ABSTRACTS

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EFFECT OF N-3 POLYUNSATURATED FATTY ACIDS ON OXIDATIVE STRESS MARKERS AND RESOLVIN E1 IN OBESE ASTHMATIC ADOLESCENTS WITH HYPERTRIGLYCERIDEMIA

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

Objective: To evaluate the effect of supplemental omega-3 fatty acid daily (2.0 g eicosapentaenoic acid (EPA) and 1.0 g docosahexaenoic acid (DHA)) for 12 weeks on oxidative stress markers and Resolvin E1 in obese asthmatic adolescents with hypertriglyceridemia.

Methods: The study was controlled, 12-week parallel group intervention trial involving 47 obese asthmatic adolescents with hypertriglyceridemia (the level of triglyceride is higher than 150 mg/dl) randomized to either omega-3 fatty acid treatment (n=21) or placebo (n=26). Insulin, lipid profile, Resolvin E1 (RvE1) and oxidative stress markers including advanced glycation end products (AGEs), Glutathione (GSH), and oxidized low-density lipoprotein (oxidized LDL) were measured at baseline and endpoint.

Results: Compared with placebo, the supplement of omega-3 for 12 weeks reduced triglycerides, insulin and HOMA in obese asthmatic adolescents with hypertriglyceridemia. Moreover, Omega-3 fatty acid decreased oxidized LDL and AGEs and increased RvE1. However, no changes were observed in GSH after treatment.

Conclusion: These results suggest that supplement treatment with omega-3 may be useful as an adjuvant therapy in obese asthmatic adolescents with hypertriglyceridemia. (HIM/2011/004 and HIM/2015/042)

ACHIEVING PERSONALIZED METABOLIC AND FUNCTIONAL CARE GOALS IN ADULTS WITH TYPE 2 DIABETES BY UTILIZING THE DIABETES CROSS-DISCIPLINARY INDEX (DXDI©) TO IMPROVE SELF-MANAGEMENT, TREATMENT SATISFACTION, AND HEALTH LITERACY

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Purpose: Personalized health goals require active patient engagement within an integrated, multidisciplinary, team-based care model. However, patients commonly experience fragmented care provided by a collection of primary and specialty clinicians. Our goal was to emphasize the multi-disciplinary care, as well as utilize the Diabetes Cross-Disciplinary Index (DXDI©) to visually orient the patient's long-term health goals in a chronic disease.

Methods: A 69-year-old African American man with T2D was referred to the Western Diabetes Institute (WDI) for integrated, multidisciplinary care 4 weeks s/p right transmetatarsal amputation (TMA) for contiguous osteomyelitis related to recurrent foot ulcerations, peripheral neuropathy, and treatment non-adherence. He had profound functional impairment and difficulty performing activities of daily living (ADLs) at presentation to WDI. Upon initial presentation to WDI, we performed a comprehensive evaluation. Clinical variables were assessed and stratified using the Diabetes Cross-Disciplinary Index (DXDI©). Variables included glycemic control (A1C); low-density-lipoprotein (LDL) level; systolic blood pressure (SBP); diastolic blood pressure (DBP); kidney health; eye health; periodontal health; foot health; functionality based on Functional Independence Measure (FIM) and Lower Extremity Functional Scale (LEFS); body mass index (BMI) and waist circumference (WC); Patient Health Questionnaire-9 (PHQ-9) depression screen; and smoking status. We organized a personalized integrated care plan, which included diabetes self-management education emphasizing nutrition, oral health, exercise, and medication adherence. We gauged clinical progress throughout the 18-month period utilizing the DXDI© as a visual shared decision-making tool. We administered the Perceived Diabetes Self-Management Scale (PDSMS), Spoken Knowledge in Low Literacy of Diabetes (SKILLD), and the Diabetes

Treatment Satisfaction Questionnaire (DTSQ) surveys at baseline and 18 months (Table) to assess the impact of DXDI© and the integrated care model on patient activation and engagement.

Conclusions: After 18 months of integrated, DXDI©-supported team-based care, glycemic control improved with a decline of A1C from 9.3% to 6.6% (Figure). DXDI© augments integrated care that promotes measurable improvements in self-management perception, treatment satisfaction, and health literacy to achieve personalized metabolic and functional goals.

Table. Patients Surveys: Baseline and 18 Months Follow-up

Patient Surveys	Initial Presentation	18-month Follow-up
Perceived Diabetes Self-Management Scale (PDSMS)	27/40	37/40
Diabetes Treatment Satisfaction Questionnaire (DTSQ)	24/36	36/36
Spoken Knowledge in Low Literacy in Diabetes scale (SKILLD)	8/10	10/10

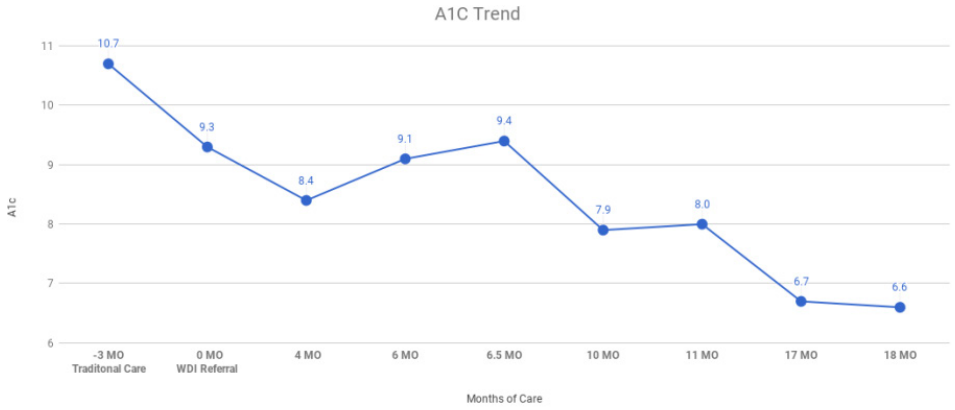

Figure. A1C Trend: Baseline through 18 Months.

STAGING TYPE 2 DIABETES MELLITUS

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In January 2017, the ADA has issued a new staging system for type 1 diabetes

	Stage 1	**Stage 2**	**Stage 3**
Stage	Autoimmunity	Autoimmunity	New-onset hyperglycemia
	Normoglycemia	Dysglycemia	Symptomatic
	Presymptomatic	Presymptomatic	
Diagnostic criteria	Multiple autoantibodies	Multiple autoantibodies	Clinical symptoms
	No IGT or IFG	Dysglycemia: IFG and/or IGT	Diabetes by standard criteria
		FPG 100-125 mg/dL (5.6-6.9 mmol/L)	
		2-h PG 140-199 mg/dL (7.8-11.0 mmol/L)	
		A1C 5.7-6.4% (39-47 mmol/mol) or ≥10% increase in A1C	

However, the stages of type 1 diabetes are not amenable to intervention for the time being. Many trials to reverse type 1 diabetes did not succeed or had a marginal effect (Trial Net)2. On the other hand, type 2 diabetes maybe prevented or delayed to a great extent at early stages the so called "prediabetes" through lifestyle changes and drugs, eg, metformin. To our opinion, the term prediabetes underestimates the importance of this clinical condition. Around 5—10% of people with prediabetes become diabetic every year. Macrovascular diabetic complications are more common in prediabetes compared to the general population. Prediabetes is linked with increased risks of major manifestations of vascular disease. Cross-sectional studies provide evidence in favor of vascular risk effects of mild or moderate hyperglycaemia because an excess prevalence of coronary disease is reported in people with fasting or postload hyperglycaemia lower than the diabetic threshold3,4 Compared with coronary disease, less certainty exists with respect to cerebrovascular disease and aortic aneurysm. Diabetes is a known risk factor for ischaemic and haemorrhagic stroke, but whether risk increases before development of diabetes remains to be established5 IGT was associated with increased risk of coronary death and total cardiovascular death, independent of the concentration of FPG, although the converse was not the case. Irrespective of whether basal or challenged blood glucose concentration is more important for atherogenesis,average glucose concentra-tions, indexed by HbA1c concentration, predict incident coronary disease. The epidemiological relation between prediabetes and macrovascular disease can be confounded by clustering of vascular risk factors within individuals. Blood glucose in the prediabetic range is correlated with many risk factors, including general and central obesity, blood pressure, and triglyceride and lipoprotein concentrations5 Individual-level evidence from prospective studies suggests that fasting hyperglycaemia, postload glucose, and HbA1c are all robust predictors of vascular mortality3,4 and, according to multivariable adjusted analyses, these associations are independent of vascular risk factors such as obesity, blood pressure, triglyceride, and lipoproteins.4,5 In addition. Microvascular complications are also prevalent in this condition. Prediabetes has been linked to increased risk of early forms of nephropathy and chronic kidney disease, defined by methods such as urinary albumin excretion rate and estimated glomerular filtration rate7-11 NHANES, 1999—2006, showed that the prevalences of microalbuminuria and macroalbuminuria increase as glycaemia worsens—ie, from normoglycaemia (6% prevalence of microalbuminuria and 0·6% prevalence of macroalbuminuria), to IFG (10% and 1·1%), undiagnosed diabetes (29% and 3·3%), or diagnosed diabetes (29% and 7·7%)12 As regards neuropathy, it was found that the strongest supportive evidence is for the association between prediabetes and autonomic neuropathy in particular Studies of prediabetes and sensorimotor neuropathy suggest that small demyelinated fibres might be implicated in IGT and early diabetic neuropathy. Distal intraepidermal nerve fibre density, quantitative sudomotor testing, total sweat volume and arm-to-foot sweat responses, deep tendon reflexes, and temperature sensation are sensitive markers of sensorimotor neuropathy, whereas tests such as the Michigan neuropathy screening instrument, calibrateded tuning fork, and classical nerve conduction tests, and vibration and temperature perception thresholds, might not detect neuropathy in prediabetic people. Finally, evidence is accumulating for increased prevalence of idiopathic polyneuropathy (eg, idiopathic sensory or painful neuropathy, and sensory or small-fibre-only neuropathy) in individuals with prediabetes, with IGT more strongly related to painful than non-painful neuropathy.18-23 Prediabetes might be associated with an increased risk of diabetic retinopathy, although findings vary depending on how diabetic retinopathy is detected. In a study of more than 5000 Pima Indians, retinopathy ascertained by direct ophthalmoscopy was associated with prediabetic status. Measures of retinal vascular changes, such as lower arteriole-to-venule ratio and increased retinal arteriole or venular calibre, have also

been related to prediabetes or increased risk of diabetes, although evidence is not entirely consistent. DDA Executive Board suggest the following stages to be appropriately used for type 2 diabetes staging according to diagnostic criteria and intervention modalities.

Stages	Stage 1	Stage 2	Stage 3
Diagnostic criteria	Diabetes risk score ≥5	IFG and/or IGT	Overt diabetes
Intervention	Life style modification	Life style modification+ metformin	Life style modification +metformin +other drugs

ALBUMINURIA ASSOCIATED WITH A HISTORY OF FOOT ULCER IN PATIENTS WITH TYPE 2 DIABETES: OPPORTUNITIES FOR SCREENING AND ANNUAL MONITORING IN AMBULATORY PODIATRIC CLINICS

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Purpose: Albuminuria can be predictive of morbidity and mortality in patients with type 2 diabetes (T2D), particularly in those hospitalized with diabetic foot ulcers (DFU). Annual albuminuria monitoring, a standard of medical care in people with T2D, is suboptimal in practice and tends to decline over time. The purpose of this pilot study was to assess albuminuria prevalence using point-of-care (POC) testing in a cross-section of patients presenting to an ambulatory podiatric clinic.

Methods: Enrolled subjects gave informed consent and completed a brief questionnaire that encompassed their past medical, surgical, and social history; demographic information; tobacco use history; exercise frequency; and reason for their podiatric clinic appointment. A voided urine specimen was obtained and analyzed using the semi-quantitative Clinitek microalbumin 2 reagent strips to determine the urine albumin-creatinine ratio (UACR). Data were analyzed using the SAS software for Windows version 9.3 (Cary, NC). Chi-square analyses were conducted to determine the association between clinical variables. *P*-value <0.05 was considered statistically significant.

Results: Data on 85 subjects were evaluable and analyzable.

Table 1. Prevalence of Chronic Illness

	N (%)
T2D	41 (48%)
Hypertension	32 (38%)
History of stroke	5 (6%)
History of DFU	28 (33%)

Table 2. Distribution of semi-quantitative UACR results

	N (%)
normal (<30 mg/g)	60 (70.6%)
microalbuminuria (30-300 mg/g)	17 (20%)
macroalbuminuria (>300 mg/g)	8 (9.4%)

Table 3. Comparison of association between Albuminuria and History of DFU

	Normal	Microalbuminuria N (%)	Macroalbuminuria N (%)	P-values
DFU Status				0.0028
History of DFU	13 (46.4%)	10 (35.7%)	5 (17.9%)	
No History of DFU	47 (82.5%)	7 (12.3%)	3 (5.3%)	

Table 4. Prevalence of Albuminuria in relation to Type 2 Diabetes and History of Foot Ulcer

	N	UACR ≥30 mg/g N (%)	P-values*
Combination of T2D and DFU			0.0006
A: T2D and no history of foot ulcers	17	5 (29.4%)	
B: T2D with history of foot ulcers	24	15 (62.5%)	
C: no T2D and no foot ulcers	40	5 (12.5%)	

**Four subjects with history of foot ulcers but no diabetes were excluded from the final analysis due to small sample size.*

Conclusion: Patients with T2D and a history of foot ulcers were twice as likely to have albuminuria as compared to those without a history of DFU and five times more likely than those with neither T2D nor history of foot ulcers. Using POC UACR testing in an ambulatory podiatric clinic offers a convenient and practical setting for screening and annual monitoring for albuminuria in patients with a history of DFU.

ACCEPTANCE OF SELF-ADMINISTERED SUBCUTANEOUS INJECTIONS OF ALIROCUMAB IN PATIENTS WITH TYPE 2 DIABETES AND MIXED DYSLIPIDEMIA: AN ANALYSIS OF THE ODYSSEY DM-DYSLIPIDEMIA STUDY

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Introduction: ODYSSEY DM-DYSLIPIDEMIA (NCT02642159) demonstrated significant reduction in non-high-density lipoprotein cholesterol (non-HDL-C) with alirocumab versus usual care (no additional lipid-lowering therapy; fenofibrate; ezetimibe; omega-3 fatty acid; nicotinic acid) in individuals with type 2 diabetes (T2DM) and mixed dyslipidemia. Alirocumab was administered subcutaneously every 2 weeks. A patient-reported outcome (PRO) was assessed to understand the acceptance of self-injection.

Objective: To measure treatment acceptance of alirocumab self-injections and compare individuals on insulin versus non-insulin anti-hyperglycemic agents. METHODS: The Injection for Treatment Acceptance (I-TAQ), a 22-item validated PRO assessing treatment acceptance on four domains, was administered at Weeks 8 (baseline) and 24 to individuals randomized to alirocumab. Domain scores and an overall summary score from the I-TAQ were converted to a 0–100 scale, with higher score indicative of higher acceptance. The Mann-Whitney test for continuous data was used to assess for significance in the change from baseline scores. Analyses were performed on alirocumab-treated patients who self-injected and completed the I-TAQ on at least one time-point.

Results: In total, 249 individuals were included in the analysis. Baseline acceptance scores were similar between the two groups. Mean domain scores at baseline were: perceived efficacy (58.78), acceptance of side effect (96.40), injection self-efficacy (89.26), injection convenience (87.29). Scores did not differ between baseline to Week 24, nor between the two groups.

Conclusion: The acceptance of alirocumab injections was high overall, irrespective of prior experience with insulin injections. These results show that alirocumab is associated with favorable ease of use, convenience, and side effect profile.

GENETIC SUSCEPTIBILITY OF VITAMIN D RECEPTOR (VDR) GENE VARIANTS (BSMI, TAQI AND FOKI) TO CORONARY ARTERY DISEASE IN ASIAN INDIANS

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Vitamin D receptor is a probable candidate gene for the development of Coronary artery disease (CAD). The present study was planned to examine the role of single nucleotide polymorphisms (SNPs) in VDR gene and CAD risk in Indians. For this purpose, we included 410 CAD patients and 414 controls to examine the 3 SNPs (*BsmI*, *TaqI* and *FokI*) in VDR gene using PCR-RFLP method. In addition, the anthropometric and biochemical characteristics were done in all the subjects. The CAD patients shows pronounced abdominal adiposity reflected by their significantly higher waist circumference (90.7±10.6 vs. 87.5±11.4, p=0.000), waist to hip ratio (0.99±0.10 vs. 0.93±0.10, p=0.000), even at the normal BMI values suggested for Asian Indians. Dyslipidemia, was an established risk factor for development of CAD. The genotyping data revealed that *BsmI*-bb genotype might be associated with 2.2-fold increased risk (OR=2.19; 95% C.I. = 1.48-3.19; p=<0.001) whereas *FokI*-TT homozygotes had a 3.5 fold increased risk for the development of CAD (OR = 3.53; 95% C.I. = 2.33-5.36; p=<0.001). Furthermore, no significant relationship of *TaqI* polymorphism with CAD risk was observed (OR; 1.35, 95% C.I.; 0.91-1.99, p = 0.161). In conclusion, present study demonstrated a significant association of *BsmI* and *FokI* variants of VDR gene with augmented possibility of CAD development in Asian Indian population. The conventional risk factors such as age, abdominal obesity and dyslipidemia were independently linked with the amplified risk of CAD. However, metabolic characteristics are not very affected by VDR gene polymorphisms in Asian Indians.

ASSOCIATION OF HBA1C, SERUM URIC ACID AND NON HDL CHOLESTEROL IN TYPE 2 DIABETES PATIENTS

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Bir Hospital

Introduction: Diabetes mellitus (DM) is a metabolic disease resulting from either insulin deficiency or/and insulin resistance. It is a leading cause of death worldwide. Incidence of cardiovascular events is increased two to four times among diabetic patients when compared with non-diabetic. Hyperglycemia causes increased activity of hepatic lipase that leads to increased clearance of HDL while impaired catabolism of VLDL causes decreased formation of HDL. Thus, the HDL levels decrease in type 2 diabetes. The reduction of cardiovascular risk by lowering low-density lipoprotein cholesterol (LDL-C) is well documented, and LDL-C remains the main target of lipid lowering therapy. However, not all patients with cardiovascular risk have elevated LDL-C. There is growing recognition that non-high-density lipoprotein cholesterol (Non-HDL-C) is strongly related to cardiovascular risk. National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) has recommended using non-HDL cholesterol in assessing CVD risk in patients with diabetes. HbA1c and serum uric acid concentrations are also the independent risk factors and predictors of CVD.

Aims and Objective: To find the association of HbA1c, serum uric acid and Non-HDL-C along with the pattern of dyslipidemia in type 2 DM and correlate HbA1c with fasting blood glucose.

Materials and Methods: This is a hospital based study conducted in Bir hospital. Patients with diagnosis of diabetes for 3 years or more duration were selected for the study. This is a hospital based descriptive and observational study. This study was conducted Bir Hospital from January 2015 to December 2015. The data including the duration of diabetes, physical examination findings and HbA1c, serum uric acid and Lipid profile were collected using preformed proforma. The data was analyzed by computer program, statistical package for social sciences (SPSS). The results were analyzed in tabulated forms and using bar diagrams. Mean values of plasma glucose, lipid profile, HbA1c and standard deviations were calculated. Association of various variable with HbA1c, uric acid and Non HDLc were calculated. Correlations with HbA1c, uric acid and other lipids parameters along with TC/HDLc, LDLc/HDLc and TG/HDLc were calculated using Pearson's Correlation Coefficient. P-values were calculated for these variables.

Results: This study included 125 patients aged between 34 to 81 years. 52% of the patients were male with the mean age of 55.08±1.11 years. The mean duration of diabetes was 6.44± 3.42 years. The mean of FBS, PPBS and HbA1c was 181.84±59.08 mg/dl, 269.48±78.24 mg/dl and 9.68±1.95 %. The mean serum uric acid was 5.68±0.87 mg/dl. Among the diabetes patients, 47.7% of male and 46.6 had uric acid level below 5.5mg/dl. 30% and 43.35 of male and female had uric acid in between 5.5-6.5mg/dl. 21.53% and 10% of male and female respectively had uric acid level more than 6.5mg/dl. In this study, desirable cholesterol was 43.2% with borderline and very high risk was 36.0% and 20.8% respectively. Similarly, 32% had normal LDL level and near optimal, borderline and high risk was 45.6%,16% and 5.6% and 36% of patients had decreased HDLc level and TG was elevate in 68.8%. Among the individual lipid profile HDL was normal in 64% of patients while LDL was in normal in 32%. Among the Cardiac risk ratio, Non-HDL cholesterol was deranged in 80%, TC/HDLc in 39.2%, and LDLc/HDLc deranged in 0.8%. HDL was decreased in 15.2 % of males and 20.8 % of females. Derangements in total cholesterol were seen in 58.3% of females and 55.4 % of males. Dyslipidemia in LDL groups were more in males as compared to females (73.3% and 63.2 % respectively). The dyslipidemia among males was 70.7 % and among the females was 66.6% respectively. Non HDLc were elevated in both male and female in this study. There was positive correlation of total cholesterol and fasting blood sugar with HbA1c (p value<0.001). However, there is no association of HbA1c with uric acid level. There is the strong correlation of Non HDLc with TC/HDLc and LDLc /HDLc (p-value <0.001).

Conclusion: The association between abnormal lipid levels and cardiovascular risk is evident among patients with diabetes mellitus. In this study there is the correlation with FBS, HbA1c and NON HDLc cholesterol. Hence Non-HDL cholesterol proves to be more sensitive and a better predictor of cardiovascular risks than LDL cholesterol. HbA1c and serum uric acid concentrations are also the independent risk factors and predictors of CVD in diabetes patients which were not correlated in this study. Key words Dyslipidemia, Non-HDLc, Uric acid, Diabetes

IL-4 GENE LENTIVIRAL TRANSDUCTION TO MATURE ADIPOCYTES HAS POSITIVE LONG-TERM EFFECTS ON THEIR INSULIN SENSITIVITY, BUT THESE EFFECTS ARE NOT MEDIATED BY STAT6

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Obesity is a growing problem associated with high risks of metabolic abnormalities. Activation of latent inflammation in adipose tissue of obese individuals can cause insulin resistance and lead to development of metabolic diseases. We hypothesized that IL-4 is able to influence adipocytes directly and restore their insulin signaling activity in insulin resistant states. Previously, we have shown, that IL-4 in concentration 50 ng/ml restores activity of insulin signaling (phosphorylation of IRS-1, Akt and AS160) after induction of IR with palmitic acid without any action on adipogenic differentiation. After that we have created mature adipocytes 3T3-L1 with hyperexpression of IL-4 by lentiviral transduction. After lentiviral transduction with IL-4 we observed high expression (70 ng/ml) in transgenic cells. Studies of their insulin sensitivity have shown that hyperexpression of IL-4 in adipocytes has positive effect not only on insulin signaling activity, but also on glucose uptake. We have checked possible mechanisms of action IL-4 on mature adipocytes. We have demonstrated, that classic IL-4 activated trans-factor STAT6 activates (immunoblotting) and translocates to nucleus (ICC) in response to IL-4 only on condition less than 6 hours of incubation. Long-term effects of IL-4 on insulin sensitivity of mature adipocytes didn't mediate by STAT6. The data obtained indicate that anti-inflammatory cytokine IL-4 can promote insulin sensitivity of adipocytes. Nevertheless, mechanisms of long-term effects of IL-4 to mature adipocytes remain unclear. It is possible, that IL-4 inhibits inflammation activated kinases that impair insulin cascade in adipocytes. These findings indicate the potential use of IL-4 for the IR treatment. This work was supported by RFBR grant #17-34-80026.

IDENTIFYING THE SEVERITY DEPRESSION AMONG PATIENTS DIAGNOSED WITH HYPERTENSION. DO WE NEED EMOTIONAL SUPPORT GROUPS?

Arooj Fatima

Sir Ganga Ram Hospital

Background: Depression plays an important role among patients diagnosed with hypertension. It is believed that hypertensive distress is recognized as major psychological issue in Pakistan. Our study aims to identify hypertension associated distress among Pakistani patients diagnosed with type II hypertension. We also aim to find out the relationship among depression, distress caused by hypertension and cardiovascular diseases.

Methods: A cross sectional study was conducted in Sir GangaRam Hospital Lahore during February 2015 to June 2016. Total 80 patients diagnosed with hypertension were included in the study. Blood pressure and certain laboratory investigations were done including total cholesterol, LDL, VLDL and HDL. A personalized health questionnaire was used to classify depression among patients. Hypertension distress scale was used to identify hypertension distress and other factors such as social distress, interpersonal distress, physician related distress, emotional distress and regimen related distress.

Results: The rate of depression was 39% among patients diagnosed with hypertension. 8% were categorized as mild depression, 14% moderate depression and 17% with severe depression. Hypertensive depression was found in 71% of the selected population. Rates of social distress, interpersonal distress, physician related distress, emotional distress, regimen related distress were 23%, 33.5%, 17.8%, 73.4% and 42.6 respectively. There was no association between depression and low HDL.

Conclusions: Our study concludes that hypertensive distress is very common among patients in Pakistan and this is an alarming condition for Pakistani population. We need to develop and modify our management plans in order to combat this deadly distress. Mass media should be involved in order to raise awareness about hypertensive distress and depression.

KNOWLEDGE ASSESSMENT OF TYPE 2 DIABETES MELLITUS IN PAKISTAN

Arooj Fatima

Sir Ganga Ram Hospital

Objective: We aim to assess the knowledge, behavioral and environmental risk factors and complications of type 2 Diabetes Mellitus among non-diabetics in Pakistan.

Methodology: A cross sectional study was conducted in peripheral areas of Lahore, Pakistan during the month of January 2015. A structured questionnaire was established that targeted 350 population >18 years. The questionnaire was designed to access knowledge, associated risk factors and complications of Diabetes Mellitus. Knowledge was assessed and risk assessment scoring was performed according to the guidelines of American Diabetic Association. Using SPSS, data was analyzed, frequencies were calculated, and p-values were determined to find associations between the variables.

Results: Out of 350 people subjected to the survey, only 130 adults (37%) had any awareness of Diabetes Mellitus. Knowledge regarding cause, signs, symptoms, risk factors and complications was found inadequate. Practices regarding diet and life style were also found unsatisfactory. Awareness of risk factors was present in 110 (31%) of targeted population. About 41% individuals were found obese and 28% were overweight and on risk assessment score 62% were found at high risk, 48% at low risk of developing diabetes mellitus. Awareness of complications was present only in 16%. Gender male, education and urban residence showed significantly better knowledge regarding diabetes but scored more on risk assessment scale due to poor dietary habits and lack of physical activity.

Conclusion: We concluded that a significant number of people have little or no awareness of Diabetes Mellitus. A formal, structured approach should be designed to deliver the necessary educational information especially in the peripheral areas of Pakistan. The proportion of individuals found high risk and low risk needs further screening for diabetes. It should be our ultimate goal to prevent the morbidity and mortality of Diabetes Mellitus among non-diabetics by raising public awareness of the disease through outreach programs and mass media.

MATERNAL ENDOTHELIUM AND RISK OF DEVELOPING CARDIOVASCULAR DISEASES

Arooj Fatima

Sir Ganga Ram Hospital

Objective Background: In Pakistan, it has been strongly suggested that women with hypertensive disorders of pregnancy are at risk of developing cardiovascular disorders. Our objective was to ascertain the persistence of endothelial activation in hypertensive pregnancies compared to women with normal pregnancies.

Methods: Case control study design was chosen in two matched group. Endothelial activation was determined by the evaluation of adhesion molecules namely P selectin, E-selectin, Intercellular adhesion molecules-1(ICAM-1) and vascular cellular adhesion molecules-1 (VCAM-1).

Results: In the first study, adhesion molecules were measured in 40 women with hypertensive pregnancies and in a matched control group with an uncomplicated pregnancy one month and three months after delivery. In the second study, adhesion molecules were measured in 40 patients with a history of HELLP syndrome several years after pregnancy and in 40 matched controls. Shortly after the delivery, increased levels of soluble adhesion molecules were found in women with hypertensive complications. However, women with uncomplicated pregnancy did not have any increase level of soluble adhesion molecules. Significant differences were still present, several years after delivery comparing levels of adhesion molecules in women with a history of HELLP syndrome with those found in control patients. An abnormal activation of endothelium was seen in hypertensive pregnancies.

Conclusion: It has also been concluded that is abnormal activation of endothelium remains increased even after delivery which pre disposes the patient towards cardiovascular disorder. The risk of cardiovascular complications including ischemic heart diseases, chronic hypertension and stroke is more commonly seen in women experiencing HELLP syndrome.

HYPERGLYCEMIA AND BETA CELL FUNCTION IN PREGNANCY

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Background: Hyperglycemia is the most common metabolic disorder in pregnancy and it complicates one in six pregnancies. AIM To evaluate beta cell function and prevalence of Hyperglycemia first detected in pregnancy.

Method: It was an observational study of 300 women with singleton pregnancy. Fasting serum c-peptide (FCP) and Oral Glucose Tolerance Test (OGTT) were done. Hyperglycemia first detected in pregnancy was diagnosed using World Health Organization (WHO) 2013 criteria. Homeostatic model assessment 2 calculator was used to calculate beta cell function (HOMA2%β), insulin resistance (HOMA2IR) and insulin sensitivity (HOMA2%S). They were followed up to delivery.

Results: The prevalence of Gestational Diabetes Mellitus was 22%, Diabetes in Pregnancy (DIP) was 2% and the rest had normal glucose tolerance (NGT). The mean age (years) of subjects with NGT was 30.1± 4.4, GDM 32 ± 3.9, and DIP 35.3 ± 2.3. The median FPG (mmol/l) IQR for NGT, GDM and DIP were 3.7 (3.3-4.2), 5.2 (5.2-5.6), and 7.4 (7.1-7.5) respectively. The median 2HPG (mmol/l) for NGT, GDM and DIP were 4.9 (4.1 – 6.0), GDM 7.7 (7.0 – 8.2), DIP 10.7 (9.0 – 12.5) respectively. The median FCP (nmol/l) were 0.3 (0.3 – 0.4), 0.5 (0.4 – 0.7), 0.7 (0.3 – 0.9) respectively. The differences in beta cell function between NGT, GDM and DIP were all statistically significant using the HOMA calculators.

Conclusion: The prevalence of hyperglycemia first detected in pregnancy is high. Pregnant women with hyperglycemia have greater pancreatic beta cell dysfunction and increased rate of adverse pregnancy outcomes.

IMPROVEMENT OF INFLAMMATORY AND CARDIOMETABOLIC BIOMARKERS IN OBESE ADOLESCENTS AFTER LONG-TERM LIFESTYLE INTERVENTION

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Background: Evidences have demonstrated that long-term lifestyle intervention is considered an important strategy in reducing inflammation and cardiovascular risks in obese children and adolescents. However, further exploration is needed to identify mechanism that can better modulate the link between the inflammation and caridometabolic risk factors in obese subjects.

Objective: The purpose of the present study was to evaluate if long-term lifestyle intervention can improve the inflammatory and cardiometabolic biomarkers. The second aim was to evaluate if there is association between changes in anthropometrics, inflammatory and cardiometabolic biomarkers in obese adolescents submitted to a 2-year lifestyle intervention.

Methods: The study involved 32 obese adolescents (12.6±1.9 years), who were divided according to their response to intervention at endpoint of the first year: Response with reduced Zscore-BMI (R, n=21) and Non-response without reduced Zscore-BMI (NR, n=11). The lifestyle intervention consisted of a 2-year period of nutritional and physical activity recommendation.

Results: After 1-year intervention, the obese subjects with R improved in the metabolic profile, inflammatory (leptin) and cardiometabolic (PAI-1) biomarkers, such improvement maintained after 2-year intervention. In contrast, the obese subjects with NR only showed decreased triglycerides and total cholesterol after 2-year intervention. No difference was observed in adiponectin and RBP4 in both groups after 2-year intervention. Additionally, changes in leptin and PAI-1 were positively associated with changes in BMI after 1-year and 2-year intervention in R subjects.

Conclusion: Our results support that long-term lifestyle intervention could control inflammatory and cardiometabolic biomarkers in obese adolescents, which is associated with reduction in body weight.

EVALUATION OF THE GLUCOCARD SHINE EXPRESS BLOOD GLUCOSE MONITORING SYSTEM'S EASE OF USE

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Arkray USA

Background: It is important that Blood Glucose Monitoring Systems (BGMS) are easy to use since they are a critical tool used in the self-management of diabetes, including the prevention of micro and macrovascular complications. The "Ease of Use" consumer study is typically evaluated as part of the FDA 510(k) approval process for BGMS.

Purpose: The objective of this study was to evaluate the Ease of Use of the GLUCOCARD Shine Express BGMS.

Methods: A total of 20 subjects aged 26 to 89 participated in the study at ARKRAY in Minneapolis, Minnesota during August 2018 by performing a fingerstick self-test and answering a questionnaire directed at the Ease of Use of the device and test strip. All of the subjects responded to the topics in the questionnaire which included, "Removing a Test Strip from Bottle", "Inserting a Test Strip into Meter", "Removing a Test Strip from Meter", "Performing a Blood Glucose Test from your Fingertip" and "Reading Meter Display". The subjects were asked to rate the topics as Very Easy, Easy, OK, Difficult, or Very Difficult. For evaluation purposes, these topics were grouped as Positive [Very Easy/Easy/OK] and Negative [Difficult/Very Difficult].

Results: All of the subjects scored the GLUCOCARD Shine Express BGMS favorably with all five questions receiving positive ratings [Very Easy/Easy/OK]. Only "Removing a Test Strip from Bottle" received one OK response with the remaining scores being Very Easy or Easy.

Conclusion: The GLUCOCARD Shine Express BGMS scored an overall average 100.0% positive Ease of Use rating by the subjects.

THE SMALL MOLECULE INDIRUBIN-3'-OXIME ACTIVATES WNT/B-CATENIN SIGNALING AND INHIBITS INSULIN RESISTANCE AND OBESITY

Seol Hwa Seo; Olivia mina Choi; Kang-Yell Choi

Yonsei University

Adipocytes have a fundamental role in regulating whole-body metabolic homeostasis by storing and releasing fuel-based on energy demands. However, excess storage of energy causes obesity, type 2 diabetes, metabolic diseases and atherosclerosis. There have been recent efforts to suppress obesity through pharmacological treatment; however, these treatments have had limited efficacy and serious side effects. Therefore, a major need in the treatment of obesity is to identify for a safe therapeutic agent that reduces adipose tissue and inhibits obesity on a long-term basis. Recent studies have assigned particular importance to the activated Wnt/b-catenin pathway because of its role in inhibiting adipogenesis. Activation of the Wnt/b-catenin pathway leads to increased levels of b-catenin and a concomitant decrement of PPARg and C/EBPa, transcription factors that activate the expression of adipocyte genes. The Wnt signaling pathway may therefore be an attractive target for the development of anti-obesity drugs. In light of this, we used a systematic cell-based screening approach to identify small-molecule activators of the Wnt/b-catenin pathway and examined their anti-adipogenic effects. From a chemical library of pharmacologically active compounds, we selected indirubin-3'-oxime (I3O), a synthesized analog of indirubin, as a model compound to characterize the effects of activating the Wnt/b-catenin pathway with respect to inhibiting adipogenesis in vitro and obesity in vivo. In this study, we show that I3O may be an effective yet safe therapeutic agent to inhibit adipogenesis in 3T3-L1 preadipocytes, and may prevent obesity and metabolic syndrome in vivo by activating the Wnt/b-catenin pathway. Thus, I3O potentially represents a new class of anti-obesity drugs.

PERSICARIA HYDOPIPER (L.) SPACH AND ITS INGREDIENTS, ISOQUERCITRIN AND ISORHAMNETIN, INHIBIT ADIOPOCYTE DIFFERENTIATION OF 3T3-L1 CELLS BY ACTIVATING THE WNT/B-CATENIN PATHWAY

Eun-Hwan Kim; Soung Hoon Lee; Kang Yell Choi

Yonsei University

Obesity, which is related to metabolic syndrome and is associated with liver disease, represents an epidemic problem demanding effective therapeutic strategies. Evidence shows that the Wnt/β catenin pathway is closely associated with obesity and that small molecules regulating the Wnt/β catenin pathway can potentially control adipogenesis related to obesity. Eleven plant extracts activating the Wnt/β catenin pathway were screened by using HEK293 TOP cells retaining the Wnt/β catenin signaling reporter gene. An extract of Persicaria hydropiper (L.) Spach was found to activate Wnt/β catenin signaling. P. hydropiper is grown worldwide in temperate climates and is found widely in Southeast Asia. The P. hydropiper extract inhibited the differentiation of adipocyte 3T3 L1 cells. Isoquercitrin and isorhamnetin, constituents of P. hydropiper, also activated Wnt/β catenin signaling and suppressed the differentiation of 3T3 L1 cells. These results indicate that isoquercitrin in P. hydropiper suppresses the adipogenesis of 3T3 L1 cells via the inhibition of Wnt/β catenin signaling. P. hydropiper and isoquercitrin may therefore be potential therapeutic agents for obesity and its associated disorders.

PERFORMANCE OF THE GLUCOCARD® SHINE EXPRESS BLOOD GLUCOSE MONITORING SYSTEM COMPARED TO FDA 2016 GUIDANCE ACCURACY CRITERIA

Julie Walker, RN, BSN, PHN; Patricia Gill, BA, MLT; Danielle Maher, BS; John Gleisner, BS, PhD

Arkray USA

Background: Blood Glucose Monitoring Systems (BGMS) are important tools used in the management of diabetes mellitus. Accurate BGMS readings are needed to prevent potential micro and macrovascular complications due to uncontrolled blood glucose levels. The FDA's 2016 Guidance, "Self-Monitoring Blood Glucose Test Systems for Over-the-Counter (OTC) Use", is FDA's recommendation for measuring the accuracy of OTC BGMS. The accuracy boundaries of the guidance require that 95% of all results fall within ±15% of reference and 99% within ±20% of reference.

Purpose: This study evaluated the GLUCOCARD® Shine Express BGMS performance against the accuracy boundaries set by the FDA's 2016 Guidance.

Methods: Three lots of test strips were evaluated in a side-by-side comparison at ARKRAY in Minneapolis, Minnesota. Blood samples were drawn from the fingertip of people with diabetes (n=180) by trained laboratory professionals in July 2018. Reference values were obtained using the YSI Model 2300 Analyzer. Data was evaluated against the accuracy boundaries of the FDA's 2016 Guidance for Self-Monitoring Blood Glucose Test Systems for OTC Use.

Results: All three lots of GLUCOCARD® Shine Express BGMS performed within the accuracy boundaries. 98.9% (178/180) of the combined results for the three lots fell within the ±15% of reference and 100.0% (180/180) were within ±20% of reference. Overall bias was 0.3% and the correlation coefficient (r) was 0.99.

Conclusion: The GLUCOCARD® Shine Express BGMS performed within the accuracy boundaries of the FDA's 2016 Guidance for Self-Monitoring Blood Glucose Test Systems for OTC Use.

EVALUATION OF EMPATHIC COMMUNICATION IN THE PHYSICIAN-TO-PATIENT RELATIONSHIP AND GLYCEMIC CONTROL IN POPULATION WITH TYPE 2 DIABETES MELLITUS

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Introduction: Empathic communication between the physician and patients have been suggested to own potential impact on patient's attitude toward his disease (1,2). However, there are no studies specifically designed to assess the role of assertive Physician-to-Patient Communication (Ph-t-PaC) in control of diseases such as Type 2 Diabetes Mellitus (t2DM) (3).

Objective: To evaluate the quality of empathic Ph-t-PaC and glycemic control in population with t2DM.

Material and methods: Cross-sectional, observational study design. Physicians (Internal Medicine, n=4), prescribing pharmacological therapy and performing medical follow up for metabolic control of patients with t2DM, participated in the study. The Jefferson Scale of Patient Perceptions of Physician Empathy (JSPPPE) was applied to patients with t2DM immediately after medical consultation and a 8-hours fasting venous blood sample was obtained (HbA1c was determined by standard ELISA method). The distribution of HbA1c was compared according to an empathy cutoff during Ph-t-PaC, as reported by the patient. In addition, Spearman's correlation analysis between the values obtained in the JSPPPE and HbA1c was performed.

Table. Population Characteristics (n=36)

Physicians	# Pts attended/ physician	Age	% male	Empathy (JSPPPE)	HbA1c
Physician No. 1	8	54 ± 8.1	50.0	33 ± 1.2	8.7 ± 1.9
Physician No. 2	12	60 ± 12.1	66.6	34 ± 1.1	8.7 ± 2.7
Physician No. 3	10	59 ± 12.8	60.0	34 ± 1.2	9.5 ± 4.3
Physician No. 4	6	69 ± 12.2	33.3	34 ± 0.4	7.7 ± 4.3

Results: A total of 36 patients with t2DM participated in the study (Table). We observed values of HbA1c that were slightly lower in the group with higher JSPPPE score (for JSPPPE >34, HbA1c 8.5±3.5; JSPPPE <34, HbA1c 9.1±3.0). In addition, we found that Ph-t-PaC was related with HbA1c, but in different ways according to each physician (Figure), being negative correlations the most significant.

Conclusion: The quality of communication between physician-to-patient is related to indicators of glycemic control in population with t2DM.

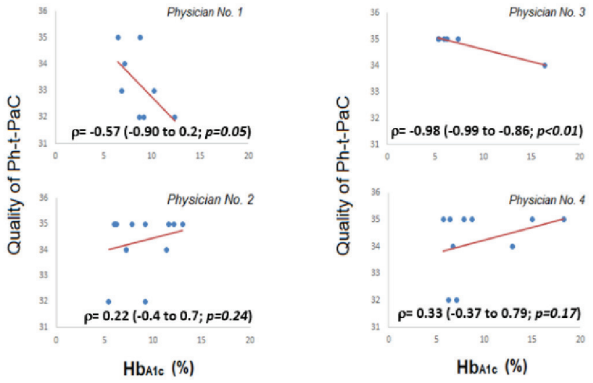

Fig. Relation of Ph-t-PaC with HbA1c, divided by each physician.

ADIPONECTIN SECRETION BY PRIMARY HUMAN ADIPOCYTES IN PATIENTS WITH AND WITHOUT REMISSION OF TYPE 2 DIABETES MELLITUS AFTER BARIATRIC SURGERY

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National Medical Center, "20 de Noviembre" ISSSTE

Introduction: The remission of type 2 Diabetes Mellitus (t2DM) after bariatric surgery has been associated with the secretion of several adipokines, where adiponectin plays a key role. Adipocytes are largely responsible for adiponectin production; however, adipocyte's basal production of adiponectin or their stimulated production have not been explored during t2DM remission.

Aim: To characterize adiponectin secretion by cultured primary human adipocytes in patients with and without remission of t2DM after bariatric surgery.

Methods: This observational, longitudinal study. Candidates for bariatric surgery were included. Clinical and biochemical data, as well as plasma adiponectin (ELISA), were recorded at recruitment and after 6 months from bariatric surgery. Clinical follow up was performed in order to document remission of t2DM. During bariatric surgery, primary human adipocytes were derived from omental fat, and adiponectin production was evaluated at control and niacin-stimulated culture conditions.

Results: Fifteen patients were included, and 8 (53%) of them showed t2DM remission. Higher (P=0.002) plasma adiponectin was observed in patients with t2DM remission after 6 months from surgery. Besides, significant difference (P=0.04) was documented in primary human adipocytes after niacin stimulation.

Conclusion: Increase in plasma adiponectin concentration and stimulated adipocyte's response of adiponectin secretion in culture were related with remission of t2DM after bariatric surgery.

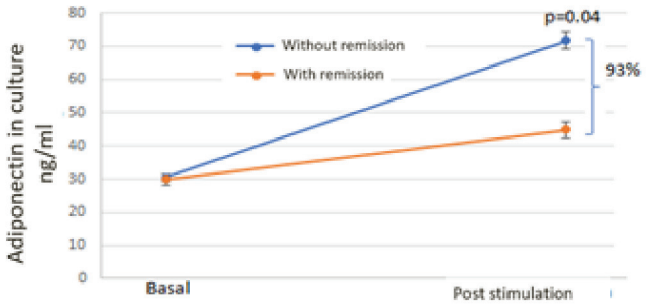

Fig. 1. Basal adiponectin concentration in culture, and after niacin stimulation.

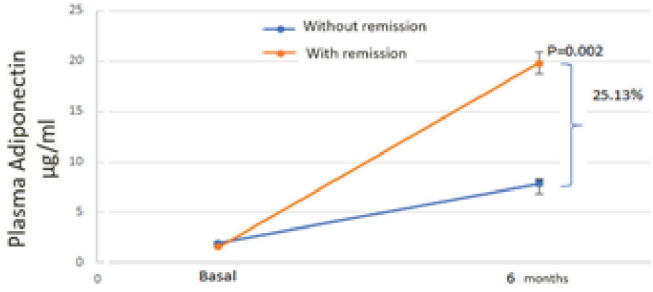

Fig. 2. Basal plasma adiponectin concentration and after 6 months from bariatric surgery.

LOW DOSE SPIRONOLACTONE SUPPRESSES GLYCOGEN SYNTHASE KINASE-3 AND PREVENTS OBESE-INSULIN RESISTANCE IN ESTROGEN-DEPRIVED RATS

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Background: Various hormonal therapies have been formulated to combat the cardiovascular disease (CVD) risks in postmenopausal women but the beneficial effects have not been consistent. Elevated glycogen synthase kinase-3 (GSK-3) has been associated with abnormal cardiometabolic effects. Spironolactone is a well-known antagonist of mineralocorticoid receptor.

Objectives: We therefore tested the hypothesis that estrogen deprivation will cause obese-insulin resistance and elevated GSK-3 that would be accompanied by increased mineralocorticoid and glucocorticoid. We also aimed at testing the hypothesis that low-dose spironolactone would ameliorate these abnormalities by replenishing estrogen and suppressing mineralocorticoid/glucocorticoid/GSK-3 pathway. Methods: Ten weeks old female Wistar rats were divided into four groups; sham-operated (SHM), spironolactone (SPL; 0.25 mg/kg) and ovariectomized (OVX) rats treated with or without spironolactone daily for 8 weeks after which analyses were done.

Results: The results indicate that estrogen deprivation through ovariectomy caused obesity with insulin resistance (IR) that are accompanied by increased pancreatic-β cell dysfunction, glucose intolerance, platelet/lymphocyte ratio, hyperinsulinemia, atherogenic dyslipidemia, GSK-3, corticosterone, aldosterone and depressed 17β-estradiol. Treatment with spironolactone reversed all these abnormalities.

Conclusion: Low-dose spironolactone improves obesity and IR, which appears to involve replenishment of estrogen and suppression of GSK-3 along with circulating mineralocorticoids and glucocorticoids. Therefore, spironolactone may be an adjuvant pharmacological therapy for cardiometabolic disorder induced by estrogen deprivation.

NOVEL COUNTER REGULATORY EFFECTS OF INSULIN AND ISOPROTERENOL ON NA+/H+ EXCHANGE IN RAT ADIPOCYTES

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Epididymal fat cells are very sensitive to pH changes; alkaline pH stimulates, while acidic pH inhibits, both the insulin receptor binding affinity (IRBA) and glucose transport (GT) activity (1,2). Fat cells possess an amiloride-sensitive Na+/H+ exchange mechanism which regulates intracellular pH (pHi) by a Na+-specific and pH-dependent mechanism (3). The Na+/H+ exchanger is very responsive to insulin and isoproterenol (Iso), the main regulators of GT (3, 4). We studied the activity of the Na+/H+ exchanger, a major regulator of pHi, in the absence of HCO3- and in the presence of ouabain, an inhibitor of Na+/K+ ATPase. Alterations of the pHi were monitored with 2',7'-bis (carboxyethyl)-5 (6)-carboxy-fluorescein (BCECF) and Na+ transport was monitored by measuring 22Na+ uptake. The results have shown that Iso (300 nM), which is known to inhibit both IRBA and GT by 50% (5), decreases the resting pHi from 7.26 ± 0.05 to 7.03 ± 0.09, p<0.05. Also, Iso completely inhibited the recovery of the acidified pHi and the 22Na+ uptake by 81% by blocking the Na+/H+ exchanger (control: 0.365 ± 0.019, Iso 0.069 ± 0.006 nmoles/105 cells/2.5 min, p<0.0001). Both of these effects are induced via β2-adrenergic receptor stimulation, adenylate cyclase activation, and a cAMP-dependent mechanism (4). Insulin (1 nM), which is known to increase the IRBA and GT (6), raised pHi by 0.1-0.2 units and increased 22Na+ uptake by >15% over control cells by stimulating the Na+/H+ exchanger. Moreover, insulin blocked the inhibitory effect of Iso and alkalinized the Iso-acidified pHi from 7.03 ± 0.09 to 7.18 ± 0.04, p<0.05; an effect mediated via the activation of the Na+/H+ antiport. Also, insulin blocked the inhibitory effect of Iso on 22Na+ uptake and increased Na+ influx by >400% (Iso: 0.059 ± 0.007, insulin+Iso: 0.244 ± 0.014 nmoles/105 cells/2.5 min, p<0.009). Thus, pHi is regulated mainly through the antagonistic actions of insulin and Iso on the Na+/H+ exchanger. The effects of insulin and Iso on pHi and GT occur simultaneously, suggesting the regulatory role of pHi on GT: acidic pHi inhibits while alkaline pHi stimulates glucose transport. Whether the two functions are taking place at the same time in parallel without affecting each other or whether pHi changes affect one of the intermediate steps of the insulin or Iso signaling pathways, still needs to be elucidated. 1) Sonne et al., J.B.C. 256: 6250, 1981. 2) Toyoda et al., J.B.C. 261: 2117, 1986. 3) Arsenis et al., Endocrinology 136: 1920, 1995. 4) Arsenis et al., Endocrinology 136: 3128, 1995 5) Arsenis et al., Endocrinology 119: 50, 1986. 6) Olefsky et al., Diabetes 30: 148, 1981.

EFFECTIVENESS OF PANCHKARMA BASED HEART FAILURE REVERSAL THERAPY IN PATIENTS OF HEART FAILURE WITH DIABETES MELLITUS: AN OBSERVATIONAL STUDY

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Heart failure (HF) is one of the most common forms of cardiovascular disease, which is defined pathologically by inability of heart to perform its routine function i.e. to get filled and pump out blood to the other parts of the body. The prevalence of HF is continuously increasing globally. In Swedish Natural Diabetes Registry, it was found that incidence of HF increased linearly with increase in glycosylated hemoglobin (HbA1C). The present study was undertaken with the pursuit of studying the effectiveness of heart failure replacement therapy/HFRT on VO2 max, HbA1c, systolic blood pressure (SBP), diastolic BP (BP), BMI and dependency on conventional medicines. The present study was observational one, conducted at Madhavbaug clinics all over Maharashtra, India. Total duration of study was two years from May 2016 to April 2018 and included patients of HF with HbA1c > 6.5. HFRT was given for minimum 7 settings over a period of 90 days (±15 days). All the parameters mentioned above were measured again at day 90 and finding were compared with baseline. 33 patients completed HFRT and were included for analysis. VO2 max showed significant improvement from 16.91±5.94 at baseline to 29.81±6.57 at day 90 (p<0.0005). HbA1c reduced from 8.34±1.53 at baseline to 6.77±1.56 at day 90 (p<0.0005), BMI from 27.90±3.2 to 25.68±2.94 (p<0.0005), SBP from 132.52±17.33 mmHg at baseline to 123.94 at day 90 (p<0.01) and DBP from 81.16±9.62 at baseline to 76±7.47 mm Hg at day 90 (p<0.01). The study findings showed significant improvement in all vital parameters of HF and diabetes i.e. VO2max, BMI, SBP, DBP which is anticipated to have a positive impact on patient's health status.

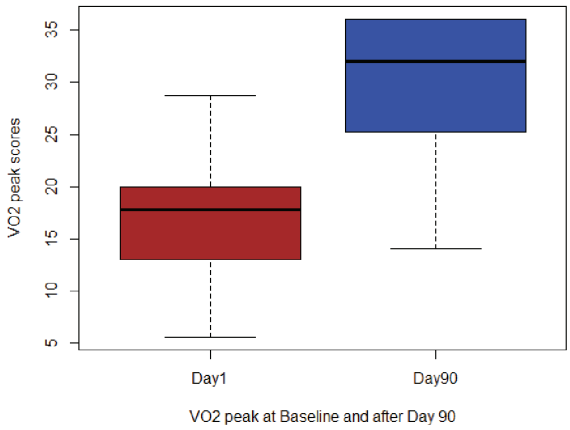

Fig. Comparison of VO2 peak at Baseline and Day 90

IMPACT OF AYURVEDA-BASED HEART FAILURE REVERSAL THERAPY PROGRAM ON 2D ECHOCARDIOGRAPHY AND VO2PEAK IN CHRONIC HEART FAILURE PATIENTS WITH REDUCED EJECTION FRACTION (> 40)

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In India, it is estimated that 1.3 and 4.6 million people are affected by CHF, which roughly means a prevalence of 0.12–0.44 %. Echocardiography is very valuable in the risk stratification of HFrEF (heart failure with reduced ejection fraction) patients. The patients with heart failure have shown reduced functional capacity, which in turn affects quality of life. Also, VO2peak (maximum aerobic capacity and independent predictor of mortality) can be derived from cardiac stress testing. Thus, this study was conducted to observe the impact of Ayurveda-based Heart Failure Reversal treatment with 2D-echocardiography and maximum aerobic capacity improvement on patients suffering from HFrEF. This observational study was conducted from April 2017-April 2018, wherein the data of HFrEF patients who attended out-patient departments (OPDs) at Madhavbaug clinics in Nashik, Maharashtra were identified. Data of patients who were administered HFRT (60-75 minutes) with minimum 7 sittings over 90 days (± 15 days) were considered. The Panchkarma treatment used under this program are Snehana i.e. oleation, Swedana i.e. passive heat therapy, Hridaydhara i.e. concoction dripping treatment and Basti i.e. per rectal drug administration. Variables like 2D echo, VO2 peak, SBP, DBP and BMI were compared between day 1 and day 90 of the HFRT. Out of 13 enrolled patients, mostly males (9) were considered for data analysis. There was significant improvement in 2D echo by 12.85% (from 25.62 ± 5.55 to 38.46 ± 7.47) and VO2peak by 1.78 (from 11.69 ± 1.7 to 13.47 ± 1.62; p<0.001) after the 90th day of therapy as compared to baseline. There was reduction in SBP(p<0.55), DBP (p<0.81), BMI (p<0.21) but was not significant. Ayurveda-based HFRT was found to be effective in management of HFrEF patients with the improvement in 2D echocardiography and VO2 peak.

CARDIOPROTECTIVE ACTION OF AYURVEDA HERBS ALONG WITH LOW CARBOHYDRATE DIET IN ADULT INDIAN WOMEN WITH OBESITY

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Obesity is strongly associated with coronary heart disease and it is known as an independent risk factor for the development of numerous cardiac diseases such as coronary heart disease (CHD), heart failure (HF), and sudden death because of its impact on the cardiovascular system and other risk factors in the CVD population. Hence, this study was conducted to observe the efficacy of Obesity Care Plan and Low Carb Diet on obese adult Indian women. This observational study was conducted from August 2017-April 2018. Data of female obese patients (BMI >28 kg/m2) who had received minimum 7 sittings over 90 days (±15 days) and were following diet plan (800 kcal) consisting 35% carbohydrate, 25% protein, 40% fat. diet in the out-patient departments (OPDs) at Madhavbaug clinics in Kolhapur, Maharashtra was identified. The patients were administered with Panchkarma therapy namely Snehana i.e. oleation (Azadirachta indica), Swedana i.e. passive heat therapy and Basti i.e. per rectal drug administration (Dolichos biflorus, Piper betle and Gymnema sylvestre). In this study, the variables namely Weight, body mass index (BMI), abdominal Girth, SBP, DBP and dependency on concomitant medicines were assessed on day 1 and day 90 follow-up. Seventeen female patients (mean age: 47.06 ± 9.7 yrs) were considered for analysis. There was significant reduction in BMI by 3.39 kg/m^2 (from 32.72 ± 4.52 to 29.33 ± 2.77; p<0.001) and abdominal girth by 5.85 cm (from 101.91±6.71 to 96.06±5.64; p<0.001). Also, weight by 7.91 kg (from 77.07± 9.5 to 69.16±6.51; p<0.001), SBP by 22.41 mmHg (from 134.71±19.72 to 112.29±11.49; p<0.001) and DBP by 16.24 (from 90.59±10.88 to 74.35±9.12; p<0.001) also showed significant reduction. Dependency on concomitant medicines was reduced, with number of patients on no concomitant medicines increasing from 52% to 70%. Obesity Care Plan and Low Carb diet was found to be effective by reducing BMI and abdominal girth in adult Indian women with obesity.

IMPACT OF PANCHKARMA THERAPY AND DIETARY MANAGEMENT ON RESTORATION OF NORMAL GLUCOSE METABOLISM TYPE II DIABETIC PATIENTS: AN OBSERVATIONAL STUDY

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Type-II Diabetes is known as progressive condition which becomes worse as age progresses, despite of all pharmacological measures type-II diabetic has to start insulin therapy after 10 years. Central obesity is prime cause of insulin resistance and impaired glucose metabolism. Several studies in have already suggested that weight reduction can reduce insulin resistance and restore normal beta cell function. So here in this study we plan to observe effect of Low Carbohydrate diet with panchkarma on restoration of normal glucose metabolism. In this observational study, the data of 39 patients (history diabetes and HbA1c > 6.5) from January 2017-April 2018 in the out-patient departments (OPDs) at Madhavbaug clinics was collected. These patients received panchkarma treatment and had followed a diet plan of 800kcal with low-carbohydrate and moderate fat and protein diet. HbA1c, body mass index (BMI), abdominal girth, dependency on medications were assessed on baseline and after 6-month follow-up of treatment. Fasting, and 120 minutes blood glucose levels were also measured on 6-month follow-up, based on reducing blood sugar levels all antidiabetic medicines were tapered. OGTT was performed after Hba1c drops to >6 % with all antidiabetic medicines tapered. 39 participants (25 males, 14 females) were enrolled. Mean HbA1c measured at 6-month followup was significantly lower than that on baseline by 1.65% (from 7.55 ± 1.33 to 5.9 ± 0.49, p<0.001) and mean BMI by 2.94 kg/m2 (from 27.06 ± 3.5 to 24.12 ± 2.69, p<0.001). Dependency on concomitant medicines was also reduced from number of patients increased from not taking OHA medicine on baseline to 60-day follow-up (23% to 53%). Also, we observed that among these 39 subjects, 22 subjects were found to be OGTT negative (FPG: < 100 mg/dl and 2h-PG: < 140 mg/dl) and 17 subjects were found to be Prediabetic (FPG: < 126 mg/dl and 2h-PG: 140-199 mg/dl). Panchkarma treatment and dietary management was found to be effective in the glycemic control as well restoration of normal glucose metabolism in type-II diabetes.

ASSESSMENT OF THE CORRELATION WITH INSULIN RESISTANCE AND CHRONIC COMPLICATIONS AMONG THE BLACK AFRICAN POPULATION

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Studies showed that insulin resistance may even accelerate the progression of moderate to high risk for developing type 1 diabetes. Clinically, insulin resistance in patients with type 1 diabetes is often recognized by high insulin requirements. The data so far show that in patients with type 1 diabetes there is an association between the presence of metabolic syndrome and diabetic nephropathy and poor glycemic control. Hence this study was aimed to assess to assess the correlation with insulin resistance and chronic complications among the black population. It is also aimed to assess the balance of carbohydrate and lipid metabolism in patients included in the study. This study cross-sectional observational held for a period of three years 2014-2017 the Department of Health Promotion and Public Health at the University College Hospital Ibadan. Calendar exploring patients in the study consisted of an initial full evaluation at inclusion in the study group. We conducted a study of 400 subjects with type 1 diabetes (232 men and 168 women). Chronic complications and major risk factors for type 1 diabetes complications were analyzed in these patients. In our study, the statistical analysis performed observed that insulin resistance measured by the constant low eGDR appears associated with all chronic complications of type 1 diabetes. Thus, insulin resistance assessed by eGDR (estimated glucose disposal rate) ≤ 7.5 mg- kg^{1} min^{-1} was found in 166 patients (41.5%), the average being 10.06 ± 5.56 mg eGDR kg^{-1} min^{-1}. Of the 166 patients with insulin, 66.3% were male and 33.7% female. Age, gender, positive family history of diabetes, duration of the disease, smoking, waist-hip ratio, BMI and dyslipidemia in patients with type 1 diabetes with or without insulin resistance were statistically significantly different. There is a higher prevalence of insulin resistance among patients with disease duration of more than 7-10 years, those with a family history of diabetes (50.6% vs 32.5%) in hypertensive (89.2% compared to 26 5%) and in those with dyslipidemia (61.9% vs 35.1%, $P<0.001$).

METABOLIC DIFFERENCES AMONG CHILDREN OF DIFFERENT ETHNICITIES ARE MAGNIFIED WHEN HEPATIC INSULIN EXTRACTION IS INCLUDED

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[1]Cedars Sinai Medical Center, Diabetes and Obesity Research Institute; [2]University of Alabama at Birmingham

Disposition index (DI) combines insulin sensitivity (SI) and beta-cell function (acute insulin response AIRg), and is a predictor of type 2 diabetes (T2DM). Insulin clearance, an important factor in glucose metabolism, is not included, yet can vary among ethnic groups. Our aim is to examine the differences among the DI in different ethnicities, and group subjects considering not only SI and AIRg, but also fractional hepatic insulin extraction (FEL). We used data from 203 normal glucose tolerant children that underwent FSIGT [55 African American (AA), 88 European American (EA), 60 Hispanic American (HA), ages 7-13 years, mean BMI = 19 kg/m^2, basal glucose = 99 mg/dL, insulin = 78 pM, C-peptide = 511 pM]. Recent studies proved that HA and AA adults have an increased risk of developing T2DM. However, such studies are of interest for children of different ethnicities. The three DI hyperbolas, associated with ethnic groups (Figure 1*A*), are similar to each other. In contrast, cluster analysis also including FE_L (Figure 1*B*), reveals that in these children 3 different clusters exist, (silhouette values > 0.6 in 63% of subjects in cluster 1, 87% in cluster 2, and 95% in cluster 3), and they do not necessarily coincide with ethnicity. Thus, FEL differs among children and it needs to be considered, together with SI and AIRg, in order to clarify diabetes risk among children of different ethnicities.

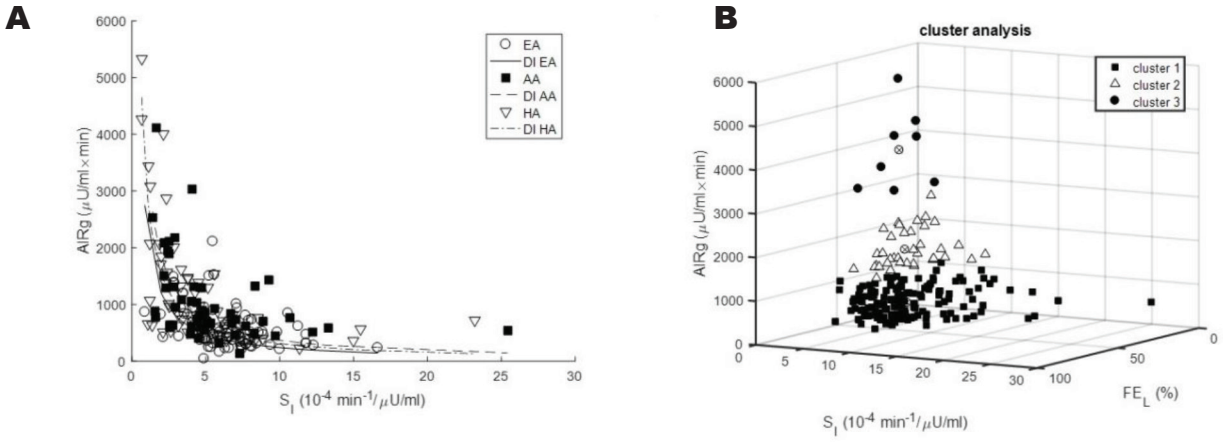


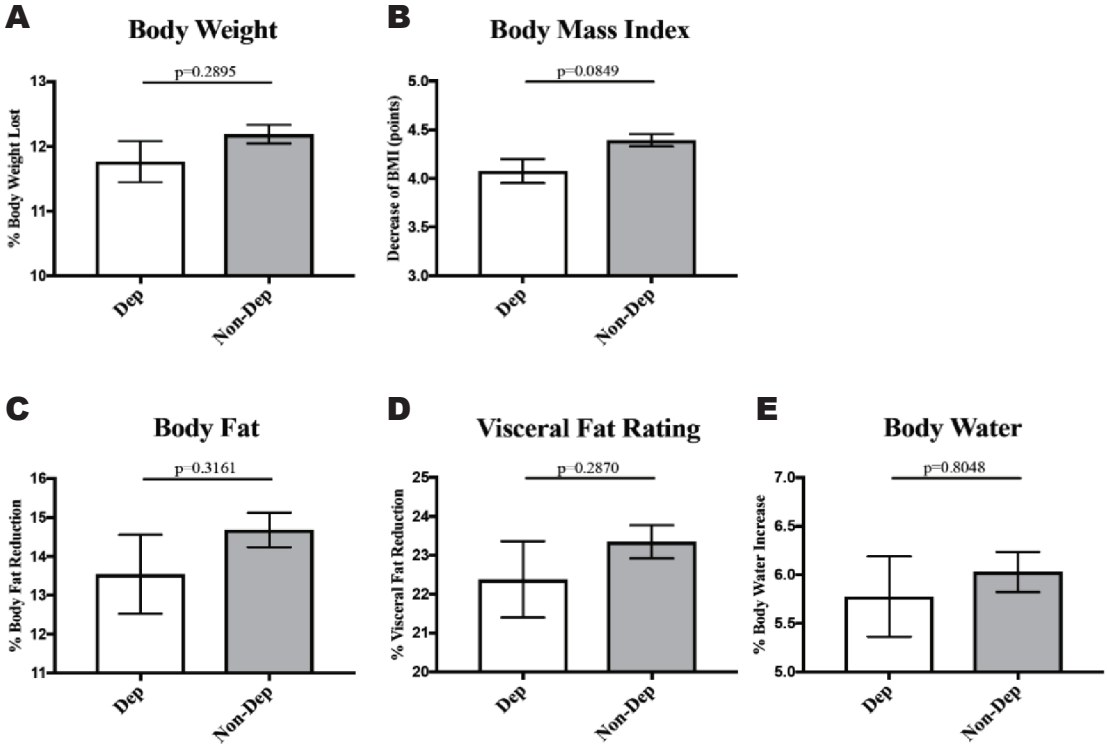
Fig. 1. *A*) Disposition index hyperbolas and individual AIRg and S_I values divided into EA, AA, and HA ethnicities. *B*) Cluster analysis: subjects were divided into 3 clusters; the centroids of each cluster are represented as well.

INTENSE WEIGHT LOSS PROGRAM EFFECTIVE FOR PARTICIPANTS PRESCRIBED ANTIDEPRESSANTS

Gerald C. Dembrowski, DC; Jessica W. Barnes, PhD

20Lighter Program

A growing body of evidence suggests pharmacologic treatment with antidepressants may increase risk of obesity. With ~12% of Americans 12 years or older prescribed at least one antidepressant and data also showing use increases with age, it is critical to understand how they may impact weight loss. Here we present data collected from the 20Lighter Program (T20LP), an intensive weight reduction program, to assess changes in body composition in participants taking antidepressant medications versus participants not prescribed medications for major depressive disorder. Overall, 14% of the participants completing T20LP between June 2016-2017 reported taking one or more prescription antidepressants (SSRI, NDRI, or other). The entire cohort had a median age of 50 ± 9.4 and Body Mass Index (BMI) of 35.1 ± 6.1. From baseline to 6wk, each group (Dep; non-Dep) showed statistically significant and clinically meaningful reductions in body weight (%) (**A**; 11.7 ± 0.3; 12.1 ± 0.1), BMI (pts) (**B**; 4.0 ± 0.1; 4.3 ± 0.0), body fat (%) (**C**; 13.5 ± 1.0; 14.6 ± 0.4), visceral fat (%) (**D**; 22.3 ± 0.9; 23.3 ± 0.4), and increases in body water (%) (**E**; 5.7 ± 0.4; 6.0 ± 0.2). We found those on antidepressant medication(s) performed equally well as those who were not taking medication. While longer follow-up is required, T20LP doctor-supervised program provides clinically relevant improvements in body composition, risk factors, and quality of life in those prescribed medications for major depressive disorder and related conditions. Our data suggest T20LP successfully complements current and historic psychopharmacologic treatment by reducing weight, body fat %, visceral fat, and addressing risk factors associated with weight gain and obesity.



ASSOCIATION OF URINARY COTININE-VERIFIED ACTIVE AND PASSIVE SMOKING WITH HYPERURICEMIA: AN ANALYSIS OF A POPULATION-BASED NATIONALLY REPRESENTATIVE SAMPLE

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Department of Family Medicine, Kosin University Gospel Hospital

Hyperuricemia is an independent risk factor of gout, hypertension, diabetes, and cardiovascular disease. Although several previous studies have been conducted, the effects of smoking on hyperuricemia has not been established. Self-reported smoking status is not a reliable way to measure smoking exposure in particular among women. The present study aimed at estimating the association of cotinine verified active and passive smoking with hyperuricemia in a nationally representative Korea population. A total 5,365 subjects (2,356 men and 3,009 women) aged ≥19 were included in this population-based cross-sectional study. Subjects' smoking status was categorized into active, passive and none smokers according to self-report questionnaire and urinary cotinine levels. Linear regression analysis was used to estimate the association between smoking exposure and serum uric acid levels. Multivariate logistic regression analysis was performed to evaluate the effects of smoking on hyperuricemia. Cotinine verified active and passive smoking rate was 38.6% and 12.0% in men and 8.7% and 12.6 % in women respectively. Although active and passive smoking is associated with increasing serum uric acid levels and risk of hyperuricemia in women, no significant association was observed in men. Active and passive smoking were associated with increasing risk of hyperuricemia especially in Korean women. Public health effort should be implemented to reduce active and passive smoking rate to decrease potential harmful effect of hyperuricemia on cardio-metabolic health especially in women.

MONITORING OF IONIC CURRENTS OF FEW MOLECULES IN EXHALED BREATH BY A SIMPLE BREATH ANALYZER: A NEW-GENERATION POINT-OF-CARE DIAGNOSTIC TOOL FOR SCREENING EARLY STAGE AND TYPE 2 DIABETES

Chiranjit Ghosh[1]; Prabuddha Mukhopadhyay[2]; Shibendu Ghosh[2]; Manik Pradhan[1]

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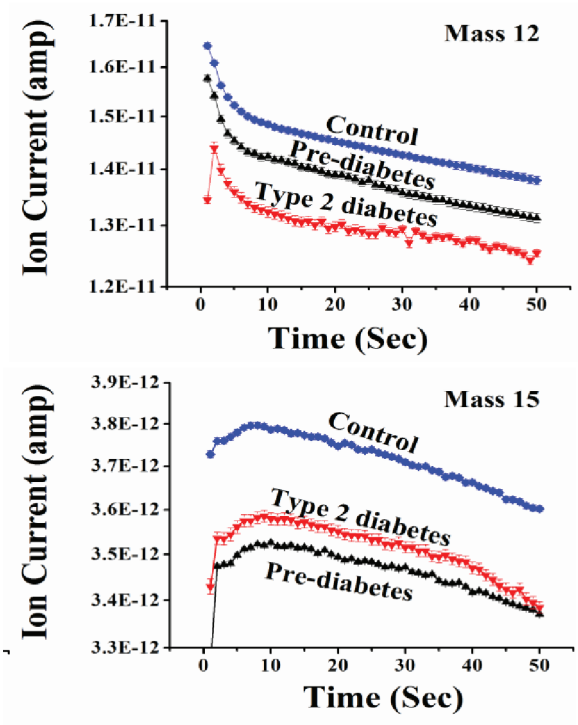
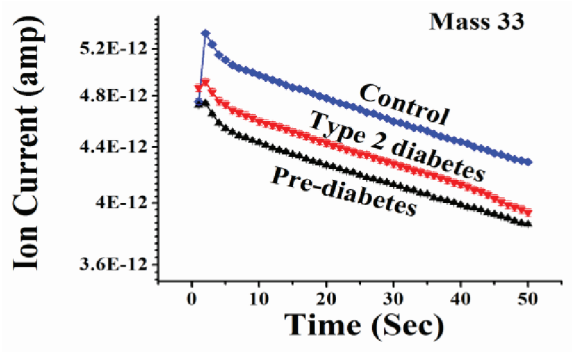
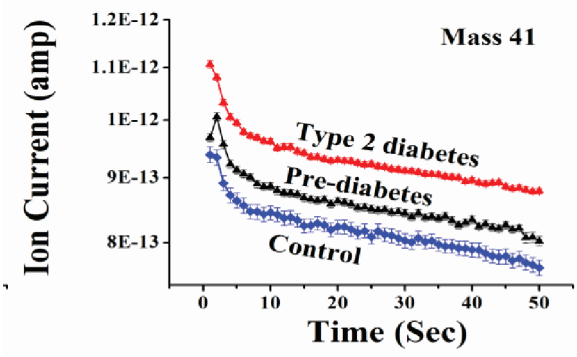
At present, pre-diabetes (PD) and type 2 diabetes (T2D) are diagnosed by means of oral glucose tolerance test, glycosylated hemoglobin test etc. These methods are invasive and therefore need the blood samples. The aim of study was to diagnose PD and T2D from the breath analysis by utilizing a simple breath analyzer, specially designed in our laboratory. Breath samples were collected and analyzed before and after oral administration of non-radioactive 13C-glucose. From the ion-current measurements of several molecules by breath analyzer, we can clearly distinguish the controls, pre-diabetes and type 2 diabetes. We found the least enrichment of 45 mass (13CO2) in exhaled breath in type 2 diabetes than pre-diabetes and controls. This may be due to that the labelled glucose uptake is impaired due to insulin resistance and results in blunted isotope enriched 13CO2 production in exhaled breath samples of T2D. We also observed significant changes in the ion currents of additional few masses (12, 15, 21, 41, 42 and 33) in type 2 diabetes than control. The changes in ion-currents of these masses during respiration may be associated with the metabolic defect of type 2 diabetes during OGTT. Our observations suggest that a simple breath analyzer may serve as a non-invasive point-of-care diagnostic tool for routine clinical practices as well as for large-scale diabetes screening purposes.







DOES THYMOSIN A1 CONSTITUTE AN INDEPENDENT RISK FACTOR FOR DIABETIC CARDIOMYOPATHY IN T2DM PATIENTS?

S. Papazoglou; D. Richter; A. Trikas; M. Aslam; U. Jaffer; C. Pantos; C. Stefanadis; P. Nihoyannopoulos; K. Toutouzas; D. Tousoulis; N. Standfield

Cardiac Dept. Euroclinic, Athens, Cardiology Dept. Hippokration University Hospital, Faculty of Medicine, University of Athens, Greece; ''ELPIS" General Hospital, Athens, Greece; Vascular Surgery Dept. Hammersmith Hospital, Faculty of Medicine, Imperial College Healthcare NHS Trust, London, UK

Purpose: T2DM is one of the most prevalent systemic diseases with an unprecedented cardiovascular impact. The pathophysiology of metabolic syndrome and insulin resistance has been a landmark in clinical research that interconnected various biomarkers to the pathogenetic mechanisms of Type 2 Diabetes Mellitus. Diabetic Cardiomyopathy consists a clinical entity referring mainly to the structural alterations on the myocardium due to systemic insulin resistance and subsequent increased levels of circulating blood glucose. The aim of this study was to investigate that decreased thymosin a1 levels consist an independent risk factor for Diabetic Cardiomyopathy in T2DM patients.

Methods: 419 (216 male, 203 female) T2DM patients were recruited on this study. Age range of the patients was between 47-79 years. All patients were admitted for standard laboratory evaluations following the updated clinical practice guidelines for T2DM and Ultrasound Echocardiographic assessment. HbA1c levels were used to measure dysglycemic variations in T2DM patients and were considered to be significant when >6.5% (48 mmol/mol). Left Atrial Pressure in mmHg was assessed in order to evaluate the severity of Diabetic Cardiomyopathy and considered significant when L.A.P >11.9 mmHg. Thymosin a1 were considered to be pathological in both male and female T2DM patients when <540 pg /ml. Data were analyzed using multiple analysis of variance (MANOVA) and logistic regression. Data are presented as mean ± standard deviation and level of significance was accepted when $P<0.05$.

Results: Data were analyzed on 419 (216 male, 203 female) T2DM patients. 117 (27.9%) had thymosin a1 433 ± 47 pg/ml, HbA1c 7.1 ± 0.3 % and LAP 12.6 ± 0.3 mmHg. 158 (37.7%) patients had thymosin a1 399 ± 46 pg/ml, HbA1c 7.9 ± 0.2 % and LAP 13.3 ± 0.2 mmHg. 144 (34.4%) with thymosin a1 317 ± 62 pg/ml and HbA1c 8.7 ± 0.8 % and LAP 13.7 ± 0.2 mmHg. In patients with Diabetic Cardiomyopathy increased LAP levels ($P = 0.018$) coexist with increased HbA1c levels ($P = 0.0067$) when there are markedly decreased levels of circulating thymosin a1 $P<0.001$.

Conclusion: Decreased thymosin a1 levels is an independent risk factor for Diabetic Cardiomyopathy in T2DM patients.

ELEVATED TRIGLYCERIDES (≥150 MG/DL) AND HIGH TRIGLYCERIDES (200–499 MG/DL) ARE SIGNIFICANT PREDICTORS OF HOSPITALIZATION FOR KIDNEY DISEASE: A REAL-WORLD ANALYSIS OF HIGH-RISK STATIN-TREATED PATIENTS

Peter P. Toth[1]; Sephy Philip[2]; Michael Hull[3]; Craig Granowitz[2]

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Background: Dyslipidemia in kidney disease (KD) involves increased levels of triglycerides (TG) and TG-rich lipoproteins, with only minor changes in LDL-C. The increasing prevalence of diabetic kidney disease and the shared atherogenic lipid profile between kidney disease and diabetes underscores the importance of understanding dyslipidemia in these patients. Previous studies suggest elevated TG and new-onset KD are associated. Additional data are needed on the role of hypertriglyceridemia and new-onset KD.

Methods: This retrospective administrative claims analysis of the Optum Research Database included statin-treated

patients (age ≥45 y) with diabetes and/or atherosclerotic cardiovascular disease similar to those in the recently completed REDUCE-IT study. Cohorts included patients with elevated TG (≥150 mg/dL; n=27, 471), with high TG (200–499 mg/dL; subgroup of elevated TG cohort; n = 13,411), and a comparator cohort (TG <150 mg/dL and HDL-C >40 mg/dL; n = 32,506) and were followed for ≥6 months. Hazard ratios were calculated from multivariate analyses controlled for patient characteristics and comorbidities using the Cox proportional hazards model.

Results: Higher rates of hospitalization for new-onset KD were found in the elevated (31%) and high (45%) TG cohorts (Table).

Conclusions: In a real-world analysis of statin-treated patients with high cardiovascular risk, elevated TG (≥150 mg/dL) and high TG (200–499 mg/dL) were found to be significant predictors of hospitalization for new-onset KD, identifying hypertriglyceridemia as a potential KD risk factor. Future analyses from REDUCE-IT may shed light on hypertriglyceridemia in diabetes and KD and the potential role of eicosapentaenoic acid in treating patients with diabetes and KD.

Table. Effects of Triglycerides on New-Onset Hospitalization for KD in Statin-Treated Patients With High CV Risk (Multivariate Analysis)*

Analysis	Hazard Ratio	95% CI	*P* Value
TG ≥150 mg/dL vs comparator†	1.311	1.228–1.401	<0.001
TG 200–499 mg/dL vs comparator†	1.451	1.339–1.572	<0.001

*New-onset KD was analyzed as inpatient stay for KD in the follow-up period in patients without evidence of baseline KD. Covariates included TG cohort, age (45–54, 55–64, ≥65 y), gender, insurance coverage type, geographic region of enrollment, and baseline clinical characteristics (diabetes, atherosclerotic CV disease, LDL-C laboratory result in relation to median).
†Comparator cohort: TG <150 mg/dL and HDL-C >40 mg/dL.

IN TYPE 2 DIABETIC PATIENTS SERUM VANIN 1 LEVELS AND RELATIONSHIP BETWEEN METABOLIC PARAMETERS

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Background and aims: Diabetes mellitus is chronic metabolic disease which requires continuous medical care due to a lack of insulin or the defect on insulin effect and organism can not benefit enough from carbonhydrate, fat and protein. We examine Vanın 1 molecule which might be effective in preventing and treating complications of diabetes in preclinical trials and methabolic parameters in drug naive newly diagnosed diabetic patients. Today, despite all the research on in ensuring the optimal glycemia in diabetes patients and complications of diabetes reached the pandemic level worldwide, it failed to reach the desired goal. For this purpose,many molecules have been found will be effective in the treatment of diabetes and/or inhibitory to the growth of potential complications. Many of these molecules have been promising through preclinical studies but clinical studies have not supported it. We also examined in our study the relationship between Vanin 1 molecule and the prevention of complications and the treatment of diabetes and metabolic parameters,which might be effective in preclinical studies.

Materials and methods: Patients was included in admitted to the internal medicine and endocrinology clinics of our hospital in 2017 according to the study protocol. BMI of these patients, waist circumference, systolic and diastolic blood pressure were measured. Fasting blood glucose, serum lipids, ALT, AST, urea, creatinine, HbA1c, 2.hr plasma glucose, fasting insulin, hs-CRP, HOMA-IR, carotid intima-media thickness and serum vanin 1 levels were examined.

Results: 41 patients with newly diagnosed type 2 diabetic patients with 41 control group was enrolled the study. Diabetes group of 26 patients were women,15 were male and 25 patients in the control group of women and 16 were men.Level of serum vannin-1 (Type 2 DM = 2.30 (1.37-8.78), control = 2.00 (0.70-6.60), p = 0.030*) were found to be significantly higher in diabetic patients with newly diagnosed. Also vanin-1 level positive correlation between HOMA-IR, waist circumference, BMI, KIM, serum levels of fasting insulin and fasting blood glucose. In addition, vanin1 was correlated positively in the statistically significant positive correlation between the level in the individuals in both groups and the KIM thickness as a marker of cardiovascular risk. No statistically significant difference was found between the other variables and serum vanin 1 level.

Conclusion: Vanin level has been an increased of newly diagnosed diabetic patients. Also, in our study, vanin level shows a significant positive correlation with KIM, waist circumference, BMI, HOMA-IR insulin resistance. Vanin 1 which thought to be involved in the pathogenesis of particularly diabetes, CVD and metabolic syndrome, can be used as risk factor and as a potential therapeutic target in these diseases.

EICOSAPENTAENOIC ACID (EPA) INHIBITS OXIDATION OF MEMBRANE LIPIDS IN A MANNER DISTINCT FROM OTHER LONG CHAIN FATTY ACIDS *IN VITRO*

Samuel C.R. Sherratt, BS[2]; R. Preston Mason, PhD[1,2]

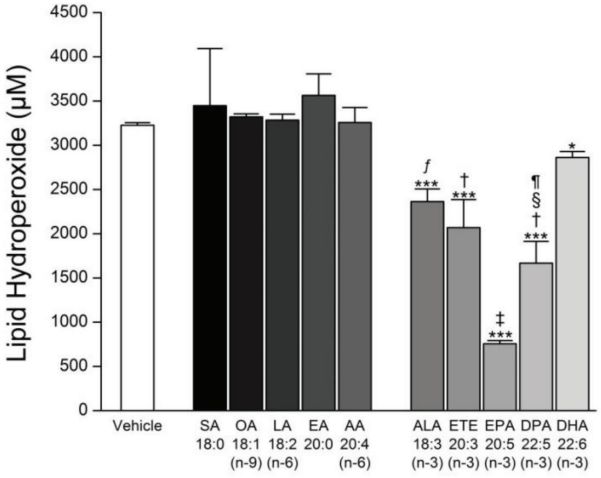
[1]Brigham & Women's Hospital, Harvard Medical School, Boston, MA; [2]Elucida Research LLC, Beverly, MA

Background: The unstable atherosclerotic plaque contains oxidized lipid and cholesterol crystals. Under conditions of oxidative stress, the fatty acid (FA) eicosapentaenoic acid (EPA, 20:5, ω-3) inhibits cholesterol crystal formation. The antioxidant activity of EPA compared to other long-chain FAs is not understood. We compared the membrane lipid oxidation properties of the following FAs: SA (18:0), OA (18:1, n-9), LA (18:2, n-6), ALA (18:3, n-3), EA (20:0), ETE (20:3, n-3), AA (20:4, n-6), EPA (20:5, n-3), DPA (22:5, n-3), and DHA (22:6, n-3).

Methods: Iodometric approaches were used to measure lipid hydroperoxide (LOOH) formation in dilinoleoylphosphatidylcholine vesicles prepared at a 0.6:1 cholesterol-to-phospholipid mole ratio, in the absence or presence of FAs at 5 and 10 μM, at 37°C. Lipid oxidation was stimulated with copper sulfate (0.1 μM) for 48 hours.

Results: At 5 μM, EPA reduced LOOH levels by 77% versus vehicle ($p<0.001$). DHA, ETE, DPA and ALA inhibited oxidation by only 11, 36, 48, and 27%, respectively ($p<0.05$ for DHA; $p<0.001$ for other treatments). The activity of EPA was 279, 174, 121, and 213% greater than that observed for DHA, ETE, DPA, and ALA, respectively ($p<0.001$). The remaining FAs had no antioxidant activity. Similar results were observed at 10 μM.

Conclusion: These data suggest that EPA, due to its unique hydrocarbon chain length and number of double bonds, is able to insert efficiently into the membrane bilayer where it inhibits membrane lipid oxidation. This structure/function mechanism may contribute to increased atheroprotective benefits with EPA as compared to other fatty acids.



***$p<0.001$ versus vehicle; *$p<0.05$ versus vehicle ‡$p<0.001$ versus all treatments; †$p<0.001$ versus DHA; §$p<0.01$ versus ALA; ¶$p<0.05$ versus ETE; ƒ$p<0.01$ versus DHA (Student-Newman-Keuls multiple comparisons test). Values are mean ± SD.

SGLT2 INHIBITOR DAPAGLIFLOZIN REDUCES HYPERFILTRATION AND PREVENTS GLOMERULAR FILTRATION RATE DECLINE IN RODENT MODELS OF DIABETIC NEPHROPATHY

François Briand[1]; Sisse A. Nørgaard[2]; Masami Shinohara[3]; Emmanuel Brousseau[1]; Nourdine Faresse[1]; Takeshi Ohta[4]; Yasushi Kageyama[3]; Fredrik Sand[2]; Thierry Sulpice[1]

[1]Physiogenex; [2]GLP-1 & T2D Pharmacology, Novo Nordisk A/S; [3]CLEA Japan Inc., Tokyo, Japan; [4]Japan Tobacco Inc., Osaka, Japan

Background: SGLT2 inhibitors (SGLT2i) may have protective effects on the kidney in diabetic nephropathy (DN). To evaluate the impact on kidney function, we here evaluated the effects of the SGLT2i dapagliflozin on glomerular filtration rate (GFR) in animal models of DN.

Methods: To evaluate the effects on hyperfiltration, db/db mice fed a high protein diet (60% kcal from protein, known to accelerate DN) were treated with vehicle or dapagliflozin 10mg/kg orally once daily for 4 weeks. To evaluate the effects on GFR decline, uni-nephrectomized Spontaneously Diabetic Torii (SDT) fatty rats were fed a 0.3% salt diet and treated without (control) or with dapagliflozin at 1mg/kg/day in the diet for 10 weeks. To measure GFR, animals were injected i.v. with FITC-sinistrin or FITC-inulin.

Results: In db/db mice, dapagliflozin significantly blunted hyperglycemia, increased fasting plasma ketone levels and urine glucose excretion. Dapagliflozin significantly reduced proteinuria and creatinine clearance by 36% and 45%, as well as hyperfiltration with a 12% and 21% reduction in GFR at 2 and 4 weeks of treatment, respectively (both p<0.05). In SDT fatty rats, dapagliflozin significantly reduced % HbA1c, systolic and diastolic blood pressure. While control rats showed a 64% GFR decline at 5 weeks of treatment, dapagliflozin markedly prevented this decline with a 71% higher GFR vs. control (p<0.01). Although GFR became similar at 10 weeks in both groups, dapagliflozin also improved glomerulosclerosis, inflammation and fibrosis.

Conclusion: Dapagliflozin shows significant benefits on kidney dysfunction by reducing hyperfiltration and preventing GFR decline in animal models of DN.

REVISITING THE HYPERINSULINEMIC EUGLYCEMIC CLAMP EXPERIMENT IN CONSCIOUS RODENTS, THE GOLD-STANDARD TO EVALUATE THE EFFICACY OF DRUGS ON INSULIN RESISTANCE AND GLUCOSE HOMEOSTASIS

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Background: To better evaluate the efficacy of drugs targeting insulin sensitivity, we aimed to validate several insulin resistant and diabetic animal models, with different setting of the hyperinsulinemic euglycemic clamp (HEC) experiment, the gold-standard to measure insulin sensitivity.

Methods: Insulin resistance were induced in C57BL6/J male mice fed a 60% high fat diet (DIO mice). Whole body/hepatic insulin resistance and NAFLD were induced in Sprague Dawley rats with a high fat/cholesterol/fructose/cholic acid diet (IR rats). Diabetes was induced in Wistar rats with a single streptozotocin injection at 60mg/kg i.v. (STZ rats). Radioactive (3H-glucose and 14C-2-deoxyglucose), one- or two-step HEC were performed to evaluate either insulin sensitizer pioglitazone in DIO mice and IR rats, or insulin analogues lispro and glulisine in STZ rats.

Results: In DIO mice, pioglitazone significantly reduced hyperglycemia and hyperinsulinemia, improved oral glucose intolerance, and impacted immune cells population in mesenteric fat using flow cytometry. During a one-step HEC, pioglitazone repressed hepatic glucose production (HGP) and improved peripheral insulin sensitivity, with higher muscle and adipose tissue glucose uptake. In IR rats, pioglitazone also improved hyperinsulinemia and significantly reduced hepatic triglycerides levels. During a two-step HEC, pioglitazone significantly reduced HGP and peripheral insulin sensitivity. In STZ rats, a head-to-head comparison during a one-step HEC demonstrated that lispro better represses hepatic glucose production, while glulisine better blunts lipolysis.

Conclusion: Our experimental setting combining animal models and HEC identifies the mechanism by which a drug compound affects insulin resistance and associated diseases such as low-grade inflammation, dyslipidemia and NAFLD.

DAPAGLIFLOZIN PRESERVES RENAL FUNCTION IN PATIENTS WITH TYPE 2 DIABETES: A LONGITUDINAL META-ANALYSIS OF ESTIMATED GLOMERULAR FILTRATION RATE ACROSS CLINICAL TRIALS

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Background: The sodium-glucose cotransporter 2 inhibitors (SGLT-2is) empagliflozin and canagliflozin showed renal benefits in patients with type 2 diabetes (T2D) in the EMPA-REG and CANVAS-R trials, respectively. This analysis aims to assess whether the SGLT-2i dapagliflozin provides renal benefits and to inform the decision to initiate a renal outcome trial (NCT03036150).

Methods: This model-based meta-analysis used individual serial estimated glomerular filtration rate (eGFR) measurements from randomized, double-blind, placebo-controlled phase 2 and 3 trials of dapagliflozin in T2D. Effects of patient characteristics on rate of eGFR change were included if significant.

Results: The analysis included a total of 4894 patients and 58,626 eGFR measurements from 8 studies. Patients received placebo or dapagliflozin 1, 2.5, 5, or 10 mg once daily for up to 2 years. Pooled mean baseline characteristics were age 60 years, HbA1c 8.2%, and eGFR 78.5 mL/min/1.73m2. In placebo-treated patients, eGFR declined steadily over time (0.3 mL/min/1.73m2/year). Dapagliflozin-treated patients showed a small immediate decline (~2 mL/min/1.73 m^2, placebo-corrected); eGFR loss slowed thereafter, leading to dose-dependent net preservation and increase of eGFR over 2 years. Following the initial drop, the rate of eGFR change increased by +1.2 and +1.4 mL/min/1.73m2/year for dapagliflozin 5 mg and 10 mg, respectively. Treatment effect was larger in women than men; no other covariates were identified, indicating similar benefits across the subgroups studied.

Conclusion: This is the first integrated, model-based analysis to show that dapagliflozin prevents progressive loss of renal function in patients with T2D over 2 years and supports the ongoing renal outcome study.

POOLED DATA ANALYSIS OF COMPOSITE ENDPOINTS FROM THE DEPICT-1 AND DEPICT-2 STUDIES USING DAPAGLIFLOZIN COMPARED TO PLACEBO ADDED TO ADJUSTABLE INSULIN IN TYPE 1 DIABETES

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Background: Adjunct therapy with insulin-independent agents may improve glycemic control in patients with type 1 diabetes (T1D). This pooled analysis of data from the DEPICT-1 and DEPICT-2 studies evaluated the effect of dapagliflozin, a selective sodium-glucose cotransporter-2 inhibitor, on the proportions of patients with T1D on adjustable insulin treatment achieving an HbA1c reduction of ≥0.5% from baseline to week 24 with no body weight gain or an HbA1c reduction of ≥0.5% from baseline to week 24 with no severe hypoglycemia or diabetic ketoacidosis (DKA).

Methods: Patients (n=1591) with T1D with inadequate glycemic control (HbA1c 7.7–11.0%) on insulin for ≥12 months with a total insulin dose of ≥0.3 U/kg/day for ≥3 months before screening, BMI ≥18.5 kg/m^2, and C-peptide <0.7 ng/mL, were randomized to receive dapagliflozin 5 mg/day plus insulin (n = 530), dapagliflozin 10 mg/day plus insulin (n = 529), or placebo plus insulin (n = 532). Logistic regression, with adjustment for study, baseline HbA1c, and randomization stratification factor, was performed.

Results: Patient demographics and baseline characteristics were comparable across study groups. Greater proportions of patients in the 2 dapagliflozin/insulin groups than in the placebo/insulin group achieved HbA1c reductions of ≥0.5% without weight gain or reduction in HbA1c of ≥0.5% without hypoglycemia or DKA (Table). The odds ratios for both composite endpoints were greater in the dapagliflozin/insulin groups versus the placebo/insulin group.

Conclusion: In patients with T1D inadequately controlled with adjustable insulin, adjunct therapy with dapagliflozin may improve glycemic control with less risk of weight gain and without severe hypoglycemia or DKA.

Table. Composite endpoint analysis

	5 mg DAPA/INS (n=530)	10 mg DAPA/INS (n=529)	PBO/INS (n=532)
HbA1c reduction ≥0.5% with no body weight gain[a] (baseline to week 24)			
Number of patients	522	521	526
Patients achieving composite endpoint, n (%)[b]	201 (38.5)	221 (42.4)	57 (10.8)
Odds ratio vs PBO/INS (95% CI)	5.4 (3.9, 7.6)	6.5 (4.7, 9.1)	
HbA1c reduction ≥0.5% with no severe hypoglycemia or DKA (baseline to week 24)			
Number of patients	522	521	526
Patients achieving composite endpoint, n (%)[b]	229 (43.9)	236 (45.3)	116 (22.1)
Odds ratio vs PBO/INS (95% CI)	2.9 (2.2, 3.9)	3.2 (2.4, 4.2)	

Abbreviations: CI = confidence interval; DAPA = dapagliflozin; DKA = diabetic ketoacidosis; INS = insulin; LOCF = last observation carried forward; PBO = placebo.
[a]Weight gain is defined as body weight at week 24 (LOCF) being greater than at baseline.
[b]n (%) is the number of patients in the full analysis data set with non-missing baseline and week 24 (LOCF) values.

EFFECT OF ADDING DAPAGLIFLOZIN AS AN ADJUNCT TO INSULIN ON URINARY ALBUMIN TO CREATININE RATIO OVER 52 WEEKS IN ADULTS WITH TYPE 1 DIABETES

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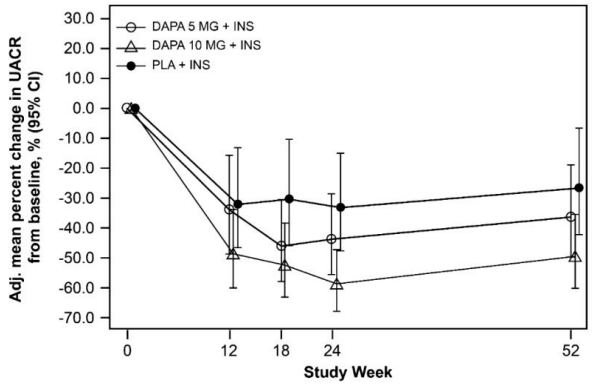
Background: In the DEPICT-1 and DEPICT-2 studies, dapagliflozin, added as adjunct to insulin in adult patients with inadequately controlled type 1 diabetes (T1D; glycated hemoglobin 7.5–10.5%), improved glycemic control and body weight and was well tolerated.

Methods: This pooled post hoc analysis of the DEPICT-1 and DEPICT-2 studies evaluated the effect of dapagliflozin on urinary albumin to creatinine ratio (UACR) in patients with T1D with baseline albuminuria.

Results: UACR was recorded at baseline for 548, 565, and 532 patients treated with dapagliflozin 5 mg, dapagliflozin 10 mg, and placebo, respectively. Albuminuria was present at baseline in 80, 84, and 87 patients in these treatment arms, respectively. Among the 251 patients with albuminuria, baseline renal function was normal in 93 (estimated glomerular filtration rate [eGFR] >90 mL/min/1.73 m^2), mildly impaired in 131 (eGFR ≥60 or <90 mL/min/1.73 m^2), and moderately impaired in 27 (eGFR <60 mL/min/1.73 m^2). Changes in eGFR appeared similar across the treatment arms (data not shown). However, dapagliflozin treatment resulted in dose-dependent reductions in UACR at weeks 12, 18, 24, and 52 (Figure). The difference in UACR between the dapagliflozin 10 mg and placebo arms was significant from weeks 18–52. At week 52, the differences in UACR between dapagliflozin 10 mg and placebo and dapagliflozin 5 mg and placebo were –31.12% (95% CI –49.94, –5.22) and –13.30% (95% CI –37.24, 19.79), respectively.

Conclusion: Treatment with dapagliflozin appears to provide dose-dependent reductions in UACR, suggesting renoprotective effects in patients with T1D with baseline albuminuria.



Adj, adjusted; CI, confidence interval; DAPA, dapagliflozin; INS, insulin; PLA, placebo; UACR, Urinary Albumin to Creatinine Ratio

Fig. Adjusted mean percent change in UACR (mg/g) from baseline.

POOLED ANALYSIS OF THE DURATION OF TYPE 1 DIABETES IN DAPAGLIFLOZIN VS PLACEBO ON ADJUSTABLE INSULIN THERAPY FROM DEPICT-1 AND DEPICT-2: EFFECTS ON GLYCEMIA, WEIGHT AND INSULIN DOSAGE

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Background: In the DEPICT-1 and DEPICT-2 phase 3 studies in patients with type 1 diabetes (T1D), dapagliflozin improved glycemic control and reduced body weight and insulin dose versus placebo, without increasing hypoglycemia. Pooled data from DEPICT-1 and DEPICT-2 were analyzed to assess the impact of T1D duration on the effects of dapagliflozin.

Methods: Patients with T1D (n=1591; age 18–75 years; HbA1c 7.7–11.0%; BMI ≥18.5 kg/m^2; C-peptide <0.7 ng/mL; prescribed insulin for ≥12 months before enrollment; total insulin dose ≥0.3 IU/kg/day for ≥3 months before screening) were randomized to add dapagliflozin 5 mg (n=530), dapagliflozin 10 mg (n=529), or placebo (n=532) to insulin. End points included adjusted mean change in HbA1c and percent changes in total daily insulin dose and total body weight from baseline to week 24. End points were analyzed by T1D duration tertile (<12.9, ≥12.9 to ≤23.5, or ≥23.5 years). No formal statistical testing was done.

Results: Patients with the longest T1D duration tended to have slightly smaller HbA1c reductions and greater weight loss (Table); no noticeable changes were observed in placebo-treated patients in any tertile. When plotted as continuous variables, correlation coefficients between HbA1c change and T1D duration for dapagliflozin 5 mg, dapagliflozin 10 mg, and placebo were 0.05635, 0.11214, and –0.09277, respectively. No trends were evident for insulin dose or other analyzed parameters.

Conclusion: Patients with the longest T1D duration demonstrated smaller HbA1c reduction but greater weight loss than those with shorter T1D duration when treated with dapagliflozin as add on to insulin therapy.

Table. Changes in major end points from baseline to week 24

	T1D duration <12.9 y			T1D duration ≥12.9 to ≤23.5 y			T1D duration >23.5 y		
BL age, y	37.6 (13.99)			40.1 (12.88)			50.0 (10.40)		
	BL	**Wk 24**	**Adj. mean change[a] (95% CI)**	**BL**	**Wk 24**	**Adj. mean change[a] (95% CI)**	**BL**	**Wk 24**	**Adj. mean change[a] (95% CI)**
HbA1c, %									
PBO[b]	8.54 (0.65)	8.63 (0.94)	0.13 (0.01, 0.24)	8.50 (0.66)	8.39 (0.86)	–0.05 (–0.16, 0.07)	8.38 (0.66)	8.29 (0.85)	–0.08 (–0.19, 0.02)
DAPA 5 mg[c]	8.62 (0.73)	8.09 (0.94)	–0.46 (–0.57, –0.35)	8.48 (0.71)	8.13 (0.84)	–0.34 (–0.46, –0.23)	8.36 (0.64)	7.96 (0.78)	–0.40 (–0.51, –0.29)
DAPA 10 mg[d]	8.54 (0.72)	8.01 (0.86)	–0.51 (–0.62, –0.40)	8.51 (0.63)	8.02 (0.78)	–0.43 (–0.54, –0.32)	8.35 (0.61)	8.00 (0.75)	–0.36 (–0.47, –0.25)
Total body weight, kg									
PBO[b]	76.09 (16.05)	76.40 (16.59)	0.19 (–0.47, 0.85)	82.84 (20.45)	82.56 (21.27)	–0.39 (–1.02, 0.25)	85.31 (18.39)	85.80 (18.38)	0.10 (–0.51, 0.71)
DAPA 5 mg[c]	77.39 (16.97)	75.80 (17.01)	–2.92 (–3.53, –2.31)	80.25 (17.26)	78.46 (16.89)	–3.00 (–3.60, –2.39)	82.29 (19.28)	79.87 (18.89)	–3.35 (–3.96, –2.73)
DAPA 10 mg[d]	77.84 (18.10)	75.42 (16.95)	–2.98 (–3.58, –2.37)	82.00 (17.93)	78.70 (17.55)	–3.87 (–4.49, –3.25)	83.29 (17.35)	79.93 (17.28)	–4.30 (–4.89, –3.71)

Abbreviations: Adj. = adjusted; BL = baseline; CI = confidence interval; DAPA = dapagliflozin; PBO = placebo; SD = standard deviation; T1D = type 1 diabetes; wk = week; y = years

Data are reported as mean (SD) unless otherwise indicated.

[a]BL to Wk 24; b n=521; c n=521; d n=524

PHYSIOLOGIC RESPONSE TO ORAL GLUCOSE TOLERANCE TESTING IDENTIFIES PROGRESSORS AND NON-PROGRESSORS TO TYPE 2 DIABETES IN CLINICAL PRACTICE (STOP DIABETES)

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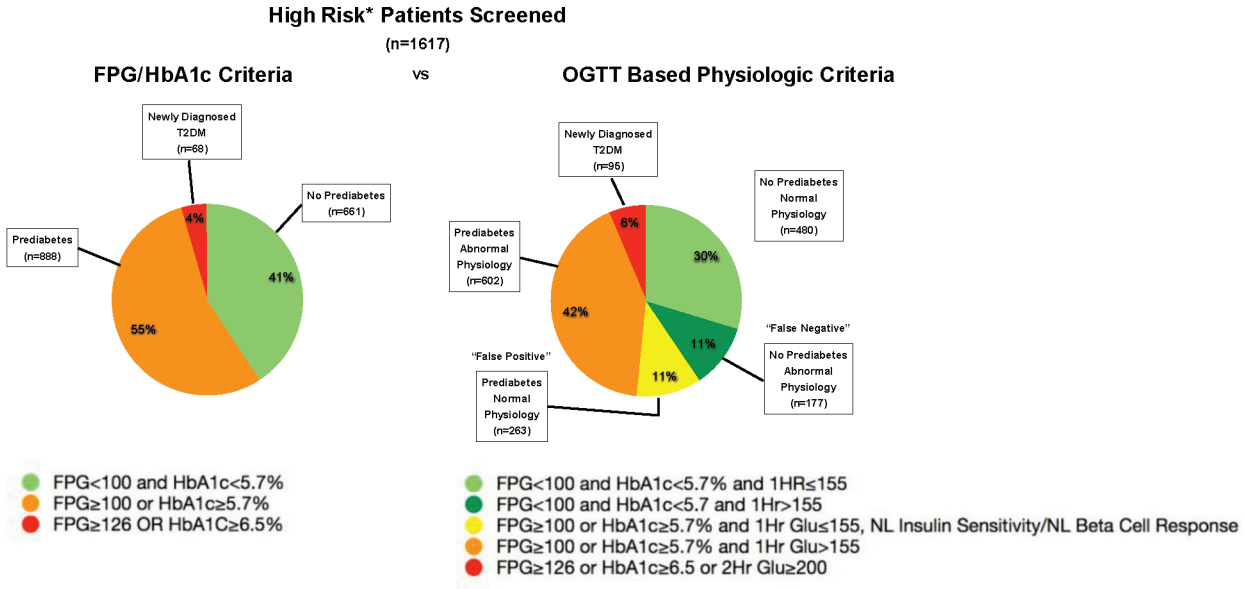
Objective: To compare fasting plasma glucose (FPG) and/or HbA1c vs. physiologic response to oral glucose tolerance test (OGTT), in identifying high risk patients likely to progress, or unlikely to progress to type-2 diabetes (T2DM).

Methods: 1617 patients at risk for developing T2DM from a clinical practice were screened with an OGTT with plasma glucose, insulin and c-peptide concentrations. Prediabetic patients were identified by FPG or HbA1c (n=888) and categorized as low risk (LR) for progression to T2DM based upon 1-Hr plasma glucose ≤155mg/dL, normal insulin sensitivity (Matsuda Index), and beta cell response (disposition index). No treatment was recommended (mean=5.6 years, n=195). Prediabetic patients at high-risk (HR) based upon abnormal physiology were recommended pharmacologic treatment. 200 patients declined and were recommended lifestyle modification (LS, mean=2.6 years). Progression to T2DM was assessed.

Results: Annual rate of progression to T2DM was 0.3% in the LR group and 4.1% in HR group (p<0.001). Prediabetic patients in the LR group were followed with FPG and HbA1c (n=107), or FPG, HbA1c and OGTT (n=88). The hazard plots for progression to T2DM for both groups yielded p<0.001 compared to prediabetics with abnormal physiology (LS) who declined treatment. Screening with FPG/HbA1c generated 30% "False Positives", 27% "False Negatives" and missed 2% of patients with undiagnosed new onset T2DM.

Conclusion: Using physiologic measures derived from OGTT including 1-hour plasma glucose >155mg/dL, insulin sensitivity and beta cell response, patients at risk for developing T2DM in clinical practice can be identified as "Low Risk" or "High Risk" of progressing to T2DM.



*Risk factors for diabetes—in addition to being overweight or obese or being age 45 or older—include the following:

- being physically inactive
- having a parent, brother, or sister with diabetes
- having a family background that is African American, Alaska Native, American Indian, Asian American, Hispanic/Latino, or Pacific Islander
- giving birth to a baby weighing more than 9 pounds or being diagnosed with gestational diabetes—diabetes first found during pregnancy
- having high blood pressure—140/90 mmHg or above—or being treated for high blood pressure
- having HDL, or "good," cholesterol below 35 mg/dL, or a triglyceride level above 250 mg/dL
- having polycystic ovary syndrome, also called PCOS
- having impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) on previous testing
- having other conditions associated with insulin resistance, such as severe obesity or a condition called acanthosis nigricans, characterized by a dark, velvety rash around the neck or armpits
- having a history of cardiovascular disease

HYPERINSULINEMIA TRENDS IN U.S. ADULTS WITHOUT DIABETES

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Evidence suggests hyperinsulinemia is associated with a plethora of clinical outcomes, including type 2 diabetes, cardiovascular disease, and metabolic syndrome. With more than two-thirds of U.S. adults being classified as overweight/obese, examining changes in insulin values over time is important due to its established relationship with ubiquitous chronic diseases.

Purpose: Estimate the prevalence and assess the trends in hyperinsulinemia is U.S. adults without diabetes between 1999 and 2014.

Methods: A fasting sub-sample of all male (n=8230) and nonpregnant females (n=8955) (≥20 years of age) who participated in the 1999-2014 National Health and Nutrition Examination Survey (NHANES) were utilized in the analyses. Hyperinsulinemia was calculated using the weighted 75th percentile of log-fasted insulin among adults who had fasting blood glucose values <126 mg/dL, answered no to a diabetes question, and reported taking no diabetes medications.

Results: The geometric mean (28.2%) proportion of U.S. adults without diabetes with hyperinsulinemia increased by ~10% from 1999 to 2014 (*P* for trend <0.001). The age-adjusted prevalence of hyperinsulinemia increased 23% between the 1999-2006 (27.6%) and 2007-2014 (34%) (*P*<0.05) NHANES data cycles. Overall, compared to females and those with normal waist circumference, males and adults with excess abdominal adiposity were found to have greater prevalence rates of hyperinsulinemia, 33.7% vs. 28.2% and 49.1% vs. 13.7% respectively, (*P* for both <0.05). Furthermore, body mass index (BMI) was found to be positively associated with hyperinsulinemia (*P* for trend <0.001).

Conclusion: Hyperinsulinemia rates have significantly increased among U.S. adults. Central adiposity and BMI are both strongly associated with hyperinsulinemia.

DAPAGLIFLOZIN AND CARDIOVASCULAR MORTALITY AND DISEASE OUTCOMES IN TYPE 2 DIABETES PATIENTS SIMILAR TO THE DECLARE-TIMI 58 PARTICIPANTS: A NATIONWIDE OBSERVATIONAL STUDY

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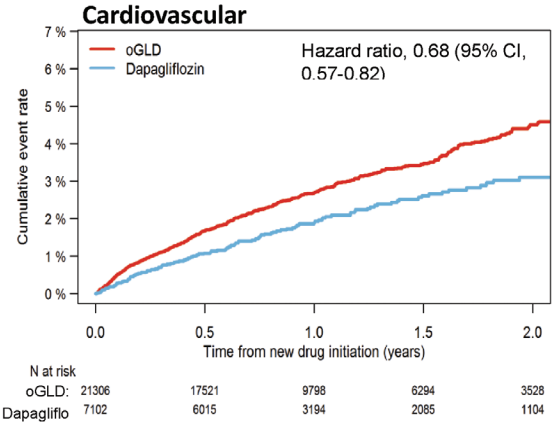
Aims: To investigate the cardiovascular (CV) safety and event rates of dapagliflozin versus other glucose lowering drugs (oGLD) in a real-world type 2 diabetes population after applying the main inclusion criteria and outcomes from DECLARE-TIMI 58.

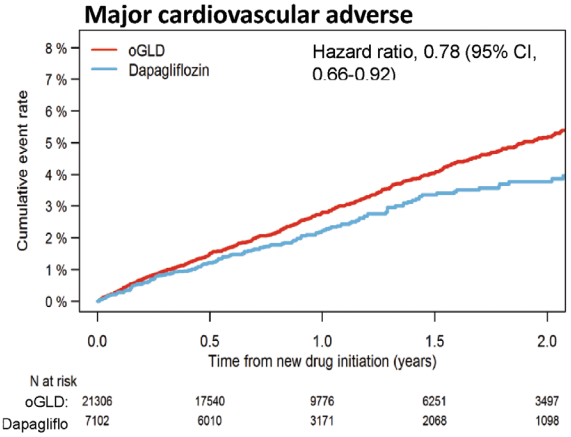
Methods: Patients with new use of dapagliflozin or oGLD were identified in nationwide health care registries during 2013-2016. Patients were included if satisfying the main cardiovascular DECLARE-TIMI 58 inclusion criteria at baseline; ≥40 years and established CV disease, or with risk factors (men ≥55 and women ≥60 years with hypertension or dyslipidemia). Propensity scores for the likelihood of dapagliflozin initiation were calculated followed by 1:3 matching. Dual-primary DECLARE-TIMI 58 outcomes were CV mortality or hospitalization for heart failure (HHF) and major CV adverse events (MACE; CV mortality, myocardial infarction or stroke), respectively. Cox survival models were used to estimate hazard ratios (HR).

Results: A total of 28,408 new use were identified, forming the DECLARE-like population (mean 66 years, 34% with established CV disease). Mean total follow-up time was 1.1 years (31,853 patient-years). Dapagliflozin versus oGLD displayed 32% lower risk of CV mortality or HHF (0.68; 0.57-0.82) and 22% lower risk for MACE (HR, 95% confidence interval; 0.78; 0.66-0.92), see Figure. Each of CV mortality and HHF risks were lower; 0.56 (0.38-0.82) and 0.70 (0.57-0.87), respectively. No significant risk associations for myocardial infarction and stroke; 0.81 (0.63-1.05) and 0.90 (0.69-1.16), respectively.

Conclusion: In real-world DECLARE-like patients, dapagliflozin versus oGLD had lower event rates of cardiovascular mortality and morbidity, including hospitalization for heart failure.

This study was sponsored by AstraZeneca,





Kaplan-Meier curves comparing on-treatment 1:3 propensity score matched type 2 diabetes patient groups of new users of dapagliflozin versus other glucose lowering drugs (oGLD) for major adverse cardiovascular event (MACE) and CV mortality or hospital events for heart failure (HHF).

DAPAGLIFLOZIN AND HEALTHCARE COSTS IN TYPE 2 DIABETES PATIENTS SIMILAR TO THE DECLARE-TIMI 58 PARTICIPANTS: A NATIONWIDE OBSERVATIONAL STUDY

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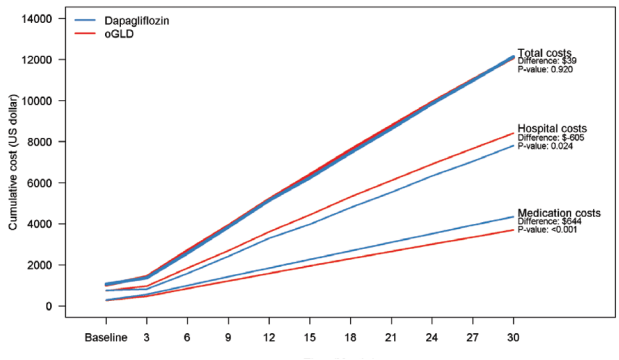
To investigate how cardiovascular disease (CVD) and mortality benefits with dapagliflozin versus other glucose lowering drugs (oGLD) translates into healthcare costs in a real-world type 2 diabetes population after applying main inclusion criteria and outcomes from DECLARE-TIMI 58 study. Patients with new use of dapagliflozin or oGLD were identified in nationwide health care registries during 2013-2016. Patients were included if satisfying the main cardiovascular DECLARE-TIMI 58 inclusion criteria at baseline; ≥40 years and established CVD, or with risk factors (men ≥55 and women ≥60 years with hypertension or dyslipidemia). Propensity scores for the likelihood of dapagliflozin initiation were calculated followed by 1:3 matching. Actual costs for hospital care (hospitalizations and outpatient hospital visits) and drug dispenses were calculated and cumulatively summarized per patient during 30-months. A total of 27,376 patients; 6,844 dapagliflozin and 20,532 oGLD, were identified. The groups were well balanced, mean age 66.4 years, 34% had a cardiovascular disease, and mean 12-months healthcare cost prior to index was $4,077. Total mean cumulative cost was similar in the dapagliflozin group versus the oGLD group; $12,144 versus $12,105, difference $39 (95%CI -$498, $522; p=0,920). The dapagliflozin group was associated with significantly lower hospital costs; -$605 (-$1,120, -$117; p=0.024), and significantly higher drug costs, $644 ($556 to $726; p<0.001) compared to oGLD. Hospital costs related to CVD were numerically lower for dapagliflozin, -$169 (-$393, $51; p=0.096). In real-world DECLARE-like patients, dapagliflozin was associated with a similar total healthcare cost compared to oGLD with beneficial CVD risk reduction shown in other studies.

This study was sponsored by AstraZeneca.



ADDITION OF ORAL MEDIUM CHAIN TRIGLYCERIDE AND OMEGA-3 FISH OIL FOR PROMPT CONTROL OF SEVERE HYPERTRIGLYCERIDEMIA

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Severe hypertriglyceridemia has few promptly effective treatments. A medium chain triglyceride (MCT) and omega-3 fish oil (Om3F) rich diet reduced serum triglycerides (trigly) from 1601 mg/dl to 554 mg/dl in 7 days (Hauenschild, 2010). Combined use of Brain & Cardiac Complement (BCC) a similar, naturally flavored 4:1 emulsion of MCT:Om3F, with diabetic diet and pharmacotherapy is exemplified in the following cases. A 63 y.o. type 2 diabetic man with history of pancreatitis and therapy nonadherence had trigly 2208 mg/dl. He took niacin 500 mg once vs. prescribed 3 times daily and refused fibrates. He took pitavastatin 4 mg daily and BCC 15 ml with 2 g Om3F twice daily. Within 24 days his trigly was 154 mg/dl. A 65 y.o type 2 diabetic man, with trigly 1698 mg/dl improved to 370 mg/dl in 39 days on pitavastatin 4 mg nightly and BCC 15 ml with 2 g Om3F twice daily. A 41 y.o. nonadherent type 2 diabetic man with HbA1c 14.6% had trigly 1081 mg/dl, unchanged after 3 days of atorvastatin 80 mg nightly and a hospital diabetic regimen. Within 7 days of added BCC 15 ml with 2 g Om3F and niacin 500 mg 3 times daily his trigly was 118 mg/dl. MCT:Om3F emulsion 15 to 45 ml daily, together with Om3F, 4 to 6 g daily, optimized diabetic control and pharmacotherapy is promptly effective for severe hypertriglyceridemia. Palatable MCT:Om3F (BCC) may help therapy adherence. Reference: Hauenschild A, Bretzel RG, Schnell-Kretschmer H et al. Ann Nutr Metab. 2010:56(3):170-5.

IMMUNE MODULATION THERAPY OF INSULIN RESISTANCE

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Our novel immune modulation (IM) therapy of insulin resistance (IR) included: 4 g omega-3 fish oil daily, >2000 units vitamin D3 daily, >400 mg/kg IV immunoglobulin (IVIg) at least monthly and, within FDA guidelines, autologous stem cells, mesenchymal (MSC) from liposuction, or very small, primordial (PSC) from plasma. Representative case summaries follow. A 69 y.o. woman had SQ PSC; in 6 wks, liquid gastric emptying T-1/2 was 14 min (normal <30 min) vs. prior 94 min. Two similar women with interstitial cystitis and deficiencies of thyroid, adrenal, gonadal and B12 had IVIg for autoimmune cerebritis. Despite high diabetes mellitus risk with antiGAD 58.5 U/ml (normal <5.0 U/ml) n the younger, 41. y.o., who had IV MSC, and severe pancreatitis post Whipple surgery for Sjogren's in the older, 61 y.o., who had IV PSC, neither developed diabetes. A 68 y.o. woman with hepatic cirrhosis, ascites, encephalopathy, CHF and mitral insufficiency chose IV MSC over hospice. In one month her cognition and liver function were normal. In 3 mos her cholesterol rose 100 mg/dl; she refused chest pain therapy and died of cardiac arrest, the only serious complication in 58 cases. A 74 y.o., type 2 diabetic man with COPD, CAD and stroke had IV MSC and in 6 wks serum creatinine 2.10 mg/dl fell to 1.68 mg/dl and his rest O2 use 5 l/min fell to zero. IM therapy of IR can be remarkably effective; however, its duration of action, and also its safety in high-risk cardiac patients, need further study.

EFFECTS OF PROBUCOL ON K562 CHRONIC MYELOGENOUS LEUKEMIA CELL LINE

F. Aktan; A. Koc; Z. Buyukbingol; A.Z. Karabay

Chronic myeloid leukemia is a hematopoietic stem cell disease characterized by the existence of Bcr/Abl oncogene and protein which result with constitutive activation of tyrosine kinase, and uncontrolled cell proliferation and apoptosis resistance. Imatinib, a tyrosine kinase inhibitor, is the first choice in the treatment of CML, but problems such as therapy resistance lead investigators to discover new drug candidates. Cholesterol lowering drugs are one of the most widely used drugs in the world to prevent cholesterol accummulation in blood wessels. Probucol is among these drugs which has been acclaimed to improve heart failure. In this study, probucol, an anti-cholesterolemic drug was tested for its effects on cell proliferation and apoptosis in K562 chronic myeloid leukemia cell line originating from a late stage CML patient of blast crisis. Cell viability was determined with MTT assay spectrophotometrically. Our results showed that probucol did not inhibit cell viability at the concentrations (0.1-10 uM) tested. In the literature, anti-proliferative and apoptotic effects have been suggested for probucol in ovarian cancer cells, glioma cells and athymic nude Mouse xenografted human head and neck squmous carcinoma cells. Since we could not find a significant viability inhibitor activity for Probucol in K562 chronic myeloid leukemia cells, we can conclude that modulation of cell viability by probucol may depend on the dysregulated biochemical pathway in every different cancer type. We suggest to examine its effects on chronic myeloid leukemia in more detail to understand its main action mechanism in this cell line.

BASELINE CHARACTERISTICS OF PATIENTS WITH AND WITHOUT DIABETES IN STELLAR-3 AND 4 - TWO GLOBAL PHASE 3 CLINICAL TRIALS FOR ADVANCED FIBROSIS DUE TO NONALCOHOLIC STEATOHEPATITIS (NASH)

Zobair M. Younossi[1]; Eric J. Lawitz[2]; Vincent Wai-Sun Wong[3]; Manuel Romero-Gomez[4]; Takeshi Okanoue[5]; Michael Trauner[6]; Deyuan Jiang[7]; Kathryn Kersey[7]; Georgia Li[7]; Bryan J. McColgan[7]; Robert P. Myers[7]; C. Stephen Djedjos[7]; Stephen A. Harrison[8]; Zachary Goodman[1]; Quentin M. Anstee[9]

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Background: Greater than 50% of patients with diabetes are estimated to have NASH. Here we describe the baseline characteristics of patients with and without diabetes enrolled in two randomized, placebo-controlled, Phase 3 trials of selonsertib, an apoptosis signal-regulating kinase 1 (ASK1) inhibitor, for the treatment of advanced fibrosis due to NASH.

Methods: Patients recruited from over 400 sites in 24 countries underwent liver biopsy and were eligible based on presence of NASH and advanced fibrosis (stage F3-F4). Enrollment was stratified by diabetes status.

Results: A total of 1679 patients were enrolled including 1239 (74%) with diabetes (70% among F3 and 77% among F4). As expected, patients with diabetes had higher values of glucose (131 vs 98 mg/dL), hemoglobin A1C (6.9% vs 5.5%), and BMI (33.1 vs 31.5 kg/m^2) compared to those without diabetes (all p<0.05). While serum ALT and AST did not differ between groups, patients with diabetes had higher GGT (73 U/L vs 57 U/L) and more severe liver stiffness as estimated by FibroScan® (16.8 vs 14.0 kPa, all p<0.001). While metformin was the most commonly prescribed diabetes medication (~70%), SGLT-2 and GLP-1 mediations were also used in approximately 20% of enrolled patients with diabetes.

Conclusion: Diabetes is an important risk factor for advanced fibrosis due to NASH; ~70% of patients enrolled in these global Phase 3 trials have diabetes. In addition, patients with diabetes appear to have more severe liver fibrosis.

CALIBRATING REGIONAL DIFFERENCES IN DIABETES COMPLICATIONS AND MORTALITY FOR THE BUILDING, RELATING, ASSESSING, AND VALIDATING OUTCOMES (BRAVO) MODEL

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Tulane University

Objectives: To improve the BRAVO diabetes model based on the ACCORD study cohort in the United States (US), we aimed to calibrate the regional variations in risks of diabetes complications in the non-US regions as its globalization module.

Methods: A systematic literature review was conducted to identify eligible clinical trials to support calibration. The BRAVO model was used to simulate CVD outcomes based on the baseline characteristics of clinical trial cohorts. We optimized the regression methods to estimate regional variations of US, Europe, Asia, and other regions in six key outcomes, including myocardial infarction (MI), congestive heart failure (CHF), stroke, angina, revascularization, and mortality.

Results: Among the 18 clinical trials identified to support the calibration process, the regional variations were found in four cardiovascular outcomes. Compares to other regions, individuals from US were found to have higher risk of MI (hazard ratio (HR): 1.64, 95% confidence interval (CI):1.41~1.91), and revascularization (HR: 3.6, 95% CI: 2.94~4.41). Individuals from Europe were found to have lower risk of stroke (HR: 0.61, 95% CI: 0.46~0.81)), and individuals from other regions besides US, Europe and Asia were found to have lower risk of CHF (HR: 0.18: 95% CI: 0.06~0.58). The simulated outcomes were regressed on observed outcomes through an ordinary least squared (OLS) model, with an intercept (0.026), slope (1.005), and r-square (0.789) indicating good prediction accuracy.

Conclusion: The globalization module for the BRAVO model shows an improved prediction accuracy when the diabetes simulation model is applied on populations from both US and non-US regions.

IMPROVED REAL-WORLD OUTCOMES FOR TYPE 2 DIABETES PATIENTS ON BASAL-BOLUS INSULIN THERAPY SWITCHING TO INSULIN GLARGINE 300 U/ML VS. 1ST GENERATION BASAL INSULINS

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Objective: To comparatively evaluate real-world clinical outcomes in type 2 diabetes (T2D) patients on basal-bolus insulin therapy (BBT) who switched their basal insulin (BI) to either insulin glargine 300 U/mL (Gla-300) or a 1st generation BI (1G-BI).

Methods: This retrospective observational study used electronic medical records from the Predictive Health Intelligence Environment database (IBM Explorys). Adults (≥18 years) with T2D on BBT who switched their BI were studied. Patients in the Gla-300 and 1G-BI cohorts were propensity-score matched (1:1). Endpoints were: glycated hemoglobin (A1C) change from baseline and target attainment (<7.0% and <8.0%) at 6 months; hypoglycemia (ICD-9/ICD-10 and/or plasma glucose ≤70 mg/dL, or inpatient/emergency department [ED]-associated), with 6 months or variable (until discontinuation or 6 months) follow-up.

Results: Baseline demographics and clinical characteristics were similar: Gla-300 (N=1486) vs. 1G-BI (N=1486; insulin glargine 100 U/mL, 29.4%; insulin detemir, 70.6%). Comparing matched groups at 6 months, mean A1C reduction was similar (0.52% vs. 0.45%; p=0.317), as was attainment of A1C goals <7.0% (16.0% vs. 19.0%; p=0.054) and <8.0% (43.5% vs. 41.8%; p=0.483). At 6 months (fixed duration), adjusting for baseline hypoglycemia, Gla-300 patients had significantly fewer all hypoglycemia events (0.76 vs. 0.95 events per patient per year [PPPY]; p=0.036). With variable follow-up, Gla-300 patients had significantly fewer all hypoglycemia events (0.63 vs. 0.77 PPPY; p<0.001) and inpatient/ED-related events (0.15 vs. 0.25 PPPY; p<0.001).

Conclusion: In patients with T2D on BBT, switching to Gla-300 vs. 1G-BIs was associated with similarly improved glycemic control, but significantly lower risk of hypoglycemia and inpatient/ED-related hypoglycemia.

HIGH REAL-WORLD HEALTHCARE COSTS IN NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)/NON-ALCOHOLIC STEATOHEPATITIS (NASH) COMPENSATED CIRRHOSIS (CC) PATIENTS WITH AND WITHOUT TYPE-2 DIABETES MELLITUS (DM): A LARGE GERMAN DATABASE STUDY

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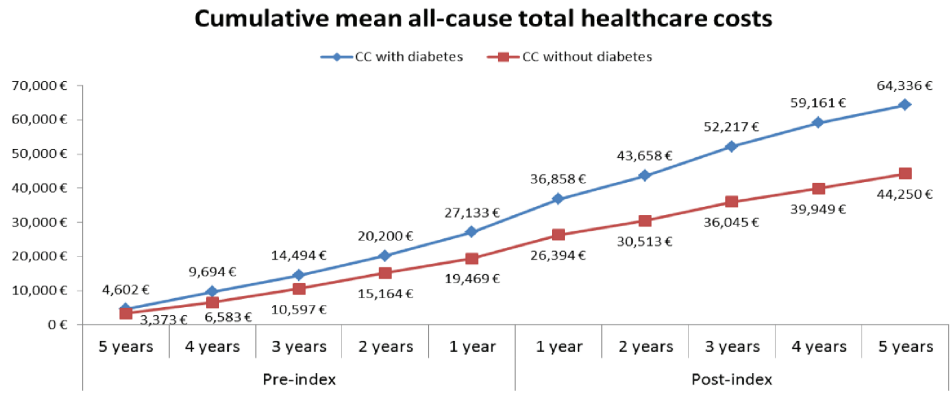
Background and Aims: This study examined the comorbidities and healthcare costs among German NALFD/NASH DM and non-DM patients once they were diagnosed with CC.

Method: Adult patients with NAFLD/NASH diagnosis from 2011-2016 were identified from the InGef claims. CC diagnosis followed the NASH/NAFLD diagnosis (first CC diagnosis as the index date). Patients were stratified by DM or non-DM status and excluded if they had other causes of liver disease. All-cause mortality was evaluated within 1-year post index. Mean annual healthcare costs were examined for patients with 1-5 years of CE pre- and post-index.

Results: The study included 555 NAFLD/NASH CC patients – 307 with DM (68.1 years) and 248 non-DM (63.7 years). DM patients had a high prevalence of additional comorbidities – hypertension 90%, obesity 53%, and dyslipidemia 61%, which were higher than in non-DM patients. The total healthcare costs for all study patients in the 1-year post-index period cumulated to €2,985,320 and €1,717,607 for DM and non-DM patients, respectively. Mean annual healthcare costs increased to €9,724 and €6,926 for DM and non-DM patients respectively. (P<0.001 for DM vs. non-DM, pre- vs post-index) The cumulative mean total costs increased 137% and 127% over five-year period for DM and non-DM patients, respectively. (Figure).

Conclusion: In the 5 years following CC diagnosis German NAFLD/NASH DM patients experienced an increase of over €37,000 in cumulative costs and non-DM patients a nearly €25,000 increase. Improved patient management and treatment options are needed to improve patient outcomes and reduce healthcare costs.



SUBSTANTIAL HEALTHCARE UTILIZATION (HCU) AND COSTS AMONG NON-ALCOHOLIC STEATOHEPATITIS (NASH) PATIENTS WITH COMORBID DIABETES MELLITUS (DM): REAL-WORLD ANALYSIS OF 2007-2015 US MEDICARE DATA

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Background and Aims: Diabetes mellitus (DM) is a known risk factor for NASH. Data on HCU and costs in NASH patients with compensated cirrhosis (CC) by DM status is lacking. This study evaluated the impact of concurrent DM on HCU and costs among NASH patients with CC.

Method: The study population was extracted from 2007-2015 US Medicare 20% sample data and included NASH/Non-Alcoholic Fatty Liver Disease (NAFLD) patients (identified via ICD codes) with CC aged ≥18 years. First CC diagnosis date marked the index date. Patients with other (non-NAFLD) causes of liver disease were excluded. HCU and costs were analyzed and adjusted to annual values in 2015 USD.

Results: The cohort included 3,775 NASH/NAFLD CC patients with mean age 67.0 (±10.9) years and 63.3% females. Comorbidity burden was high in CC DM patients - hypertension 97.1% and hyperlipidemia 95.3%. For CC DM patients, mean inpatient visits were 0.52 (pre) vs. 0.99 (post) (p<0.001), and for CC non-DM patients, mean inpatient visits were 0.37 (pre) vs. 0.76 (post) (p<0.001). The total costs for CC DM patients were $20,646 (pre) vs. $35,359 (post) (p<0.001), and for CC non-DM patients were $15,633 (pre) vs. $27,953 (post) (p<0.001).

Conclusion: When stratified by DM status, impact of CC diagnosis on HCU and costs among NASH/NAFLD patients was substantial – costs increased by 71.3% (CC DM) and 78.8% (CC non-DM). Early identification and effective treatment of NASH/NAFLD DM patients is needed to reduce the risk of disease progression and higher associated HCU and costs.

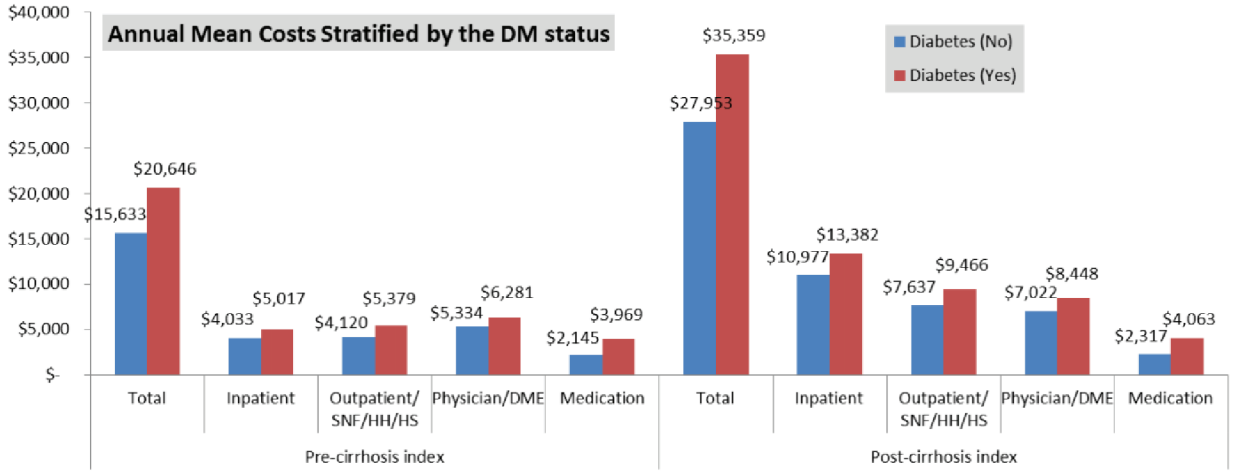

Fig. Durable medical equipment (DME); Skilled nursing facility (SNF); Home health (HH); Hospice (HS)

WHOLE BLOOD T_{2S} AND T_{2P} AS BIOMARKERS FOR EARLY INSULIN RESISTANCE: POTENTIAL FOR POINT-OF-CARE SCREENING

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Prediabetes and metabolic syndrome identify individuals with increased cardiometabolic risk. However, by the time those conditions develop, a significant decline in pancreatic insulin secretion has already occurred. To preserve beta cell function and arterial wall integrity, an optimal screening and intervention strategy would identify at-risk individuals earlier. Here we describe a new approach for detecting early metabolic dysregulation, a condition that includes compensatory hyperinsulinemia (early insulin resistance) and subclinical inflammation. The method uses a fingerstick drop of whole blood and a tabletop magnetic resonance device about the size of a toaster. It measures the ^1H transverse relaxation times (T_2) for the plasma supernatant (T_{2s}) and the cell pellet (T_{2p}) of settled anti-coagulated whole blood. No chemical reactions or reagents are required, and the measurement takes 3 minutes. In a discovery cohort of 43 asymptomatic non-diabetic subjects, remarkably strong bivariate correlations were observed between T_{2p} and markers of poor metabolic health, namely hyperinsulinemia, inflammation and dyslipidemia. By contrast, T_{2s} correlated with red blood cell count and hematocrit, even though the supernatant was devoid of blood cells. Upon varying the ratio of supernatant to pellet, we observed that T_{2s} was inversely proportional to the sixth power of hematocrit. Thus, a magnetic susceptibility gradient from the paramagnetic pellet was enhancing T_2 relaxation in the supernatant. After mathematically correcting for this gradient, T_{2s} can be used to calculate plasma water T_2, another early marker of poor metabolic health. This approach is powerful and practical, and shows promise for translation into clinical point-of-care settings.

EFFECTS OF A STRUCTURED EDUCATIONAL INTERVENTION PROGRAM ON METABOLIC CONTROL OF PATIENTS WITH TYPE 2 DIABETES

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The disease burden of diabetes is increasing worldwide, particularly in developing countries. The IDF reported that currently 425 million adults suffer from it. In Mexico, diabetes and its complications are among the leading causes of death. According to the American Diabetes Association, nutritional counseling, intensive lifestyle change and education are recommended in order to achieve the goals of control. The approach to managing diabetes must be fundamentally comprehensive, this being the best example of the good results of teamwork with health professionals trained with an educational-therapeutic vision. The aim of the present study was to evaluate the effects of a dietetic-motivational and educational strategy in a group of type 2 diabetes patients. We evaluated the effect of an intervention based on education during 3 months in 70 patients with type 2 diabetes mellitus. The anthropometric and metabolic characteristics of the group were determined at the beginning and at the end of the study (attached table). At the end of the study, a statistically significant decrease in fasting glucose was found from 194.2 ± 70.0 to 158.5 ± 61.1 (P = 0.024), blood cholesterol from 210.7 ± 28.9 to 184.2 ± 37.3 (P = 0.020) and body weight of 76.5 ± 18.7 to 75.4 ± 18.9 (P = 0.004). Additionally, a clinically significant decrease in HbA1c from 8.1 ± 2.8 to 7.2 ± 2.3 was found. This work confirms the importance of nutritional treatment and therapy based on education, especially working with groups to reduce cardiovascular risk and control metabolic parameters.

Table. Characteristics of the group at the beginning and end of the study

Variable	Before the intervention	5 months after the intervention	P value
Age (years)	57.5 ± 8.9		
Height (m)	147.0 ± 30.6		
Glucose (mg/dl)	194.2 ± 70.0	158.5 ± 61.1	0.024
Colesterol (mg/dl)	210.7 ± 28.9	184.2 ± 37.3	0.020
Triglicéridos (mg/dl)	213.7 ± 88.5	183.7 ± 73.2	0.256
Weight (kg)	76.5 ± 18.7	75,4 ± 18.9	0.004
Waist circumference (cm)	102.9 ± 11.7	102.3 ± 12.3	0.624
Waist to hip index	0.95 ± 0.06	0.96 ± 0.05	0.063
HbA1c (%)	8.1 ± 2.8	7.2 ± 2.3	0.122

Paired *t*-tests were used in comparing means; $^*P < 0.05$ is significant (two-tailed).

VARIATIONS IN ADULT TYPE 2 DIABETES PREVENTION PROGRAMS FOR LATINOS IN THE US: A SYSTEMATIC LITERATURE REVIEW OF THE PAST 14 YEARS

Daniel Lopez; Michelle Seu; Anisha Bellur; Aaron Esagoff; Ozlem Equils

MiOra

Background: Latinos are at a higher risk of obesity, type II diabetes, and diabetes-related mortality. Objective: To assess the efficacy of different diabetes intervention techniques and use of community health workers for Latinos. Search Strategy: We searched the American Diabetes Association Database using search terms "diabetes prevention", "community", "health", "healthcare workers", and "promotora". We obtained over 12,000 results, looked through the first three pages generated per each search term, and eliminated articles not focused on type II diabetes or the use of lifestyle changes to combat type II diabetes. No year restriction was applied. Selection criteria: We found 12 articles, selecting only randomized control trials (RCTs) studies on Latinos and adults in the USA.

Data collection and analysis: Four independent investigators reviewed the literature following the Cochrane Handbook guidelines; external authors were contacted when additional information was necessary.

Main results: From the 12 RCTs studies (17269 participants) on Latinos and adults (13578 females, 3691 males, average age 51.9 ± 3.5) in the USA, all utilized interviews, ranging from semi-structured to unstructured, with standard diabetes assessments to assess their intervention success. Interventions involved socioeconomically altered diabetes prevention programs, improving results through psychosocial mechanisms such as social support, goal attainment, and emotional support.

Authors' conclusions: To enhance diabetes prevention programs for minorities like Latinos, emphasis on the socioeconomic intricacies and available health support system(s) to address psychosocial health is necessary for improving programs' successes.

PATIENT PROFILE AND BURDEN OF ILLNESS: CHRONIC KIDNEY DISEASE (CKD) IN A POPULATION WITH TYPE 2 DIABETES (T2D)

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Objective: Using a large US claims database, this retrospective study compared patient characteristics, healthcare utilization and expenditure between T2D patients with and without CKD.

Methods: Adult patients who had ≥1 T2D diagnosis (ICD-9-CM 250.x0/2; ICD-10-CM E11.x) in 2015, with continuous enrollment and ≥1 serum creatinine measurement during 2015 were included. Patients were categorized into CKD (eGFR <60mL/min/1.73m^2) and non-CKD (eGFR ≥60mL/min/1.73m^2) groups. Healthcare utilization and cost in 2015 was assessed and compared between CKD and non-CKD groups.

Results: 434,556 T2D patients were included in the study and 111,697 (25.7%) had CKD. Compared with non-CKD patients, T2D-CKD patients were older (mean 74 vs. 62 years), more female (55.8% vs. 49.3%), and Caucasian (68.9% vs. 60.1%; all p<0.001). CKD patients had more comorbidities than non-CKD patients (Elixhauser index: 5.7 vs. 3.9, p<0.001; diabetes complication: 52% vs. 28%). Comparing CKD vs. non-CKD patients, 54.6% vs. 61.7% received oral antidiabetes drugs (biguanides, 34.0% vs. 54.1%; sulfonylureas, 27.4% vs. 20.8%; linagliptin, 2.5% vs. 1.5%; SGLT2 inhibitors, 2.1% vs. 5.5%); 20.6% vs. 12.1% received insulin (all p<0.001). More CKD vs. non-CKD patients had been hospitalized (21.4% vs 11.4%; p<0.001) and had emergency department visits (30.4% vs 19.6%; p<0.001). Average annual healthcare costs for CKD patients were significantly higher than for non-CKD patients ($24,740 vs $14,885; p<0.001).

Conclusions: T2D-CKD patients were older and had more comorbidity including diabetes complication such as coronary artery disease and retinopathy compared with non-CKD patients. They also had limited treatment options and significantly greater healthcare utilization and cost than non-CKD patients.

INDEPENDENT AND COMBINED EFFECT OF THE UCP2 45-BP INDEL POLYMORPHISM WITH PGC-1A GLY482SER, SEDENTARY LIFESTYLE AND SMOKING ON METABOLIC SYNDROME DEVELOPMENT

Csép Katalin; Bálint Ágnes; Szigeti Eszter

University of Medicine and Pharmacy Tg, Mures, Romania

Mitochondrial dysfunction and oxidative stress are involved in insulin resistance and metabolic syndrome development, though the cause-effect relationship remains unclear. Overexpression of the widely expressed uncoupling protein UCP2 associates with decreased ROS production, while its potentially functional 45-bp INDEL polymorphism was reported inconsistently with metabolic disturbances. We proposed to investigate the role of this frequent variant of a gene central for mitochondrial function on disease risk, in combination with the common Gly482Ser polymorphism of the transcriptional coactivator PGC-1α controlling UCP2 and crucial for mitochondrial biogenesis, as well as sedentary lifestyle and smoking characterized by added oxidative stress. 306 middle-aged persons from a central Romanian region were investigated in a case-control study. Metabolic syndrome was diagnosed according to the IDF criteria, lifestyle characteristics were assessed by PhenX-based questionnaires, and genotyping was done by PCR-RFLP. Minor allele frequency in cases and controls was 26.96/21.34%; no significantly increased disease risk (OR=1.43, p=0.19, CI95%= 0.86-2.39) or genotype-dependent differences in metabolic parameters, age at onset of manifestations or complications could be demonstrated for UCP2-INDEL solely. As compared to wild-type homozygous persons, however, carriers of variant combinations for both genes showed an increased risk (OR=2.02, p=0.05), further augmented in sedentary lifestyle and smoking combined with carrier status (OR: 5.12 and 3.28 respectively, p<0.002). In conclusion, the UCP2 45-bp INDEL polymorphism-associated predisposing effect for metabolic syndrome may become manifest in case of gene and environment interactions, such as PGC-1α, sedentary lifestyle or smoking, presumably by increased mitochondrial oxidative stress, potentially addressed by genotype-based personalized interventions.

DIABETES AWARENESS WITHIN THE INDIAN COMMUNITY

Anisha Bellur; Caitlyn Kellogg; Daniel Lopez; Dr. Ozlem Equils

MiOra

Background: Diabetes rates increase for low- and middle-income countries, such that India, which had 31.7 million diabetic people in 2000, is expected to more than triple by 2030. Studies have shown a vegetarian or vegan diet can help control the effects of diabetes. Objective: To assess Indian community members' knowledge about the effects of a vegetarian diet on diabetes.

Methods: An IRB-approved (WIRB No 1924863-44007609), 32-question online survey about personal history with diabetes and dietary habits was distributed to an international Indian temple community and through a messaging app. Individuals were educated on healthy lifestyles, and results were analyzed by differences in subjects' body measurements, dietary habits, and family obesity and diabetes trends between non-vegetarians and vegetarians.

Results: 71 people completed the study. 40.0% (6/15) of non-vegetarians have struggled with weight compared to 25.0% (14/56) of vegetarians. 20.0% (3/15) of non-vegetarians indicated a family-obesity trend compared to 10.7% (29/56) of vegetarians. 40.0% (6/15) of non-vegetarians and 51.8% (29/56) of vegetarians had a family-diabetes trend. All non-vegetarians (15/15) indicated not having diabetes while 5.5% (3/56) of vegetarians indicated having diabetes. Of the vegetarians, 48.2% (27/56) believed dieting could help manage diabetes while 30.4% (17/56) believed a vegetarian diet could. Of the non-vegetarians, 77.3% (11/15) believed dieting helps manage diabetes and 13.3% (2/15) believed becoming vegetarian would help.

Conclusion: A vegetarian diet can help those struggling with weight gain. A lack of understanding of diet's impact on diabetes suggests further educational efforts are needed for such communities.

TRANSLATION AND CROSS-CULTURAL ADAPTATION OF THE FINNISH DIABETES RISK SCORE INTO BRAZILIAN PORTUGUESE LANGUAGE

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Background and aims: The Finnish Diabetes Risk Score (FINDRISC) is an instrument that predicts the risk of developing diabetes in 10 years. The aim of this paper is to describe the process of translation and cross-cultural adaptation of FINDRISC into a Brazilian Portuguese language and its reliability study.

Method: The Transcultural translation and adaptation followed the recommendations of the principles of good practice for cross-cultural adaptation of research tools developed by the 10-step International Society for Pharmacoeconomics and Outcomes Research task force. The reliability study was performed by analyzing the level of agreement between the test-retest responses of FINDRISC-BR using the Kappa Coefficient.

Results: There was 100% understanding of the instrument translated and adapted by users and health professionals: physicians, registered dietitian nutritionist, nurses and nursing technicians. The Kappa coefficient values of the FINDRISC-BR variables revealed a Concordance level close to 1.0, indicating the instrument's Adequate Reliability (Table).

Conclusion: The transcultural translation and adaptation process of the Finnish Diabetes Risk Score for Brazilian Portuguese and its reliability study demonstrated satisfactory evidence to be used in the practice of Primary Health Care in the Brazilian context.

Table. Kappa coeficiente values and concordance level

	Kappa coefficient	CI95%
Age	0.96	0.92 – 1.00
Body Mass Index	0.92	0.85 – 0.99
Waist Circumference	0.92	0.86 – 0.99
Physical Activity	0.78	0.64 – 0.94
Fruit and vegetable intake	0.63	0.41 – 0.84
Use of medication for high blood pressure	0.93	0.85 – 1.00
Impaired glucose metabolism	0.96	0.88 – 1.00
Family History of Diabetes	0.87	0.77 – 0.96

CI = confidence interval

CONTEMPORARY REAL WORLD CHARACTERISTICS AND DIABETES MANAGEMENT IN CHILDREN AND ADOLESCENTS WITH TYPE 1 (T1D) AND TYPE 2 (T2D) IN THE U.S.

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Objective: To describe characteristics and diabetes management in children and adolescents with Type 1 (T1D) and Type 2 (T2D) diabetes as recorded in the Electronic Medical Records (EMR) from U.S. health care centers.

Methods: Data were drawn from a subset of the TriNetX federated network of EMRs from approximately 39 million patients in 36 Health Care Organizations predominately in the U.S. EMR data from patients <18 years old coded using International Classification of Diseases (ICD) 9/10 codes corresponding to T1D or T2D diagnosis in the network on or before October 15, 2018 were queried.

Results: In all, 15,644 patients coded as T1D and 3,056 patients coded as T2D were included in the present study. Based on EMR data, diagnoses of both T1D and T2D increased with age. T1D was slightly higher in males than females and was highest in white youth. Glycemic control, as measured by HbA1c, tended to worsen with increasing age over the pediatric age range, with highest values in adolescents aged 10-17 years with T1D.

Conclusion: These results point to considerable potential variation in the coding of diagnoses and management for pediatric diabetes. The amalgamation of real world data from multiple sources presents several issues, including gaps and inconsistencies arising from differences in study design and methodologies for collection. However, these results can provide important insight into the current landscape of diabetes among children and adolescents in the U.S. and also reveal a need for education to enable more rigorous attention to proper coding of youth with diabetes.

Table. EMR database summary of diabetes characteristics among 15,644 pediatric patients

	T1D				*T2D*			
	All N=15,644	<6 yrs old N=823	6-9 yrs old N=2,429	10-17 yrs old N=12,392	All N=3,056	<6 yrs old N=337	6-9 yrs old N=281	10-17 yrs old N=2,438
Age, years	13 (4)	4 (1)	9 (1)	14 (2)	13 (4)	3 (1)	8 (1)	14 (2)
Age at diagnosis, years[a]	10 (6)	3 (2)	8 (2)	13 (2)	13 (7)	2 (2)	8 (5)	14 (3)
BMI percentile	38.99 (35.75)	29.37 (25.94)	34.49 (29.34)	40.66 (37.37)	35.30 (26.84)	24.23 (24.54)	20.14 (10.72)	39.12 (27.51)
Sex (%) (f/m)	47/51	40/60	48/51	47/51	43/57	47/52	50/50	59/41
Race (%) (white/black/unknown)	67/10/22	83/5/7	66/9/24	67/10/22	50/27/20	53/24/19	58/20/19	48/28/20
OAD treatment (% by treatment)	12	22	15	10	41	28	25	45
Insulin treatment (%)[b]	66	62	66	66	21	9	11	24
Insulin pump use (%)	17	11	15	18	1	3	0	1
CGM use (%)	4	5	4	3	0	0	0	0
HbA1c, %	9.09 (2.25)	8.72 (2.02)	8.80 (2.05)	9.16 (2.29)	7.32 (2.36)	6.64 (2.23)	6.57 (1.90)	7.34 (2.37)
Glucose, mg/dL[c]	237.02 (142.05)	234.17 (153.04)	234.44 (148.05)	237.73 (140.02)	143.59 (90.30)	115.94 (82.85)	120.38 (68.31)	148.24 (91.87)
FPG, mg/dL[d]	158.26 (127.04)	NA	104.57 (28.03)	165.63 (133.40)	102.66 (35.40)	92.00 (0)	91.67 (8.81)	103.18 (36.13)

Abbreviations: BMI = body mass index; CGM = continuous glucose monitor; FPG = fasting plasma glucose; HbA1c = hemoglobin A1c; OAD = oral antidiabetic.
Data are mean ± (standard deviation) unless otherwise stated.
[a]Age at diagnosis was calculated for all network patients who satisfied the criteria, regardless of current age. [b]Some patients in the database will have received insulin prescriptions outside of the network (i.e., at a local clinic) and therefore would not be captured in these data. [c]Glucose measured in serum, plasma or blood from the most recent lab result for each patient who satisfied the criteria. Fasting status is not specified. [d]Values presented only for patients with a confirmed fasting status in serum or plasma.

USING METABOLIC MARKERS TO IDENTIFY INSULIN RESISTANCE IN PREMENOPAUSAL WOMEN WITH AND WITHOUT POLYCYSTIC OVARIAN SYNDROME

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Background: Insulin resistance is associated with increased risk for type 2 diabetes mellitus and cardiovascular disease. Determining insulin resistance is invasive and time-consuming, and thus not routinely done in clinical practice. Simple metabolic markers to predict insulin resistance exist but have not been validated in premenopausal women or women with polycystic ovary syndrome (PCOS).

Objective: To evaluate the ability of metabolic markers associated with insulin resistance to identify premenopausal women with/without PCOS who are insulin resistant.

Design/Setting: Cross-sectional analysis

Participants: 242 nondiabetic premenopausal overweight/obese women with and without PCOS.

Methods: Insulin resistance was quantified by the steady-state plasma glucose during the modified insulin-suppression test. Metabolic markers (body mass index, lipid and lipoprotein concentrations, fasting glucose) were evaluated for their discriminative ability to identify participants with insulin resistance, using area under the receiver-operating characteristic curve (AUC) analysis. Optimal cut-points were identified and evaluated for the predictive power.

Results: Triglyceride/HDL cholesterol (TG/HDL-C) ratio was the best marker overall (AUC 0.75, 95% confidence interval (CI) 0.86 - 0.81). In the PCOS subset, the total cholesterol (TC)/HDL-C ratio performed slightly better (AUC 0.85, 95% CI 0.74 - 0.95). Optimal cut-points for TG/HDL-C ratio were 1.6 and 1.3, respectively, for premenopausal women without and with PCOS, and 3.0 for TC/HDL ratio in women with PCOS.

Conclusion: TG/HDL-C ratio, and TG/HDL-C ratio or TC/HDL-C ratio can identify insulin resistance in premenopausal women without and with PCOS, respectively. These metabolic markers can be used to tailor lifestyle and medical interventions to improve health outcomes in premenopausal women.

Table. Optimal cut-points for metabolic markers

Marker	SSPG ≥ 180 mg/dL	SSPG < 180 mg/dL	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV	Positive LR (95% CI)	Negative LR (95% CI)
A) Overweight/obese pre-menopausal women without PCOS: Prevalence of insulin resistance = 50%								
Triglycerides-HDL cholesterol ratio ≥ 1.6	77 (72)	30 (28)	77 (75 - 79)	58 (56 - 60)	72	64	1.82 (1.36 - 2.44)	0.4 (0.27 - 0.6)
Triglycerides-HDL cholesterol ratio < 1.6	23 (36)	41 (64)						
HDL cholesterol < 44 mg/dL	45 (80)	11 (20)	45 (44 - 46)	85 (82 - 87)	80	52	2.9 (1.62 - 5.2)	0.65 (0.53 - 0.8)
HDL cholesterol ≥ 44 mg/dL	55 (48)	60 (52)						
Total cholesterol-HDL cholesterol ratio ≥ 3.7	63 (73)	23 (27)	63 (61 - 65)	68 (66 - 70)	73	56	1.94 (1.34 - 2.8)	0.55 (0.41 - 0.74)
Total cholesterol-HDL cholesterol ratio < 3.7	37 (44)	48 (56)						
B) Pre-menopausal women with PCOS: Estimated prevalence of insulin resistance = 66%								
Triglycerides-HDL cholesterol ratio ≥ 1.3	43 (83)	9 (17)	90 (87 - 92)	61 (58 - 64)	83	74	2.29 (1.36 - 3.85)	0.17 (0.07 - 0.41)
Triglycerides-HDL cholesterol ratio < 1.3	5 (26)	14 (74)						
HDL cholesterol < 52 mg/dL	39 (87)	6 (13)	81 (79 - 84)	74 (70 - 77)	87	65	3.11 (1.54 - 6.27)	0.25 (0.13 - 0.47)
HDL cholesterol ≥ 52 mg/dL	9 (35)	17 (65)						
Total cholesterol-HDL cholesterol ratio ≥ 3.0	47 (80)	12 (20)	98 (95 - 101)	48 (45 - 51)	80	92	1.88 (1.27 - 2.79)	0.04 (0.01 - 0.29)
Total cholesterol-HDL cholesterol ratio < 3.0	1 (8)	11 (92)						
C) Non-PCOS and PCOS women combined: Estimated prevalence of insulin resistance = 51%								
Triglycerides-HDL cholesterol ratio ≥ 1.7	103 (77)	30 (23)	70 (68 - 71)	68 (66 - 70)	77	59	2.18 (1.59 - 2.98)	0.45 (0.34 - 0.6)
Triglycerides-HDL cholesterol ratio < 1.7	45 (41)	64 (59)						
HDL cholesterol < 44 mg/dL	76 (84)	14 (16)	51 (50 - 53)	85 (83 - 87)	84	53	3.45 (2.08 - 5.73)	0.57 (0.47 - 0.69)
HDL cholesterol ≥ 44 mg/dL	72 (47)	80 (53)						
Total cholesterol-HDL cholesterol ratio ≥ 4.2	82 (84)	16 (16)	55 (54 - 57)	83 (81 - 85)	84	54	3.26 (2.04 - 5.21)	0.54 (0.44 - 0.66)
Total cholesterol-HDL cholesterol ratio < 4.2	66 (46)	78 (54)						

Abbreviations: CI = confidence interval; HDL = high density lipoprotein; NPV = negative predictive value; PPV = positive predictive value; SSPG = steady-state plasma glucose.