P 5: Value of the UKPDS risk score in the screening of asymptomatic type 2 diabetic patients for coronary stenoses and artery stiffness

Azzedine Belhadj-Mostefa, Daoud Roulta, Paul Valensi

1 Internal Medicine, Faculty of medicine, CHU Benbadis, Constantine, Algeria; 2 Endocrinology, Diabetology, Nutrition, Jean Verdier Hospital, Bondy, France

Rationale and aims: In patients with type 2 diabetes silent coronary disease was shown to be predictive of major cardiac events. Thus, the detection of silent myocardial ischemia (SMI) and silent coronary stenoses is challenging. Artery stiffness is also associated with a worse prognosis. The aim of this study was to examine the value of the UKPDS risk score for coronary events in the algorithm of screening for SMI, coronary stenoses and artery stiffness in patients with type 2 diabetes.

Patients and Methods: We included 116 patients (65 women and 51 men), aged 55.4 ± 11.8 years, without known cardiovascular disease and with normal resting ECG but at high cardiovascular risk. SMI was assessed on an ECG stress test, and a coronary angiography was carried out in the patients with SMI. Significant coronary stenoses (SCS) were defined as ≥ 70% (or 50% for the main left coronary artery). The 10-year coronary risk of non fatal events was estimated using the UKPDS risk score for coronary events in the algorithm of screening for SMI, coronary stenoses and artery stiffness in patients with type 2 diabetes.

Results: The prevalence of hypertension, obesity, dyslipidemia, nephropathy and smoking was 61.2%, 47.2%, 52.6%, 36.2 and 6%, respectively. SMI was found in 59 patients. A coronary angiography was performed in 51 of them, and 22 (15 men and 7 women) had SCS. The coronary risk score was 18.8±16.0%, and was significantly higher in men than in women (29.4±18.3% vs 10.6±6.8%, p<10^-5). The score did not differ according to the presence or absence of SMI (20.4±18.2% vs 17.2±13.5%, p=0.28) but was significantly higher in the patients with SCS than in those without (29.5±21.4% vs 14.1±9.9%, p<0.001), even after gender adjustment (p<10^-5). A score ≥15% significantly predicted SCS (sensitivity 72%, specificity 66%, positive and negative predictive values 61% and 71%; AROC 0.76±0.06, p<0.001). The score was higher in the patients with PWV ≥11 m/s (21.8±15.9% vs 12.8±10.1%, p<0.001), even after gender adjustment (p<10^-5). A score ≥15% also significantly predicted a PWV ≥11 m/s (sensitivity 50.8%, specificity 71%, positive predictive value 71.1% and negative predictive value 50.8%, AROC: 0.60±0.05, p<0.001).

Conclusion: In this population of type 2 diabetic patients at high cardiovascular risk, an UKPDS risk score for non fatal coronary events ≥ 15% was associated with a significantly increased risk of artery stiffness and silent coronary stenoses. This score may help in screening patients who should be tested for these disorders.

P 6: Markers of systemic inflammation and ApoAI-containing HDL subpopulations in women with and without diabetes.

G.T. Russo, E.L. Romeo, A. Giandalia, A. Alibrandii, K.V. Horvathi, A. Di Benedetto, D. Cucinotta, B. Azcalosi

1 Dipartimento di Medicina Interna, Università di Messina; 2 Lipid Metabolism Laboratory, JM-USDA- Human Nutrition Research Center on Aging Tufts University, Boston, MA-USA; 3 Dipartimento di Scienze Statistiche, Università di Messina

Background and aims: Atherosclerosis is a blood vessel inflammatory disease. Besides their role in reverse cholesterol transport (RCT), HDL particles may affect the atherosclerotic process through the modulation of subclinical inflammation. Notably, HDL are a heterogeneous class of particles, differing in size, composition and, probably, in their anti-inflammatory properties. The potential relationships between HDL sub-particles and inflammatory markers have never been explored in diabetic women, who typically shows dysfunctional HDL. In this work, we investigated the relationship between different HDL subclasses and major inflammatory markers in a group of women with and without type 2 diabetes.

Materials and Methods: Eighty type 2 diabetic and 80 control CHD-free women, not taking any hypolipidemic or hormonal drug, and matched for age and menopausal status, participated to the study. Clinical, lifestyle, common laboratory parameters, as well as inflammatory markers and HDL ApoAI-containing subpopulations with two gradient gel electrophoresis technique were measured in all participants.

Results: When comparing HDL subpopulations profile in women with and without diabetes, diabetic women showed a decrease of the larger alfa-1 (P=0.006), alfa-2 (P=0.005), and pre alfa-1 HDL (P=0.02), and higher levels of the smaller, lipid poor alfa-3 HDL particles (P=0.02). Diabetic women also had higher hsCRP and IL-6 serum levels than non diabetic ones (age- and BMI-adjusted P<0.001, both), whereas no difference in resistin concentration were noted.

Overall, inflammatory markers showed significant inverse correlations with the larger ApoAI containing HDL subclasses, and positive correlations with the smaller, less atheroprotective HDL particles. In particular, hsCRP inversely correlated with alfa-1 (P=0.01), pre alfa-1 (P=0.001), and pre alfa-2 (P=0.02); IL-6 inversely correlated with alfa-1 (P<0.001), alfa-2 (P<0.001), pre alfa-1 (P<0.001), pre alfa-2 (P=0.02), and positively with alfa-3 HDL (P=0.03). No correlations between resistin and HDL subpopulations were found. Similar correlations were also noted when considering diabetic and control women, separately, although these correlations were less numerous, especially in controls. These relationships were also confirmed by univariate regression analysis, especially in the diabetic group.

Conclusions: Our data show that the larger, more atheroprotective HDL subclasses were associated with lower hsCRP and IL-6 levels, whereas the smaller, lipid poor alfa-3 HDL particles were associated with an increase of these inflammatory markers. These associations were more pronounced in type 2 diabetic women, who typically show dysfunctional HDL.

These data suggest that different HDL subclasses may influence CHD risk also through altered anti-inflammatory properties.

P 7: Does choice of antidiabetic and/or antihypertensive treatment influence progression of nephropathy in hypertensive type 2 diabetic patients?

S. Jelic

Bezanijska Kosa Clinical-Hospital Center, University Clinic for Internal Medicine, Endocrinology Department, School of Medicine, University of Belgrade, Belgrade, Serbia

Background and aims: It is well known that coexistence of arterial hypertension and type 2 diabetes significantly multiply cardio-renal risks. But the question remains – is it enough to strictly control blood glucose and blood pressure no matter how? Is the choice of treatment also important?

So, the aim of this study was to assess the influence of the choice of antidiabetic and/or antihypertensive treatment on the rate of nephropathy progression in hypertensive type 2 diabetic patients, during long-term follow-up period.

Methods: The study included 126 (62 female/64 male) hypertensive type 2 diabetic patients (mean age: 50.45±5.61 years; duration of treatment: 5±2.3 years) who were divided into two groups (n=63 in each) according to their treatment with the following: 1) glimepiride (G), a representative of the first generation of antidiabetic drugs; 2) sitagliptin (S), a representative of the new generation of antidiabetic drugs; 3) amlodipine (A), a representative of the new generation of antihypertensive drugs; and 4) valsartan (V), a representative of the angiotensin II receptor blockers.
of diabetes: 10.03±4.91 years and duration of hypertension: 11.32±5.38 years). Patients were assigned to antidiabetic and antihypertensive treatment aiming to attain pre-defined level of glycemic (HbA1c < 7%) and blood pressure control (<130/85 mmHg). Nephropathy progression parameters, average annual increment of microalbuminuria (Δ UAE) and deterioration of glomerular filtration rate (Δ GFR), were prospectively followed-up for a mean period of 6.28 (0.88) years. Statistical analysis was performed using the STATISTICA 4.5 program (StatSoft, Tulsa, OK, USA). The significance of differences was evaluated using the Kruskal-Wallis test. A value of p<0.05 was accepted as statistically significant.

Results: A total of 62 (49.2%) patients achieved good glycaemic control while tight blood pressure control was achieved and maintained in 76 (60.3%) patients. Choice of antidiabetic treatment did not significantly influence the quality of glycaemic control (P=0.4233), while choice of antihypertensive drugs significantly influenced the quality of achieved blood pressure control (P=0.0357), speaking in favor of ACEI.

Choice of antidiabetic treatment did not significantly influence the rate of microalbuminuria progression as well as the rate of deterioration of glomerular filtration both in patients with good (P=0.641 and P=0.837, respectively) and those with poor glycaemic control (P=0.305 and P=0.256, respectively). However, choice of antihypertensive treatment significantly influenced the rate of microalbuminuria progression (P=0.011) as well as the rate of deterioration of glomerular filtration (P=0.0013), but only in those with tight blood pressure control.

Conclusion: Independently from the quality of achieved glycaemic control, choice of the antidiabetic treatment did not significantly influence the rate of nephropathy progression in hypertensive type 2 diabetic patients. However, choice of antihypertensive treatment significantly influenced the rate of progression of microalbuminuria and the rate of deterioration of glomerular filtration but only in those patients in whom good control of blood pressure was achieved.

P 8: Peripheral insulin resistance influence the presence of hypertension in overweight type 2 diabetic patients

Medical Faculty, University of Belgrade, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia, Belgrade, Serbia

Backgrounds and Aims: Increased obesity is closely related to insulin resistance (IR) promoting the development of type 2 diabetes (T2D) and cardiovascular disease. IR represents a well established risk factor for development of hypertension, but the significance of the associations between the IR and obesity in the development of hypertension in overweight patients with type 2 diabetes (T2D) still remains unclear. We analyzed the levels of insulin resistance in: overweight T2D patients with hypertension (group A, n=48, 30±BMI ≥22.5kg/m2), overweight T2D patients without hypertension (group B, n=43, 30±BMI ≥22.5kg/m2) and overweight nondiabetics without hypertension (group C, n=40, 30±BMI ≥22.5kg/m2).

Materials and Methods: Patients were aged 40-70 years, matched by gender, duration of diabetes, with optimal metabolic control (HbA1c=6.5±0.6%). Hypertension was defined as systolic BP ≥140 and diastolic BP ≥90mmHg measured by sphygmomanometer, or by established use of antihypertensive drugs. Assessment of IR were done with two complementary indexes of insulin sensitivity: (1) oral glucose insulin sensitivity (OGIS) index derived from 75 g oral glucose tolerance test and (2) homeostasis model assessment of insulin resistance (HOMA-IR) determined from fasting glucose and plasma insulin (PI) levels. PI and levels were measured by RIA method.

Results: We have found significantly higher PI levels in group A (P=0.045) and C vs B; P=0.005). Simultaneously, there was no significant difference in the level of HOMA-IR among diabetics (A: 9.43±2.69; B: 7.52±2.08; C: 5.73±1.83; A vs B p=NS; A vs C and B vs C p<0.05), reflecting hepatic insulin sensitivity. However, lowest OGIS were found in group A, being significantly lower in group A in comparison to group B (A: 38.05±4.24; B: 29.33±3.13; C:21.34±2.23mU/ml, A vs B; A vs C and B vs C p<0.05). Simultaneously, we have not found significant correlation between PI and presence of hypertension (r=0.177, p=NS). Also, there was no significant correlation between HOMA-IR and presence of hypertension among diabetics (r=0.218, p=NS).

Conclusion: Our results imply that increased peripheral insulin resistance compared to hepatic insulin resistance stronger influence the presence of hypertension in overweight type 2 diabetic patients. Moreover, this association was not depending of obesity.

P 9: Taurine protects against impairment of mitochondrial function and oxidative stress in the heart of rats with fructose-induced insulin resistance

N. Gorbenko, T. Zryagina, O. Borikov, A. Shalamay, O. Ivanova
Institute of Endocrine Pathology Problems, Pharmacology, Kharkiv, Ukraine

Background and aims: Taurine (2-aminoethanesulfonic acid) is a free amino acid found in substantial amounts in all mammalian tissues. Recently, data is accumulating that show the effectiveness of T against diabetes mellitus, insulin resistance and its complications, including retinopathy, nephropathy, neuropathy, atherosclerosis and cardiomyopathy, independent of hypoglycemic effect. Numerous experimental and several clinical studies demonstrated that T helps the cardiovascular system through a variety of mechanisms including modulation of intracellular calcium concentration, antagonism of angiotensin II action, membrane-stabilizing, antioxidant, and lipid-lowering effects. The aim of the study was to assess the effects of T on mitochondrial respiratory chain activity and lipid peroxidation in the heart of prediabetic rats fed a high-fructose diet.

Materials and Methods: Male Wistar rats were divided into three groups: the control group fed on a regular diet (C, n=8), the high fructose-fed group (F, n=8), which had free access to 250 g/L solutions of fructose for 8 weeks and the fructose-fed group treated with taurine (F+T, n=8) for 8 weeks (100 mg/kg/day per os). Mitochondria were isolated by differential centrifugation from the hearts of fed rats. Oxygen consumption rate was measured polarographically at 37°C using a Clark-type oxygen electrode with either glutamate/malate or succinate as energy substrates of complex I or II, respectively. Levels of lipid hydroperoxides, reduced glutathione (GSH) and glutathione reductase (GR) activity were determined in mitochondrial preparations. Result: We found reduction of NAD-dependent substrate oxidation rate in metabolic state 3 in the heart mitochondria of rats with fructose-induced insulin resistance by 20% in comparison with intact control (p<0.02). However, FAD-dependent substrate oxidation rate was not changed in all experimental groups. Administration of T normalised the rate of glutamate/ malate oxidation in the state 3 (F+T:F=0.94±3.97 vs F:T:6.6±1.5; C:82.60±7.48 nmol/min of protein, p<0.05) and the values of respiration control (F+T:F=5.38±0.32 vs F:T:4.63±0.25; C:5.83±0.35, p<0.02). Improvement of mitochondrial function in the