CLINICAL STUDY

Endothelial dysfunction correlates with plasma fibrinogen and HDL cholesterol in type 2 diabetic patients with coronary artery disease

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Abstract

Objective: Assessment of endothelial dysfunction (ED) in type 2 diabetic patients with coronary artery disease (CAD) and estimation of correlation of ED with metabolic parameters: low HDL, hypertriglyceridemia, obesity, systolic blood pressure and with inflammatory-hemostatic parameters: CRP and fibrinogen.

Patients and methods: 42 patients (age 60.0±8.5 years) with diagnosed type 2 diabetes and CAD were randomly included in a cross sectional study. B-mode ultrasound system with a linear transducer 7.5 MHz was used for evaluation of flow mediated vasodilation in brachial artery (FMV). FMV was presented as the percentage increase in brachial artery diameter, within 30 s after limb ischemia, previously provoked by cuff inflation. Percentage value up to 10 % was defined as ED.

Results: Bivariate linear correlation model presented significant correlation between plasma fibrinogen and FMV percentage, with r -0.47, p<0.01. Presence of ED correlates linearly with plasma level of HDL <1.03 mmol/L (r -0.35, p<0.03). Multivariate analysis using Backward Wald model presented fibrinogen (OR 3.14, 95 % CI 0.87–11.28) and low HDL (OR 5.16, 95 % CI 0.53–60.39) as factors correlated with the presence of endothelial dysfunction.

Conclusion: These results presented plasma fibrinogen level and low HDL <1.03 mmol/L as factors, independently correlated to the presence of endothelial dysfunction in type 2 diabetic patients with coronary artery disease (Tab. 8, Fig. 1, Ref. 25). Full Text (Free, PDF) www.bmj.sk.

Key words: endothelial dysfunction, fibrinogen, HDL, type 2 diabetes, coronary artery disease.

Endothelial dysfunction (ED) is a functional marker of atherosclerosis. ED presented as peripheral impaired endothelial-dependent vasodilation (FMV) has been established in type 2 diabetes patients (pts) (1, 2). The degree of endothelial impairment correlates with glycemic control, nitric oxide bioavailability, and plasma level of lipids and inflammatory markers: cholesterol, HDL, LDL cholesterol, CRP and fibrinogen in general population and population with coronary artery disease (3–5). Some studies addressed the effects of use of statins and ACE inhibitors’ therapy on the abnormalities of endothelial function (6, 7).

Objectives

We hypothesized that ED in type 2 diabetes could correlate with metabolic syndrome parameters: low HDL, hypertriglyceridemia, and obesity. A measurement of ED will also be performed to assess whether it correlates with inflammatory and hemostatic parameters: fibrinogen and CRP.

Patients and methods

Study population

42 randomized patients were included in a cross sectional study. All of them were with diagnosed diabetes type 2 and coronary artery disease. Diabetes mellitus type 2 is defined by the criteria of International Diabetes Federation. Coronary artery disease in our study is defined as asymptomatic coronary artery disease, confirmed by coronary angiography. The study excluded patients with primary hyperlipidemia, established kidney failure, anemia and re-

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Acknowledgement: Paper is a part of a project: Coronary artery disease and type 2 diabetes, granted by a Ministry of Science and Education of Republic of Macedonia, No. 08-2436/2/2003.
cent diabetic ketoacidosis. All patients signed written informed consent for inclusion in to the study. The study was conducted according to the Helsinki declaration for clinical studies.

**Study protocol**

All patients were evaluated for the following parameters: age, duration of diabetes, used drugs, risk factors for coronary artery disease: arterial hypertension, hyperlipidemia, and metabolic syndrome’s components: low HDL, hypertriglyceridemia, obesity, systolic pressure and inflammatory-hemostatic parameters: CRP and fibrinogen.

Blood pressure was measured with a standard sphygmomanometer in a sitting position and presented as a mean value of two readings (in mmHg). Arterial hypertension was defined as systolic blood pressure ≥130 mmHg, or/and diastolic pressure ≥85 mmHg, or as antihypertensive drugs used. Anthropometric measurements were made with patient wearing lightweight clothing and no shoes. Weight was presented in kilograms (kg) and Body mass index (BMI) in kg/m². Waist and hip circumferences were measured by a plastic tape meter at the level of the umbilicus and of the major trochanter.

The following standard laboratories were performed in the evaluated patients: enzymatic methods for assessment of: total cholesterol, in the presence cholesterol oxidizes, triglycerides, in the presence of glycero kinase and HDL fraction with direct method. LDL fraction was evaluated with Friedewald formula. Non-HDL cholesterol was determined as difference between total cholesterol and HDL cholesterol. Fibrinogen and CRP were analyzed with turbidimetric method.

According to ATP III criteria: hypertriglyceridemia was defined as value of triglycerides ≥1.7 mmol/L and low HDL as value of <1.03 mmol/L. Obesity was defined as BMI >30 kg/m².

B-mode ultrasound system with a linear transducer 7.5 MHz (HP Agilent S 4500) was used for evaluation of peripheral impaired endothelial-dependent vasodilation in brachial artery. Lumen diameter was defined as distance between media-adventitia interfaces of far and near wall. FMV was presented as the percentage increase in brachial artery diameter, within 30 s after limb ischemia, previously provoked by cuff inflation. Percentage value up to 10 % was defined as ED (12, 13).

**Statistical analysis**

SPSS 10 packet for statistical analysis was used. Data are expressed as mean ±SD. Pearson model was used for bivariate linear analysis. P value ≥0.05 was considered statistically significant. Univariate and multivariate logistic regression analyses were conducted to identify variables predictive of carotid artery disease. The significance of the variables in the multivariate logistic regression model was assessed by the Wald chi² test and CIs.

**Results**

Study population was in age range 60.0±8.5 years and with mean diabetes duration 8.5±6.1. In Table 1 the values of metabolic parameters were presented.

Endothelial dysfunction was detected in 33 pts (78.6 %), 30.9 % (13 pts) were obese, 57.1 % (24 pts) had hypertriglyceridemia, 76.2 % (32 pts) with arterial hypertension, and 61.9 % (26 pts) had low HDL. Patients were taking drugs as is shown in Table 2.

Bivariate linear correlation model showed significant correlation between plasma fibrinogen and FMV percentage, with r -

**Fig. 1. Linear correlation between plasma fibrinogen and FMV.**
0.47, p<0.01 (Fig. 1). Presence of ED correlates linearly with plasma level of HDL <1.03 mmol/L (r = -0.35, p<0.03).

Multivariate analysis using Backward Wald model presented fibrinogen (OR 3.14, 95% CI 0.87–11.28) and low HDL (OR 5.16, 95% CI 0.53–60.39) as factors, independently influencing the presence of endothelial dysfunction (Tab. 3). When Forward Wald analysis was applied only fibrinogen presented as predictor of ED presence.

Discussion

Endothelial dysfunction has been presented in type 2 diabetic population, previously. Almost 80% of our investigated patients presented with endothelial dysfunction.

ED reflects the presence and extent of atherosclerosis. Therefore it is not surprising that CAD risk factors are in relationship with ED (8–10). Presence of ED correlates with plasma level of HDL <1.03 mmol/L, by our data. MRFIT study presented the relationship between low HDL and diabetic atherosclerosis and prognosis of these patients (11). Low HDL has been shown in relationship to functional impairment of arteries in type 2 diabetes by our data. HDL has been presented with vasoprotective effect, and its imbalance is in relationship with enhanced brachial reactivity. Other explanation is that presence of ED is due to the control of risk factors. HDL in type 2 diabetes is usually under controlled. No association was found between ED and systolic pressure and LDL, which could be explain by proper treatment with antihypertensive and hypolipemic drugs.

The degree of endothelial impairment correlates with glycemia (12). Hyperglycemia affects multiple mechanisms that exchange oxidation, thrombosis and inflammation (13). Regarding this thesis endothelial dysfunction should be in correlation with thrombotic and inflammatory parameters. Inflammation, per se CRP contributes with endothelial dysfunction (14). Our data present a correlation with linear and logistic regression model between plasma fibrinogen and percentage of FMV. Plasma fibrinogen could open new insights in type 2 diabetic population, as a promoter of enhanced endothelial function.

It is possible that ED represents the cumulative effects of risk factors on the vessels and these patients with a higher grade of risk factors will be more prone for severe atherosclerosis and higher risk for future vascular events. These observations contribute and raise the question whether assessment of endothelial dysfunction in type 2 diabetes can be used in risk stratification (15, 16).

Study limitation

The population of this study is not large. Underestimation and overestimation of lumen diameter could not be excluded. It relates to several factors, the first one is the time of second measurement of lumen diameter after cuff deflation, and as the one second the location of cuff. Using beat-to-beat analysis may lead to more precise estimation of FMV of brachial artery.

Conclusion

These results presented plasma fibrinogen level and low HDL <1.03 mmol/L as factors, independently correlated to the presence of endothelial dysfunction.

References


Received February 20, 2007.
Accepted June 22, 2007.