 2 diabetes having duration of ≥ 6 years were studied. All the patients were investigated for ABI and interarm systolic blood pressure difference.

Most of the patients (62.22%) were males and male to female ratio was 1.64:1. 40% of the patients presented with age between 61 to 70 years. The duration of diabetes was between 10 to 15 years in 31.11% of the patients and mean duration was 20.04 ± 6.93 years. Most of the patients (42.22%) were on oral hypoglycaemic agents. The history of coronary artery disease was present in 31.11% of the patients. The interarm systolic blood pressure difference of ≥ 10 mm Hg was noted in 37.78% of the patients. Based on ABI most of the patients (46.67%) had mild and 33.33% had moderate peripheral vascular disease. IASBP difference ≥ 10 mm Hg was noted in 17 patients and of these, all the patients had PVD (100%). Mild PVD was noted in 11.76% and moderate in 88.24% ($p < 0.001$). Comparison of mean IASBP difference with severity of PVD showed an increasing trend in the mean values with severity of disease that is, as the PVD severity increased the mean IASBP difference increased and mean IASBP values differed significantly in all the grades of PVD based on ABI ($p < 0.001$). The linear correlation of ABI and IASBP difference showed strong negative correlation, depicting increase in IASBP difference with decrease in ABI and vice versa ($R = -0.919$; $R^2 = 0.8447$; $p < 0.001$). An IASBP of ≥ 10 mm Hg prompts physician for signs of peripheral vascular disease.

EFFICACY AND TOLERABILITY OF ITCA 650 (CONTINUOUS SUBCUTANEOUS EXENATIDE) IN POORLY CONTROLLED TYPE 2 DIABETES WITH BASELINE A1C $> 10\%$

Robert R. Henry; Julio Rosenstock; Michelle A. Baron

VA San Diego Healthcare System, San Diego, CA and University of California, San Diego, La Jolla, CA Dallas Diabetes and Endocrine Center at Medical City, Dallas, TX, Intarcia Therapeutics, Boston, MA

Background and Aims: ITCA 650, the injection-free GLP-1 receptor agonist that provides continuous SC exenatide for up to 12 months from a single sub-dermal placement, is undergoing extensive clinical evaluation in multiple Phase 3 double-blind studies. This report represents the first 6 month, open-label experience with ITCA 650 mini-pumps from an ongoing multicenter study in subjects with type 2 diabetes who did not meet enrollment criteria

for the double-blind placebo controlled trial because of A1C $> 10\%$.

Materials and Methods: Entrance criteria for this open-label trial were: A1C $> 10\%$ to $\leq 12\%$, age 18-80 years, BMI 25-45 kg/m², and on stable (≥ 3 months) diet and exercise and/or monotherapy or any combination of metformin, sulfonylurea, and thiazolidinedione. Treatment was initiated by placing a 3-month ITCA 650 mini-pump delivering 20 mcg/day, which was then replaced by a 6-month ITCA 650 mini-pump delivering 60 mcg/day for 26 weeks. Pre-study oral antidiabetic agents (OADs) were maintained unchanged for the 39 week of treatment. The primary endpoint was change in A1C from baseline to week 39.

Results: At the time of this initial interim analysis, 50, 39, and 25 of the 60 subjects enrolled had completed 13, 19, and 26 weeks of treatment; respectively. Mean baseline characteristics for the entire cohort ($n = 60$) were A1C 10.7%, age 52.1 yrs, BMI 32.1 kg/m², duration of diabetes 8.9 yrs, OAD use 69%. Mean reductions of A1C at Weeks 13 ($n = 50$), 19 ($n = 39$), and 26 ($n = 25$) were -2.5% , -2.9% , and -3.2% , respectively. A1C reductions $\geq 2\%$ were achieved by 78% of subjects who completed at least 13 weeks of treatment; 50% achieved $> 3\%$ and 22% achieved $\geq 4\%$ reductions. A1C targets of $< 7\%$ were achieved in 22% of subjects who had completed at least 13 weeks of treatment. Adverse events were consistent with previous trials with ITCA 650.

Conclusion: ITCA 650 has the potential to markedly improve glycemic control in patients with severe hyperglycemia and longstanding diabetes.

CORRELATION OF INTERARM SYSTOLIC BLOOD PRESSURE DIFFERENCE TO ANKLE BRACHIAL INDEX (ABI) IN DETECTING PERIPHERAL VASCULAR DISEASE IN TYPE TWO DIABETES MELLITUS PATIENTS – A ONE YEAR CROSS SECTIONAL STUDY IN KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM

Dr. Arathu Darshan; Dr. VA Kothiwale; Dr. Shekhar Ramchandra Bhise

Kle University JN Medical College Belgaum Karnataka, India

Peripheral vascular disease is a major macrovascular complication of diabetes mellitus. The ABI is useful in the diagnosis of both symptomatic and asymptomatic PAD. Interarm systolic blood pressure differences have been studied in patients with various manifestations of vascular

disease. The present study was attempt to examine whether interarm differences in SBP and ABI correlate in diagnosing PVD among the patients with type 2 diabetes mellitus. The present cross-sectional study was conducted for a period of one year from January 2013 to December 2013 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 45 patients with type 2 diabetes having duration of ≥ 6 years were studied. All the patients were investigated for ABI and interarm systolic blood pressure difference.

Most of the patients (62.22%) were males and male to female ratio was 1.64:1. 40% of the patients presented with age between 61 to 70 years. The duration of diabetes was between 10 to 15 years in 31.11% of the patients and mean duration was 20.04 ± 6.93 years. Most of the patients (42.22%) were on oral hypoglycaemic agents. The history of coronary artery disease was present in 31.11% of the patients. The interarm systolic blood pressure difference of ≥ 10 mm Hg was noted in 37.78% of the patients. Based on ABI most of the patients (46.67%) had mild and 33.33% had moderate peripheral vascular disease. IASBP difference ≥ 10 mm Hg was noted in 17 patients and of these, all the patients had PVD (100%). Mild PVD was noted in 11.76% and moderate in 88.24% ($p < 0.001$). Comparison of mean IASBP difference with severity of PVD showed an increasing trend in the mean values with severity of disease that is, as the PVD severity increased the mean IASBP difference increased and mean IASBP values differed significantly in all the grades of PVD based on ABI ($p < 0.001$). The linear correlation of ABI and IASBP difference showed strong negative correlation, depicting increase in IASBP difference with decrease in ABI and vice versa ($R = -0.919$; $R^2 = 0.8447$; $p < 0.001$) An IASBPD of ≥ 10 mm Hg prompts physician for signs of peripheral vascular disease.

INFLAMMATORY BIOMARKERS AND DIABETES AS PREDICTORS OF CHD IN MESA

Douglas S. Harrington, MD, FACP;
Americo Simonini, MD, FACC

*Cedars-Sinai Heart Institute, Los Angeles, CA USA
& Keck School of Medicine, University of Southern California*

Acute coronary syndrome (ACS) is the main cause of coronary artery disease (CAD) mortality. Insulin resistance and diabetes are significant factors increasing risk of CAD. In 50% of individuals, the initial presentation of CAD is a myocardial infarction (MI) or cardiac death. Current multifactorial absolute risk methods in clinical practice only predict 60%–65% of cardiovascular risk. Atherosclerosis is a disorder of the arterial wall caused by oxidized lipids and inflammatory cells. Most heart attacks (60%–83%) occur at the site of a non-obstructive plaque. Exercise testing or cardiac imaging only diagnose high grade coronary stenosis and fail to identify many at-risk asymptomatic patients because obstructive coronary plaque (stenosis of $>50\%$) is most often *NOT* the site of the cardiovascular event. Significant lipid elevation occurs in fewer than 50 percent of patients with ACS, MI, and unstable angina. Recent evidence from MESA (Multi-Ethnic Study of Atherosclerosis) suggests that biomarkers correlate with ACS risk (inflamed unstable soft plaque). In MESA, use of a biomarker algorithm significantly improves identification of at risk patients frequently missed by current methods. The protein-based algorithm includes seven proteins from pathways implicated in vulnerable plaque formation: CTACK, Eotaxin, Fas Ligand, HGF, IL-16, MCP-3, and sFas. The algorithm was 43% more predictive than Framingham models (clinical net reclassification). This algorithm identified 61% of patients who went on to experience an event. This novel risk algorithm, developed and validated in independent cohorts, demonstrates clinical utility for assessing the true risk of CHD events in intermediate risk and diabetic patients.