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CORRELATION OF SERUM APO – PROTEINS (APO – A1 & APO –B) TO C - PEPTIDE IN NEWLY DIAGNOSED TYPE -2 DIABETES MELLITUS – IMPACT ON CVD RISK EVALUATION

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Aim:
The present study was planned to establish the correlation between C – peptide & metabolic parameters like apo – proteins in newly diagnosed type – 2 diabetics for an early evaluation of CVD risk of these patients.

Background:
With an ever increasing incidence of both type – 2 DM & CVD in most urban populations, there has been a demand for newer techniques that could help in the early detection of the risk of this disease complex.

Materials: & Methods:
The present study has been conducted in 280 subjects (100 healthy controls & 180 – type – 2 DM patients) The diabetics were all newly diagnosed & were analysed for anthropometric (BMI), clinical (Blood pressure) & biochemical (FBS, Lipid profile, apo – proteins) parameters.

Statistical Analysis:
It was done using the students -‘t’ test and spearman’s coefficient of correlation.

Results:
The newly diagnosed type – 2 diabetics presented with obesity, hypertension, hyperglycaemia, dyslipidaemia, raised Apo – B & C – peptide levels & reduced Apo –A1 & a statistically significant association of C – peptide was observed with FBS, TG, Apo – B & CVD risk ratio apo – B/ Apo – A1.

Conclusion:
Serum C – peptide levels in type -2 diabetic subjects at diagnosis can be used as a tool for an early evaluation of CVD risk of these patients.

The traditional lipid profile values are a marker of CVD risk can be further attenuated by measuring the serum apo – proteins apo –B & A1 and their ratios that can help an early CVD risk evaluation.

Keywords:
HYPERTENSION, OBESITY & NON - HDLC IN NEWLY DIAGNOSED TYPE – 2 DIABETIC FEMALES OF WESTERN RAJASTHAN – A CVD DISASTER

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Aim:
To evaluate the CVD risk in the female type 2 diabetic patients at diagnosis.

Background:
India faces dual epidemic of diabetes and CVDs. Hypertension affects approximately 70% of patients with diabetes and is approximately twice as common in persons with diabetes as in those without. The hypertensive diabetic women with coronary heart disease appeared to be under-diagnosed.

Materials & Methods:
The study included 148 subjects (healthy controls – 50 females, DM -2 – 98 females). The patients were selected on the basis of symptomatology & a FBS > 126 mg / dl. They were then analysed for BMI, BP, serum Insulin, HOMA – IR, C – peptide, Lipid profile, apo – B & A1. CVD risk was assessed using non – HDLc, T.Chol/HDL and apo – B/apo A1 ratios.

Statistical Analysis:
It was done using the students -‘t’ test and spearman’s coefficient of correlation.

Results:
The female DM -2 patients presented with raised BMI, hyperinsulinemia, HOMA - IR & raised serum C – peptide, dyslipidaemia, raised non – HDLc, apo – B, (p<0.0001, HS) & reduced apo -A1 (p<0.0001, HS) as compared to the healthy controls. Hypertension was observed in 39.79% female diabetics. There was a significantly raised blood pressure than in controls (SBP - 134.24±18.72 mm of Hg v/s 114.72± 3.93 mm of Hg; p<0.000; DBP – 86 ± 8.93 mm of Hg v/s 77.92 ± 3.75 mm of Hg; p<0.0001 ). The correlative analysis showed a strong association of SBP in the female type – 2 diabetics with FBS (r= 0.24 p = 0.01 [S]) & with the potential CVD risk biochemical parameters (Insulin – r = 0.31 p = 0.0014 [VS]; HOMA – IR – r = 0.25 p = 0.012[S]; C – peptide – r = 0.34 p = 0.001[VS] & T.Chol/HDL (r= -0.28; p=0.005 [VS]). Non – HDLc had a strong association with insulin (r = 0.28 p =0.0052 VS), HOMA – IR (r = 0.31 p = 0.0019 VS), SBP(r=-0.27 p=0.0058 VS).

Conclusion:
The newly diagnosed type two diabetic females higher CVD risk is explained by significantly raised BMI, greater mean systolic & diastolic blood pressure and a high non – HDLc which in turn are strongly associated to potential CVD risk factors -hyperinsulinemia, HOMA –IR & CVD risk ratios. The coexisting hypertension & type – 2 DM should be thus aggressively managed specially in female diabetics, which are otherwise ignored in view of the female gender factor.

Keywords:
Dyslipidaemia, HOMA – IR, hypertension, C – peptide, CVD risk ratios

Abbreviations:
CVD – cardiovascular diseases, FBS – fasting blood sugar, SBP – systolic blood pressure, DBP – diastolic blood pressure, IR – Insulin resistance, NS – non significant, HS – highly significant, VS – very significant, S – significant.
THE CLINICAL CHARACTERISTICS OF ACANTHOSIS NIGRICANS IN OBESE ADOLESCENTS IN CHINA

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Purpose:
Acanthosis Nigricans (AN) is among the most common dermatologic manifestations of obesity and hyperinsulinemia. In this study, we aimed to find the clinical and laboratory differences among the AN, OB and normal adolescents.

Methods:
The data of 135 obese patients (60 with AN and 75 without AN) visiting our department from July, 2010 to February 2012 were collected and 20 age-matched healthy volunteers were included in this study. The physical examinations, lipid profile, measurement of fat distribution by DEXA were measured in all the participants. Glucose tolerance test with the secretion of insulin and C peptides in each point was performed in all participants. We also measured the thyroid function and adrenal function to evaluate the endocrine change of these patients. Fat liver accumulation was quantitative by MRS.

Results:
AN group had higher body weight, body mass index, waist circumference, waist/hip ratio, internal adipose, basal metabolism rate and total cholesterol level. Compared with the control group, there were higher percentage body fat, trunk fat and upper-limb fat in AN and OB groups. Although AN group had higher percentage of body fat than OB group, there was no difference in the fat distribution between the two groups. AUC\textsubscript{I} in the AN and OB groups was significantly higher than that in the control group. AN group had lower QUICKI, McAuley, AUC\textsubscript{G}/AUC\textsubscript{I} and IAI than OB and control groups, but higher I\textsubscript{0} and HOMA-IR (p< 0.05).

Conclusions:
AN patients is popular in obese and had more severe insulin resistance and fat liver accumulation with an high inflammation states. The fat distribution is different to the obese and normal. AN was a dermatologic marker of severe obesity and insulin resistance in obese adolescents in China.
PROFILE OF ADIPOKINES IN OBESITY ADOLESCENTS WITH ACANTHOSIS NIGRICANS

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Purpose:
Adipokines play an important role in the obesity related diseases. In this study, we aim to investigate its effect in obesity adolescents with acanthosis nigricans.

Methods:
36 obese patients (14 with AN and 22 without AN) visiting our department from July, 2010 to February 2012 participated our trial and 20 age-matched healthy volunteers were included in this study. The physical examinations, lipid profile, measurement of fat distribution by DEXA were measured in all the participants. Glucose tolerance test with the secretion of insulin and C peptides in each point was performed in all participants. Adipokines (Serum leptin, adiponectin and chemerin) levels were measured by ELASA. Inflammation factors as TNF-a, FFA and sCRP were also measured at same time.

Results:
The differences of serum leptin levels among the three groups were significant, the highest in AN group and the lowest in control group. The serum chemerin levels were higher in the AN and OB group than that in the control group (p<0.05), but there was no significant difference between the two groups. The serum leptin and chemerin levels were positively correct with BMI, FMI, waist/hip ratio, LDL, percentage body fat, truncal fat, I0 and HOMA-IR. After adjustment for sex, age and BMI, only waist/hip ratio, I0 and HOMA-IR had a negative correction with serum leptin level in the study population. Interestingly, Serum adiponectin is high and have significantly difference in AN group which different with diabetic obesity patients.

Conclusions:
There was an increase serum leptin and chemerin in obesity adolescents with acanthosis nigricans, leptin level was significantly higher in AN than obesity group,, which may be related to the severity of obesity and leptin resistance. The increasing of adiponectin play a potential protective affect which is different from diabetic patients.
EFFECT OF SITAGLIPTIN ON LIVER FAT ACCUMULATION IN TYPE 2 DIABETIC PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE

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Objective:
The purpose of this study was to observe the Sitagliptin effect on lipid metabolism and liver fat accumulation in diabetic patients with nonalcoholic fatty liver disease.

Methods:
17 diabetic patients with NAFLD received sitagliptin treatment for 24 weeks (100mg, qd ). T2DM was diagnosed according to the 1999 WHO criteria. NAFLD was diagnosed according to the criteria of 2010 Chinese Society of Hepatology and the fat liver was quantitative by MRS. Physical examination (waist circumstances, WC; body mass index, BMI;) and serum cytokines (leptin, adiponectin and chemerin), inflammation factors (TNF-a, sCRP, FFA), insulin secretion, glucose and lipid profiles (fasting blood glucose FBG; HbA1c, triglycerides, cholesterol, ALT, AST) were measured before and after sitagliptin treatment.

Results:
All the patients had the significant improvement in glucose metabolism after treatment. The liver function and inflammation states was improved and ALT, Leptin were significantly decreased, lipid profile was significantly changed. The fat liver was also improved but there was no statistical significance.

Conclusion:
Sitagliptin can not only improve the glucose metabolism in type 2 diabetic patients but also can improve the lipid metabolism in diabetic patients with nonalcoholic fatty liver disease, the potential mechanism was under further investigation. Weight loss and the reduction of inflammation factors possible contribute to the lipid profile improvement.
Objective:
The aim of this study is to investigate the relationship and its correlation between liver fat content quantitative measured by MRS and body fat distribution measured by Dual-energy X-ray Absorptionmetry (DEXA).

Methods:
68 NAFLD patients were recruited in our outpatient department from July, 2010 to February 2012 and NAFLD was diagnosed according to the criteria of 2010 Chinese Society of Hepatology. All subjects receive MRS and DEXA measurement at same time. The waist circumstances (WC), hip circumstances (HP) and Waist hip ratio (WHR), body mass index (BMI) were measured at same time. All subjects received serum total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein(LDL) and HbA1c measurement. Body fat (BF), Fat-free mass index (FFMI), Fat mass index (FMI), Lean mass index (LMI) and fat distribution were observed and calculated. Body fat distribution was calculated and compared to the liver fat content respectively.

Results:
1. There are linear correlation between liver fat content and waist circumference, BMI, the respectively correlation coefficient were 0.381, 0.383 (P < 0.01).
2. Liver fat content and body fat content has correlation and the correlation coefficient were 0.355 and 0.395(P < 0.05).
3. Liver fat content and body fat content has correlation and the correlation coefficient were 0.355 and 0.395(P < 0.05).
4. Male Liver fat content has much stronger correlation with FMI, upper part fat (UP%) and Trunk% than that of female patients, (male 0.581, 0.479, 0.709 VS female 0.31, 0.312, 0.29).

Conclusions:
Liver fat content and body fat distribution were positively correlated. The higher body fat content and upper body fat content were characteristics of fat distribution in subjects with NAFLD and the trunk fat can possibly reflect the liver fat content in clinical practice.

Keywords:
Non-alcoholic fatty liver disease, DEXA, fat distribution
MALNUTRITION RISK IN NEWLY HOSPITALIZED OBESE INDIVIDUALS: MR NOI

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Background:
It is estimated that 20-50% of hospitalized individuals are malnourished. The co-existence of malnutrition in obese, newly hospitalized patients has not been evaluated.

Objectives:
To estimate malnutrition prevalence among newly hospitalized overweight/obese patients; to characterize malnutrition by body weight category; and to assess associations between BMI, duration of hospitalization and in-hospital death in malnourished patients.

Design:
Cross sectional survey in newly hospitalized human patients.

Methods:
All adults newly admitted to internal medicine and surgical departments at the E. Wolfson Medical Center, Holon, Israel, during the five-week data acquisition period, were screened for malnutrition risk using the NRS 2002. An age-adjusted score of ≥ 3 on the NRS 2002 defined malnutrition. Malnutrition was compared across body weight categories: underweight (BMI<18.5 kg/m²), normal (BMI 18.5-24.99 kg/m²), overweight (BMI 25-29.99 kg/m²) and obese (BMI≥ 30 kg/m²). Overweight/obese subjects were compared by malnutrition status.

Results:
A total of 431 individuals were analyzed, of whom 243 were overweight/obese (BMI≥25 kg/m²). Of these, 58 (23.9%) were malnourished. Compared to adequately nourished overweight/obese subjects, malnourished overweight/obese patients had significantly prolonged duration of hospitalization: 11.7±18.9 (median 5, 1-123 days) vs. 5.3±6.7 (median 4, 0-65 days), (p=0.001). In-hospital mortality was 6.9% among malnourished vs. 0.5% among adequately nourished overweight/obese patients, p=0.003.

Malnutrition increased duration of hospitalization and in-hospital mortality risk in both overweight/obese and normal weight patients.

Discussion:
Malnutrition is a frequent finding in newly hospitalized overweight/obese adults. Elevated BMI does not affect duration of hospitalization. In-hospital mortality rates are similar for normal weight and overweight/obese individuals.
RISK FACTORS FOR THE METABOLIC SYNDROME IN CANADIAN ADULTS

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Background:
There is little is known about the predisposing risk factors for Metabolic Syndrome (MetS). No studies have compared the predisposing risk factors for MetS using the Adult Treatment Panel (ATP III) and the International Diabetes Federation (IDF) definitions.

Objective:
The purpose of this study was to examine and to compare the relationship between MetS and its associated risk factors according to both definitions.

Methods:
The Canadian Heart Health Survey was a cross-sectional probability sample survey conducted in all 10 Canadian provinces between 1986 and 1992. The present study is based on 4724 men and 4712 women from five provinces (Alberta, Manitoba, Ontario, Quebec and Saskatchewan) for whom full anthropometric measurements and data on all components of MetS were available. MetS was defined according to ATP III and IDF definitions. A weighted analysis using SPSS PASW Complex Samples (version 18) was used to conduct stepwise logistic regression analysis to identify risk factors significantly associated with MetS (p < 0.05).

Results:
According to ATP III, 17.9% and 15.3% of men and women have MetS, while according to IDF, 23.8% and 17.3% of men and women have MetS, respectively. Older age and low level of physical activity were significant risk factors for the MetS regardless of gender and definition. Higher level of education and alcohol consumption were additional significant protective factors for women, whereas retirement and being unemployed were additional significant risk factors for men.

Conclusion:
Both definitions identify the same risk factors which include demographic, socio economic factors, and lifestyle habits.

Funding:
This research was funded by New Emerging Team grant from the Canadian Institutes for Health Research and the Heart and Stroke Foundation of Canada.
PREDICTION OF MAJOR ADVERSE CARDIAC EVENTS AFTER COMPLETE REVASCULARIZATION BASED ON THE LEVEL OF HDL CHOLESTEROL - INTERMEDIATE FOLLOW-UP

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Introduction:
Plasma concentrations of HDL cholesterol (HDL-h) and risk of coronary artery disease (CAD) are in a strong inverse correlation, and patients with elevated HDL-h are at greater risk for severe CAD.

Objective:
To determine the impact of lower levels of HDL-h in assessing risk for CAD or the incidence of MACE (major adverse cardiac events) after a complete heart revascularization in the follow-up period of one and six months.

Methodology:
The reference value for HDL-h was ≤1.03mmol/L in men and ≤1.29mmol/L in women, according to International Diabetes Foundation criteria. We evaluated the incidence of MACE (myocardial infarction, angina, acute heart failure) after percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). CAD was graded as binary (have or don't have CAD).

Results:
The study included 140 pts. who underwent PCI (88pts., 80% men) and CABG (52pts., 77% men), 60±8.7 years. Lower HDL-h was more prevalent in men than women (43% vs. 26.3%) (chi-square=1705, df=1, p<0.001). Lower HDL-h was more frequent in patients ≤50 years (55.5%) than in older ones (chi-square=14:57, df=2, p<0.001). 71.4% of patients with lower HDL-h and 64.7% of those with elevated had statins therapy for a period more than one month (p<0.045). Frequency of CAD for those who have or do not have lower levels of HDL-h (chi-square=7.04, df=4, p=0.133) were nonsignificant. Incidence of MACE during follow-up didn't depend on levels of HDL-h (p=0.154).

Conclusion:
Lower level of HDL-h was more frequent in younger men and did not correlate with the degree of CAD or MACE during follow-up.
EVALUATION OF MAJOR ADVERSE CARDIAC EVENTS IN HIGH-RISK PATIENT GROUPS AFTER COMPLETE REVASCULARIZATION – INTERMEDIATE FOLLOW UP

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Introduction:
Heart revascularization generally consists of the prevention of disease progression and attendant suffering after it is clinically obvious and a diagnosis established.

Objective:
Certain subgroups of patients, such as those older than 65, young patients (≤50y) with diabetes type 2 (DM), obese patients (BMI≥30kg/m2) or patients with severe systolic dysfunction (LVEF≤30%), were evaluated and compared to the rest of the group in terms of higher risk for complications during and after complete revascularization.

Methodology:
The study group underwent percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) at Dedinje Institute for Cardiovascular Diseases. We evaluated the incidence of MACE (major adverse cardiac events), which includes myocardial infarction, angina, and acute heart failure, among those who underwent PCI or CABG for a period of one month and six months.

Results:
The study included 188 consecutive patients after coronaryography, 60±8.7 years, 77% men. Patients ≥65 years (34.6%), the incidence of MACE (after first vs. six months), (chi-square=0.122, df=1, p=0.727) vs. (chi-square=0.018, df=1, p=0.892), ns. Patients ≤50 years with DM (6.9%), MACE (chi-square=0.059, df=1, p=0.807) vs. (chi-square=0.138, df=1, p=0.710), ns. Patients BMI ≥30kg/m2 (4.3%), MACE (chi-square=0.018, df=1, p=0.892) vs. (chi-square=1.870, df=1, p=0.171), ns. Patients with EF ≤30% (14.4%), MACE (chi-square=1367, df=1, p=0.242) vs. (chi-square=0.488, df=1, p=0.485), ns.

Conclusion:
Up-to-date approach to myocardial revascularization in centers which specialize in these types of interventions, leads to the reduced incidence of complications in high-risk groups of patients regardless of the type of revascularization.
INDICATORS OF PEROXIDE-INDUCED CHEMILUMINESCENCE OF BLOOD SERUM WITH INSULIN RESISTANCE IN PATIENTS WITH CHRONIC HEPATITIS C

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The Aim:
To study was to examine the intensity of ultra-low luminescence of blood serum (computer chemiluminescence) in patients with chronic hepatitis C, combined with insulin resistance.

Method:
Analysed the spontaneous chemiluminescence (CL) induced by hydrogen peroxide chemiluminescence, area hemiluminescence in 45 chronic hepatitis C patients (38 men and 7 women aged 24 to 39 years) with the presence (group 1 - 16 patients) or absence of insulin resistance (group 2 - 29 patients).

Result:
We have established that in the presence of insulin resistance (group 1), the level of induced CL was higher than in group 2 (15.3 ± 0.7 conventional units, 11.6 ± 0.6 conventional units, respectively, P <0,001 for Mann-Whitney), in an area hemiluminogram group rates are also higher than group 2 patients studied (235.1 ± 10.6 conventional units, 191.3 ± 11.2 conventional units, respectively, P <0,001 for the Mann-Whitney ). When conducting discriminant analysis, we found that the most discriminant features is - induced chemiluminescence ($F = 23.4; P <0,001$), with a value of discriminant function coefficient of $F$ for the area hemiluminogram - $F = 11.9 (P <0,001)$. By the method of mathematical divider we have calculated the value of the induced CL - 14.1 standard units, which has the highest diagnostic screening opportunities for verification of insulin resistance in patients with chronic hepatitis C. The proposed test exceeds the level of induced CL in the serum to more than 14.1 standard units, has a sensitivity of 87% and a specificity of 81%.

Conclusions:
Insulin resistance in patients with chronic hepatitis C accompanied by an increase in the concentration of peroxidative substances in the blood serum, which confirms a high level of peroxide-induced chemiluminescence. The excess of the intensity of this indicator over 14.1 conventional units can be used to verify the screening of insulin resistance in patients with chronic hepatitis C.
ELECTRON MICROSCOPIC CHANGES IN LIVER TISSUE OF PATIENTS WITH CHRONIC HEPATITIS-C, COMBINED WITH INSULIN RESISTANCE

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The aim:
To investigate the ultramicroscopic changes in liver tissue of patients with chronic hepatitis C with and without insulin resistance.

Method:
There has been a study of liver biopsy in 14 patients with a moderate degree of activity of chronic hepatitis C. Of these patients, 8 patients (group 1) had not been verified for insulin resistance and 6 patients (group 2) were expressed resistant to insulin.

Results:
In biopsies of patients of group 1, it was found as follows: single deposition of lipid granules mainly in the liver lobules of centro-lobular zone, the high activity of the degradation of lipid granules in centro-lobular zone, hypertrophy and hyperplasia of mitochondria, increase in the number of lipid granules and lipo-phagocytic signs of degradation of the surface layer.

In group 2 patients, there was a significant progression of steatosis of hepatocytes in the peri-portal areas and centro-lobular zone, decreased degradation of lipid granules, disruption of mitochondrial cristae, an increase in the activity of Kupffer cells, increasing the number of cells and degranulation of ITO, their phenotypic transformation of fibroblasts in the growing accumulation of collagen fibres in the space of Disse.

Conclusion:
The presence of insulin resistance in patients with chronic hepatitis C progression is accompanied by significant deposits of lipid granules in periportal hepatocytes and centro-lobular zones, a significant decrease in the degradation of lipid granules and the progression of cell transformation in fibroblasts ITO, mainly in the centro-lobular area of liver.
SEVERE BURN-INDUCED ACUTE INSULIN RESISTANCE MEDIATED BY TRANSIENT HYPERGLYCEMIA-TRIGGERED AGES PRODUCTION

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Brief clarification:
Basic research on acute insulin resistance.

Hyperglycemia has been well recognized among patients suffering severe burns and is identified as an independent factor for poor outcomes of critical illness. Here, we report our findings of the dynamic profile of acute insulin resistance (AIR) following severe burns in rats (third-degree, comprising 40% of total body surface area) and its underlying mechanism. Two peaks of blood glucose were observed at 30 min (increased by 13%, p<0.05) and 3 h (increased by 35%, p<0.01) respectively after burns. Specifically, the two peaks of hyperglycemia had a definite pattern over time and amplitude, especially the 2nd peak was significantly positively-related to rat mortality following burns. Meanwhile AIR was detected as evidenced by blunted glucose tolerance, decreased phospho-Akt and increased serum insulin (>200% over baseline) 3 h after burns. Furthermore, carboxymethyllysine (CML), a dominate advanced glycation endproduct (AGE), was increased after the 1st hyperglycemia peak 1 h post-burn (p<0.01) together with increased ROS production. More importantly, early treatment with sRAGE (soluble receptor for AGE, 3 μg/kg BW) inhibited the 2nd hyperglycemia peak and alleviated AIR. Finally, inhibiting the 1st hyperglycemia with early (but not later) insulin treatment (2.5 U/kg BW) following burns not only decreased CML level, but also blocked the 2nd hyperglycemia peak and alleviated AIR. These results suggest that the first hyperglycemia peak after severe burns triggers AGEs production which induces AIR, resulting in adverse outcomes of severe burns. Early insulin treatment alleviates AIR and improves survival following burns via inhibition of hyperglycemia and the resultant AGEs production.
Ischemic heart disease as one of cardiovascular disease becomes a major public health problem worldwide. Diabetes mellitus is a major risk factor for IHD patients, which have 2-3 times more likely to develop IHD. A cross-sectional study was carried out in Punjab Institute of Cardiology Lahore, Pakistan on ischemic heart disease subjects (n=200) of age group of 40-65 years to study the frequency of type 2 diabetes and the relative prevalence of hyperglycemia, dyslipidemias and hypertension. The subjects were divided into two groups, group I (with diabetes) and group II (without diabetes). Out of total 200 patients the prevalence of diabetes was observed in 60% subjects. The mean ± SEM values of blood pressure, total cholesterol, serum triglycerides and LDL were significantly higher in group I as compare to group II. However the mean value of HDL was higher in group I as compare to group II but the difference among the group was non-significant (p >0.05). Overall results had shown that the prevalence of hyperglycemia, dyslipidemias and hypertension was higher in diabetics with IHD as compared to those without Diabetes. Therefore, it is concluded that the prevalence of conventional risk factors is quite significant in Pakistani IHD population.

**Keywords:**
IHD, type 2 Diabetes, risk factors.
DIRECT AND INDIRECT PARAMETERS OF INSULIN SENSITIVITY IN ASSESSMENT OF THE DEGREE OF CORONARY ARTERY DISEASE AND PROGNOSIS AFTER CORONARY ARTERY BAY-PASS SURGERY – INTERMEDIATE FOLLOW UP

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Introduction:
HOMA-index and metabolic syndrome (MetSy) are direct and indirect parameters of insulin sensitivity. Ability to predict major cardiac adverse events (MACE) after coronary artery bay-pass grafting (CABG) with these parameters of insulin sensitivity is still controversial.

Methodology:
Study group included patients who underwent CABG. MetSy is defined by International Diabetes Foundation criteria. HOMA-index was calculated as mathematical formulation of the values of fasting glucose and insulin. We evaluated the incidence of MACE, which included myocardial infarction, angina, and acute heart failure, during the follow-up periods of one and six months.

Results:
52 patients underwent CABG (78.8% men, 63±7y.). The mean value of HOMA-index was 9.7±9. HOMA-index was significantly elevated in MetSy patients (chi-square=666.7, df=1, p=0.002). HOMA-index and frequencies of patients with MetSy were higher in the group that had three or more blood vessel diseases compared to those who have one or two-vessel disease, but statistically nonsignificant. HOMA-index was higher in the group with MACE after one and six months, nonsignificant (p=0.226 vs. p=0.791). The mean values of upper quartile of HOMA-index was 9.2 (26.9%). The mean value of HOMA-index in MACE group did not exceed the limit defined for insulin resistance (9.06±8)(chi-square=296.05, df=1, p=0.036). Patients in upper quartile of HOMA-index did not have significantly more MACE after one or six months (p=0.246 vs. p=0.478). Patients with MetSy did not have significantly more MACE after one or six months (p=0.834 vs. p=0.906).

Conclusion:
MetSy and HOMA-index were not predictor for MACE after cardiac by-pass surgery, during intermediate follow-up.
ENLARGEMENT OF AORTA: MAY BE AN OCCUPATIONAL DISEASE?

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Background:
Enlargement of aorta may eventually progress to thoracic aorta aneurysm (TAA). Prolonged isometric type training or heavier strenuous exercise activity due to nature of some professions may be an important causative factor for the development of TAA. Latter issue is of potential to death unless it is diagnosed and managed earlier. We evaluated retrospectively the aortic diameters among middle aged subjects exposed to isometric type training or strenuous sports activity.

Material and Method:
We retrospectively analyzed the echocardiographic measurement reports recorded during the periodical examinations of personnel. Subjects were grouped as those having daily strenuous training activities and those having ordinary sports activity. Clinical features and parameters of left ventricle and aorta measured by echocardiography were compared among groups.

Results:
Diameters of aorta at root (33.5±1.9 vs 35.4±3.0) and at ascending level (34.1±2.2 vs 36.8±2.9) and also left atrium (36.2±2.2 vs 37.4±2.2) were significantly enlarged in subjects exposing daily strenuous isometric type training program. Also diastolic blood pressure was significantly lower (78.3±6.0 vs 73.8±5.9 mmhg, p=0.005) in those group. Although left ventricular internal diameter at diastole was slightly increased it was not statistically significant. There was not any statistically significant difference in comparisons of other echocardiographic parameters of left ventricle and systolic blood pressure among groups.

Conclusion:
Dilatation and subsequently the aneurysm of aorta may be an occupational disease due to nature of some professions such as security, athletes, heavy workers etc. Echocardiography is a convenient method of imaging which could easily applicable either at pre-participation screening or at periodical examination of those subjects. Earlier detection of TAA and limitation of such strenuous activities may be the initial lifesaving measures for them.

Key words:
aortic aneurysm, heavy workers, weight lifting, strenuous sports, echocardiography.

Group Statistics:

<table>
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<tr>
<th>Patient type</th>
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<td>70.7±5.7</td>
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TISSUE LEVELS OF ADIPONECTIN AND LEPTIN IN HUMAN CORONARY ATHEROSCLEROTIC PLAQUES

Karaduman, M1, Sengul, A2, Oktenli1, C, Pekel, A2, Yesilova1, Z, Musabak, U3, Sanisoglu, SY4, Gunay, C4, Baysan, O5, Kocar, IH1, Tatar, H5, Ozata1, M

Departments of Internal Medicine1, Immunology2, Biostatistics3, Cardiovascular Surgery4, and Cardiology5, Gülhane Military Medical Academy, TR-06018 Etilk-Ankara, Turkey

Background:
Leptin was originally thought to be an anti-obesity hormone, but it is also a crucial molecule for a number of diverse physiological processes, such as inflammation, immune function and atherosclerosis.

Adiponectin has a variety of anti-inflammatory functions against atherosclerosis. There is but little information available about any link between the levels of adiponectin and leptin in coronary atherosclerotic plaque specimens.

Aim:
We wished to analyze tissue levels of adiponectin and leptin in the plaques obtained from coronary artery bypass grafting (CABG) and to evaluate whether there is any relationship between these variables and diabetic state.

Patients and Methods:
Thirty-seven coronary atherosclerotic plaque specimens were derived during the elective CABG surgery. Immediately after the procedure, all extracted atherosclerotic plaques were frozen and stored at -80 C until the tissue homogenization.

Coronary artery specimens from thirty seven consecutive patients (28 men and 9 women) at time of CABG procedure and pre-procedural blood samples were obtained. Tissue concentrations of adiponectin and leptin in the atherosclerotic plaques were measured.

Diabetes was diagnosed in patients with dietary treatment or antidiabetic medication or current fasting plasma glucose level higher than 7 mmol/l.

Results:
The main finding of the present study that tissue levels of leptin is associated negatively with adiponectin in atherosclerotic plaques. Adiponectin levels were significantly lower in patients with diabetes mellitus than patients without diabetes mellitus. These differences in the variables between the presence and absence of diabetes mellitus remained significant after adjusting for age, gender, BMI, and statin use. Atherosclerotic tissue levels of these substances are also altered in diabetes. The mean tissue levels of leptin is higher in patients with diabetes mellitus than without diabetes mellitus. There was a positive association between leptin and plasma glucose in all patients. Atherosclerotic tissue levels of leptin were significantly higher in patients with diabetes.

The main finding of the present study that tissue levels of leptin is associated negatively with adiponectin. Atherosclerotic tissue levels of these substances are also altered in diabetes.

TABLE 1
Clinical and Laboratory Characteristics of Study Patients (n = 37)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th></th>
</tr>
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<td>Age, years</td>
<td>59.11 ± 10.06</td>
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<tr>
<td>Body mass index, kg/m2</td>
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<tr>
<td>Male, %</td>
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<td>Plasma fasting glucose, mmol/l</td>
<td>6.95 ± 2.81</td>
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<tr>
<td>Tissue concentrations*</td>
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<tr>
<td>Adiponectin, μg/ml*</td>
<td>22.97 ± 2.34</td>
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<tr>
<td>Tissue concentrations*</td>
<td></td>
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<tr>
<td>Leptin, pg/ml</td>
<td>10503.86 ± 11894.16</td>
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</table>
Data are mean ± S.D.
*Atherosclerotic tissue levels

**TABLE 2**
Comparisons of the Tissue Levels of Parameters between the Patients With (n = 17) and Without (n = 20) Diabetes Mellitus

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Diabetes mellitus (+)</th>
<th>Diabetes mellitus (-)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin (μg/ml)</td>
<td>21.87 ± 2.05</td>
<td>23.90 ± 2.18</td>
<td>0.006</td>
</tr>
<tr>
<td>Leptin (pg/ml) *</td>
<td>3.43 ± 0.07</td>
<td>3.28-3.57</td>
<td>0.006</td>
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</tbody>
</table>

**Conclusions:**
Present data provide confirmatory data to prior publications dealing with detection and quantification of various adipocytokines in atherosclerotic plaques. Our results raise a question that diabetic state, in addition to other psychopathological mechanisms, may create a chronic inflammatory situation in atherosclerotic process.
THE IMMUNOLOGICAL IDENTIFICATION OF LEPTIN ON HUMAN BREAST CANCER TISSUE AND NORMAL MAMMARY GLAND

Karaduman, M1, Ozet, A2, Sengul, A2

1Etimesgut Military Hospital, Dept. Internal Medicine and Surgery, Ankara, Turkey, 2Gulhane School of Medicine, Department of Medical Oncology, Ankara, Turkey

Objective:
Incidence of cancer is higher in obese individuals, which has not been clearly understood. The relationship of obesity as a risk factor for cancer is complex. Leptin levels are high in individuals with breast cancer. In this study, we aimed to compare levels of leptin in tissue suspensions in samples from breast cancer and normal tissues

Methods:
We included 30 consecutive patients with operable breast cancer and another 30 individuals whose biopsies were benign. All the patients were informed on the study and consented for reserving a part of the biopsy specimen for research purposes. They were then homogenized in homogenization solution. Leptin were studied in homogenized solutions by ELISA using Human Leptin elisa kit.

Body mass indexes for all the individuals were calculated. Menopausal status, types of surgery, tumor size, lymph node status, hormonal status for patients.

Statistical analyses were performed by using Statistical Package for Sciences.

Results:
Normal mammary epithelial cells did not express a significant level of leptin, whereas carcinoma cells showed positive staining for leptin 25 (83%) cases. Both normal epithelial cells and carcinoma cells expressed a significant level of leptin. However, over-expression of leptin, as determined by staining intensity. The expression of leptin showed a significant correlation with the level of leptin expression.

Conclusion:
Leptin may have a promoting effect on the carcinogenesis and metastasis of breast cancer, possibly in an autocrine manner. Functional inhibition of leptin may be effective for the prevention and treatment of breast cancer.
EFFICACY OF AUTOLOGOUS FAT STEM CELL TRANSPLANTATION IN TYPE 1 AND TYPE 2 DIABETICS

Barrenechea E, Lucero F, Paspaliaris B, Lucero L

Veterans Memorial Medical Center, Philippines

Objective:
To determine the efficacy of autologous fat stem cell transplantation in the management of type 1 and type 2 diabetics.

Materials and Methods:
Type 1 and Type 2 diabetics who are on either oral hypoglycemic agents and/or on insulin where baseline studies in the form of blood chemistries including Hemoglobin A1C and C-peptide determinations will be done. They will be subjected to the autologous fat transfer stem cell procedure.

Results:
Thirty five (35) diagnosed patients with diabetes mellitus were included in the study.

Significant decrease in FBS, creatinine levels and triglyceride from baseline to the end of the study (one year) was seen. No significant change was seen in these parameters - C-peptide, CBC, liver function and urinalysis proved the safety of the procedure.

Conclusions:
The significant decrease in the fasting blood sugars, creatinine and triglycerides from baseline to the end of the study as well as the decrease of the level of Hemoglobin A1C is highly significant for the type 2 diabetics. The other benefits are reduction of oral hypoglycemic agents in some of the patients (20%) and reduction or adjustment of insulin (10%) doses for the others.

The subjective benefits cannot be overlooked as majority (90%) of the patients had.

With these results, autologous fat stem cell transplantation may be one of the answers to the onslaught of diabetes in our midst.
ATYPICAL PROTEIN KINASE C IS ACTIVATED BY AMPK ACTIVATORS, METFORMIN AND AICAR, AND LIMITS AMPK-DEPENDENT IMPROVEMENTS IN LIPOGENIC AND GLUCONEOGENIC ENZYME EXPRESSION IN HEPATOCYTES OF TYPE 2 DIABETIC HUMANS

Farese, RV, Sajan MP

Medical and Research Services, James A. Haley Veterans Medical Center; Tampa, Florida, Division of Endocrinology and Metabolism, Department of Internal Medicine, University of South Florida College of Medicine, Tampa, Florida.

We recently reported that, whereas insulin activation of Akt and its regulation of gluconeogenesis are diminished in hepatocytes of type 2 diabetic (T2DM) humans, atypical protein kinase C (aPKC) is paradoxically increased and causes excessive expression of lipogenic and gluconeogenic factors that provoke/abet metabolic syndrome features of obesity, dyslipidemia, hyperinsulinemia, and glucose intolerance. Presently, metformin is widely used to improve hepatic gluconeogenesis, presumably through activation of 5’-AMP-dependent protein kinase (AMPK). However, metformin reportedly increases aPKC activity in mouse liver, and this may offset salutary effects of AMPK. Here, we compared metformin and experimental AMPK activator, AICAR, to aPKC inhibitor, ICAP, which potently diminishes expression of lipogenic and gluconeogenic factors in human hepatocytes. Metformin and AICAR indeed activated aPKC in human hepatocytes, in parallel with, and presumably secondary to, AMPK activation. Whereas ICAP largely reversed insulin-dependent and T2DM-dependent increases in lipogenic factor expression, such expression trended upward in non-diabetic hepatocytes, and was not diminished in T2DM hepatocytes treated with metformin and AICAR. Also, whereas ICAP diminished gluconeogenic enzyme expression in both the absence and presence of concurrent insulin treatment in both non-diabetic and T2DM hepatocytes, metformin and AICAR diminished gluconeogenic enzyme expression only in insulin-treated T2DM hepatocytes.

Conclusions:
In T2DM: failure to diminish expression of hepatic lipogenic enzymes may limit metformin effects on lipid abnormalities; dependence of gluconeogenic enzyme suppression on concurrent insulin treatment may limit metformin effects on glucose metabolism as insulin secretion diminishes; aPKC inhibition is more effective than combined AMPK/aPKC activation in diminishing hepatic lipogenic and gluconeogenic pathways.
STANDARD RISK FACTORS, HOMA-IR AND METABOLIC SYNDROME IN PREDICTION OF CORONARY ARTERY STENOSIS

Nikolić, A1,2, Nikolić, D1,3, Stanimirović, V4, Šumarac-Dumanović, M1,5

1Faculty of Medicine, University of Belgrade, Serbia, 2Cardiovascular Institute Dedinje, 3University Medical Center Bezanijska Kosa, 4Medicines and Medical Devices Agency of Serbia, 5Institute for Endocrinology CCS

Background:
Standard risk factors, direct (homeostatic model assessments (HOMA-IR)) and indirect (Metabolic Syndrome-MetSy) assessments of insulin-resistance are associated with cardiovascular diseases but they have a different predictive value on the degree of coronary artery disease (CAD).

Aims:
To evaluate significance of the standard risk factors, HOMA-IR and MetSy in the presence of CAD in patients submitted to cardiac catheterization.

Methods:
The study included 837 patients (60±8,7 years, (27-84 y.), 77% men, underwent clinical, laboratory and angiographic evaluation and were classified as CAD (extensiveness of CAD were graded as one, two, three, four and more vessels disease) or no-CAD (absence of coronary artery disease).

Results:
MetSy was present in 81.6% vs. 77.5% of those in CAD/no-CAD groups (Chi-square=1.7, df=1, p=0.18). The extensiveness of CAD was with no differences between patients with or without MetSy (Chi-square=8, df=4, p=0.08). Mean value of Tg 2.1±1.7mmol/L (p=0.076 vs. p=0.533), HTA 128±21mmHg (p=0.377) were insignificant, HTA (in different degrees of CAD, p<0.05), HDL 1.1±0.3mmol/L (p<0.001 vs. p=0.001), DM2 6.56±2.3mmol/L (p<0.03 vs. p=0.001), were statistically significant in CAD/no-CAD vs. different degrees of CAD. TG/HDLc index 2.2±2.9 vs. 1.1±1.4 was higher in the CAD/no-CAD group analysis, p=0.01, respectively graded CAD, p=0.196. HOMA-IR was insignificant between CAD/no-CAD groups, 9.19±8.6 vs. 7.72±4.6, p=0.501. HOMA-IR was insignificant in different degrees of CAD, p=0.587.

Conclusions:
MetSy, HOMA-IR, HTA (CAD/no-CAD), elevated triglyceride are not and lower HDL, DM2, TG/HDLc index (CAD/no-CAD), HTA (different degrees of CAD) are positively associated with angiographic CAD, and may be useful for risk stratification for CAD.
DYSLIPIDEMIA AND CORONARY HEART DISEASE MORTALITY (CHDM): TIME FOR THE MEDICAL PROFESSION TO CATCH UP WITH THE INSURANCE UNDERWRITERS!

Lardinois, CK

*Renown Health, University of Nevada School of Medicine, Reno, Nevada*

For over two decades the focus of dyslipidemia therapy has been on the LDL-C. These recommendations were based on studies showing that lowering LDL-C reduced CHDM. Diabetes patients have significantly higher rates of CHDM compared to the general population despite identical LDL-C. LDL-C suffers from the fact that it does not address critical triglyceride-rich atherogenic lipoproteins like very-low-density lipoprotein, very-low-density lipoprotein remnant and intermediate-density lipoprotein, which are commonly elevated in patients with and without diabetes. LDL-C alone also fails to recognize the importance of HDL-C. Therefore the time has come for dyslipidemia recommendations to focus on something other than LDL-C.

Areas of interest include non-HDL-C, ApoB, Apo A-1, ApoB/Apo A-1 ratio, LDL-Particles, HDL-Particles, LDL-P/HDL-P ratio, LDL-size (small dense) and HDL-size (buoyant HDL 2b). Another important parameter virtually ignored by the medical profession is the TC/HDL-C ratio (see table below). When the baseline TC/HDL-C ratio is >5 prior to any intervention, 8/9 studies showed a significant reduction in CHDM. In contrast when the baseline ratio was <5 only 3/12 studies showed any reduction in CHDM.

<table>
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<th>Study</th>
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<th>LDL-C Post</th>
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<td></td>
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<td></td>
<td></td>
<td>Fluvastatin</td>
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</table>

Summary:
There is clearly a critical threshold for the TC/HDL-C ratio (<5) for which further modulating of any lipid parameters (↑HDL-C and/or ↓LDL-C) offers little additional CHDM benefit. Underwriting Cholesterol for Life Insurance Companies only look at the TC and TC/HDL-C ratio in assessing risk. They do not look at LDL-C or triglycerides! The time has come for the medical profession to
get on board with the insurance companies and determine CHDM risked based on TC and TC/HDL-C ratio.
LEFT VENTRICULAR GEOMETRY OF CONCENTRIC HYPERTROPHY IN YOUNG OBESE SUBJECTS IS ASSOCIATED WITH INCREASED CAROTID INTIMA MEDIA THICKNESS

Aparci1, M1, Isilak, Z2, Yalcin, M1, Arslan, Z3, Erdal, M4, Kardesoglu, E2

1Etimesgut Military Hospital, Cardiology Service, Ankara, Turkey, 2Haydarpasa Training Hospital, Department of Cardiology, Istanbul, Turkey, 3Gelibolu Military Hospital, Cardiology Service, Canakkale, Turkey, 4Etimesgut Military Hospital, Family Medicine Service, Ankara, Turkey

Aim:
Carotid intima medial thickness (CIMT) is closely associated with abnormal elastic properties of arteries and also increased cardiovascular events. We evaluated the CIMT in young obese subjects grouped according to the hypertrophy type of left ventricle geometry.

Material and Method:
We evaluated the echocardiography examination results and carotid intima medial thickness measurements from the medical recordings of young obese subjects. Left ventricular mass and mass index was calculated by using Devereux formula and Dubois formula for BSA (body surface area, g/m2). Also LV hypertrophy index was calculated. Then concentric hypertrophy was defined as LVMI >50 g/m2; LVH index ≥4.4 and eccentric hypertrophy was defined as LVMI >50 g/m2; LVH index <4.4. We compared CIMT among groups designed according to the LV hypertrophy type.

Results:
Systolic (129.5±19.2 vs 135.5±15.9, p=0.190) and diastolic (82.8±14.1 vs 83.8±17.2, p=0.793) blood pressures were slightly higher in concentric hypertrophy group but not statistically significant. CIMT was also increased (0.48±0.03 vs 0.51±0.05, p=0.012) in concentric hypertrophy group.

Conclusion:
Carotid intima media thickness in significantly increased in young obese patients with LV concentric hypertrophy. It may be representative of any increased arterial shear stress or insult in those patients and also may indicate future cardiovascular events.

Keywords:
young, obesity, carotid intima media thickness, left ventricle geometry.
ASSOCIATION BETWEEN INSULIN SENSITIVITY AND LDL PARTICLE SIZE AND CHOLESTEROL DISTRIBUTION IN LATINO YOUTH

Ryder, JR¹, Vega-López, S¹², Kim, JY¹, Djedjos, CS³, Shaibi1, GQ²³⁴

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Obesity and insulin resistance place youth at higher risk for cardiovascular disease (CVD), but the mechanisms are poorly understood. In adults, insulin resistance is associated with the formation of small, dense low-density lipoprotein (LDL) particles, which contributes to CVD outcomes independent of LDL-cholesterol concentrations. However, limited data in youth exist. The purpose of this investigation was to examine the associations between insulin resistance and LDL particle size and cholesterol distribution in Latino youth.

One hundred and twenty nine Latino youth (16.3±2.5 years) were assessed for LDL-cholesterol (92.5±27.6 mg/dL), LDL particle size (272±2.4 Å), and distribution of cholesterol among LDL subfractions (7.3±4.7 %area). A 2-hour oral glucose tolerance test was performed with 30 minute sampling of plasma glucose and insulin to estimate insulin sensitivity as determined by Matsuda Index.

After adjusting for age and gender, insulin sensitivity was positively associated with LDL particle size (r=0.25; p=0.005) and inversely associated with cholesterol in small LDL subfractions (r=-0.30; p=0.001). These associations remained significant after further adjusting for LDL-cholesterol concentrations (r=0.22; p=0.02 and r=-0.24; p=0.007, respectively).

These data suggest that insulin resistance in youth contributes towards a more atherogenic lipoprotein phenotype, which includes smaller LDL particles and more cholesterol in small LDL subfractions. Therefore, interventional strategies that focus on improving insulin sensitivity may decrease CVD risk by shifting lipoproteins towards a less atherogenic profile.
CLINICAL FEATURES OF AVIATORS WITH CORONARY ARTERY DISEASE DOCUMENTED WITH MULTISLICE CT ANGIOGRAPHY

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Aim:
Coronary artery disease (CAD) is one of the incapacitating causes during flight operation among aviators which is currently crowding in number. So we aimed to detect the clinical features that could identify aircrew with coronary artery disease.

Material and Methods:
We retrospectively analyzed medical recordings of 26 (15 pilot and 11 technical stuff aviator) aircrew to who were diagnosed as coronary artery disease by MSCT angiography. We compared the clinical features (age, body mass index, systolic and diastolic blood pressure, and etc), coronary risk factors (hypertension, diabetes, smoking, family history, hyperlipidemia and etc) and ST and T wave changes at resting ECG, treadmill test (TT), and laboratory findings of subjects.

Results:
Demographics were not significantly different except age (46.2±5.1 vs 40.0±2.5) among pilots and other aircrew. ST depression <0.05 mV and T wave inversion (0.03 mV) were found on 53.8% and 23.1% of resting ECG, respectively. 53.8% of patients had the family history of coronary artery disease. All of the subjects had ECG changes diagnosed as 76.9% equivocal and 23.1% positive on TT. 73.1% of patients were overweight. Family history was found to be statistically correlated with coronary artery disease (p=0.023<0.05, ß=0.445). Diabetes and hypertension were absent whereas hyperlipidemia, smoking, and low HDL were lower in study group. Nevertheless, 73.1% of patients were overweight whereas 15.4% was obese and only %11.5 was of normal weight.

Conclusion:
Periodical examination of aircrew should include at least a resting ECG and inquiry of family history of an atherosclerotic heart disease. ECG changes such as minimally ST and T wave changes should not be overlooked or ignored. Also equivocal TT results may indicate further coronary imaging. Since detection of any coronary artery disease which could potentially challenge public safety through aviation accidents is clinically important and allows an effective primary prevention of aviators. Additionally overweight which could potentially be source of multiple cardiovascular problems in the future is a common problem among aircrew probably due to physical inactivity. Lifestyle modifications are necessary for a healthier aircrew population and less cardiovascular events.

Keywords:
aviation, coronary risk factors, atherosclerosis, multi-slice CT coronary angiography, family history, overweight.
INCREASED LEVELS OF GAMMA GLUTAMYL TRANSFERASE IS ASSOCIATED WITH INCREASED RISTOCETIN AGGREGATION IN YOUNG OBESE SUBJECTS

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Aim:
Gama glutamyl transferase-γ (GGT) is a liver enzyme which was recently reported to be found associated with increased atherosclerotic cardiovascular disease in adults. We aimed to evaluate retrospectively the results of aggregation tests (Ristocetin-, ADP-, and Epinephrine induced aggregation) performed in young obese subjects. and its association with levels of GGT.

Material and Method:
Medical recordings of 56 young obese individuals were analyzed and demographics (age, body weight and height, body mass index), laboratory parameters (AST, ALT, GGT, FBG, etc), and aggregation tests results were recorded. Data were compared among the groups designed according to the levels of GGT as ≤40, 40-80, ≥80.

Results:
Age and BMI were not different among groups whereas body weight and height are higher in patients with higher GGT levels. Also ALT and AST levels were higher in those patients (Table1). When we compared aggregation test results among groups designed to the GGT levels we observed that ristocetin aggregation (77.0±5.5, 74.7±1.7, and 65.0±1.7, p= 0.000) significantly shortened whereas ADP (62.6±12.1, 65.5±6.8, and 74.2±2.0, p= 0.018) Epinephrine aggregation (65.2±16.8, 66.7±8.2, and 71.2±2.2, p=0.535) durations prolonged as the levels of GGT enzymes increased (Table 2).

Conclusion:
Ristocetin aggregation test represents the von Willebrand Factor associated coagulation pathway and increased in associated with increased levels of GGT in obesity. Additionally response to ADP and epinephrine induced aggregation was prolonged in associated with increased levels of GGT. Increased ristocetin induced aggregability may explain the increased thromboembolic events associated with obesity and it may suggest an increased activity or levels of vWF in obesity. Also GGT enzyme level is closely associated with enhanced aggregation probably associated with increased vWF activity and its routine follow up may aid to indicate increased aggregability in obese subjects. Additionally prolonged ADP and epinephrine aggregation test may be an explanatory mechanism for the reported data about the decreased sensitivity to antiaggregating effects of both acetylsalicylic acid and thienopyridines in obesity.

Keywords:
obesity, gama glutamyl transferase, ristocetin, aggregation.
ROLE OF BMI AND LEFT VENTRICULAR HYPERTROPHY INDEX ON PREDICTION OF LEFT VENTRICULAR DIMENSIONS IN YOUNG OBESE SUBJECTS

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Aim:
Obesity is closely associated with heart failure. But which type of heart failure could be develop and its onset could not be predicted yet. In this study we aimed to evaluate the role of BMI and LV hypertrophy index in prediction of left ventricular dimensions and geometry pattern in young obese individuals.

Material and Method:
We evaluated the echocardiography examination results and measurements from the medical recordings of young obese subjects. Echocardiographic parameters of left ventricle and mitral inflow were recorded. Left ventricular mass and mass index was calculated by using Devereux formula and Dubois formula for BSA (body surface area, g/m2). Also LV hypertrophy index was calculated. Then concentric and eccentric hypertrophy was defined as LVMI >50 g/m2; LVH index ≥4.4 and <4.4, respectively. We compared those parameters among groups designed according to the LV hypertrophy type, BMI, and etc.

Results:
LV internal diastolic (50.7±7.2 vs 43.3±3.8, p=0.00) and systolic (33.1±5.6 vs 27.4±2.1, p=0.00) diameters and volumes (101.5±22.6 vs 83.5±16.6, p=0.001) (32.3±7.4 vs 27.6±5.2, p=0.005) were found to be significantly increased in eccentric hypertrophy group in comparison according to LV hypertrophy index. Furthermore mitral inflow A velocity increased (0.77±0.12 vs 0.97±0.29, p=0.001) and also deceleration time (205.5±65.1 vs 242.4±52.4, p=0.015) prolonged whereas E velocity (0.72±0.22 vs 0.61±0.18, p=0.031) decreased in concentric hypertrophy group. However it was not observed any significant difference among groups designed according to the BMI 40 kg/m2. LV hypertrophy index<0.44 could indicate the enlargement of LV parameters whereas index ≥0.44 indicate concentric hypertrophy and also dependency to contribution of atrial contraction to the diastolic volumes which may indicate progression to diastolic heart failure.

Conclusion:
LV hypertrophy index may be used in follow up and may aid to identify the risk of what type of heart failure have an obese subject. Perhaps losing weight and life style changes must be first choices of treatment of obesity. However we must be ready and could predict the further cardiovascular morbidities in obese patients.

Keywords:
young, obesity, left ventricular hypertrophy, left ventricle geometry.
THE LONG-TERM EDUCATION IMPACT ON DIABETES EDUCATION FOR OLDER PEOPLE: A SYSTEMATIC REVIEW

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Background:
Although enthusiasm is growing for diabetic education programs for older people, data regarding their effectiveness and long term impact on their self management were neglected.

Purpose:
To systematically review DM education that has long-term effects of self-management for diabetes older people.

Data Sources:
The authors searched multiple sources dated through September 2007, including the Cochrane Library, MEDLINE, PsycINFO, and Nursing and Allied Health databases, and bibliographies of 50 previous reviews.

Methods & Data Extraction:
Computerized databases were searched for English-language controlled studies assessing the effect of long term education for older people published from 1987 to 2007. Reviewers extracted study data using a structured abstraction form. Pooled of long term education program effects on older people with diabetic were used to adjustment to review.

Results:
The pooled estimate of program effects on long term education was a 0.5-percentage point reduction (95% confidence interval), a modest but significant improvement. Evidence also supports the long term education had a benefits in improving for diabetic patient self-care management in term of glycemic control.

Limitations:
Studies had variable quality, and possible publication bias was evident.

Conclusions:
Diabetes education, self-management program can be combined with new technology and results were as successful for the glycemic control for patient. The elements of the programs most responsible for benefits cannot be determined from existing data, and this inhibits specification of optimally effective or cost-effective programs.
INTERACTION BETWEEN -11391G/A AND +45T/G POLYMORPHISMS IN ADIPOQ GENE AND ENVIRONMENTAL FACTORS AND THEIR INFLUENCE ON ADIPONECTIN, CARDIOVASCULAR RISK AND INSULIN RESISTANCE IN MEXICAN SUBJECTS

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Introduction:
Adiponectin (apM1) is an adipocytokine involved in fatty acid metabolism and insulin sensitivity. Single nucleotide polymorphisms (SNPs) -11391G/A and +45T/G in ADIPOQ gene are associated with high concentrations of apM1 and lower risk of metabolic disorders.

Objective:
To analyze the interaction of the -11391G/A and +45T/G SNPs and environmental factors and their influence in apM1, cardiovascular risk and insulin resistance (RI) in Mexican subjects.

Methodology:
394 subjects with mean age of 37.16±11.5 years were grouped by BMI tertiles and SNPs genotype. Anthropometric, biochemical, dietary, clinical and physical activity parameters were evaluated. Genotyping was performed by PCR-RFLPs. Insulin and apM1 were realized by ELISA. To determine RI, was used the HOMA assay. Biochemical indicators of cardiovascular risk and glucose were determined by dry chemistry. Statistical analysis was performed with PASW software. P values <0.05, were considered significant.

Results:
56.1% of the subjects had hypoadiponectinemia and 41.5%, RI. Allele frequency of SNP -11391G/A were 0.78 for G and 0.22 for A; and SNP +45T/G were 0.66 for T and 0.33 for G. Frequency of subjects with wild genotype of both SNPs was higher in the 1st tertile compared to 2nd and 3rd tertile, (p<0.05). Couplet by tertiles, in 1st tertile, -11391GA/AA genotype had higher apM1 concentration vs -11391GG. The variability in apM1 concentration was due to RI, gender and physical activity (R²=0.224).

Conclusion:
The -11391G/A SNP had positive effect in apM1 concentrations, this decreased in relation to BMI. Environmental factors and -11391G/A SNP are related to apM1 concentrations.
HYPERTRIGLYCERIDEMIC WAIST PHENOTYPE IS A NAFTA EARLY METABOLIC MARKER IN HEALTHY NON-OBSESE YOUNG ADULT MALES

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Background:
The worldwide increase in the prevalence and incidence of non-alcoholic fatty liver disease (NAFLD) may largely be explained by the epidemic of insulin resistance. The aim of this study was to investigate whether simple combination as waist circumference and fasting plasma triglyceride (TG) concentrations is associated with early signs of NAFLD in clinically healthy non-obese young adult males.

Materials:
The 119 clinically healthy male subjects aged 25-44 years were enrolled in the study (55 with primary NAFLD by ultrasound and 64 controls). The BMI was less 30 kg/m2. The presence of an elevated waist circumference (90 cm or greater) and moderate hypertriglyceridemia (TG concentration 2.0 mmol/l or higher) is defined as hypertriglyceridemic waist phenotype.

Results:
The waist circumference was 92.3±8.4 cm in patients with NAFLD vs. 84.7±8.8 cm in controls (p<0.001). The triglyceride levels in NAFLD patients were significantly higher 1.5±1.0 vs. 1.1±0.7 mmol/l in control group (p=0.003). There was no difference between glucose and cholesterol HDL concentrations. The frequency of elevated waist circumference and NAFLD was 73.2% (OR=5.88 with 95% CI [2.66 – 13.01]). The combination of moderate hypertriglyceridemia and NAFLD was detected in 21.4% cases (OR=4.02 with 95% CI [1.22 – 13.32]). The hypertriglyceridemic waist phenotype occurred in 17.9% NAFLD patients and the OR estimation showed increase more than 2.3 times and reached 13.48 level with 95% CI [1.67 – 109.1].

Conclusion:
The present study confirms the hypothesis that hypertriglyceridemic waist phenotype in non-obese males could be a useful screening tool for the identification the high risk group for NAFLD.
PARAMETERS OF INSULIN RESISTANCE IN A REPRESENTATIVE ADOLESCENT POPULATION OF LAHORE

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Objective:
Assessment of parameters of insulin resistance in our adolescents and see if these are deranged.

Materials and Methods:
193 adolescents aged 17-25 years from various educational institutes of Lahore participated in this study. A questionnaire about family history and dietary habits was completed.

After written consent, anthropometric parameters of obesity, fasting blood sample for glucose, lipids and insulin levels were taken according to standardized methods. Fasting plasma glucose and lipids including total cholesterol (TC), HDL-cholesterol, LDL-cholesterol and triglycerides (TG) were evaluated. Out of the total, 88 samples were frozen and measured later for fasting insulin levels. HOMA1-IR was applied to relevant values. Data was calculated by SPSS 15.

Results:
Frequency distribution according to gender was 54.9% males, 45.1% females. Obesity showed increased incidence, 34.7% due to increased BMI in both genders. Out of these 29% were overweight, 5.7% were frankly obese, 20.2% had fasting serum cholesterol > 191 mg/dl; serum HDL-cholesterol < 40 mg/dl in 87.6%. 23.3% of the total had LDL-cholesterol > 200 mg/dl. Fasting serum triglycerides >185 mg/dl in about 12.5%. Fasting insulin level in 88 out of 193 samples, males 0.1711±0.22473 and females 0.1950±0.10128. HOMA 1-IR in 53 males was 0.03734±0.046990 and 31 females was 0.03782±0.022139. Both fasting insulin levels and HOMA1-IR showed statistically significant values.

Conclusion:
Deranged parameters of obesity, fasting plasma glucose, lipid, insulin and HOMA1-IR indicate some degree of insulin resistance in our adolescent population. Early onset of insulin resistance calls for early preventive measures regarding change in dietary and lifestyle habits.
PROTECTIVE EFFECT OF MORIN ON CARDIAC MITOCHONDRIAL FUNCTION DURING ISOPROTERENOL-INDUCED MYOCARDIAL INFARCTION IN MALE WISTAR RATS

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Altered mitochondrial function and free radical-mediated tissue damage have been suggested as an important pathological event in isoproterenol (ISO)-induced cardiotoxicity. This study was undertaken to know the preventive effect of morin on mitochondrial damage in ISO-induced cardiotoxicity in male Wistar rats.

Myocardial infarction (MI) in rats was induced by ISO (85 mg/kg) at an interval of 24 hours for 2 days. Morin was given to rats as pre-treatment for 30 days orally using an intragastric tube.

ISO-treated rats showed a significant elevation of mitochondrial thiobarbituric acid reactive substances (TBARS) and hydrogen peroxide (HP) level and pre-treatment with morin significantly prevented the increase of TBARS and HP level to near normality. The level of enzymic and non-enzymic antioxidants was decreased significantly in ISO-treated rats and pre-treatment with morin significantly increased the levels of superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase, glutathione reductase, and reduced glutathione to normality. The activities of mitochondrial enzymes such as isocitrate dehydrogenase, alpha-ketoglutarate dehydrogenase, succinate dehydrogenase, and malate dehydrogenase were decreased significantly in ISO-treated myocardial ischemic rats and upon pretreatment with morin restored these enzymes activity to normality. In addition, the decreased activities of cytochrome-C oxidase and NADH-dehydrogenases were observed in ISO-treated rats and pre-treatment with morin prevented the activities of cytochrome-C oxidase and NADH-dehydrogenase to normality.

Pretreatment with morin favorably restored the biochemical and functional parameters to near normal indicating morin to be a significant protective effect on cardiac mitochondrial function against ISO induced MI in rats.
Aims:
Type 2 diabetes (T2D) and impaired glucose tolerance (IGT; the pre-diabetic state) are associated with a significantly increased risk of developing cardiovascular disease and heart failure when compared to the healthy population. Despite this, there exists little discussion into the effect of T2D and IGT on cardiac torsion, the measure of “twist” during the cardiac cycle. This study will explore the effect of T2D and IGT on cardiac structure, function (including torsion) and metabolism using magnetic resonance methodologies.

Methods:
Seven adults diagnosed with IGT and T2D were age- and sex-matched to healthy controls without cardiac disease. Cardiac structure and function were assessed with high-resolution cardiac magnetic resonance imaging (MRI). High-energy phosphate metabolism was carried out with the use of 31P-MR spectroscopy in order to obtain the phosphocreatine-to-ATP ratio (PCr / ATP); a measure of metabolic efficiency.

Results:
Despite showing no significant changes in cardiac energetics (PCr / ATP), cardiac output or left ventricular mass, adults with T2D and IGT had significantly thicker left ventricular walls at diastole and systole than healthy controls and showed increased percentage thickening during contraction. The ratio of early to late ventricular filling (a measure of diastolic function) was significantly reduced (1.3 ± 0.5 vs. 2.0 ± 0.9 p < 0.0005) as well as an increased torsion (7.5 ± 1 vs. 6.2±1 degrees p = 0.039) compared to controls.

Conclusions:
Our findings suggest significant sub-clinical differences exist in cardiac structure and function in T2D and IGT. Studies are required to identify which specific differences are predictive of the excessive risk of cardiovascular disease associated with T2D and IGT.
HEART RATE AND PHYSICAL ACTIVITY ASSOCIATED WITH INSULIN RESISTANCE AND ABNORMAL GLUCOSE TOLERANCE IN A MULTI-ETHNIC COHORT

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Objective:
Resting heart rate (RHR) has been identified as an independent risk factor for cardiovascular disease and mortality, contributing to atherosclerosis, the progression of heart failure, and myocardial ischemia and infarction. This study examines the association of RHR and physical activity with insulin resistance and abnormal fasting glucose in a multiethnic cohort from North Kohala, Hawai’i.

Methods:
Cross-sectional data from 1,440 participants of Native Hawaiian, Japanese, Filipino, Caucasian, and mixed ethnic ancestries were analyzed for the study to include sociodemographics, anthropomorphic measurements, and biochemical markers. The homeostasis model was used to estimate insulin resistance from an oral glucose tolerance test. Physical activity was estimated using the Modifiable Activity Questionnaire. Multiple regression was performed using the General Linear Model.

Results:
Caucasians had lower mean RHR than all other ethnic groups; there were no statistically significant differences between other ethnic groups on mean RHR. BMI was highly associated with a higher RHR, with a p<0.0001. The log of physical activity level remained significant for both insulin resistance and abnormal glucose tolerance.

Conclusions:
In a multiethnic cohort from a rural community in Hawai’i, increased RHR and a lower level of physical activity were both independently associated with insulin resistance and abnormal glucose tolerance. Further research is needed to elucidate the mechanism explaining the role of resting heart rate in determining insulin resistance.
COMMON VARIANT OF THE ADIPOQ GENE AND ITS RELATIONSHIP WITH ADIPONECTIN, LEPTIN, INSULIN RESISTANCE AND DETERMINANTS OF METABOLIC SYNDROME IN NORTH INDIAN ADULT WOMEN

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Background:
Adiponectin (ADIPOQ) is a gene exclusively expressed in human adipose tissue. Some common variants of the adiponectin gene, affects its serum level and metabolic features of metabolic syndrome. The goal of this study was to examine the possible relationship of the common genetic variants of AdipoQ (+45T/G and +276G/T) with its level, leptin level, Insulin resistance and component of metabolic syndrome (MetS) in north Indian adult women.

Methods:
Two SNPs in the adiponectin gene were genotyped in 269 women with MetS (according to the criteria of NCEP-ATP III) and 272 women without metabolic syndrome (wMetS). Circulating adiponectin and leptin level, IR and metabolic risk factors were determined.

Results:
Significantly difference (p<0.001) were found for determinants of metabolic syndrome and lower adiponectin and HOMA-IR in MetS compared to wMetS women. The frequency of TG+GG of +45T/G was found to be significantly less (p=0.017) while mutant G allele was significantly high (p=0.008) as compared to respective wild type in MetS women. But for +276G/T gene, the frequency of mutant T allele in MetS women was found to be significantly (p=0.027) less as compared to wMetS. The mutant alleles, T and G of the +276 G/T and +45 T/G gene respectively, were associated with a lower serum adiponectin level in MetS women. Hypertension and BMI were also significantly associated with minor alleles of +276 G/T gene but only BMI was associated with +45 T/G gene in women with metabolic syndrome.

Conclusion:
The present study provides evidence that the mutant allele of +276 G/T, a common variant of adiponectin gene, is associated with lower adiponectin level, BMI and hypertension and this may contribute into the genetic makeup of the metabolic syndrome.
INCREASED SKELETAL MUSCLE VOLUME IN WOMEN WITH FAMILIAL PARTIAL LIPODYSTROPHY, 
DUNNIGAN VARIETY

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Introduction:
Familial partial lipodystrophy, Dunnigan variety (FPLD) is an autosomal dominant disorder caused by mutations in the lamin A/C (LMNA) gene. FPLD patients have extremity fat loss, hypermuscular appearance, and predisposition to metabolic disorders. However, it is unknown whether FPLD patients have increased muscle size or if it merely appears so.

Methods:
Whole body axial MRI and DXA scans were obtained on 39 females, age 18-65 y, with FPLD and 17 healthy females, matched for age and body mass index (Group1). Combined bilateral muscle volume of the thighs, calves and psoas were calculated using MRI and muscle mass in the extremities were calculated from DXA scans. Abdominal MRI scans and DXA scans were analyzed from 129 healthy, block matched women from the Dallas Heart Study (Group 2). Comparisons between FPLD and control groups were made using analysis of covariance, adjusting for height, BMI and age.

Results:
The thigh, calf and psoas muscle volumes were significantly greater in FPLD patients than in normal controls (6358 ± 1491 vs. 5198 ± 716 cc, p=0.002; 3133 ± 713 vs. 2397 ± 335 cc; p<0.001, and 210 ± 51 vs. 175 ± 34 (Group 1) and 165 ± 38 cc (Group 2), p <0.001; respectively). FPLD patients also had significantly higher arm and leg muscle mass when measured by DXA scan (p<0.001).

Conclusions:
Female FPLD patients have increased skeletal muscle volume and mass compared to normal women. The molecular mechanisms involved in increasing muscle mass in patients with FPLD remain to be determined.
HOW IMPAIRED GLUCOSE TOLERANCE INVOLVES CARDIOVASCULAR DISEASE?

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Aim:
It is well established that a major risk factor for the development of Coronary Artery Disease (C.A.D), is hyperlipidemia. However, the association of Diabetes Mellitus (D.M) and Cardiovascular Disease is also known. The aim of this study is to evaluate the severity of C.A.D in comparison to the levels of morning fasting glucose and HbA1c in pre-diabetic patients.

Methods:
The age range of 453 patients, 370 male and 83 female was between 47-74 years. All the patients were subjected to diagnostic coronary angiography for suspected C.A.D. Diagnosis was accepted when there was an angiographic evidence of Coronary Artery stenosis of 70% for most vessels and 50% for left main disease. Morning fasting glycemia and HbA1c levels were also analyzed as independent risk factors. Statistical analysis was performed using ANOVA and logistic regression analysis. Data is presented as mean± standard deviation and level of significance was accepted when p<0.05.

Results:
Of the 453 patients investigated, data from 450 patients was analyzed. 3 patients refused to use their data to any public health survey. 114 patients (25%) had fasting glycemia of 103.5± 6.7mg/dl and HbA1c levels of 5.8± 0.38 and no significant C.A.D. 116 (25%) had fasting glycemia of 104.4± 6.6 mg/dl, HbA1c 5.9± 0.37 and 1 vessel disease. 102 patients (22%) had fasting glycemia of 105.6± 5.9mg/dl, HbA1c 6.0± 0.33 and 2 vessel disease whereas, 118 (26%) had fasting glycemia of 106.1± 5.4 mg/dl, HbA1c 6.2± 0.3 had 3 vessel disease. C.A.D was more severe in patients with higher fasting glycemia (p=0.006) and higher HbA1c levels (p=0.00044) and logistic regression analysis showed glycemia (p=0.0131) and HbA1c levels (p=0.0002) to be independent significant risk factors.

Conclusion:
Morning fasting glycemia and HbA1c levels of non diabetic patients are independent risk factors and higher levels significantly increase the severity of C.A.D.
ASSOCIATION OF MUSCLE STRENGTHENING ACTIVITY WITH GLYCOSYLATED HEMOGLOBIN

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Glycosylated hemoglobin (HbA1c) is currently recommended as a marker of long-term glucose control; increased muscle mass has been shown to be inversely associated with elevated HbA1c.

Purpose:
To examine the association between muscle strengthening activity (MSA) and HbA1c in U.S. adults without diabetes.

Methods:
Sample included adults, ≥ 20 years of age (n=5,618), that participated in the 1999-2004 National Health and Nutrition Examination Survey. MSA cut points were taken from the 2012 American Diabetes Association (ADA) position statement. Three categories of MSA participation were created. Categories included a referent group reporting no MSA, some MSA (≥1 to <2 days/week), and meeting the recommendations (≥2 days/week). HbA1c was examined continuously.

Results:
Significant decreases in HbA1c levels (p<0.05) were observed in participants reporting engaging in the level of MSA that would meet ADA recommendations when compared to the referent group. HbA1c levels of those reporting some MSA, but less than the ADA recommended amount, were not significantly different (p=0.2516).

Conclusions:
Individuals reporting engaging in the level of MSA that meets the ADA MSA recommendation were found to have significantly lower HbA1c percentage compared to those reporting some MSA or no MSA. Future studies need to investigate MSA exceeding this recommendation.
ASSOCIATIONS BETWEEN HIGH SENSITIVITY C-REACTIVE PROTEIN AND SELF-REPORTED SCREEN TIME IN U.S. ADULTS: A CROSS-SECTIONAL ANALYSIS

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High sensitivity C-reactive protein (hs-CRP) has shown efficacy in predicting risk of adverse cardiovascular events. Increased screen time, in the forms of television and computer use, has been shown to be positively associated with cardio-metabolic risk.

**Purpose:**
To examine the associations between elevated hs-CRP and screen time in a nationally representative sample of U.S. adults.

**Methods:**
Study sample included adults, ≥20 years of age (n=3,811), who participated in the 2003-2006 National Health and Nutrition Examination Survey. Logistic regression was utilized to examine the association between elevated hs-CRP (>3 mg/L) and screen time.

**Results:**
Following adjustment for covariates and potential confounders, analysis excluding individuals with hs-CRP concentrations >10 mg/L revealed a significant (p=0.0039) increase in the odds of reporting ≥ 3 hours/day of screen time (OR 1.24; 95% CI 1.08-1.43) when compared to those with hs-CRP levels <3mg/L. This association remained significant (OR 1.24; 95% CI1.06-1.45, p=0.0084) following adjustment for self-reported physical activity.

**Conclusion:**
Elevated levels of hs-CRP were significantly associated with greater amounts of self-reported screen time independent of meeting the Department of Health and Human Services physical activity recommendations. Future studies need to investigate hs-CRP, objectively measured sedentary behavior, and the clinical implications for identifying associated cardio-metabolic risk factors.
To evaluate the cardioprotective potential of morin, a flavonoid on lipid peroxides and antioxidants status in isoproterenol (ISO)-induced myocardial infarction (MI) in rats. Male albino Wistar rats were pre-treated with morin (40 mg/kg) daily for a period of 30 days. After the treatment period, ISO (85 mg/kg) was subcutaneously injected in rats at an interval of 24 hr for 2 days.

ISO-administered rats showed elevated levels of thiobarbituric acid reactive substances (TBARS) and lipid hydroperoxide (LOOH) in plasma and heart while pretreatment with morin, the above parameters were significantly reduced to near normal control. ISO-administered rats showed decrease in the activities of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione-S-transferase (GST), reduced glutathione (GSH), vitamin C and vitamin E in plasma and heart and the ceruloplasmin in plasma. Morin, at a dose of (40 mg/kg/BW) reversed these above biochemical changes towards normalcy.

These findings revealed that the morin possess antilipoperoxidative and antioxidant activity in experimentally induced cardiac toxicity.
“DELAYED HYPERINSULINEMIA” AFTER ORAL GLUCOSE LOAD IS ASSOCIATED WITH SEVERITY OF CORONARY ARTERY DISEASE

Makoto Murata

Introduction:
Hyperglycemia exerts its direct detrimental effects toward the progression of atherosclerosis. However, the role of hyperinsulinemia which accompanies insulin resistance in the development of atherosclerosis is still unclear.

Hypothesis:
We hypothesize that hyperinsulinemia in response to oral glucose load is associated with the severity of coronary atherosclerosis.

Methods:
Three hundred and fifty consecutive patients (mean age 63±14 SD years; 281 male patients, 69 female patients) who underwent coronary angiography and 2-h 75-g oral glucose tolerance test (OGTT) from 2006 to 2012 were enrolled. We excluded the patients who prior use of an antidiabetic medication. Based on the number of stenotic vessels, the patients were classified into 4 groups; 0 vessel disease(0VD)(n=43), 1VD(n=164), 2VD(n=100), and 3VD(n=43), measured plasma glucose and insulin levels after 75-g oral glucose load.

Results:
Baseline characteristics were similar among the 4 groups. There were no differences glucose profiles in 75-gOGTT, homeostasis model assessment-insulin resistance (HOMA-IR) (Figure 1A). However, insulin secretion was higher in 3VD groups at 120 min whereas no significant difference in insulin secretion at 30 and 60 min (Insulin at 120min; 0VD:41(29-62) vs1VD:48(30-81) vs2VD:57(34-102) vs3VD:68(33-100) μg/ml[p=0.0041 vs0VD]; Bonfferoni level of p<0.0083) (Figure 1B).

Furthermore, insulinogenic index at 120 min was increased in 1VD,2VD and 3VD compared with 0VD despite of no significant difference in common insulinogenic index (Insulinogenic index at 120min;0VD:0.63(0.36-0.88) vs1VD:0.88(0.55-1.45)[p=0.001 vs0VD] vs2VD:0.78(0.55-1.49)[p=0.0081 vs0VD] vs3VD:1.01(0.56-1.46)[p=0.0043 vs0VD]; Bonfferoni level of p<0.0083)

Conclusions:
Despite no significant difference in insulin resistance and insulinogenic index, prolonged insulin secretion was associated with multivessel coronary artery disease. “Delayed hyperinsulinemia” may promote progression of atherosclerosis independent of postprandial hyperglycemia.
Efficacy and Safety of Colesevelam HCL as Add-On Therapy in Older (≥65 Years) Patients with Type 2 Diabetes Mellitus (T2DM)

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Colesevelam HCl was approved for T2DM based on 3 pivotal trials in subjects inadequately controlled on metformin-, insulin-, or sulfonylurea-based therapy. A post-hoc pooled analysis evaluated efficacy in subjects ≥65 years (colesevelam, n=110; placebo, n=118) versus <65 years (colesevelam, n=400; placebo, n=388).

With colesevelam (added to existing therapy), older and younger subjects had similar significant (p<0.0001) reductions from baseline in A1C (treatment difference -0.59% and -0.54%, respectively) and LDL-C (-14.7% and -15.5%, respectively). Colesevelam also decreased fasting plasma glucose, total cholesterol, non–HDL-C, and apoB, and increased apoA1 and triglycerides, similarly in both subgroups; HDL-C showed no significant changes. Safety/tolerability analysis included subjects (≥65 years: colesevelam, n=121; placebo, n=128; <65 years: colesevelam, n=446; placebo, n=434) from the pivotal trials plus a small study involving patients inadequately controlled on metformin and/or sulfonylureas. Overall adverse event (AE) incidence was slightly higher with colesevelam versus placebo in both older (66.9% vs 59.4%) and younger (58.7% vs 54.4%) subjects, with slightly lower values overall in younger subjects. Serious AE incidence in older subjects was lower with colesevelam versus placebo, and similar to younger subjects. Regarding gastrointestinal AEs, constipation incidence in older subjects was 11.6% with colesevelam and 4.7% with placebo (<65 years: 7.9% and 1.2%, respectively). Dyspepsia was less frequent in older subjects and similar between treatments. Hypoglycemia was more frequent in older subjects receiving colesevelam (5.8%) versus placebo (2.3%).

Thus, in subjects ≥65 years, colesevelam added to existing therapy had similar efficacy to that in younger subjects, and appeared safe and well tolerated.
EFFECT OF COLESEVELAM HCL MONOTHERAPY ON LIPID PARTICLES IN TYPE 2 DIABETES MELLITUS (T2DM)

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Patients with insulin resistance, compared with individuals with normal insulin sensitivity, have higher concentrations of LDL particles relative to their LDL-cholesterol (LDL-C) levels. A study was recently conducted to evaluate the effects of colesevelam monotherapy in adults with T2DM who had inadequate glycemic control (A1C ≥7.5% to ≤9.5%) with diet and exercise alone. Patients were randomized to receive colesevelam 3.8 g/day (n=175) or placebo (n=169) for 24 weeks. In addition to the typical glycemic and lipid parameters, changes in lipid particle concentrations and sizes were determined by nuclear magnetic resonance spectroscopy.

As expected, at baseline the mean LDL-C level (119 mg/dL) was modestly elevated above the optimal level, whereas the mean LDL particle concentration (LDL-P; 1587 nmol/L) was borderline high to high (Mora et al. Atherosclerosis 2007). At Week 24 with last observation carried forward, colesevelam versus placebo produced a significant reduction in total LDL-P (least squares mean treatment difference -143 nmol/L; p<0.0001); significant reductions were also seen in large (p=0.002), small (p<0.05), and very small (p=0.03) LDL-P. There were also increases in VLDL particle size (+2.8 nm; p=0.001) and associated reductions in small VLDL particle concentration (-5 nmol/L; p=0.03). In addition, with colesevelam versus placebo there was increased HDL particle size (+0.1 nm; p<0.0001), associated with increases in large (+0.5 µmol/L; p=0.007) and medium (+0.8 µmol/L; p=0.02) HDL particle concentration.

In conclusion, colesevelam monotherapy in patients with T2DM resulted in generally favorable changes to the lipoprotein particle profile compared with placebo.
EFFICACY AND SAFETY OF COLESEVELAM HCL AS MONOTHERAPY FOR TYPE 2 DIABETES MELLITUS (T2DM)

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A study was recently conducted to evaluate colesevelam HCl as monotherapy in adults with T2DM who had inadequate glycemic control (A1C $\geq$7.5\% to $\leq$9.5\%) with diet and exercise alone. Patients were randomized to receive colesevelam 3.8 g/day (n=175) or placebo (n=169) for 24 weeks. Subjects’ mean age was 52.2 years, 51.3\% were male, and the mean duration of T2DM diagnosis was 4.1 years.

At Week 24 with last observation carried forward, colesevelam showed reductions from baseline in A1C (least squares (LS) mean treatment difference -0.27\%; $p=0.01$) and fasting plasma glucose (-10.3 mg/dL; $p=0.04$). Colesevelam versus placebo also decreased LDL-C (-11.2\%; $p<0.0001$), total cholesterol (-5.1\%; $p=0.0005$), non-HDL-C (-7.4\%; $p=0.0001$), and apoB (-6.5\%; $p=0.0001$), and increased apo A1 (+2.4\%; $p=0.04$) and TG (median treatment difference +9.7\%; $p=0.03$). Colesevelam had no significant effects on index of insulin resistance by homeostatic model assessment (HOMA-IR; LS mean treatment difference -0.46; $p=0.53$), fasting (-0.75 μIU/mL; $p=0.60$) or 2-hour postprandial (+8.09 μIU/mL; $p=0.13$) insulin levels. The most frequently reported adverse events in the colesevelam group were back pain (colesevelam, 5.1\%; placebo, 0.6\%), headache (colesevelam, 4.6\%; placebo, 2.9\%), diarrhea (colesevelam, 4.0\%; placebo, 1.8\%), urinary tract infection (colesevelam, 4.0\%; placebo, 8.8\%), and hypoglycemia (colesevelam, 4.0\%; placebo, 0.6\%).

In conclusion, colesevelam monotherapy resulted in clinically significant improvements in glycemic and most lipid parameters in patients with T2DM, with no new or unexpected safety and tolerability issues. The lack of significant changes in HOMA-IR index or in fasting or 2-hour postprandial insulin suggests that colesevelam treatment did not affect insulin sensitivity.
ABO BLOOD GROUP FREQUENCY IN CORONARY AND ISCHEMIC HEART PATIENTS VISITING PIC, LAHORE

Anwar, N

The present study was designed to study the relationship between blood groups and CVDs i.e. IHD and CHD. The study was done at Punjab Institute of Cardiology, Lahore from March 2012- July 2012. For this purpose 430 samples were collected and divided into two groups, 230 control and 200 cardiac subjects. Their blood groups were determined by a simple and widely used method of blood typing using Anti-A serum, Anti-B serum and Anti-D serum. Out of 200 cardiac subjects, 109 were IHD patients and 91 were CHD patients.

The percentage of males and females in control and cardiac group was 63.5% and 36.5% respectively. Mean age of controls was 34.3±0.71 (years), and of cardiac group was 56.4±0.86 (years). Mean BMI of control and cardiac group was 23.8±0.29 (kg/m2), and 26.4±0.33 (kg/m2) respectively. 54% of the cardiac subjects were smokers, 45% had a family history of cardiac disease. Diabetes was reported in 53.5% subjects. Hypertension was present in 58.5% of them. Only 35.5% do exercise daily. 58.5% of the subjects used food cooked in ghee. The prevalence percentage of blood group A, B, AB, and O in control group was 20.9%, 34.4%, 12.6%, and 32.2% respectively and in cardiac group 34% were in blood group A, 29% in blood group B, 14% in blood group AB, and 23% in blood group O. Blood group B was most common in general population, and in cardiac group blood group A was dominant. The prevalence of Rh positive among control group was found to be 92.6% and in cardiac group it was 90.5%. Rh negative prevalence in control was 7.4%, and in cardiac group was 9.5%.

Keywords:
Punjab Institute of Cardiology (PIC), Cardiovascular diseases (CVDs), Ischemic Heart Disease (IHD), Coronary Heart Disease (CHD), Rhesus (Rh)
Insulin resistance leads to increased levels of insulin necessary to control plasma glucose levels and results in persistent hyperinsulinemia and hyperglycemia. Some studies indicate that signs of mitochondrial dysfunction in beta cells may precede evidence of beta cell damage\(^1,2\). Hence, hyperinsulinemia may contribute to the development of beta cell deterioration in T2DM. Insulin was shown to increase death of pancreatic beta cells and exacerbate the effects of H2O2 on their viability\(^3\).

Here, we investigated the possibility that insulin may adversely influence pancreatic β cells through activation of apoptotic pathways. Effects of insulin on cell viability were conducted on 3 pancreatic β cell lines, isolated mouse and human islets, as well as on 3 non-pancreatic beta cell lines. Cell viability was estimated by measurements of LDH and by Cell-Titer Blue viability assay. Caspase activity was also determined.

Treatment of beta cells or islets with insulin for 24 hr caused a decrease in viability and increase in caspase 3/7 activity. Decreased viability induced by H2O2 could also be increased by insulin. These effects were specific to insulin and selective for pancreatic β cells. Viability of non-pancreatic beta cells was not decreased by insulin. \(^z\)-VAD-fmk and Nec-1 abrogated both the increase in caspase activity and the decrease in viability of Min6 cells induced by insulin.

The findings indicate that prolonged elevated levels of insulin, alone or in combination with other factors, may adversely affect pancreatic beta cells by activating apoptotic and other mechanisms that lead to beta cell deterioration and death.

Adiponectin is a known beneficial adipokine, improving insulin sensitivity and reducing inflammation. The aim of this study was to clarify the autocrine effects of adiponectin on 3T3-L1 adipocytes function.

Preadipocytes were treated with Adiponectin from 2 days following confluency until the 12th day of differentiation. Rate of proliferation as measured by XTT reagent was increased by adiponectin. Adiponectin did not affect mRNA expression of adiponectin or AdipoR2, but increased that of AdipoR1. PPARgamma and perillipin mRNA expressions were lower in adiponectin-treated adipocytes. This was accompanied by a reduction in triglyceride accumulation as measured by Oil-red-O staining and TG assay kit. In order to clarify whether lipolysis or lipogenesis are regulated by adiponectin, glycerol release and mRNA expression of FAS, HSL and ATGL were measured. Although mRNA expression of HSL was not affected by adiponectin, basal lipolysis was increased. In addition, FAS expression was inhibited by adiponectin, indicating that adiponectin regulates both lipolysis and lipogenesis pathways.

To investigate the effect of adiponectin on inflammatory response induced by LPS, cells were treated with adiponectin during differentiation process ("chronic") or 24 hours before induction of inflammation in differentiated adipocytes ("late"). LPS induced inflammatory response, as indicated by 40 fold increase in IL6 mRNA expression. While "late" treatment reduced LPS-induced IL6 expression by 42%, "chronic" adiponectin completely blocked LPS-induced IL6 expression.

In conclusion, elevated adiponectin concentration at differentiation may lead to increased adipocyte number, with reduced lipid content and high resistance to inflammatory stimuli. The molecular mechanisms mediating these effects are currently being investigated.
INSULIN SENSITIVITY IS IMPROVED BY THE BEDUIN MEDICINAL PLANT, SARCOPOTERIUM SPINOSUM

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Introduction:
Sarcopoterium spinosum (Thorny burnet) is an abundant plant in Israel, used by Beduin medicinal practitioners for the treatment of diabetes. In our previous study we validated the anti-diabetic activity of S.spiniosum. The aim of this study was to clarify its mechanism of action.

Methods:
In-vivo studies were performed on KK-Ay mice given the extract for 6 weeks. Insulin tolerance test was performed, and pancreata were stained by H&E in order to measure relative islet area. Mechanisms of action were investigated in L6 myotubes using Western blot analysis and confocal microscopy.

Results:
S. spinosum extract reduced fasting blood glucose level and improved insulin sensitivity in treated mice. Hypertrophic islets were detected in diabetic, but not in S.spiniosum-treated mice. In L6 myotubes, S.spiniosum phosphorylated PTEN on ser380 and thr382/383, which are known to inhibit PTEN activity. Phosphorylation of PKB, supposed to be higher as PTEN activity reduced, was measured. Surprisingly, neither ser473 nor thr308 was phosphorylated by S.spiniosum. However, translocation of PKB from cytoplasm to membrane and to the nucleus was detected. Regarding the downstream events of PKB activation; GSK phosphorylation and glucose uptake were increased by the extract. We assume that the active ingredients in S.spiniosum activated PKB by a mechanism which is independent of ser473 and thr308 phosphorylation. Other post translation modifications are currently being analyzed in order to understand further this unique PKB activation.

Conclusion:
Identifying the active molecules and clarifying its mechanism of action may lead to the development of new agents for the treatment of insulin resistance.
N-ACETYL-CYSTEINE (NAC) SUPPLEMENTATION IMPROVES INSULIN SENSITIVITY: BIOMARKERS FOR REDOX STATE MUST BE IDENTIFIED

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Meta analyses conclude that antioxidant supplementations have no beneficial effects on the prevalence of type 2 diabetes (T2D). These disappointing results conflict with most in-vitro and in-vivo studies showing damage of oxidative stress and benefits of antioxidants on insulin sensitivity and β-cell function. We assume that there is an optimal redox state that normally should be maintained. If shifted, disturbances in β cell function and in insulin sensitivity appear. The aim of this study is to clarify the dose-response effect of antioxidant supplementation in-vivo on the progression of T2D.

Methods:
Experiments were conducted on KK-Ay mice, given NAC at different concentrations (200-1800 mg/kg/day) for 6 weeks. Glucose and insulin tolerance tests were performed and plasma insulin and lipid peroxidation were measured. Insulin signaling pathway was followed in soleus muscle and pancreas stained by H&E.

Results:
Although lipid peroxidation was reduced in all concentrations used, glucose intolerance was not corrected in the 200 mg/kg/day treated mice. While 600, 1200 and 1800 mg/kg/day NAC were all found to improve glucose tolerance, only the 1200 mg/kg/day treatment increased insulin sensitivity as indicated by improved insulin tolerance test, reduced plasma insulin and accordingly low HOMA-IR. Islet hypertrophy was also corrected only in the 1200 mg/kg/day treated animals.

Conclusion:
The inconsistency in literature regarding antioxidant and prevention of diabetes may result from the lack of clear guidelines for effective doses. There is a need to find certain biomarkers for the target oxidative state that should be maintained in order to obtain optimal outcomes.
A NOVEL COMPOUND FROM CASEARIA ESCULENTA (ROXB.) ROOT AND ITS EFFECT ON CARBOHYDRATE METABOLISM IN STREPTOZOTOCIN-DIABETIC RATS

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Casearia esculenta root (Roxb.) is widely used in traditional system of medicine to treat diabetes in India. An active compound 3-hydroxymethyl xylitol (3-HMX) has been isolated and its optimum dose has been determined in a short duration study and patented. In the present study, the long-term effect of 3-HMX in type 2 diabetic rats has been investigated.

An optimum dose of 3-HMX (40 mg/kg body weight) was orally administered for 45 days to streptozotocin-diabetic rats for the assessment of glucose, insulin, hemoglobin (Hb), glycated hemoglobin (HbA1c), hepatic glycogen, and activities of carbohydrate metabolizing enzymes, such as glucokinase, glucose 6-phosphatase, fructose 1,6-bisphosphatase and glucose-6-phosphate dehydrogenase and hepatic marker enzymes, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gammaglutamyl transferase (GGT) in normal and streptozotocin-diabetic rats.

3-HMX at 40 mg dose produced similar effects on all biochemical parameters studied as that of glibenclamide, a standard drug. Histological study of pancreas also confirmed the biochemical findings. These results indicate that 3-hydroxymethyl xylitol, the compound from C. esculenta, possesses antihyperglycemic effect on long-term treatment also.
DIFFERENTIAL EFFECTS OF APPENDICULAR MUSCLE MASS UPON INSULIN RESISTANCE IN NON-DIABETIC LEAN AND OVERWEIGHT INDIVIDUALS

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Background:
Skeletal muscle plays an important role in glucose disposal. Admixture of fat and muscle in overweight/obese individuals may limit the accuracy of muscle mass determination.

Objective:
To determine if appendicular muscle mass (AMM) is associated with homeostasis model assessment of insulin resistance (HOMA-IR) in lean versus overweight/obese individuals.

Methods:
Retrospective, cross-sectional data collected between 1999 and 2011 from 14 outpatients aged 18-88 (median 41.5) years. Population stratified as lean (body mass index <25 kg/m2) or obese/overweight (BMI ≥25 kg/m2). Outcome measure was HOMA-IR. Predictor variables of AMM and truncal fat mass determined from whole body dual-energy x-ray absorptiometry (DEXA) scans. Covariates in multiple regression analyses were ethnicity, sex and truncal fat.

Results:
Increased AMM was associated with increased truncal fat in overweight/obese (Pearson correlation coefficient 0.47, p=0.01) but not lean individuals (PCC 0.45, p=0.14). HOMA-IR was inversely related to AMM in lean (PCC -0.77, p=0.03), but not overweight/obese individuals (PCC 0.21, p=0.54). Adjusted associations of AMM (continuous, per 10%) with insulin resistance showed a 1% decrease in HOMA-IR per 10% increase in AMM in lean individuals (0.993, 95% confidence interval (CI) -0.007 to -0.00001), but no association in overweight/obese individuals (0.999, 95% CI -0.0008 to 0.006).

Conclusions:
Increased AMM is associated with decreased insulin resistance in lean but not obese/overweight individuals. The correlation between AMM and truncal fat in obese/overweight individuals suggests that DEXA measurements of muscle mass include intramuscular fat. Future investigations to determine methods of body composition which are accurate regardless of general adiposity status are warranted.
BERBERINE ALLEVIATES MESENTERIC ARTERY ENDOTHELIAL DYSFUNCTION BY IMPROVING INSULIN SENSITIVITY IN TYPE 2 DIABETIC RATS

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Objective:
Insulin resistance causes vascular complications in type 2 diabetes mellitus. Berberine (BBR) has been shown to lower blood glucose and regulate lipid metabolism, but whether BBR can enhance insulin-induced vasodilatation and the underlying mechanism remains unclear. In the present study, we investigated the effects of BBR on mesenteric artery endothelium in diabetic rats and the underlying mechanisms.

Methods:
Diabetes was induced in streptozotocin-treated (30 mg/kg, i.p.) male Sprague-Dawley rats fed on high-fat diet for 8 weeks. The diabetic rats were then administered with saline or BBR (200 mg/kg/d) intragastrically for 4 weeks.

Results:
BBR treatment significantly improved the mesenteric arteries endothelium-dependent vasodilatation in diabetic rats. Insulin-induced vasodilatation was also significantly improved (38.67±4.46% vs. 7.54±2.90%, n=12, p<0.01) in BBR-treated diabetic rats compared with that in saline-treated diabetic rats. The effects of BBR were blunted by PI3K inhibitor wortmannin. In high glucose (25 mM) and palmitate (500 nM)-induced insulin resistant human mesenteric artery endothelial cell line Ealy 926, BBR alone could not improve Ealy 926 viability, but co-treatment of BBR (25 μM) with insulin (1 nM) enhanced cell viability. Meanwhile, co-treatment of BBR with insulin significantly increased phosphorylation of IRS-1, Akt and eNOS in cultured Ealy 926.

Conclusions:
BBR improves insulin-induced endothelium-dependent vasodilatation and enhances mesenteric endothelial insulin sensitivity through activation of mesenteric endothelial IRS-1 and eNOS in type 2 diabetic rats.

Keywords:
berberine, insulin sensitivity, diabetes, endothelial function
BERBERINE PREVENTS CORONARY ARTERY ENDOTHELIAL APOPTOSIS AND ENHANCES INSULIN-INDUCED CORONARY VASODILATATION VIA ENDOTHELIUM-DEPENDENT PI3K-AKT-ENOS PATHWAY IN TYPE 2 DIABETIC RATS

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Objective:
Coronary heart disease (CHD) is a leading cause of death in diabetics. Recent studies report promising effects of berberine (BBR), an isoquinoline alkaloid widely used in Chinese herbal medicine, on regulating blood glucose and lipid metabolism. We are interested to investigate effects of BBR on coronary artery dysfunction in diabetic rats.

Methods:
Male Sprague-Dawley rats were treated with streptozotocin (30 mg/kg, i.p.) and fed with high-fat diet for 8 weeks to induce type 2 diabetes. The diabetic rats were intragastrically administered with saline or BBR (200 mg/kg/d) daily for 4 weeks.

Results:
Endothelium-dependent vasodilatation (53.7% vs 11.2%, n=12, p<0.01) was enhanced in BBR-treated diabetic rats compared with saline-treated diabetic rats. In addition, insulin-induced vasodilatation of coronary arteries was significantly improved by BBR treatment (39.3% vs 5.2%, n=12, p<0.01). Serum nitride oxide production was increased (n=12, p < 0.05) in BBR-treated diabetic rats compared with that in non-treated diabetic rats. TUNEL staining of coronary artery endothelium showed that BBR treatment reduced apoptosis. HUVECs cell apoptosis induced by high glucose and high fatty acid (HG/HF, 25 mM glucose and 500 nM palmitate) was also decreased by BBR. Meanwhile, BBR up-regulated phosphorylation of Akt, eNOS and GSK3β in HUVECs cells. The effects of BBR were blunted by PI3K inhibitor wortmannin.

Conclusion:
Our results suggest that BBR prevents coronary artery endothelial apoptosis and enhances insulin-induced vasodilatation via endothelium-dependent PI3K-Akt-eNOS pathway in type 2 diabetic rats.

Keywords:
diabetes, berberine, insulin, coronary artery, endothelial function
Objective:
The aim of the study is to investigate the characteristic of body composition among male and female adults with different body weight.

Methods:
We performed a study on 61379 healthy adults (39855 male and 21527 female) referred to the health examination center of Chinese PLA general hospital between May/2005 to February/2011. BMI, body composition including body fat, water, muscle, protein, mineral salt content were measured by anthropometric measurements and bioelectrical impedance analysis (BIA). The data were analyzed among groups divided by gender, age and BMI.

Results:
1.) The prevalence of overweight and obesity defined by BMI is significantly higher in the male group than in the female (P<0.01);
2.) Within a certain age range (<60 in male, <70 in female), the prevalence of both overweight and obesity defined by BMI increased with age (P<0.01);
3.) The fat mass percentage is significantly higher in female than in male (95% CI 24.6% ~ 37.4% vs. 18.7% ~ 31.3%, P<0.01);
4.) Body fat mass percentage progressively elevated with increase of BMI, while there is a decreasing trend of the other body composition. The male subjects had higher percentage of muscle, water and mineral salt (P<0.01), while the percentage of protein was higher in the female group (P<0.01).

Conclusion:
1.) The female has more fat mass than male under the same level of BMI. So it is more reasonable to introduce adiposity for the evaluation of obesity, especially in women.
2.) There might be a relationship between the increased risk of cardiovascular and cerebrovascular diseases, impaired glucose tolerance, dyslipidemia and higher fat mass percentage, modification of body composition in obesity adults.

Keywords:
bioelectrical impedance; body composition; obesity; fat mass percentage.
ASSOCIATION BETWEEN INSULIN RESISTANCE AND INSULIN, PLASMA GLUCOSE, HBA1C AND C-PEPTIDE IN DIABETIC PATIENTS FROM SAUDI ARABIA

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We determined the insulin resistance (HOMA IR) and evaluated its association with insulin, C-peptide, fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) in 47 diabetic patients and 38 control subjects attending the Armed Forces Hospital, Riyadh, Saudi Arabia.

There was a significant increase in the levels of FPG (11.51 ± 0.55 mmol/L versus 5.29 ± 0.13 mmol/L, P < 0.001) and HbA1c (9.49 ± 0.31% versus 6.44 ± 0.19%, P < 0.001) in diabetic patients as compared to controls. Although the levels of C-peptide (951.17 ± 100.69 mmol/L versus 861.18 ± 63.33 mmol/L) and insulin (25.25 ± 5.39 µU/mL versus 16.72 ± 2.03 µU/mL) did not differ significantly between the two groups, a significant increase in HOMA IR was observed in diabetic patients (11.49 ± 2.10) than control subjects (3.96 ± 0.47). In diabetic patients, 16 of 47 patients (34.04%) had HOMA IR > 10 as compared to only 2 of 38 controls (5.26 %). There was no correlation between HOMA IR and HbA1c, FPG, gender or age. However, a highly significant correlation was observed between HOMA IR and insulin (Pearson R = 0.96, P < 0.001) and C-peptide (R = 0.65, P < 0.001).

These findings show that insulin resistance is highly prevalent in diabetic patients from Saudi Arabia. HOMA IR is neither affected by glycemic control nor influenced by age or gender. FPG levels do not reflect the intensity of HOMA IR in diabetic patients. However, C-peptide can be used as a predictor of HOMA IR using optimized cut-point criteria. A longer half-life of C-peptide than insulin also favors its biomarker utility with less fluctuation.
WHAT IS THE SIGNIFICANT CUT-OFF LEVEL OF ALBUMINURIA FOR SUBCLINICAL ATHEROSCLEROSIS IN THE GENERAL POPULATION?

Nho, KW\textsuperscript{1}, Kim, JS\textsuperscript{1}, Kim, JH\textsuperscript{1}, Kim, SM\textsuperscript{2}, Kim, SB\textsuperscript{1}

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Background:
The aim of this study was to estimate the cutoff level of microalbuminuria for subclinical atherosclerosis through evaluating all carotid, coronary and peripheral arteries in the general population.

Methods:
The study population included a total of 1,692 persons (male 1,069, female 623), ages 22 to 83 years, who participated in health screening at Asan Medical Center. The participants performed all coronary CT, carotid doppler US, ankle-brachial index and pulse wave velocity with urine albumin to creatinine ratio (UACR). The subjects who had at least one of the following were “atherosclerosis group”: 1) coronary CT: coronary calcium score >400, 2) carotid doppler US: plaque or intimal thickening is visible sonographically, 3) ankle-brachial index <0.9, 4) pulse wave velocity >8.5 m/s.

Results:
Among 1,692 participants, 510 persons were classified to atherosclerosis group. Mean ages of the two groups were 59.2 ± 8.6 and 52.6 ± 8.9 years, male were 77.5% and 57.0% in “atherosclerosis group” and “non-atherosclerosis group”, respectively. Median ± range of UACR was significantly increased, 8.50 (95% CI: 7.60-9.55) mg/g in the atherosclerosis group and 7.05 (95% CI: 6.60-7.55) in the non-atherosclerosis group (p=0.017). In ROC curves for UACR to identify atherosclerosis, the optimal cutoff value of UACR was 7.75mg/g (sensitivity; 47.5%, specificity; 69%, 56 percentile). The gender-specific cutoff points were 6.45mg/g (sensitivity; 50.0%, specificity; 70.1%, 59 percentile) in men and 8.45mg/g (sensitivity; 62.7 %, specificity; 63.0 %, 64 percentile) in women. In multivariate analysis for atherosclerosis, male gender was the most powerful independent predictor for atherosclerosis and smoking, hypertension, HbA1c, age and BMI were independently associated with atherosclerosis. Microalbuminuria tended to be higher in atherosclerosis group but was not statistically significant by multivariate analysis in both genders.

Conclusion:
In this study, we have shown the cut-off value of albuminuria for atherosclerosis was much lower than traditional level of microalbuminuria using the ROC curve.
Impact of metabolic syndrome and adiponectin on oxidized low-density lipoprotein levels in statin-treated diabetic patients with coronary artery disease


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Adiponectin is an adipocyte-derived factor exerting insulin sensitizing effects. A decrease in circulating adiponectin levels may be involved in the pathogenesis of obesity-associated insulin resistance, diabetes and cardiovascular disease. This paper shows clinical data indicating that metabolic syndrome and adiponectin are closely associated with oxidized low-density lipoprotein levels in statin-treated diabetic patients with coronary artery disease.

Background and Aims:
Lowering of low-density lipoprotein (LDL) with statin has been an established strategy for cardiovascular prevention. Serum oxidized LDL levels have been recognized as a predictive marker for future events. However, it has been unclear what determines oxidized LDL levels under standard prevention with statins. In this study, we aimed to clarify the clinical factors associated with oxidized LDL levels in statin-treated diabetic patients with coronary artery disease (CAD).

Methods:
This study was conducted on 184 diabetic patients with proven CAD who were treated with statins. Serum concentrations of malondialdehyde-modified LDL (MDA-LDL) and various parameters of cardiovascular risk factors were measured. Extent of CAD was defined as number of segments with ≥ 50% stenosis or stent-implantation assessed by angiography or computed tomography.

Results:
The ratio of MDA-LDL to LDL-C levels (MDA-LDL/LDL-C) was significantly correlated with triglyceride (p<0.001), high-density lipoprotein cholesterol (HDL-C) (p<0.001) and adiponectin (p<0.01), but not with HbA1c or the extent of CAD. Patients with metabolic syndrome (MS) had significantly higher MDA-LDL/LDL-C than those without MS (p<0.01). Number of MS components was significantly associated with MDA-LDL/LDL-C (p<0.001). Additional treatment with pioglitazone or angiotensin II receptor blockers did not show a significant reduction in MDA-LDL/LDL-C.

Conclusion:
Oxidized LDL levels may be associated with several features of MS characterized by serum triglyceride, HDL-C and adiponectin levels, independently of the extent of CAD, in statin-treated diabetic patients.
ADIPONECTIN LEVELS PROVIDE INCREMENTAL VALUE TO DIABETES AND HYPERTENSION IN PREDICTING MULTIVESSEL CORONARY ARTERY PLAQUES

Matsuda, M, Tamura, R, Kishida, N, Nishimoto, O, Nakamoto, K, Nishiyama, H, Kawamoto, T

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Adiponectin is an adipocyte-derived factor having insulin sensitizing effects. A decrease in circulating adiponectin levels may be involved in the pathogenesis of obesity-associated insulin resistance, diabetes and cardiovascular disease. This paper shows that adiponectin levels provide incremental value to diabetes and hypertension in predicting multivessel coronary artery plaques.

Background and Aims:
Although multi-slice computed tomography coronary angiography (CTCA) is useful in non-invasively evaluating early stage of coronary artery disease (CAD), the criteria for selecting CTCA remain unclear. This study aimed to clarify the risk factors associated with multivessel coronary artery plaques determined by CTCA, which might be useful as a potential strategy for identifying high-risk patients who need CTCA.

Methods:
This study was performed on 201 patients who underwent CTCA for screening for CAD between 2009 and 2011. We evaluated the relationship between the extent of coronary atherosclerosis, determined by CTCA, and various parameters, including serum adiponectin levels.

Results:
Age- and gender-adjusted odds ratio (OR) for serum adiponectin levels of ≤8.3 μg/mL—the optimal cutoff-point determined by receiver operating characteristic (ROC) curve analysis—for multivessel coronary plaques was 2.93 (95% confidence interval (CI): 1.53–5.74). Multivariate analysis revealed that serum adiponectin levels of ≤8.3 μg/mL, diabetes mellitus, and hypertension were significantly associated with multivessel coronary plaques and cumulatively associated with the extent of coronary atherosclerosis; age- and gender-adjusted ORs of 2 and 3 of the factors for multivessel coronary plaques were 5.58 (95% CI: 1.84–25.98) and 14.14 (95% CI: 3.58–74.04), respectively, as against none of the factors. Even in the absence of symptoms on exertion, this cumulative association remained significant.

Conclusions:
Low levels of serum adiponectin, diabetes mellitus, and hypertension may have independent and incremental associations with the extent of coronary atherosclerosis in patients without documented CAD, irrespective of the presence or absence of symptoms.
ASSOCIATION OF OBESITY WITH LEFT ATRIAL ENLARGEMENT: DIFFERENCE IN QUANTITATIVE ASSESSMENTS WITH ECHOCARDIOGRAPHY AND THREE-DIMENSIONAL RECONSTRUCTED CT IMAGES

Tamura, R, Matsuda, M, Nishimoto, O, Nakamoto, K, Nishiyama, H, Kawamoto, T

Department of Cardiology, Kure Medical Center and Chugoku Cancer Center

Background and Aims:
Obesity has been reported to be associated with left atrial enlargement (LAE). However, it has been unclear whether ectopic fat depots, including visceral, subcutaneous or pericardial fat, may contribute to obesity-mediated LAE. Here we aimed to clarify the clinical association of LAE with ectopic fat depots.

Methods:
We evaluated left atrial size in 100 consecutive patients undergoing cardiac MDCT and echocardiography, without coronary artery disease, mitral regurgitation or systolic dysfunction with ejection fraction <50%. Parasternal long-axis diastolic diameter of left atrium (LAD) was measured by echocardiography. Left atrial volume (LAV) and pericardial fat volume (PFV) was quantitatively measured using three-dimensional reconstructed CT images. Visceral and subcutaneous fat area (VFA, SFA) was measured by abdominal CT.

Results:
Both LAD and LAV were significantly correlated with left ventricular diastolic diameter (p<0.005, p<0.001) and left ventricular mass (p<0.005, p<0.0001), but not with relative wall thickness or E/A. Regarding adiposity and ectopic fat depots, LAD was significantly correlated with BMI (p<0.0001), VFA (p<0.0001) and PFV (p<0.005), but not with SFA. On the other hand, LAV was weakly associated with BMI (p=0.05) and not with VFA, SFA or PFV.

Conclusion:
Since left atrium has geometric structure, LAD and LAV show different aspects on the association with ectopic fat depots: LAE assessed by LAD but not LAV is closely associated with visceral obesity.
UNDERESTIMATION OF BODY MASS INDEX AND PREVALENCE OF OBESITY

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Western Diabetes Institute, Western University of Health Sciences, Pomona, California

Background:
Previous studies, including the US NHANES III, have indicated that African-Americans and Hispanics have higher prevalence of obesity. Their self-perception of body mass index (BMI) category may be a crucial factor in this phenomenon. This pilot study aims to assess people’s perception and knowledge about obesity in a city with 77.8% of African-Americans and Hispanics. Hopefully, this will increase providers’ understanding of patients’ barriers to weight management.

Methods:
Surveys addressing demographics and weight perception were distributed to patients and their companions at the Patient Care Center of Western University of Health Sciences in Pomona, California over a three-week period. A total of 104 adults were surveyed. After completing the survey, the subjects’ weight and height were measured to calculate their BMI.

Results:
Table 1 presents the findings pertaining to each group. The results showed that Hispanics had the highest average BMI. Interestingly, 55.55% and 54.39% of African-Americans and Hispanics respectively underestimated their BMI, while none of the Non-Hispanic White subjects did. Overall, 9.9% subjects reported an ideal BMI category that was higher than their perceived healthy BMI. More than 75% of the subjects across all groups recognized type 2 diabetes, hypertension, hypercholesterolemia, coronary artery diseases, and sleep apnea as obesity-associated diseases.

Conclusions:
In this study, both weight perception and knowledge about obesity were investigated. The results identified the possible contribution of poor self-assessment of BMI and ideal weight to the overall higher prevalence of obesity among African-Americans and Hispanics. When conducting patient education, providers should consider taking different race/ethnicity groups’ perceptions of weight into account.

Table 1. The average body mass index (BMI), overall knowledge about the concept of BMI category, perception of current BMI, perception of healthy and reported ideal BMI category, and knowledge about medical consequences associated with obesity among Pomona community members (n = 104).

<table>
<thead>
<tr>
<th>All Race/Ethnicity Groups</th>
<th>Non-Hispanic White (n = 13)</th>
<th>African-American (n = 10)</th>
<th>Hispanic (n = 64)</th>
<th>Other (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Average Measured BMI (kg/m²)</td>
<td>32.33 ± 8.76</td>
<td>31.89 ± 9.09</td>
<td>31.45 ± 8.76</td>
<td>34.04 ± 8.75</td>
</tr>
<tr>
<td>Male</td>
<td>30.07 ± 8.44</td>
<td>32.50 ± 8.32</td>
<td>27.14 ± 3.12</td>
<td>31.84 ± 8.90</td>
</tr>
<tr>
<td>Female</td>
<td>33.35 ± 9.11</td>
<td>31.68 ± 9.80</td>
<td>33.31 ± 9.93</td>
<td>34.98 ± 8.61</td>
</tr>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Knowledge about the Concept of BMI Category</td>
<td>Yes 38 (36.54%)</td>
<td>9 (69.23%)</td>
<td>3 (30.00%)</td>
<td>17 (26.56%)</td>
</tr>
<tr>
<td></td>
<td>No 66 (63.46%)</td>
<td>4 (30.77%)</td>
<td>7 (70.00%)</td>
<td>47 (73.44%)</td>
</tr>
<tr>
<td>Perception of Current BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>Overestimated</td>
<td>4 (4.49%)</td>
<td>1 (9.09%)</td>
<td>0 (0.00%)</td>
<td>2 (3.51%)</td>
</tr>
<tr>
<td>Precisely predicted</td>
<td>49 (55.06%)</td>
<td>10 (90.91%)</td>
<td>4 (44.44%)</td>
<td>24 (42.11%)</td>
</tr>
<tr>
<td>Underestimated</td>
<td>36 (40.45%)</td>
<td>0 (0.00%)</td>
<td>5 (55.55%)</td>
<td>31 (54.39%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Perceived Healthy Weight Reported as BMI Category (&quot;For a person of your height, what would be a healthy weight?&quot;)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
</tr>
<tr>
<td>Normal</td>
<td>52 (51.49%)</td>
<td>7 (58.33%)</td>
<td>3 (30.00%)</td>
<td>31 (50.00%)</td>
<td>11 (64.71%)</td>
</tr>
<tr>
<td>Overweight</td>
<td>42 (41.58%)</td>
<td>4 (33.33%)</td>
<td>7 (70.00%)</td>
<td>26 (41.94%)</td>
<td>5 (29.41%)</td>
</tr>
<tr>
<td>Obese</td>
<td>7 (6.93%)</td>
<td>1 (8.33%)</td>
<td>0 (0.00%)</td>
<td>5 (8.06%)</td>
<td>1 (5.88%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subjects’ Reported Ideal BMI Category Compared to Perceived Healthy BMI Category (&quot;What is your ideal weight that you would like to maintain?&quot;)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ideal &lt; Healthy</td>
<td>6 (5.94%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>6 (9.68%)</td>
<td>0 (0.00%)</td>
</tr>
<tr>
<td>Ideal = Healthy</td>
<td>85 (84.16%)</td>
<td>10 (83.33%)</td>
<td>8 (80.00%)</td>
<td>52 (83.87%)</td>
<td>15 (88.24%)</td>
</tr>
<tr>
<td>Ideal &gt; Healthy</td>
<td>10 (9.9%)</td>
<td>2 (16.67%)</td>
<td>2 (20.00%)</td>
<td>4 (6.45%)</td>
<td>2 (11.76%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Knowledge of Medical Consequences Associated with Obesity</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 Diabetes</td>
<td>96 (92.31%)</td>
<td>13 (100.00%)</td>
<td>8 (80.00%)</td>
<td>60 (93.75%)</td>
<td>15 (71.43%)</td>
</tr>
<tr>
<td>High Blood Pressure</td>
<td>96 (92.31%)</td>
<td>12 (92.31%)</td>
<td>8 (80.00%)</td>
<td>60 (93.75%)</td>
<td>16 (76.19%)</td>
</tr>
<tr>
<td>High Cholesterol</td>
<td>91 (87.50%)</td>
<td>10 (76.92%)</td>
<td>8 (80.00%)</td>
<td>56 (87.50%)</td>
<td>17 (80.95%)</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>92 (88.46%)</td>
<td>12 (92.31%)</td>
<td>7 (70.00%)</td>
<td>56 (87.50%)</td>
<td>17 (80.95%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>73 (70.19%)</td>
<td>11 (84.62%)</td>
<td>6 (60.00%)</td>
<td>44 (68.75%)</td>
<td>12 (57.14%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>32 (30.77%)</td>
<td>5 (38.46%)</td>
<td>4 (40.00%)</td>
<td>18 (28.13%)</td>
<td>5 (23.81%)</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>46 (44.23%)</td>
<td>10 (76.92%)</td>
<td>3 (30.00%)</td>
<td>24 (37.50%)</td>
<td>9 (42.86%)</td>
</tr>
<tr>
<td>Gynecological Problem</td>
<td>35 (33.65%)</td>
<td>5 (38.46%)</td>
<td>3 (30.00%)</td>
<td>19 (29.69%)</td>
<td>8 (38.10%)</td>
</tr>
<tr>
<td>Sleep Apnea / Respiratory Problem</td>
<td>78 (75.00%)</td>
<td>12 (92.31%)</td>
<td>6 (60.00%)</td>
<td>47 (73.44%)</td>
<td>13 (61.90%)</td>
</tr>
<tr>
<td>Liver and Gall Bladder Disease</td>
<td>56 (53.85%)</td>
<td>10 (76.92%)</td>
<td>5 (50.00%)</td>
<td>31 (48.44%)</td>
<td>10 (47.62%)</td>
</tr>
</tbody>
</table>
**Objective:**
To compare the performance of methods of stratifying patients with prediabetes by the 5-year likelihood of progression to type 2 diabetes (T2DM).

**Background:**
Approximately 80 million US adults have prediabetes, and their individual risk of progressing to T2DM varies considerably. Tests to identify patients most likely to progress are important to effectively focus prevention resources.

**Methodology:**
In this post-hoc analysis, we identified a prediabetic population in the Botnia Study (n=789, 48% female, age 48.9±12.5 years, FPG 105.2±8.3 mg/dL, A1C 5.5±0.4%, mean±SD). Performance was estimated for 12 stratification strategies, including common clinical risk factors two diabetes risk scores based on combinations of clinical risk factors and biometric tests (Framingham and San Antonio), and the PreDx test that utilizes biomarkers from multiple pathways in the pathogenesis of T2DM to generate a score corresponding to the 5-year likelihood of incident T2DM. Performance was assessed by positive predictive value (PPV), odds ratio (OR), positive predictive ratio (PPR), and number needed to treat (NNT) to prevent 1 case of T2DM with lifestyle intervention. The PreDx score was compared to other strategies by computing performance in 10,000 bootstrap replicates.

**Results:**
Forty subjects (5.1%) converted to T2DM within 5 years. The PreDx test had the best performance for each metric. Superior performance was maintained in >95% of the bootstrap trials for most comparisons.

<table>
<thead>
<tr>
<th>Methodology</th>
<th>% PPV *</th>
<th>OR*</th>
<th>PPR*</th>
<th>NNT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PreDx Score &gt;8</td>
<td>20</td>
<td>6.4</td>
<td>5.3</td>
<td>14</td>
</tr>
<tr>
<td>2-hr OGTT 140-199 mg/dL</td>
<td>14 (89%)</td>
<td>5.7 (55%)</td>
<td>5.0 (59%)</td>
<td>20 (89%)</td>
</tr>
<tr>
<td>A1C 6.0-6.4%</td>
<td>15 (80%)</td>
<td>4.6 (73%)</td>
<td>4.0 (75%)</td>
<td>18 (80%)</td>
</tr>
<tr>
<td>San Antonio Heart Study Risk &gt;12.5%</td>
<td>6 (&gt;99%)</td>
<td>3.8 (67%)</td>
<td>3.6 (72%)</td>
<td>50 (&gt;99%)</td>
</tr>
<tr>
<td>Obesity + Family History</td>
<td>10 (99%)</td>
<td>3.2 (90%)</td>
<td>3.0 (91%)</td>
<td>30 (99%)</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>9 (&gt;99%)</td>
<td>3.2 (89%)</td>
<td>3.0 (91%)</td>
<td>32 (&gt;99%)</td>
</tr>
<tr>
<td>BMI ≥30 kg/m2</td>
<td>10 (98%)</td>
<td>2.7 (95%)</td>
<td>2.6 (96%)</td>
<td>28 (98%)</td>
</tr>
<tr>
<td>Met. Synd. + Obesity</td>
<td>10 (98%)</td>
<td>2.7 (96%)</td>
<td>2.5 (97%)</td>
<td>28 (98%)</td>
</tr>
<tr>
<td>FPG 110-125 mg/dL</td>
<td>8 (&gt;99%)</td>
<td>2.0 (&gt;99%)</td>
<td>1.9 (&gt;99%)</td>
<td>38 (&gt;99%)</td>
</tr>
<tr>
<td>Age ≥65 y</td>
<td>8 (&gt;99%)</td>
<td>1.7 (99%)</td>
<td>1.6 (99%)</td>
<td>37 (99%)</td>
</tr>
<tr>
<td>Framingham Heart Study Risk &gt;12.5%</td>
<td>5 (&gt;99%)</td>
<td>1.7 (85%)</td>
<td>1.7 (86%)</td>
<td>58 (99%)</td>
</tr>
<tr>
<td>Family History T2DM</td>
<td>5 (&gt;99%)</td>
<td>1.0 (99%)</td>
<td>1.0 (99%)</td>
<td>58 (&gt;99%)</td>
</tr>
</tbody>
</table>

(*) Frequency of superior PreDx performance is shown in parentheses
Conclusion:
The Predx test showed the best overall performance compared to other biometric lab tests, clinical risk factors, and diabetes risk scores. This was followed by the 2-hr OGTT glucose concentration.
Insulin resistance (IR) has been proven to increase the risks for cardiovascular complications in type 2 diabetes mellitus. Recently, IR has also been shown to play a bigger role in the natural history of type 1 diabetes mellitus (T1DM) disease process than is commonly recognized. The objectives of this study are to determine the prevalence of IR among Filipino adults with T1DM and to describe the clinical features of T1DM with IR.

This cross-sectional study recruited 83 adults with long standing (≥1 yr duration) T1DM in Philippine General Hospital. Mixed-meal stimulated C-peptide level was done to confirm the diagnosis of T1DM. IR was determined using the validated clinical scoring, estimated glucose disposal rate (eGDR) with the formula of: eGDR= 24.31 – (12.22 x Waist-to-hip ratio) – (3.29 x 1 if with hypertension or on anti-hypertensive or x 0 if no hypertension) – (0.57 x HbA1c). Subjects with eGDR of ≤ 7.5 mg/kg/min were considered to have IR.

The prevalence rate of IR found to be 54.2%. Among these subjects 84.4% had family history of diabetes, 80% had diabetes ketoacidosis, 46.7 % were either overweight or obese, 68.9% were hypertensive and 97.8 % were dyslipidemic. Majority had more than 10-year duration of disease and daily insulin dose of > 1 unit/Kg body weight.

The result of this study showed a high prevalence rate of IR among Filipino adults with long standing T1DM. Hypertension, older age, longer duration of disease and a higher waist-to-hip ratio were significantly higher in T1DM subjects with IR.
THE CONUNDRUM OF BIRTH WEIGHT IN WELL-CONTROLLED GDM: RELATIONSHIP WITH MATERNAL BMI, WEIGHT GAIN AND GLYCEMIC STATUS AT DIAGNOSIS

Umakanth, S, Bhat, SK

Dr. TMA Pai Hospital, Melaka Manipal Medical College, Manipal University, Manipal, India

Introduction:
Ensuring an uncomplicated pregnancy, delivery and a healthy child in pregnant women with gestational diabetes mellitus (GDM) is the combined responsibility of obstetricians, physicians and pediatricians. The importance of adequate birth weight in avoiding complications cannot be overemphasized. In this retrospective study we have attempted to find a relationship of birth weight with maternal pre-pregnancy weight, weight gain during pregnancy and maternal glucose intolerance.

Objective:
To evaluate the relationship of birth weight with maternal pre-pregnancy BMI, change in BMI at 24-28 weeks (ΔBMI@GCT) and total change in BMI (ΔBMI@TERM).

Methods:
We performed a retrospective analysis on 109 pregnant women with GDM diagnosed using 3-hour 100 g oral glucose tolerance test (GTT) with at least two abnormal values. Pre-pregnancy BMI was ascertained from antenatal records along with total weight gain, weight gain until glucose challenge test (GCT) at 28 weeks, oral GTT values, and changes in BMI during the course of pregnancy were also recorded. Thirty-seven cases were excluded due to non-availability of pre-pregnancy weight or poor glycemic control (HbA1c>6.5% at 34-36 weeks) and remaining 72 cases were analyzed using IBM SPSS® v20.0.

Results:
There was a highly significant correlation between birth weight and ΔBMI@GCT (Pearson correlation R=0.681, p<0.001), ΔBMI@TERM (Pearson correlation R=0.563, p<0.01) and GTT value at 1 hour (Pearson correlation R=0.568, p<0.01), while there was positive insignificant correlation with maternal age, GCT, other GTT values and gestational age at delivery. By multiple regression analysis, it was found that birth weight = 2462.7 + 144.7 (ΔBMI@GCT) grams.

Conclusion:
In well-controlled GDM, birth weight has a more significant relationship with change in BMI at GDM diagnosis than at term.
Objective:
The purpose of this study was to evaluate the association of pre-gravid body mass index (BMI), gestational weight gain on glycemic response to universal glucose challenge test (50-g GCT).

Method & Design:
A prospective analysis of a cohort of 301 antenatal women with singleton pregnancy attending a secondary care center was done. Effect of pre-gravid BMI and gestational weight gain assessed by proportional change in BMI (until the time of GCT) on 50-g glucose challenge test was evaluated. Pre-gravid BMI < 23 was considered as normal BMI and > 23 was considered as high BMI for this study. Statistical analysis was done using IBM SPSS® v20.0.

Results:
In women with normal BMI, proportional BMI gain until GCT had a statistically significant relationship with GCT values (Proportional BMI gain= 5.7+1.9%, GCT= 125.8+30.4 mg/dL, Pearson correlation R=0.224, p<0.01). However, in women with high BMI, proportional BMI gain until GCT was lower and did not have any significant relationship with GCT values (Proportional BMI gain= 4.3+1.6%, GCT= 121.4+25.6 mg/dL, Pearson correlation R=-0.106, p=0.387).

Conclusion:
In women with normal BMI, proportional BMI gain had a positive and significant linear relationship with GCT. This was probably because this group of women had a higher proportional BMI gain, while women with higher BMI had a modest weight gain. A proportional BMI gain of >5.7% in women with normal pre-gravid BMI may warrant an OGTT without the need for GCT as they are very likely to have an abnormal GCT.
CONTRIBUTION OF METABOLIC SYNDROME TO ATHEROSCLEROSIS PROCESS

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Aim:
To study the association between metabolic syndrome (MS) and atherosclerosis in hypertensive patients.

Materials and Methods:
We have examined 162 hypertensive men. Mean age 47.8 ± 9.5 yr. Metabolic syndrome was defined according to IDF recommendations, 2005. Standard glucose tolerance test was performed for all patients. Following a 12-hour period of fasting, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein-cholesterol (LDL-C) levels were obtained. Common carotid and brachial artery intima-media thickness (IMT) was measured by high-resolution ultrasound.

Results:
Patients were divided into 2 groups: first group – hypertensive patients with MS (n=140) and second one – hypertensive patients without MS (n=52). Both groups adjusted by age, duration of hypertension, SBP, DBP. Patients with MS have had significantly higher level of TC (224.0±41.9 vs 200.6±41.9 mg/dl, p=0.0008), TG (214.7±153.4 vs 160.9±83.4 mg/dl, p=0.019) and LDL-C (142.3±33.7 vs 128.1±35.6 mg/dl, p=0.011) than those without MS. LDL-C level didn’t differ between groups: 39.4±6.7 vs 41.1±9.1 mg/dl. Surrogate marker of subclinical atherosclerosis common carotid IMT was significantly higher in 1th group than 2nd one: 0.98±0.23 vs 0.87±0.21 mm, p=0.002, respectively. Moreover, brachial artery IMT was also significantly higher in hypertensive patients with MS compared with those without MS: 0.52±0.13 vs 0.46±0.12 mm, p=0.004.

Conclusion:
The presence of MS intensifies of atherosclerosis processes in hypertensive patients.
CHARACTERIZATION OF A NOVEL FASTING BLOOD TEST FOR INSULIN RESISTANCE: QUANTOSE™

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Background:
There is an unmet need for a simple measure of insulin resistance (IR). Recently we reported that the fasting blood levels of a number of metabolites correlated with insulin resistance as measured by the hyperinsulinemic euglycemic clamp, the gold standard for measuring insulin sensitivity. These metabolites were used to develop Quantose™, a novel test for IR.

Method:
Data from the RISC Study (a healthy non-diabetic cohort, n=1277) were used in an iterative process of algorithm development to define the best combination of metabolites for predicting the M value derived from the clamp. The process converged to a model consisting of a multiple linear regression (natural log transformed) on the fasting levels of α-hydroxybutyrate, linoleoylglycerophosphocholine, oleate and insulin used to calculate ln(M). The resulting score, MQ, was utilized to predict insulin resistance and the risk of progressing from NGT to IGT over a 3 year period.

Results:
MQ correlated with actual M values with an r value of 0.66. In addition, the test predicted insulin resistance and 3 year IGT progression with AUCs of 0.79 and 0.70, respectively, outperforming other simple measures such as fasting insulin, fasting glucose, HOMA-IR or BMI. Finally, the test detected subjects at risk of progression to IGT that were missed by traditional criteria.

Conclusions:
Quantose™ is a simple test for IR based on a single fasting blood sample. The MQ score may have clinical utility as an early indicator of risk for the development of prediabetes and type 2 diabetes.
IMPACT OF VITAMIN D DEFICIENCY AMONG TYPE-2 DM AND MI PATIENTS OF SOUTH INDIA

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Background:
Presence of Vitamin D deficiency in type-2 diabetes and MI patients has been established in western studies. Whether Vitamin D deficiency contributes to Insulin resistance among type-2DM is evaluated, whether Vitamin D deficiency is a risk marker of MI is unknown among south Indian population.

Method:
446 type-2 DM and 314 MI individual are compared with 57 non-diabetics for vitamin-D status. Following IRB guidelines, history, examination & anthropometrics, fasting blood sample is collected for Glucose, Lipid profile, thyroid function test insulin, c-peptide, vitamin-D and analyzed on Cobas P-800 & elecsys2020, also done is CPK, CK-MB in MI and urine microalbumin in diabetics. Statistical analysis is done using Mann-Whitney, Chi-squared test.

Result:
817 individuals, male and females were 48% and 68% as type-2DM, 47% & 21% as MI patients and 5% &11% non diabetic. Vitamin D is normal in 4% of non diabetic, 6% of Type-2DM & 15% of MI, while insufficiency of 21-29ng/ml is seen in 14% nondiabetic,14% type-2DM and 20% MI. Deficiency of <20ng/ml is 82% in non Diabetic,80% in type-2DM and 65% in MI. Statistical significance (p-value<0.001) between Non-diabetic &MI and type-2DM &MI with higher sample number is in type-2DM & MI having deficiency. Insulin resistance by HOMA-1 among vitamin D deficiency type-2DM, seen as uncontrolled hyperglycemia 83% in both fasting & post-prandial glucose, 80% have hypercholesterolemia, 86% low HDL, 87% hypertriglyceridemia while higher BMI is marked.

Conclusion:
Vitamin D deficiency linked to insulin resistance is a progressive phenomenon that maybe a risk marker of MI.
ATYPICAL PRESENTATION OF MYOCARDIAL INFARCTION: THE PHILIPPINE GENERAL HOSPITAL EXPERIENCE

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Background:
Myocardial infarction (MI) remains one of the leading causes of cardiovascular death among Filipinos. Some patients with MI present with symptoms other than typical chest pain. This leads to misdiagnosis or delay in management. At present, local studies on atypical MI, its prevalence, risk factors and outcomes are lacking. This information is important to develop a higher index of suspicion for the disease and subsequently render prompt management. Doing so may halt the catastrophic consequences of this illness.

Objectives:
Our primary objective is to determine the proportion of atypical presentation of MI in patients admitted in the Philippine General Hospital. Specifically, we aim to identify these atypical symptoms, describe and compare this population from those who presented typically based on the following demographics: age, gender, presence of hypertension, diabetes mellitus, chronic kidney disease, smoking history, lipid levels, past and family history of cardiovascular event. Our secondary objectives are to identify risk factors for atypical presentation and compare inpatient outcomes of patients with typical and atypical presentation.

Methods:
This is a descriptive-analytical study. We conducted chart review of patients diagnosed with myocardial infarction in the Philippine General Hospital during the period of October 2006 to September 2007. Chief complaint, population characteristics and inpatient outcomes were extracted. Logistics regression analysis was employed to elicit association of population characteristics to presentation of MI and outcomes. Bartlett’s Test for Variance was used to relate chief complaint with hospital stay.

Results:
We identified 97 patients admitted for MI in the period specified. Thirty eight percent (38%) presented with atypical complaints. Dyspnea (62%) was most common followed by epigastric pain (8%) and syncope (8%). Patients who presented with typical and atypical chief complaints were comparable in age, presence of hypertension, diabetes mellitus, chronic kidney disease, prior cardiovascular event, family history of cardiovascular disease and level of low density lipoprotein (LDL) and triglycerides. Four factors were identified to be significantly associated with atypical presentation namely: female gender (OR 11.54, 95% CI [1.46, 91.48]), presence of heart failure (OR 7.31, 95% CI [1.28, 42.60]), decrease in level of HDL (OR 13.7, 95% CI [1.14, 165]) and duration of smoking history (OR 1.05, 95% CI [1.0, 1.09]). Patients with atypical symptoms had significantly increased risk for mortality (OR 6.9, 95% CI [1.24, 165]) and in-hospital complications (OR 5.7, 95% CI [2.15, 16.21] with arrhythmia being the most common. Atypical MI patients also tended to have longer hospital stay, however this was not statistically significant.

Conclusion:
A considerable proportion of patients with MI presented atypically. Dyspnea was the most common atypical symptom. They are also shown to have poorer outcomes. Female gender, duration of smoking history, presence of heart failure and low HDL are associated with atypical presentation. These findings may be employed to increase the index of suspicion for the diagnosis of MI and consequently render prompt management.

Keywords:
atypical myocardial infarction, Filipinos, risk factors, outcome
MEDICAL STAFF EXPERIENCE AND ACCEPTANCE OF AN ICU INSULIN INFUSION PROTOCOL IN A TERTIARY HOSPITAL IN THE PHILIPPINES

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Introduction:
The recommended strategy for glycemic control among critically ill is use of intravenous insulin that is adjusted via a standardized insulin protocol. Critical to its successful implementation is acceptance of the implementing staff. In our hospital, we adapted and modified the Yale Insulin infusion protocol to target the current blood glucose recommendations and tailor it to our hospital’s setting. Evaluation of its performance in routine clinical practice specifically the medical staff experience has not yet been done.

Objectives:
To evaluate medical staff experience and acceptance of the protocol through a survey and focused group discussion.

Methods:
A survey followed by focused group discussions among the medical staff of the Medical and Central Intensive Care Units were done. Questionnaires were distributed to the nurses of the two ICU units and the medical residents who manned in these ICUs. The survey focused on assessment of their experience and acceptance of the insulin protocol. Focused group discussions were done after the survey to clarify and confirm the information derived from the survey.

Results:
A total of 109 medical staff (47 nurses and 62 medical residents) participated in the study. For nurses, most consider their knowledge of the protocol to be good. Majority (76.7%) of the ICU nurses felt that they had good knowledge of the IIP. Seventy-seven percent of nurses agree that the Modified Yale Insulin Infusion Protocol (IIP) is effective in controlling hyperglycemia and 57.4% felt that it prevented hypoglycemia. While 74.5% held that the protocol increases their workload due to frequent glucose checks and need for computations to adjust the drip, majority (64%) agree that it is easy to administer. Seventy percent of nurses are satisfied with the use of the protocol. Similarly, a majority (80.6%) of medical residents in the ICUs believe that the IIP is effective. While most felt that the protocol is not easy to administer (68%), a majority (64%) would still opt to use it for their patients. The staff believes that periodic training and provision of supplies are key factors in improving the protocol.

Conclusion:
Experience and acceptance of the insulin infusion protocol is generally excellent for both nurses and physicians. Despite an increase in workload, most believe the protocol to be effective and would advocate its use for ICU patients.
Mounting evidence suggests that high body iron stores, hyperglycemia and insulin resistance are biologically intertwined. The excess dietary iron is thought to be a risk factor of diabetes due to the prooxidant feature of iron. This experiment was designed to test the impact of dietary iron restriction and supplementation on functional outcome in adult, healthy rats.

Rats were fed diets containing either 10 mg / Kg or 350 mg /Kg of elemental iron for 12 wk compared with the control rats that were fed AIN-M 93 diet. Then, rats were euthanized and detailed analyses were performed.

Fasting blood glucose was markedly diminished by dietary iron restriction, moreover, hepatic glycogen content decreased with concomitant increases in skeletal muscle. In addition, dietary iron restriction resulted in a twofold increase in mRNA expression of InsR and fourfold increase in GLUT4 expression in skeletal muscle. Although the dietary iron restriction did not affect body iron status, caused hepatic low oxidative damages; however, high liver NADPH oxidase activity and increased levels of protein oxidation in muscle were observed. Chronic feeding of high iron diet increases serum and hepatic iron and resulted in elevated levels of stress markers in liver and skeletal muscle. Dietary iron supplementation did not affect either glucose uptake or glycogen content.

Thus, dietary iron deprivation may improve insulin-stimulated muscle glycogen synthesis and glucose uptake; nevertheless, the pivotal role of iron in the biological function should not be underestimated.
A NOVEL ASSAY TO SIMULTANEOUSLY MEASURE THE KINASE ACTIVITY OF PKC AND PKG-Iα, TWO ENZYMES REGULATED BY GLUCOSE LEVELS AND LINKED TO DIABETIC COMPLICATIONS

Costantino, BFB\textsuperscript{1,2}, Johlfs, MG\textsuperscript{1,2}, Fiscus, RR\textsuperscript{1,2,3}

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Protein expression levels, kinase activity and biological functions of protein kinase C (PKC) and cGMP-dependent protein kinase type-Iα (PKG-Iα) are dramatically altered by diabetes or in-vitro hyperglycemia, resulting in cellular dysfunctions. Activation of PKC by hyperglycemia and lipid metabolites is linked to specific diabetic complications, such as cardiomyopathy, atherosclerosis, and neuropathy.

Our lab has shown that PKG-Iα, activated by endogenous nitric oxide (NO) and natriuretic peptides (ANP and BNP), plays an essential role in promoting cell survival and proliferation in various mammalian cells, including neural, vascular smooth muscle and bone marrow stem cells. Hyperglycemia decreases PKG-Iα protein expression, thereby reducing PKG-Iα kinase activity, which can result in loss of cytoprotection normally mediated by NO, ANP and BNP. Measuring both PKC and PKG-Iα kinase activities in the same cell lysate is of great value in determining progression of diabetes, adding to our understanding of how these kinases contribute to diabetic complications.

Here, we present a unique strategy to measure PKC and PKG-Iα activities simultaneously using a novel near-infrared fluorescently-labeled peptide designed around the serine-32 region of histone H2B, RKRSRKE (we call nIRF-H2Btide), a selective substrate for only PKC and PKG isoforms. Difference in charge allows phosphorylated peptide to be electrophoretically separated from nonphosphorylated peptide. After separation by agarose gel, results are scanned and quantified using LI-COR Odyssey® Infrared-Imaging System. PKC-specific inhibitors are used to discriminate between PKC and PKG-Iα kinases activities.

Using our novel assay, we present data showing that PKG-Iα kinase activity is suppressed in neural cells exposed to high glucose.
PERIPHERAL MICRORNA EXPRESSION PROFILE IN PCOS: MAJOR IMPLICATIONS TOWARDS METABOLIC DYSFUNCTION

Krishna B, M, Pillai, SM, Laloraya, M

Background:
Polycystic Ovarian Syndrome is a heterogeneous metabolic disorder with an enigmatic aetiology prevalent among women of reproductive age. With the advent of microRNAs (miRNA), which regulate gene expression networks, there is a growing interest in understanding of PCOS specific miRNAome and its association with PCOS aetiology.

Objective:
We investigated the microRNA expression profile in peripheral blood under PCOS and its functional significance.

Methods & Results:
MiRNA expression profiling was performed on TaqMan Array Human MicroRNA Panel in peripheral blood of 4 normal and 4 PCOS women. Accordingly hsa-miR-451a, hsa-miR-210 and hsa–miR-494 (P-value <0.1, fold change +/- 2) were found aberrantly expressed. The results were further validated by real-time quantitative PCR. Bioinformatic Pathway analysis identified biological process including Circadian rhythm, Wnt signaling pathway, TGFβ signaling pathway, Phosphatidyl inositol pathway, Long term depression, GnRH pathway, mTOR signaling, Polyunsaturated fatty acid metabolism and Inositol phosphate metabolism are affected by the altered microRNA expression. Functional annotation clustering on DAVID identified terms implicating cardio-vascular dysfunctions. Given the targets enriched in the above biological processes, we examined the transcript level expression changes through qRT-PCR. The approach enabled us to parallel the miRNA-mRNA expression in decisive pathways of PCOS.

Conclusion:
Our work is a pioneer attempt of profiling miRNA expression in peripheral blood of PCOS patients. The potential regulatory role of these miRNAs keeps them ahead as specific candidate molecules in PCOS research, diagnosis and therapy.
INSULIN RESISTANCE AND \(\beta\)-CELL DYSFUNCTION DUE TO A SINGLE NIGHT OF SLEEP DEPRIVATION IN A DIURNAL ANIMAL


Cedars-Sinai Medical Center, Los Angeles, California

Background:
Sleep deficiency is a risk factor for the development of obesity, insulin resistance and type 2 diabetes. We have examined the impact of sleep deprivation for 1 night in a diurnal animal model of sleep restriction-induced metabolic dysfunction.

Methods:
Eleven male mongrel dogs were studied under two randomized crossover conditions—Undisturbed Sleep (UNS) and Sleep Deprivation (SD) separated by at least 2 weeks. UNS involved 1 night of undisturbed sleep, whereas SD included constant human attention from 1800-0600 to prevent sleep (0600-1800 lights on; 1800-0600 dim light [<5 lux] in both conditions). Food intake was matched across conditions for each dog and Actical data were collected to determine sleep-wake states and activity levels. Each sleep condition was followed by an intravenous glucose tolerance test, evaluation of total and visceral body fat, as well as heart function by magnetic resonance imaging, and organ fat evaluation by magnetic resonance spectroscopy for heart, liver and pancreas.

Results:
Sleep restriction resulted in a 28% reduction in insulin sensitivity [UNS 4.6(1.0) versus SD 3.1(0.4) (mU/l)-1.min-1; p<0.02], decreased glucose tolerance, calculated as the disappearance rate of glucose from minutes 5-19 after glucose bolus [UNS 3.4(0.4) versus SD 2.6(0.2) (mg.dL-1.min-1); p=0.01], and a reduction in \(\beta\)-cell function, as assessed by the Disposition Index [UNS 2519(448) versus SD 1585(155); p<0.02]. Fasting insulin and fasting glucose levels were unchanged [insulin: UNS 9.6(1.5) versus SD 10.6(1.4) (\muU/L) p=0.5; glucose: 94.2(1.5) versus 97.7(1.6) (mg/dL) p=0.1]. Weight was unchanged across conditions [UNS 29.1(1.2) versus SD 29.2(1.2) (kg); p=0.6]. Food intake on the day prior to the sleep condition was not different [UNS 656(63) versus SD 593(44) (grams); p=0.8].

Conclusions:
A single night of sleep deprivation in the dog is associated with a 28% decrease in insulin sensitivity, decreased glucose tolerance and decreased \(\beta\)-cell function. The mechanisms by which 1 night of sleep interruption causes metabolic dysfunction remain to be elucidated.
INTRA-INDIVIDUAL LP(A) VARIATION IN CARDIOLOGY OUTPATIENT SUBJECTS

Ross, D1,3, Smolgovsky, A1,3, Baca, A2,3, Gunning, K2,3, Sninsky, J1,3, Superko, HR1,3

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Background:
Individuals with >30 mg/dl Lp(a) have an increased cardiovascular disease (CVD) risk. An improved understanding of the intra-individual variation of Lp(a) will assist interpretation of biological variability and categorical thresholds for patient management.

Methods:
De-identified patient records (January 2010 and May 2011) from a mixed ethnic and gender prevention broad spectrum cardiology outpatient database (Berkeley HeartLab, Alameda, CA) were selected (n= 8,098). The intra-individual Lp(a) dynamic range was evaluated using 4-12 tests per subject. The Lp(a) assay (Diazyme) was performed on a Roche Hitachi 917. Simple precision (20 runs, same sample and day) had < 2% coefficient of variation (CV), and cumulative analytical CV was 4-5%.

Results:
Lp(a) levels can vary widely within an individual over time. The relationship between the Lp(a) level and the dynamic range was good (r2 =0.44). Nearly all individuals who remain below 30 mg/dl have narrow Lp(a) ranges (average 4.8 mg/dl males and females 5.2 mg/dl)(4423 subjects); individuals who had Lp(a) levels both below and above 30 mg/dl have higher ranges (22.7 mg/dl males and females)(824 subjects); and individuals whose Lp(a) levels remain above 30 mg/dl have an even higher range (27.7 mg/dl male/ 29.2 mg/dl female)(2851 subjects).

Conclusions:
The longitudinal variability of Lp(a) observed in this study supports and extends earlier recommendations that multiple determinations are required to accurately assess CVD risk. Caution should be used for patients in whom serum levels are near the threshold for CVD risk. Individuals with a wide range of Lp(a) levels may lack differential regulated control.
Nitric oxide (NO) was considered to potentially involve in the destruction of pancreatic β-cells in the development of type 1 diabetes. However, in recent years, it has become clear that NO has both cytotoxic and cytoprotective effects in mammalian cells. Our studies have shown basal activity of NO/soluble guanylyl cyclase (sGC)/cGMP/PKG-Iα signaling pathway is necessary to prevent spontaneous apoptosis in mouse primary/isolated pancreatic islets (model of islet-transplantation therapy). The eNOS inhibitor L-NIO, sGC inhibitor ODQ and specific-PKG-Iα inhibitor DT-2 increased apoptosis and decreased insulin secretion in the rat insulinoma β-cell line RINm5F cells. Specific PKG-Iα-siRNA gene knockdown of PKG-Iα expression (~70% knockdown confirmed by Western blot analysis, as well as decreased phospho-VASP at ser239, an indicator of endogenous PKG-Iα activity), significantly increased apoptosis by 1.5-fold and decreased insulin secretion by 25%, confirming the role of PKG-Iα in survival and insulin secretion. In PKG-Iα-knockdown RINm5F cells, Western blot analysis showed decreased pancreas duodenum homeobox-1 (PDX-1) expression, a regulator of β-cell development, survival and insulin secretion. Furthermore, phospho-Akt, phospho-eNOS (regulated by Akt at ser1177) and phospho-Foxo1a (downstream target of Akt) are decreased in PKG-Iα-knockdown RINm5F cells. Because Foxo1a is a transcriptional repressor of PDX-1, increased active Foxo1a nuclear translocation (i.e. decreased phospho-Foxo1a) causes suppression of PDX-1, hence inhibiting insulin secretion and survival in pancreatic β-cells. The data shows basal NO/cGMP/PKG-Iα activity is essential in survival and insulin secretion in pancreatic β-cells, and may provide therapeutic implications in the development of new therapeutic agents for preventing type 1 diabetes and promoting β-cell survival.
DELAYED BLOOD PRESSURE RECOVERY AND HEART RATE RECOVERY AFTER EXERCISE STRESS TEST IN WOMEN WITH METABOLIC SYNDROME

Background:
Non-electrophysiological markers of chronotropic incompetence, such as delayed blood pressure (BP) recovery and delayed heart rate recovery (HRR), have risen as independent predictors of underlying coronary artery disease (CAD).

Objectives:
The purpose of the study is to determine the pattern of non-electrophysiological markers of standard treadmill stress test in women with metabolic syndrome.

Methods:
A total of 90 post-menopausal women have been randomized for evaluation (mean age 56.5 ± 1.7). All of them underwent routine physical examination, blood lipid profile measurement, glucose tolerance tests, standard treadmill stress test according Bruce protocol, and carotid artery intima-media thickening evaluation. 31 patients were diagnosed with metabolic syndrome.

Results:
23.3% (21 patients) failed to reach 85% of age-adjusted maximum heart rate. 29% of patients had low chronotropic index. 41% patients showed delayed heart rate recovery. 38% had delayed blood pressure recovery. 34% of all evaluated patients showed evidence of increased carotid arterial intima-media thickening. After adjustment of age, BMI, lipid profile, glucose tolerance test and stress test results (delayed heart rate recovery, delayed blood pressure recovery, chronotropic index, failure to reach 85% of maximum heart rate was associated with metabolic syndrome and carotid arterial intima-media thickening in 77% of patients.

Conclusion:
Women who show impaired non-electrophysiological response to exercise stress test have close correlation with metabolic syndrome and impaired carotid arterial intima-media thickening.
EFFECT OF ANTIOXIDANTS ON THE RENAL FUNCTION, GLYCOSYLATED HEMOGLOBIN PLASMA LEVELS AND QUALITY OF LIFE IN TYPE 2 DIABETES MELLITUS PATIENTS WITH CHRONIC KIDNEY DISEASE: A CONTROLLED CLINICAL TRIAL

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Background and Aim:
Diabetic nephropathy is well-recognized as the leading cause of Chronic Kidney Disease (CKD) in the United States and other Western societies. Also represents a significant long-term complication; as well as increases the costs for health systems. Our aims were determinate the effect of antioxidants on renal function, and whether this treatment improve the quality of life (QOL) of type 2 diabetes patients.

Materials and Methods:
We designed a controlled clinical trial, randomized and single-blind. A total of 30 diabetic patients, with stage 1 and 2 of CKD; treated with renin-angiotensin-aldosterone system inhibitors at least three months before inclusion were included. The QOL was evaluated with the Diabetes QOL instrument. All patients received antioxidants and placebo twice daily. We divided all patients in two groups. The first group started administrating of placebo for one month and a half. After suspend placebo for 7 days patients continued with intake of antioxidants for another similar time. Group 2 began with antioxidants. Comparison of variables was performed using Student’s t test. We adjusted the p value by Bonferroni correction and a value <0.003 was considered significance.

Results:
Plasma levels of biomarkers were similar between groups. However, we observed significantly lowest levels of creatinine and glycosylated hemoglobin, as well as increase the QOL after intake of antioxidants in the group 1 (Table 1 and 2).

Conclusions:
The administration of a short cycle of antioxidants doesn’t improve renal function in diabetic patients with CKD, but whether decreases glycosylated hemoglobin levels and improves QOL.

Keywords:
diabetes, chronic kidney disease, albuminuria, antioxidant, quality of life

<table>
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<th>Placebo</th>
<th>Antioxidant</th>
<th>Placebo vs. Antioxidant p Value</th>
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### Table 2: Clinic and biomarkers parameters in group 2

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<td>216.6</td>
<td>NS</td>
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<td>NS</td>
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<tr>
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<td>31.2</td>
<td>NS</td>
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<td>38.6</td>
<td>38</td>
<td>NS</td>
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<tr>
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<td>46.7</td>
<td>46.5</td>
<td>NS</td>
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<tr>
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<td>4.36</td>
<td>4.4</td>
<td>NS</td>
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<tr>
<td>Glucose</td>
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<td>155.4</td>
<td>147</td>
<td>NS</td>
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<td>24</td>
<td>23.6</td>
<td>NS</td>
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<td>Creatinine</td>
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<td>0.69</td>
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<td>Hemoglobin</td>
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<td>17.56</td>
<td>NS</td>
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<td>0.001</td>
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<td>Quality of life</td>
<td>98.5</td>
<td>91.2</td>
<td>94.1</td>
<td>NS</td>
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</tbody>
</table>
GENETIC VARIANTS ASSOCIATED WITH CORONARY HEART DISEASE IN FILIPINO-AMERICAN WOMEN IS CONSISTENT WITH THE COMPLEX ADMIXTURE OF THIS ETHNIC GROUP

Ancheta, IB1, Battie, CA1, Ancheta, CV2, Conley, Y3, Volgman, AS4, Tuason, MT4, Lew, D5, Smolgovsky, A5, Rana, F6, Wilson, JA6, Sninsky, JJ5,7, Catanese, JJ5,7, Ross, DA5,7, Superko, HR5,7

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Introduction:
Genetic variants have been associated with coronary heart disease (CHD) in studies conducted mainly with Caucasian subjects. Ethnic genetic variation and the inability of risk assessment algorithms to predict many cardiovascular events led us to investigate 19 well-validated single nucleotide polymorphisms (SNPs) in Filipino-American women who are of interest because of their complex genetic ancestry.

Methods:
This study recruited self-identified Filipino-American women (n=193, mean age= 55.3 ± 7.1) in Northeast Florida. Traditional cardiometabolic risk factors (means ± SD) were determined. Subjects were genotyped for 19 genetic variants that have robust univariate associations with CHD based on the literature in non-Filipino populations.

Results:
Mean values of cardiometabolic risk factors in the entire group included: systolic blood pressure: 127.3 ± 18.5, diastolic blood pressure: 81.5 ± 10.7, triglycerides: 113 ± 62, HDL cholesterol: 62.2 ± 15.6, fasting glucose: 102 ± 24, central obesity: 37.18 ± 3.72. Fifty-five per cent of the subjects fulfilled international harmonized criteria for the metabolic syndrome. Two SNPs (rs17465637 and rs17111436) had minor allele frequencies (MAF) similar to Caucasians and one SNP (rs11556924) had an intermediate MAF between Chinese and Caucasians. An allele count risk score of these SNPs ranged from 13 to 25 and had a Gaussian distribution with mean (SD) of 19 (1.8) risk alleles.

Conclusion:
The allele frequencies of the CHD-associated variants in this cohort of Filipino–American women were consistent with the complex admixture of this ethnic group. Additional studies are warranted to discern the involvement of these variants with CHD in Filipino-American women.
INVolvement of physiological-level nitric oxide (NO)/protein kinase G type-Iα (PKG-Iα) signaling in protection against diabetic neuropathies: glucose effects on PKG-Iα expression and downstream signaling quantified by ultrasensitive capillary-electrophoresis (CE)-based nanopro1000 protein analysis system

Johlfs, MG, Coffman, R, Rosenberg, H, Fiscus, RR

Center for Diabetes and Obesity Prevention, Treatment, Research and Education; Cancer Research Program; and College of Pharmacy, Roseman University of Health Sciences (formerly the University of Southern Nevada), Henderson, Nevada

Cyclic-GMP-dependent protein kinase type-I (PKG-I) is the main protein kinase mediating biological effects of low/physiological-level nitric oxide (NO) and natriuretic peptides in vascular smooth muscle cells, uterine epithelial cells, bone marrow mesenchymal (stromal) stem cells and various malignant cells, such as breast, lung, ovarian and prostate cancer. PKG-I is also expressed in neuronal (normal and malignant) cells. PKG-I expression and downstream signaling are downregulated by elevated glucose levels, potentially contributing to diabetic neuropathies. At low/physiological-level NO, PKG-I serves a neuroprotective role, preventing spontaneous apoptosis and promoting cell proliferation. There are two splice variants of PKG-I (PKG-Iα and PKG-Iβ), potentially with different cellular functions. Our previous work implicates PKG-Iα as the dominant isoform mediating neuroprotective effects.

Here, we determined the expression of PKG-I isoforms in neuronal cells using the novel NanoPro1000 system (ProteinSimple, Santa Clara, CA), an automated CE-chemoluminescence-based immuno-quantification instrument, providing exquisitely-high sensitivity and phosphoprotein resolving power and quantification, compared with conventional Western blot analysis. The 500-fold better sensitivity of this system allows more definitive analysis of isoform expression levels. We found only PKG-Iα isoform in NG108-15 neural cells, used as a model studying NO/natriuretic peptide-induced neuritogenesis. We also used this technology to explore the effects of glucose on PKG-I expression. High levels of glucose suppressed PKG-Iα expression in both NG108-15 cells and Schwann cells, likely contributing to neuropathies. The effect of glucose on downstream targets of PKG-Iα, known to be involved in the cytoprotective effects of neuronal cells, such as BAD, CREB and VASP, was also explored.
METABOLIC SYNDROME: THE CRUX OF THE MATTER

Pretorius, HT, Idoine, JD, Menke, DE, Richards, NM, Hartsock, H

1Blue Ash Nuclear Medicine LLC, Cincinnati, Ohio, 2Kenyon College, Gambier, Ohio

Objective:
Describe a practical test to elucidate the metabolic syndrome hallmark: the coincident risk of myocardial and cerebral disease.

Methods:
Cardiac protocols included treadmill or pharmacologic stress with simple (< five time points, < nine heart regions) tracer (Tc-99m-sestamibi or Tl-201) kinetic analysis. Brain SPECT included Tc-99m-ECD or Tc-99m-HMPAO for basal and perfusion-stimulated (e.g. 500 mg acetazolamide IV) indices of cerebral perfusion, metabolism and flow reserve (CMi, CPI, FRi) and was abnormal for any of these indices > two standard deviations from mean values for 34 near normal patients.

Results:
Of 453 insulin resistant (IR) or diabetic (DM) patients with cerebral ischemia symptoms, 434 (95.9%) had abnormal brain SPECT and within 2.9±2.1 years, 184 (40.6%) had coincident cardiac disease documented. Optimized brain-heart protocols required comparable radiation and time as usual cardiac stress-rest protocols alone. Preoperative evaluation was positive in two exemplary cases, in one for coronary disease, with uneventful surgery after beta blocker therapy, and in another, positive for focal cerebro-vascular disease, associated with perioperative stroke after necessary cessation of antiplatelet therapy for breast cancer surgery. Tracer kinetic analysis was more sensitive than standard stress-rest protocols and was particularly helpful in primary and secondary prevention strategies including 15.7% (68/434) patients with improved FRi and subjective memory complaints after 4 grams daily omega 3 fish oil for > 1 year.

Conclusions:
Whenever cerebral and cardiac disease are major contributors to morbidity and mortality, and especially in metabolic syndrome patients, combined brain-heart scan protocols are efficient and effective.
INFLAMMATION FROM FAT: THE NAME OF THE BRAIN GAME?

Pretorius, HT¹, Idoine, JD², Menke, DE¹, Pendleton, KA¹

¹Blue Ash Nuclear Medicine LLC, Cincinnati, Ohio, ²Kenyon College, Gambier, Ohio

Objective:
Demonstrate abnormal cerebral flow reserve in cognitively impaired, insulin resistant (IR) patients and cerebral perfusion stimulation by coconut oil.

Methods:
Brain SPECT indices of cerebral metabolism (CMi), perfusion (CPi) and flow reserve FRi = CPi – CMi and FRr = (peak stimulated)/basal counts/mCi used Tc-99m-HMPAO, basal and perfusion-stimulated with 0.8 mg nitroglycerin sl, 500 mg acetazolamide IV or 50 g coconut oil oral. Omega 6:omega 3 ratio (O6O3R), Berkley Labs, was after > 12 hr fasting. Cognition was monitored with Test Your Memory (TYM).

Results:
In 32 near normal patients age (51±15) years, CMi was (57.0±4.1)%; CPi (67.1±4.9)%; FRi (10.2±2.6)% and TYM 47.6±1.5. In 47 cognitively impaired IR patients CMi was (53.8±6.4)%; (p < 0.004); CPi (52.6±11.7)%; (p < .0001); FRi - (1.27±12.4)%; (p < 0.0001) and TYM 35.7±4.9, (p.< 0.00001). Normalized FRi and FRr correlated in 43 cases with background < 27%, (r = 0.93) using acetazolamide or nitroglycerin and similarly in 9 cases using coconut oil (r = 0.92). By visual scan analysis, coconut oil often stimulated hypoperfused cortex preferentially. Moreover, in two cases, dietary manipulation, including two tablespoons (30 g) coconut oil daily, reduced O6O3R to 3.9 and 2.1 vs. the U.S. population average of approximately 25:1.

Conclusions:
Insulin resistant, cognitively impaired patients have abnormal cerebral flow reserve. Further studies will determine if anti-inflammatory fat therapy, such as decreasing the O6O3R may have positive effects on abnormal cerebral function.
INSULIN RESISTANCE, DIABETES MELLITUS AND LOW CEREBRAL FLOW RESERVE: FUEL TO THE FIRE OF THE DEMENTIA EPIDEMIC

Pretorius, HT1, Idoine, JD2, Menke, DE1, Richards, NM1

1Blue Ash Nuclear Medicine LLC, Cincinnati, Ohio, 2Kenyon College, Gambier, Ohio

Objective:
Clarify insulin resistance (IR), diabetes mellitus (DM) and low cerebral flow reserve contributions to stroke (S) and dementia (D).

Methods:
Among 300 patients with cerebral ischemia symptoms, brain SPECT indices of basal metabolism (CMi), stimulated perfusion (CPi) and cerebral flow reserve (FRi = CPi – CMi and FRr = net stimulated/basal counts) used parabolic renal corrections. Same day scans for FRi and FRr correlations had background < 30%. Test Your Memory (TYM) dementia cutoff was < 41/50.

Results:
In 34 near normal patients age (51.8+-14.6) years, CMi was (57.3+-4.4)%, FRi (10.0+-2.5)% and TYM 47.6+-1.5. For 43 patients with FRr calculations: (20- FRi) = 45.83(1.4- FRr)+0.87 with r = 0.93. In 128 IR cases, age (52.4+-14.2) years, FRi was -(0.24+-6.71)%; TYM (43.4+-3.6), S 14.1%, D 16.5%; similarly, in 172 DM cases, age (56.5+-12.3) years, FRi was -(0.16+-9.0)%; TYM (43.8+-5.6), S 11.6%, D 19.7%. Age of S+D patients was (56.4+-12.2) years for IR cases and (57.9+-11.7) years for DM cases. For IR patients, males were a similar 25.8% (33/128) of the total and 26.3% (5/19) of D cases; however, males comprised more, 47.7% (82/172) of total and 63.3% (19/30) of D cases among DM patients.

Conclusions:
Total S and D are similar in IR and DM, hence IR (prevalence > DM) likely contributes predominantly to overall cognitive impairment. Cost effective blood tests for amyloid fragments (Pesini P, 2012) and focused brain uptakes (Pretorius, 2005) may further clarify if DM predisposes even more to dementia in men than perimenopausal women.

Table: Comparison of Near Normals, Insulin Resistant and Diabetics Contribution to Stroke and Dementia

<table>
<thead>
<tr>
<th>Category</th>
<th># of Patients</th>
<th>Age</th>
<th>CMi</th>
<th>FRi</th>
<th>TYM</th>
<th>% Stroke</th>
<th>% Dementia</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Near Normals</td>
<td>34</td>
<td>51.8+-14.6</td>
<td>57.3+-4.4</td>
<td>10.0+-2.5</td>
<td>47.6+-1.5</td>
<td>0</td>
<td>0</td>
<td>13</td>
<td>21</td>
</tr>
<tr>
<td>Insulin Resistant</td>
<td>128</td>
<td>52.4+-14.2</td>
<td>52.3+-7.6</td>
<td>-0.24+-6.71</td>
<td>43.4+-3.6</td>
<td>14.1</td>
<td>16.5</td>
<td>33</td>
<td>95</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>172</td>
<td>56.5+-12.3</td>
<td>53.8+-6.8</td>
<td>-0.16+-9.0</td>
<td>43.8+-5.6</td>
<td>11.6</td>
<td>19.7</td>
<td>82</td>
<td>90</td>
</tr>
<tr>
<td>Total Stroke</td>
<td>39</td>
<td>60.3+-9.5</td>
<td>54.7+-6.98</td>
<td>-2.37+-8.10</td>
<td>42.3+-5.51</td>
<td>100</td>
<td>21.10</td>
<td>12</td>
<td>27</td>
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<tr>
<td>Total Dementia</td>
<td>47</td>
<td>56.2+-12.6</td>
<td>53.8+-6.38</td>
<td>0.39+-8.70</td>
<td>35.9+-4.95</td>
<td>14.89</td>
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P Values Comparing Categories

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<tr>
<th>Category</th>
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<th>FRi</th>
<th>TYM</th>
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<td>Normal VS Diabetes</td>
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<td>Normal VS IR</td>
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<td>Diabetes VS IR</td>
<td>0.08</td>
<td>0.9</td>
<td>0.5</td>
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</table>

Table: Comparison of Near Normals, Insulin Resistant and Diabetics Contribution to Stroke and Dementia
DIFFERENCES IN ADIPOSE AND LIVER TRIGLYCERIDE TURNOVER, LIPOGENESIS AND ADIPOCYTE PROLIFERATION IN OBESE INSULIN SENSITIVE AND OBESE INSULIN RESISTANT HUMAN SUBJECTS

Candice A. Allister, Cindy A. Lamendola, Colleen M. Craig, Marc K Hellerstein and Tracey L. McLaughlin

University of California, Berkeley

It is well-established that obesity is a major risk factor for the development of insulin resistance, but less attention has been given to the condition of obesity with normal insulin sensitivity. The physiological mechanisms underlying the ability to remain insulin sensitive in the obese state were explored here, using our laboratory’s technique of administering $^2\text{H}_2\text{O}$ for the quantitative measurement of triglyceride turnover, de novo lipogenesis (DNL) and cell proliferation in adipocytes. Obese human subjects were classified as insulin sensitive (IS) or insulin resistant (IR) on the basis of steady-state plasma glucose (SSPG) testing. Our data suggest that differences in adipocyte function may contribute to insulin sensitivity or resistance in obesity. Incorporation of deuterium into the glycerol and palmitate moieties of extracted triglycerides show higher total triglyceride (TG) synthesis and DNL in the subcutaneous depot of IS subjects as compared to IR subjects. This suggests a greater capacity for storage of excess calories as fat in the subcutaneous depot of IS subjects. Surprisingly, our data also show a trend towards higher adipocyte proliferation (represented by the incorporation of deuterium into deoxyribose of DNA) in the IR group as compared to the IS group. Interestingly, hepatic triglyceride synthesis (represented by plasma DNL) was significantly higher in the IR subjects as compared to the IS subjects, likely reflecting greater exposure to insulin in combination with maintenance of hepatic insulin sensitivity by lipogenic pathways. These results suggest that adipocytes, but not liver cells, of obese IR subjects are resistant to insulin’s effects on lipogenesis.