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CAROTID ULTRASOUND, BLOOD LIPIDS AND WAIST DETERMINATION CAN PREDICT A FUTURE CORONARY REVASCULARISATION IN THE TYPE 2 DIABETIC COHORT

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A b s t r a c t: The aim of the study was to identify incremental values of carotid ultrasound measurements (carotid plaques and stenosis) on the prediction of future coronary revascularization among type 2 diabetic patients. The second objective was to determine the predictive value of the assessment of blood lipids, BMI, abdominal obesity and the ankle-brachial index (ABI).

Three hundred and thirty three (333) patients with type 2 diabetes and manifested coronary artery disease were randomly selected in a cohort prospective study. Univariate and multivariate logistic regression analyses were conducted to identify variables predictive of the need for future revascularization: percutaneus coronary interventions (PCI) or coronary bypass surgery (CABG) followed 24 months after the study starting point. The presence of arterial hypertension, hyperlipidemia, physical inactivity, intermittent claudication, the value of systolic pressure, BMI, waist and hip measurement, glycemia and blood lipid fraction (total cholesterol, HDL, LDL, non-HDL, triglycerides) were entered in a model. Ultrasound measurements: carotid IMT, presence of carotid plaques and stenosis, and ABI were also included in the analysis.

Based on the univariate and multivariate findings, the presence of internal carotid artery (ICA) stenosis (OR 4,562, 95% CI 1,327–15,687), carotid plaque (OR

[*] Occurrence and Development of Coronary Artery Disease among Patients with Diabetes Mellitus Type 2 Research Project Team.

1,465, 95% CI 0,829–2,591), and increased waist measurement (OR 1,371, 95% CI 0,757–2,483) were found as significant independent predictors of future PCI. LDL and non HDL cholesterol were found to be factors independently associated with the need for future CABG by univariate analysis, which was not confirmed by multivariate analysis.

In conclusion, the current study has provided an identification of predisposing factors for the future need of coronary revascularization among type 2 diabetic patients that permits risk stratification and may facilitate improved patient selection or optimization.

Key words: carotid ultrasound, carotid stenosis, plaque, abdominal obesity, LDL, HDL, type 2 diabetes, coronary revascularization.

Introduction

Prognosis of patients with diabetes mellitus type 2 depends on the presence of macrovascular disease [1]. Two-thirds of all causes of mortality are due to macrovascular complications, and more than 75% of all hospitalizations of the diabetic population are due to diabetic vascular disease [2, 3, 4].

The American Heart Association and the European Society of Cardiology guidelines for cardiovascular risk assessment and cardiovascular disease prevention in diabetic patients include two goals: screening of asymptomatic vascular disease and proper management of already established diabetic macrovascular disease [5, 6]. These screening guidelines refer to the use of non-invasive tests: assessment of blood lipids, albuminuria, assessment of ankle-brachial index, carotid intima-media thickness (IMT), coronary stress test and cardiac computed tomography [7].

Carotid ultrasound has a potential role in the prediction of all causes of cardiovascular risks in populations with and without coronary artery disease. Although those populations also include a certain number of diabetic patients, the value of this parameter in the diabetic population needs further evaluation [8, 9].

The aim of the study was to identify if there are incremental values of carotid ultrasound measurements (carotid IMT, stenosis and presence of plaques) in the need for future coronary revascularisation among type 2 diabetic patients with coronary artery disease. The second objective was to determine the predictive value of the assessment of blood lipids, obesity, abdominal obesity and ankle-brachial index for future coronary revascularization.

Patients and methods

Research design and study population

Three hundred and thirty-three (333) patients with diabetes type 2 and CAD were randomly selected in a cohort prospective study. Type 2 diabetes

was defined based on the criteria of the International Diabetes Federation. CAD in the evaluated population is defined as symptomatic CAD, angiographycally confirmed in 325 pts.

Patients were followed for future coronary revascularization: percutaneous coronary interventions (PCI) or coronary bypass surgery (CABG), 24 months after the study starting point. The study was conducted according to the Helsinki declaration for clinical studies.

Physical examination

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 a systolic blood pressure >/= 130 mmHg, or/and diastolic pressure >/= 85 mmHg, or as antihypertensive drugs used. Anthropometric measurements were made with the patient wearing lightweight clothing and no shoes. Weight was presented in kilograms (kg) and body mass index (BMI) in kg/m^2. Waist and hip circumferences were measured with a plastic tape measure at the level of the umbilicus and of the major trohanter. According to ATP III criteria, hypertriglyceridemia was defined as a value of triglycerides >/= 1,7 mmol/L and low HDL as a value of < 1,03 mmol/L. Obesity was defined as BMI > 30 kg/m2. and increased weight as BMI > 25 and < 29,9 kg/m2. Waist circumferences > 88 cm in women and > 102 cm in men were defined as abdominal obesity.

Carotid ultrasound and Ankle-brachial index

Evaluation for carotid artery disease was done using the HP Agilent S4500 ultrasound system. Carotid IMT was measured by B-mode ultrasound using a linear transducer (7.5–10 MHz) and presented as a mean value of three measurements from both sides. Carotid IMT was defined as the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line on the scans, with the first line representing the lumen-intimal interface and the second line representing the collagen-containing upper layer of the adventitia. IMT with a value equal to or great than 0.8 mm was defined as increased IMT. Plaque was defined as a localized thickening lesion (=/>1.1 mm). Carotid stenosis (CS) > 60% was considered significant. In each longitudinal projection, the site of the greatest thickness (including plaque) was detected along the vessel from the common carotid artery to the internal carotid artery. The observer was blind to the patients' risk factors.

Continuous Doppler was used to determine the lowest and median value of the ankle-brachial index (ratio of ankle to brachial pressure). There was no inter-observer disagreement with regard to ultrasound interpretation, reported previously.

Laboratory

The following standard laboratory tests were performed in the evaluated patients: Enzymatic methods for the assessment of total cholesterol in the presence of cholesterol oxidizes, triglycerides, in the presence of glycerokinase, and the HDL fraction by direct method. The LDL fraction was evaluated using the Friedewald formula. Non-HDL cholesterol was determinate as a value of total cholesterol minus HDL cholesterol. The values of fasting venous glucose concentration were evaluated using the enzymatic-photometric method, in the presence of glucoso-dehydrogenase.

Coronary angiography

Coronary angiography was performed by an experienced invasive cardiologist blinded to the patient's risk factors. The left anterior descending (LAD), left circumflex (LCx) and right coronary artery (RCA) or posterior descending artery were considered to be diseased only if the stenosis was equal to or greater than 70% of the luminal diameter. The left main coronary artery was classified as diseased if any stenosis equal to or greater than 50% of luminal diameter was reported. The degree and distribution of coronary artery stenoses and approximal size of coronary vessels were recorded. A Gensini angiographic score was calculated for all patients. In operated patients completeness of revascularisation was defined as bypassing or having opened by PCI all significant stenosed or occluded vessels.

Statistical analysis of data

The SPSS 10 packet for statistical analysis was used. Data expressed as mean +/-SD. P value </ = 0.05 was considered statistically significant. Univariate and multivariate stepwise logistic regression analyses were conducted to identify variables predictive for future revascularization. All variables with a P value <0.1 in the univariate analysis were selected for multivariate analysis. The logistic regression forward method was used for multivariate analysis of the risk factors, and its results are reported as odds ratio (OR) and confidence interval.

Results

The study population was at an age of 60.4 $\pm$ 8.23 years. 67.3% (224) of pts were men and 32.7%(109) were women. At the starting point of the study 73.9% of pts had stable angina and 6.9% had acute coronary syndromes. The risk factors and clinical characteristics of pts are presented in Tables 1 and 2.

During two years' follow-up PCI was done among 82 pts (24.6%) and CABG among 27 pts (81%).

Table 1 – Табела 1

Risk factors and clinical characteristics of population
Фактори на ризик и клинички карактеристики

Risk factors	Pts	(%)
Arterial hypertension	262	(78,7%)
Hyperlipidemia	282	(98,8%)
Obesity	111	(34,8%)
> Weight	158	(47,4%)
Stable angina pectoris	246	(73,9%)
Nonstable angina pectoris	23	(6,9%)
Myocardial infarction (history)	177	(53,2%)

Table 2 – Табела 2

Values of estimated risk factors
Вредности на испитуваните фактори на ризик

Parameters	**Mean.**	**Std. Dev.**
Sys. TA (mmHg)	144,26	19,56
Waist (cm)	96,97	8,00
Hip	52,96	6,43
High	169,07	7,59
Weight (kg)	82,38	12,61
BMI (kg/m2)	28,75	4,07
GL (mmol/L)	8,49	2,47
HOL.	5,39	1,37
HDL	1,05	0,44
NON.HDL	4,28	1,36
LDL	3,37	1,00
TR	1,98	1,04

The presence of arterial hypertension, hyperlipidemia, physical inactivity, intermittent claudication, value of systolic pressure, BMI, waist and hip measurements, glycemia and lipid fraction (total cholesterol, HDL, LDL, non-HDL, triglycerides) were entered in a univariated model. Carotid measurements: values of mean and highest carotid IMT, presence of carotid plaques (at all, unilateral and bilateral), carotid stenosis (unilateral and bilateral) and internal carotid artery (ICA) stenosis and ankle-brachial index (mean and lowest values) were also included in the analysis.

Univariate logistic regression analysis revealed that the presence of carotid plaque, internal carotid artery (ICA) stenosis and an increased waist were independently associated with the need for new PCI (Table 3). The same variables were found to be significant independent predictors of PCI by the multivariate model: ICA stenosis with OR 4,562 (95% CI 1,327–15,687), plaque with OR 1,465 (95% CI 0,829–2,591) and increased waist with OR 1,371 (95% CI 0,757–2,483) (Table 4). Univariate analysis defined LDL and non HDL cholesterol as factors independently associated with the need for future CABG (Table 3). Multivariate analysis did not identify independent predictors for CABG.

Table 3 – Табела 3

Univariate analysis of predictors for a future coronary revascularisation
Универзитетна анализа за предскажувачи на идна коронарна реваскуларизација

Variable	Score	Sig
For PCI		
> Waist	5,362	0,021
Plaques	8,583	0,003
ICA stenosis	10,632	0,005
For CABG		
Non HDL	5,645	0,018
LDL	4,450	0,035

Table 4 – Табела 4

Multivariate analysis of predictors for future percutaneous coronary intervention
Мултиваријантна анализа за предскажувачи на идна перкутана коронарна интервенција

Variable	**B**	**S.E.**	**Wald**	**df**	**Sig.**	**Exp(B)**	**95% CI EXP (B)**	
							Lower	Upper
> Waist	0,315	0,303	1,084	1	0,298	**1,371**	0,757	2,483
Plaques	0,382	0,291	1,727	1	0,189	**1,465**	0,829	2,591
ICA tenosis	1,518	0,630	5,802	1	0,016	**4,562**	1,327	15,687

Backward Wald Model for estimated Multivariate analysis.
Log Likelihood -152,237 for > waist,
-152,545 for plaques and -156,636 for ICA stenosis

Discussion

Our results revealed carotid stenosis and the presence of carotid plaque as strong predictors of the need for PCI. Carotid IMT and plaque are important for global cardiovascular risk in CAD pts [10]. In general, carotid plaque is a superior predictor of underlying CAD in the general population to IMT. If carotid artery stenosis is presented, atherosclerosis/thrombosis in different vascular beds is more extensive [11, 12].

ABI by our data does not predict future revascularisation. Overestimation of ABI, due to diabetic mediocalcinosis, is not excluded.

Determination of the waist as a metabolic risk factor in the general population and diabetics has a prognostic value regarding future coronary events [13]. Its value, when increased, predicts a need for new PCI, according to this data. An increased waist measurement represents abdominal obesity and is closely related to pro-inflamatory and hemostatic disturbances in type 2 diabetes [5, 13].

Diabetic pts have a different response to hypolipemic treatment strategies [6]. Diabetic pts with high LDL and low HDL have a high vascular risk [14, 16]. Consistent with these observations, our data revealed LDL and HDL as factors influencing the need for new CABG.

The influence of glucometabolic control on revascularisation is still unclear. There were incomplete results of glycohemoglobin in all pts. This was a study limitation.

The problem is important due to a higher risk of in-hospital CABG, a higher incidence of stent restenosis and thrombosis and a demand for repeat coronary revascularisation in diabetic pts [6]. Risk stratification according the coexistence of the metabolic syndrome's components is mandatory for the comprehensive management of type 2 diabetes patients who present CAD [17,18]. All references mentioned address the predictive value of carotid ultrasound and blood lipids and waist determination in the population with coronary artery disease. No previous study has studied the predictive value of the metabolic syndrome's components: increased waist, LDL and HDL cholesterol for new PCI and CABG in diabetic type 2 patients, nor the incremental role of carotid plaque and stenosis in the need for future PCI.

Conclusion

The results of this study revealed the presence of internal carotid stenosis, carotid artery plaque, and abdominal obesity as significant independent predictors of future percutaneus coronary intervention in the type 2 diabetic population. LDL and non-HDL cholesterol were found as factors independently

associated with the need for future coronary bypass surgery among type 2 diabetics, but multivariate analysis did not confirm this. The current study permits risk stratification and may facilitate improved patient selection or optimization for future coronary revascularization.

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Резиме

КАРОТИДНИОТ УЛТРАЗВУК И ОДРЕДУВАЊЕТО НА КРВНИТЕ ЛИПИДИ И АБДОМИНАЛНИОТ ОБЕМ МОЖЕ ДА ПРЕТСКАЖАТ ИДНА КОРОНАРНА РЕВАСКУЛАРИЗАЦИЈА КАЈ КОХОРТИ СО ТИП 2 ДИЈАБЕТ

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Целта на студијата беше да се одредат одделните претскажувачки вредности на параметрите на каротидниот ултразвук: присуството на каротидните плаки и стеноза за идната коронарна реваскуларизација кај пациенти со тип 2 дијабет. Втората цел беше одредување на претскажувачката улога на одредените крвни липиди, индексот на телесна маса (БМИ), абдоминалната гојност и глуждно-надлактниот индекс (АБИ) за идна коронарна реваскуларизација.

Триста триесет и три пациенти со тип 2 дијабет, кои манифестираа коронарна артериска болест беа вклучени во кохортна проспективна студија. Беше изведена униваријантна и мултиваријантна логистична регресивна анализа за да се препознаат варијаблите кои ја претскажуваат потребата за

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идна реваскуларизација: перкутаната коронарна интервенција (ПКИ) и коронарната бајпас хирургија (КАБГ), следени за 24 месеци од почетокот на студијата. Присуството на артериската хипертензија, хиперлипидемијата, физичката неактивност, интермитентната клаудикација, вредноста на систолниот крвен притисок, БМИ, обемот на половината (абдоминалниот обем) и колкот, гликемијата и крвните липидни фракции (вкупен холестерол, ХДЛ, ЛДЛ, нон-ХДЛ, триглицериди) беа вклучени во моделот. Ултразвучните параметри: каротидната ИМТ, присуството на каротидната плака и стеноза, како и АБИ беа исто така вклучени во анализата.

Врз основа на резултатите од униваријантната и мултиваријантната анализа: присуството на стенозата на внатрешната каротидна артерија (OR 4,562, 95% CI 1,327–15,687), каротидната плака (OR 1,465, 95% CI 0,829–2,591) и зголемениот обем на половина (OR 1,371, 95% CI 0,757–2,483) беа најдени за значајни независни претскажувачи за идна ПКИ. ЛДЛ и нон ХДЛ холестеролот беа најдени за фактори што независно се поврзани со потребата за идна КАБГ, одредени со униваријантен модел, што не беше потврдено со мултиваријантната анализа.

Во заклучок, оваа студија ги одреди факторите што предиспонираат идна потреба за коронарна реваскуларизација кај пациентите со тип 2 дијабет, што, пак, дозволува нивна ризик стратификација, и подобрување, односно оптимизирање на селекцијата на истите.

Клични зборови: каротиден ултразвук, каротидна стеноза, плака, абдоминална гојност, LDL, HDL, `tip 2 dijabet`, коронарна реваскуларизација.

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