Diabetes, Insulin resistance
Used studies and abstracts

1) Mayaudon H, Miloche PO, Bauduceau B A new simple method for assessing sudomotor function: Relevance in type 2 diabetes. Diabetes Metab. 2010 Aug 23

METHODS: A total of 133 type 2 diabetic patients and 41 control subjects were tested. Participants placed their hands and feet on nickel electrodes, and an incremental low direct current was applied to the anode for 2min. ESC was calculated from the resulting voltage and generated current. ESC diagnostic accuracy was analyzed by ROC curve modeling, and reproducibility was assessed using Bland-Altman analysis.
RESULTS: The ESC of hands and feet was significantly reduced in diabetic patients (53+/-16muSi and 67+/-14muSi, respectively) compared with control subjects (68+/-16muSi and 80+/-7muSi, respectively; P<0.0001). ESC values had a sensitivity of 75% and specificity of 100%, with an area under the ROC curve of 0.88 at a threshold of 50% on the EZSCAN scale. Coefficients of variation in hand and foot measurements were 15 and 7%, respectively.

2) P. T. Ahamed Seyd, V. I. Thajudin Ahamed, Jeevamma Jacob, Paul Joseph K . Time and Frequency Domain Analysis of Heart Rate Variability and their Correlations in Diabetes Mellitus International Journal of Biological and Life Sciences 4:1 2008

Abstract
Diabetes mellitus (DM) is frequently characterized by autonomic nervous dysfunction. Analysis of heart rate variability (HRV) has become a popular noninvasive tool for assessing the activities of autonomic nervous system (ANS). In this paper, changes in ANS activity are quantified by means of frequency and time domain analysis of R-R interval variability. Electrocardiograms (ECG) of 16 patients suffering from DM and of 16 healthy volunteers were recorded. Frequency domain analysis of extracted normal to normal interval (NN interval) data indicates significant difference in very low frequency (VLF) power, low frequency (LF) power and high frequency (HF) power, between the DM patients and control group. Time domain measures, standard deviation of NN interval (SDNN), root mean square of successive NN interval differences (RMSSD), successive NN intervals differing more than 50 ms (NN50 Count), percentage value of NN50 count (pNN50), HRV triangular index and triangular interpolation of NN intervals (TINN) also show significant difference between the DM patients and control group.

3) Stein PK, Barzilay JI, Chaves PH, Traber J, Domitrovich PP, Heckbert SR, Gottdiener JS Higher levels of inflammation factors and greater insulin resistance are independently associated with higher heart rate and lower heart rate variability in normoglycemic older individuals: the Cardiovascular Health Study . Cardiovascular Division, Washington University School of Medicine, St. Louis, Missouri 63108, USA.

Abstract
OBJECTIVES: To explore the relationship between (1) insulin resistance and inflammation factors with (2) higher heart rate (HR) and lower heart rate variability (HRV) in normoglycemic older adults.
DESIGN: Cross-sectional population-based study.
PARTICIPANTS: Five hundred forty-five adults aged 65 and older with normoglycemia (fasting glucose <100 mg/dL) who participated in the Cardiovascular Health Study.
MEASUREMENTS: Serum levels of three inflammation proteins (C-reactive protein (CRP), interleukin 6 (IL-6), and fibrinogen); insulin resistance, quantified according to the homeostasis assessment model (HOMA-IR); HR; and four representative measures of HRV (the standard deviation of normal beat to beat intervals (SDNN), the root mean square of successive differences (rMSSD), very low frequency power (VLF), and the low- to high-frequency power ratio (LF/HF)) derived from 24-hour Holter recordings.
RESULTS: High CRP and IL-6 levels were associated with higher HR and lower SDNN and VLF after adjustment for multiple covariates, including HOMA-IR and clinical cardiovascular disease. High IL-6 was also associated with lower LF/HF. Significant univariate inverse relationships between HOMA-IR and HR and HRV were also found, but the strengths of these relationships were attenuated after adjustment for inflammation factors.
CONCLUSION: Increased levels of inflammation markers and HOMA-IR are associated with higher HR and lower

HRV. These findings suggest that inflammation may contribute to the pathogenesis of cardiovascular autonomic decline in older adults.

4) Toshiaki OTSUKA, Tomoyuki KAWADA, Masao KATSUMATA, Chikao IBUKI, and Yoshiki KUSAMA. Independent Determinants of Second Derivative of the Finger Photoplethysmogram among Various Cardiovascular Risk Factors in Middle-Aged Men. Hypertens Res Vol. 30, No. 12 (2007)

Abstract

The second derivative of the finger photoplethysmogram (SDPTG) has been used as a non-invasive examination for arterial stiffness. The present study sought to elucidate independent determinants of the SDPTG among various cardiovascular risk factors in middle-aged Japanese men. The SDPTG was obtained from the cuticle of the left-hand forefinger in 973 male workers (mean age: 44±6 years) during a medical checkup at a company. The SDPTG indices (bla and -d/a) were calculated from the height of the wave components. Multiple logistic regression analyses revealed that the independent determinants of an increased bla (highest quartile of the bla) were age (odds ratio [OR]: 1.12 per 1-year increase, 95% confidence interval [Cl]: 1.09-1.15), hypertension (OR: 1.65, 95% Cl: 1.03-2.65), dyslipidemia (OR: 1.51, 95% Cl: 1.09-2.09), impaired fasting glucose/diabetes mellitus (OR: 2.43, 95% Cl: 1.16-5.07), and a lack of regular exercise (OR: 2.00, 95% Cl: 1.29-3.08). Similarly, independent determinants of a decreased dia (lowest quartile of the d/a) were age (OR: 1.11 per 1-year increase, 95% Cl: 1.08-1.14), hypertension (OR: 3.44, 95% Cl: 2.20-5.38), and alcohol intake 6 or 7 days per week (OR: 2.70, 95% Cl: 1.80-4.06). No independent association was observed between the SDPTG indices and blood leukocyte count or serum C-reactive protein levels. In conclusion, the SDPTG indices reflect arterial properties affected by several cardiovascular risk factors in middle-aged Japanese men. The association between inflammation and the SDPTG should be evaluated in further studies.

5) Kirsi A. Virtanen, Patricia Iozzo, Kirsti Hällsten, Risto Huupponen, Riitta Parkkola, Tuula Janatuinen, Fredrik Lönnqvist, Tapio Viljanen, Tapani Rönnemaa, Peter Lönnroth, Juhani Knuuti, Ele Ferrannini and Pirjo Nuutila. Increased Fat Mass Compensates for Insulin Resistance in Abdominal Obesity and Type 2 Diabetes. Diabetes September 2005 vol. 54 no. 9 2720-2726

Abstract

To evaluate the relative impact of abdominal obesity and newly diagnosed type 2 diabetes on insulin action in skeletal muscle and fat tissue, we studied 61 men with (n = 31) or without (n = 30) diabetes, subgrouped into abdominally obese or nonobese according to the waist circumference. Adipose tissue depots were quantified by magnetic resonance imaging, and regional glucose uptake was measured using 2-[18F] fluoro-2-deoxyglucose/positron emission tomography during euglycemic hyperinsulinemia. Across groups, glucose uptake per unit tissue weight was higher in visceral (20.5 ± 1.4 μmol · min−1 · kg−1) than in abdominal (9.8 ± 0.9 μmol min−1 · kg−1, P < 0.001) or femoral (12.3 ± 0.6 μmol · min−1 · kg−1, P < 0.001) subcutaneous tissue and ∼40% lower than in skeletal muscle (33.1 ± 2.5 μmol · min−1 · kg−1, P < 0.0001). Abdominal obesity was associated with a marked reduction in glucose uptake per unit tissue weight in all fat depots and in skeletal muscle (P < 0.001 for all regions). Recent type 2 diabetes per se had little additional effect. In both intra-abdominal adipose (r = −0.73, P < 0.0001) and skeletal muscle (r = −0.53, P < 0.0001) tissue, glucose uptake was reciprocally related to intra-abdominal fat mass in a curvilinear fashion. When regional glucose uptake was multiplied by tissue mass, total glucose uptake per fat depot was similar irrespective of abdominal obesity or type 2 diabetes, and its contribution to whole-body glucose uptake increased by ∼40% in obese nondiabetic and nonobese diabetic men and was doubled in obese diabetic subjects. We conclude that 1) in abdominal obesity, insulin-stimulated glucose uptake rate is markedly reduced in skeletal muscle and in all fat depots; 2) in target tissues, this reduction is reciprocally (and nonlinearly) related to the amount of intra-abdominal fat; 3) mild, recent diabetes adds little insulin resistance to that caused by abdominal obesity; and 4) despite fat insulin resistance, an expanded fat mass (especially subcutaneous) provides a sink for glucose, resulting in a compensatory attenuation of insulin resistance at the whole-body level in men.

6) Colditz GA, Willett WC, Stampfer MJ, Manson JE, Hennekens CH, Arky RA, Speizer FE: Weight as a risk factor for clinical diabetes in women. Am J Epidemiol132 :501 – 513,1990

Abstract:
To determine the relation of body mass index (weight/height^2) with the risk of clinical non-insulin-dependent diabetes, the author's analyzed data from a cohort of 113,861 US women aged 30–55 years in 1976. During 8 years of follow-up (826,010 person-years), 873 definite cases were identified among women initially free from diagnosed diabetes. Among women of average body mass index, 23–23.9 kg/m^2 the relative risk was 3.6 times that of women having a body mass index less than 22 kg/m^2 the risk continued to increase above this level of body mass index. The authors observed a much weaker positive association with weight at age 18, and this association was eliminated after adjustment for current body mass index. Thus, weight gain after age 18 was a major determinant of risk. For an increase of 20–35 kg, the relative risk was 11.3, and for an increase of more than 35 kg, the relative risk was 17.3. Adjusting for family history did not appreciably alter the strong relation observed among women at average levels of body mass index. These data indicate that, at even average weight, women are at increased risk of clinical non-insulin-dependent diabetes and that the relation between body mass index and risk of diabetes is continuous.

7) Miyazaki Y, Glass L, Triplitt C, Wajcberg E, Mandarino LJ, DeFronzo RA: Abdominal fat distribution and peripheral and hepatic insulin resistance in type 2 diabetes mellitus. Am J Physiol Endocrinol Metab283 :E1135 –E1143,2002

Abstract
We examined the relationship between peripheral/hepatic insulin sensitivity and abdominal superficial/deep subcutaneous fat (SSF/DSF) and intra-abdominal visceral fat (VF) in patients with type 2 diabetes mellitus (T2DM). Sixty-two T2DM patients (36 males and 26 females, age = 55 +/- 3 yr, body mass index = 30 +/- 1 kg/m2) underwent a two-step euglycemic insulin clamp (40 and 160 mU. m(-2). min(-1)) with [3-3H]glucose. SSF, DSF, and VF areas were quantitated with magnetic resonance imaging at the L(4-5) level. Basal endogenous glucose production (EGP), hepatic insulin resistance index (basal EGP x FPI), and total glucose disposal (TGD) during the first and second insulin clamp steps were similar in male and female subjects. VF (159 +/- 9 vs. 143 +/- 9 cm2) and DSF (199 +/- 14 vs. 200 +/- 15 cm(2)) were not different in male and female subjects. SSF (104 +/- 8 vs. 223 +/- 15 cm2) was greater (P < 0.0001) in female vs. male subjects despite similar body mass index (31 +/- 1 vs. 30 +/- 1 kg/m2) and total body fat mass (31 +/- 2 vs. 33 +/- 2 kg). In male T2DM, TGD during the first insulin clamp step (1st TGD) correlated inversely with VF (r = -0.45, P < 0.01), DSF (r = -0.46, P < 0.01), and SSF (r = -0.39, P < 0.05). In males, VF (r = 0.37, P < 0.05), DSF (r = 0.49, P < 0.01), and SSF (r = 0.33, P < 0.05) were correlated positively with hepatic insulin resistance. In females, the first TGD (r = -0.45, P < 0.05) and hepatic insulin resistance (r = 0.49, P < 0.05) correlated with VF but not with DSF, SSF, or total subcutaneous fat area. We conclude that visceral adiposity is associated with both peripheral and hepatic insulin resistance, independent of gender, in T2DM. In male but not female T2DM, deep subcutaneous adipose tissue also is associated with peripheral and hepatic insulin resistance.

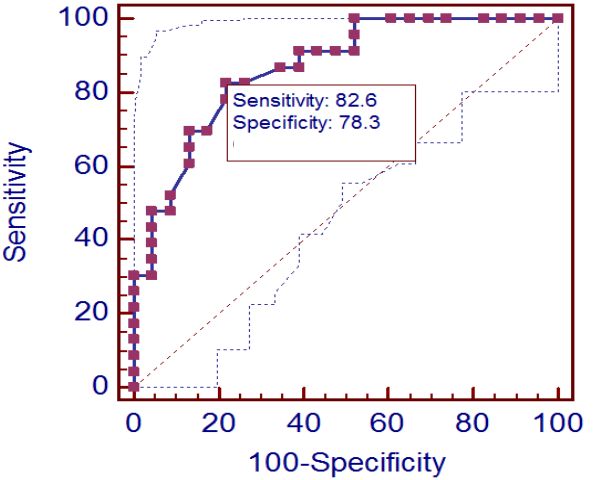
8) Ferrannini E, Natali A, Bell P, Cavallo-Perin P, Lalic N, Mingrone G: Insulin resistance and hypersecretion in obesity: European Group for the Study of Insulin Resistance (EGIR). J Clin Invest100 :1166 –1173,1997

Abstract:
Insulin resistance and insulin hypersecretion are established features of obesity. Their prevalence, however, has only been inferred from plasma insulin concentrations. We measured insulin sensitivity (as the whole-body insulin-mediated glucose uptake) and fasting posthepatic insulin delivery rate (IDR) with the use of the euglycemic insulin clamp technique in a large group of obese subjects in the database of the European Group for the Study of Insulin Resistance (1,146 nondiabetic, normotensive Caucasian men and women aged 18-85 yr, with a body mass index (BMI) ranging from 15 to 55 kg.m-2). Insulin resistance, defined as the lowest decile of insulin sensitivity in the lean subgroup (608 subjects with a mean BMI of 29 kg.m-2). Insulin sensitivity declined linearly with BMI at an age- and sex-adjusted rate of 1.2 micromol.min-1.kg FFM-1 per BMI unit (95% confidence intervals = 1.0-1.4). Insulin hypersecretion, defined as the upper decile of IDR, was significantly (P<0.0001) more prevalent (38%) than insulin resistance in the obese group. In the whole dataset, IDR rose as a function of both BMI and insulin resistance in a nonlinear fashion. Neither the waist circumference nor the waist-to-hip ratio, indices of body fat distribution, was related to insulin sensitivity after adjustment for age, gender, and BMI; both, however, were positively associated (P<0.001) with insulin hypersecretion, particularly in women. In nondiabetic, normotensive obese subjects, the prevalence of insulin resistance is relatively low, and is exceeded by the prevalence of insulin hypersecretion, particularly in women with central obesity. In the obese with preserved insulin sensitivity, risk for diabetes, cardiovascular risk, and response to treatment may be different than in insulin resistant obesity.

9) D Liao, R P Sloan, W E Cascio, A R Folsom, A D Liese, G W Evans, J Cai and A R Sharrett. Multiple metabolic syndrome is associated with lower heart rate variability. The Atherosclerosis Risk in Communities Study. Diabetes Care December 1998 vol. 21 no. 12 2116-2122

Abstract:
OBJECTIVE: To test at the population level whether people with multiple metabolic syndrome (MMS) disorders have reduced cardiac autonomic activity (CAA). RESEARCH DESIGN AND METHODS: We examined the association between the level of CAA and MMS disorders, at the degree of clustering and the segregate combination levels, using a random sample of 2,359 men and women aged 45-64 years from the biracial, population-based Atherosclerosis Risk in Communities (ARIC) Study. Supine resting 2-min beat-to-beat heart rate data were collected. High-frequency (HF) (0.15-0.35 Hz) and low-frequency (LF) (0.025-0.15 Hz) spectral powers, the ratio of LF to HF, and the SD of all normal R-R intervals (SDNN) were used as the conventional indices of heart rate variability (HRV) to measure CAA. The MMS disorders included hypertension, type 2 diabetes, and dyslipidemia. RESULTS: HRV indices were significantly lower in individuals with MMS disorders. The multivariable adjusted mean HF was 0.85 (beat/min)2 in subjects with all three MMS disorders, in contrast to 1.31 (beat/min)2 in subjects without any MMS disorder. At the segregated combination level, the multivariable adjusted means +/- SEM of HF were 1.34 +/- 0.05, 1.16 +/- 0.05, 1.01 +/- 0.17, and 1.34 +/- 0.05 (beat/min)2, respectively, for subjects without any MMS disorder, with hypertension only, with diabetes only, and with dyslipidemia only, and the means +/- SEM of HF were 0.93 +/- 0.04, 0.70 +/- 0.15, and 1.20 +/- 0.05 (beat/min)2, respectively, for subjects with diabetes and hypertension, diabetes and dyslipidemia, and hypertension and dyslipidemia. An increase in fasting insulin of 1 SD was associated with 88% higher odds of having a lower HF. The pattern of associations was similar for LF and SDNN. CONCLUSIONS: These findings suggest that MMS disorders adversely affect cardiac autonomic control and a reduced cardiac autonomic control may contribute to the increased risk of subsequent cardiovascular events in individuals who exhibit MMS disorders

According to the above clinical investigations including patients insulin resistance or type II diabetes and control group (N=1687, we do not including in the meta-analysis the studies related fat mass, obesity and insulin resistance) .However, the factor was considered in the regression analysis of our Roc curve.



ROC curve		
Variable	SDNN, FM, VO2,DELTA	
Classification variable	diagnosis	
Sample size		1687
Positive group :	diagnosis = 1	1031
Negative group :	diagnosis = 0	656
Disease prevalence (%)	50	
Area under the ROC curve (AUC)	0.866	
Standard Error [a]	0.0522	
95% Confidence Interval [b]	0.733 to 0.948	
z statistic	7.004	
Significance level P (Area=0.5)	<0.0001	