Original article **UDC: 616.379-008.64:616.13-004.6**
doi:10.5633/amm.2012.0305

RELATIONSHIPS BETWEEN METABOLIC PARAMETERS AND PLAQUE VULNERABILITY IN THE CAROTID ARTERIES IN PATIENTS WITH DIABETES MELLITUS TYPE 2

Muamer Suljić[1] and Aleksandar Jovanović[2]

In most patients with type 2 diabetes, along with the presence of disturbances of glycemic control, there are disturbances of lipid metabolism and elevated blood pressure, which are strong risk factors for the development of late, especially macrovascular complications and whose base is the vulnerable atherosclerotic plaque.

This study included a total of 101 individuals (51 patients suffering from diabetes mellitus type 2-DMT2 and 50 healthy subjects). Distribution of respondents according to the presence of hyperlipoproteinaemia, vulnerable and invulnerable atherosclerotic plaque was done. The data were analyzed by appropriate statistical tests.

Hyperlipidaemia was more prevalent in patients with DMT2 than in the control ones ($p<0.05$). Cholesterol levels were significantly higher ($p<0.05$) in subjects with DMT2 (5.74±2.69 vs. 4.82±1.11mmol/L) as well as triglycerides (1.94±2.2 compared to 1.6±1.14mmol/L) ($p<0.001$). Mean values of glucose in the group of subjects with diabetes mellitus type 2 (10.54±3.75mmol/L) and in the control group (4.53±2.14mmol/L) were significantly different ($p<0.001$). Glycosylated hemoglobin HbA1c was significantly higher in patients with DMT2 (9.30±2.26%) than control group (4.98±0.05%). Mean values of both systolic and diastolic blood pressure were significantly higher in subjects with diabetes mellitus type 2 (149.55±29.27mmHg and 87.92±17.58mmHg) compared to those in the control group (mean systolic blood pressure of 128.32±25.77 and mean diastolic blood pressure 79.11±9.51mmHg). Plaque was found in 100% of diabetic patients, as opposed to 28.12% of patients in the control group. Vulnerable plaque was found in 47.06% of patients in the group with type 2 diabetes and 6.25% in the control group. Analysis with the Mann-Whitney-test shows that the incidence of plaque and vulnerable plaque was significantly higher in DMT2 patients ($p<0.001$).

Hyperlipidaemia, hypertension and type 2 diabetes mellitus are significantly associated with atherosclerotic changes in the blood vessels. Ultrasound determination of plaque vulnerability in the carotid arteries is one of the most important criteria for the classification of patients at high risk for ischemic stroke and development of DMT2. *Acta Medica Medianae 2012;51(3):29-37.*

Key words: *hyperlipidaemia, hypertension, diabetes mellitus, plaque, carotid arteries*

Health Centre Novi Pazar, Internal Medicine Department, Novi Pazar[1]
University of Priština, Faculty of Medicine in Kosovska Mitrovica, Kosovska Mitrovica[2]

Contact: Muammer Suljić
Hercegovacka Street No. 4
36300 Novi Pazar
E-mail: muamer_suljic@yahoo.com

Introduction

Diabetes, especially type 2, is a global problem of modern age due to a marked increase in prevalence up to pandemic proportions, but also due to vascular complications. It is believed that over 60% of diabetics die from cardiovascular complications and that the mortality from myocardial infarction and stroke is 2 to 4 times higher (1).

In diabetes, there is a concurrence of several independent risk factors for cardiovascular complications. Some risk factors appear associated with diabetes, others are some of the complications of diabetes and the third ones are the result of lifestyle and habits. Traditional risk factors, such as dyslipidaemia (high triglycerides and low density lipoprotein (LDL cholesterol) and reduced levels of high density lipoprotein (HDL cholesterol), hypertension and obesity, cannot fully explain an excessive risk for vascular disease in diabetes, and the role of "non-traditional" risk factors can be extremely important (insulin resistance, endothelial dysfunction, hyperfibrinolysis, inflammation, microalbuminuria). It is clear that we should not forget genetics as a risk factor and lifestyle (smoking, physical activity) (2,3). In addition, we should note some biochemical factors which are increased in patients with diabetes and have influence on atherosclerosis, or can be the indicators of an acute phase, e.g.CRP (C-reactive protein), Interleucin 6, fibrinogen, TNF alpha (tumor necrosis factor), PAI (plasminogen activator inhibitor) (2,3). In the recent years, Lp-PLA2 (Lipoprotein-associated phospholipase A2) has been in the focus of

interest, because it can point to an inflammatory process in the vascular system.

Hyperlipidaemias pose one and some say the most important risk factor for the development of vascular diseases and atheroclerosis. Previous investigations have shown not only the quantitative but also the qualitative lipid disorders in type 2 diabetes, so that the term dyslipidemia is being increasingly used. Dyslipidemia occurs in 70-97% of all people with diabetes (4). Dislipidaemia is particularly common in type 2, either as a primary, the associated disorder (within the metabolic syndrome), or as a secondary phenomenon, due to poor glycaemic control (5).

High blood pressure (greater than 130/80mmHg) affects roughly 60-70% of people with diabetes, depending on their age, obesity and ethnicity. Hypertension is important because it represents a major growth factor of risk for the vascular diseases and it works synergistically with diabetes or hyperglycaemia (6).

As in the majority of patients with type 2 diabetes, along with the presence of disturbance of glycemic control, there are disturbances of lipoprotein and elevated arterial pressure, the modern treatment of this disease should necessarily implement a comprehensive approach, such as a good metabolic control, where both glycemic control and disorders of lipoprotein metabolism and elevated arterial pressure are corrected. In this sense, the target serum glucose, HbA1c and lipoprotein levels are defined by the level of vascular risk to which they correspond. Accordingly, HbA1c values equal to or less than 6.5%, morning glucose equal or less than 5.5 mmol/L, total cholesterol less than 4.8 mmol/L and triglycerides less than 1.7mmol/L are the values of low risk for vascular complications. Patients with the values above optimal are at risk for macrovascular and microvascular complications. In accordance with modern recommendations, there is a vascular risk for complications if blood pressure is over 130/80mmHg (7).

Morphological characteristics of atherosclerotic plaque

The basic histopathological substrate of vascular complications in diabetes mellitus is atherosclerotic plaque, and therefore, an adequate treatment of patients with vascular disease is conditioned by timely and precise diagnosis.

Ultrasonography is a sovereign method among angiographic methods for the assessment of carotid atherosclerotic plaque. It provides not only the quantitative analysis of plaque (length, width, thickness, degree of lumen stenosis), but also the qualitative analysis of plaque structure, plaque area and presence of thrombus. Plaque is defined as intraluminal focal prominence 1,4mm or more in length and 5mm or more in extent. By Color doppler ultrasound examination on longitudinal section, first we determined plaque localization on carotid artery and its length, then on the cross section we determined its position. Further, we assessed the plaque structure based on ultrasound density and edges of the plaque, and in the end we estimated the extent of stenosis based on maximal speed in the systole.

According to this quality score system, plaque can be:

Type 1: hypoehogenic and homogenic, corresponds to lipid plaque;

Type 2: entirely hypoehogenic but with heterogenic distribution echo, and more than 50% hypoehogenic elements, corresponds to lipid/fibrotic plaque.

Type 3: entirely hyperehogenic, but with heterogenic distribution echo, and more than 50% of hyperehogenic elements, corresponds to lipid/fibrotic plaque.

Type 4: hyperehogenic and homogenic, corresponds to fibrotic plaque.

Type 5: calcified plaque which has acoustic scattering shadow. Based on this analysis, the "danger" of the plaque for the occurrence of cerebrovascular disease can be estimated and whether there is an indication for surgical removal (endarterectomy) (8).

Division of plaques that have clinical implications is the division into the vulnerable (complicated, unstable) and invulnerable (uncomplicated, stable). Vulnerable plaques are those in which the exulcerated surface (ulceration in an area where there has been a separation of lipid plaque) or where there is vascular wall thrombosis (hypoechogenic structure of appositional thrombus) or hemorrhage in the plaque (anechogenic centre of plaque). These plaques are unstable, their parts tend to separate, with the possibility of distal embolization of the arteries. Hypoehogenic plaque (lipid) is vulnerable, its content can easily get into blood and react as procoagulant, making thrombus. This plaques are dangerous, unstable and can cause cerebrovascular diseases (8,9).

Aims

1. To determine the difference in the presence of hyperlipidaemia and hypertension among patients with type 2 diabetes mellitus and healthy control subjects.
2. To examine the dependence of hyperlipidaemia, hypertension and hyperglycaemia and atherosclerotic plaque vulnerability.
3. To determine the frequency of occurrence of atherosclerotic plaques in the carotid arteries in patients with type 2 diabetes mellitus compared to healthy subjects.

Examinees and methods

This prospective study analyzed a total of 101 subjects, male and female.

All subjects were divided into two test groups - group 1 patients with overt diabetes mellitus

type 2 (n=51), and group 2 - control group of healthy subjects (n=50).

According to the gender, the first group was composed of 25 males (49%) and 26 females (51%). In the second group there were 24 males (48%) and 26 females (52%).

Diabetes mellitus was diagnosed based on the fasting glucose above 7mmol/L, verified on at least two occasions, i.e. on the basis of clinical documentation and the OGTT test. Blood glucose concentration was determined by photometric analysis, the GOD-PAP method with the reference value of 3.6 to 6.1mmol/L. The values of glycosylated hemoglobin, HbA1c was assessed electrophoretically (Isolab techniques) as a percentage of total hemoglobin. The values between 4.2 % and 6.2% are taken for the standard ones.

Testing vulnerability of atherosclerotic plaques of carotid arteries by ultrasound was performed on the equipment Toshiba Cori Vision Pro (Japan, 2002.), based on the echogenicity of plaque, its global appearance, homogeneity, size, regularity of the edge and clarity of the fibrous cap. The criteria for vulnerable plaque are: homogenic hypoechogenicity (lipid plaque), trombolisis by the wall (hypoechogenic structure of appositional thrombus), haemorrhage in plaque (anehogenic midpoint of plaque) and exulceration plaque surface (ulceration on places where separation of plaque occurs).

Cholesterol in the plasma was determined by colour enzyme PAP method. Reference values were 3.63-6.7mmol/L. Triglycerides in the plasma were investigated by colour enzyme ESPA - S method, with the standard values in the range 1.7-2.3mmol. The criteria for vulnerable plaque are: homogenic hypoechogenicity (lipid plaque), trombolisis by the wall (hypoechogenic structure of appositional thrombus), haemorrhage in plaque (anehogenic midpoint of plaque) and exulceration plaque surface (ulceration on places where separation of plaque occurs).

The values of arterial blood pressure were obtained by using sphingomanometer according to the standard procedure.

Distribution of respondents by the presence of certain measured parameters – hyperlipoproteinaemia, hypertension and the presence of vulnerable and invulnerable atherosclerotic plaque is presented in percentage. Results of statistical comparisons obtained by Student's t-test and Mann-Whitney test are shown in the diagram. The results of correlation analysis are presented with corresponding tables, with a statistically significant correlation.

Results

Regarding the age, the average age of patients in the group of patients with diabetes mellitus type 2 was 62.42±10.14 years. In the control group, it was 57.63±12.12 years. The average age of patients in the control and study group were not significantly different ($p>0.05$). Mean values of glucose in the group of subjects with diabetes mellitus type 2 (10:54±3.75 mmol/L) and in the control group (4.53±2.14mmol/L) are statistically significantly different ($p<0.001$). Analyzing the mean glycosylated hemoglobin HbA1c, it can be seen that the highest values of this laboratory parameter is in the group of patients with diabetes mellitus (9.30±2.26%) and in comparison to the control group (4.98±0.05%) the difference is statistically significant. In the investigated group, 65% patients were on peroral antidiabetic drugs and 35% on insulin therapy.

Hyperlipidemia, regardless of the type of disorder, was far more frequent in patients with diabetes mellitus type 2 than in the control group. Normal values of serum lipids were found in the majority (71.87%) of subjects in the control group and the minority (49.12%) of patients with diabetes. Lipid abnormalities were observed in 50.98% of patients with type 2 diabetes mellitus, as well as 28.13% in the control group. The difference, according to the results of Mann-Whitney's test of distribution by the presence of hyperlipidaemia, was statistically significant ($p <0.05$) (Figure 1).

The mean values of total cholesterol and triglycerides in the group of patients with type 2 diabetes mellitus and the control group are shown in Figures 1 and 2. Cholesterol levels in the blood were significantly higher ($p <0.05$) in patients with type 2 diabetes mellitus (5.74±2.69 compared to 4.82±1.11mmol/L). The difference in the mean level of triglycerides in the blood between these two groups (1.94±2.2 compared to 14.1±1.6mmol/L) was even more pronounced ($p<0.001$)).

Mean values of both systolic and diastolic blood pressure were significantly higher in subjects with diabetes mellitus type 2 (149.55± 29.27mmHg and 87.92±17.58mmHg) compared to those in the control group (mean systolic blood pressure of 128.32±25.77mmHg and mean diastolic blood pressure 79.11±9.51mmHg). Student's t-test for small independent samples proved that the difference in both systolic and diastolic arterial blood pressure was statistically significant, with a value of $p <0.001$ (Figure 2).

The distribution of patients according to the presence and type of atherosclerotic plaque in the carotid arteries in the study and control groups are shown in Figures 4 and 5. Plaque was found in 100% of diabetic patients versus 28.12% of patients in the control group. Vulnerable plaque was found in 47.06% of patients with type 2 diabetes and 6.25% in the control group. Analysis of the Mann-Whitney-MAOIs test showed that the difference in the incidence of plaque and plaque vulnerability are highly statistically significant ($p <0.001$).

Hyperlipidemia, hypertension, serum glucose level and duration of diabetes were significantly correlated with the presence of atherosclerotic plaque vulnerability (Table 1). Vulnerability of atherosclerotic plaque significantly correlates with hypertension, hyperlipidemia and glucose value (Table 1). Also, in Tables 2,3 and 4, statistically

significant correlation between glucose value, hyperlipidemia and hipertension is shown, with plaque vulnerability on carotid artery. In Table 5, statistically significant correlation between diabetes mellitus and plaque vulnerability can be seen.

Discussion

Nowadays, 200 million people in the world suffer from diabetes, in our country over 500,000. Over 90% of all patients suffer from type 2 diabetes. The number of cases is increasing, life expectancy is extended, which increases the incidence of late complications of diabetes.

Although dyslipidaemia is a well-known risk factor for atherosclerosis and coronary heart disease, only the more recent studies with statins have clearly indicated that abnormalities of serum lipids increase the risk of acute ischemic stroke (AIS). People with diabetes are more prone to changes in lipid status in comparison with the general population (elevated triglycerides, low HDL cholesterol, high LDL cholesterol). The knowledge of the positive effects of lowering cholesterol on the risk of acute ischemic stroke in diabetic patients are derived in the majority of cases from the studies with patients who have a coronary disease.

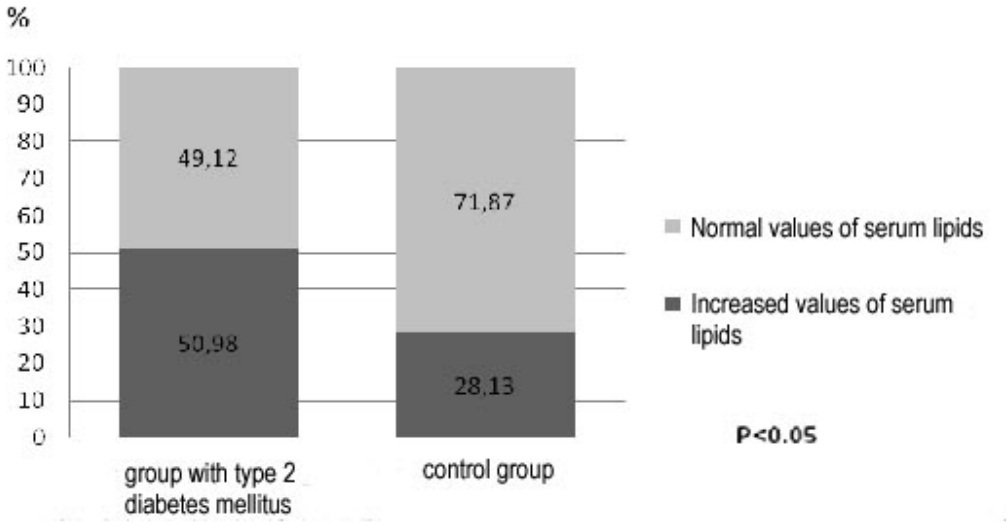

Figure 1. Distribution by the presence of hyperlipoproteinemia in the group of patients with diabetes mellitus type 2 and control group

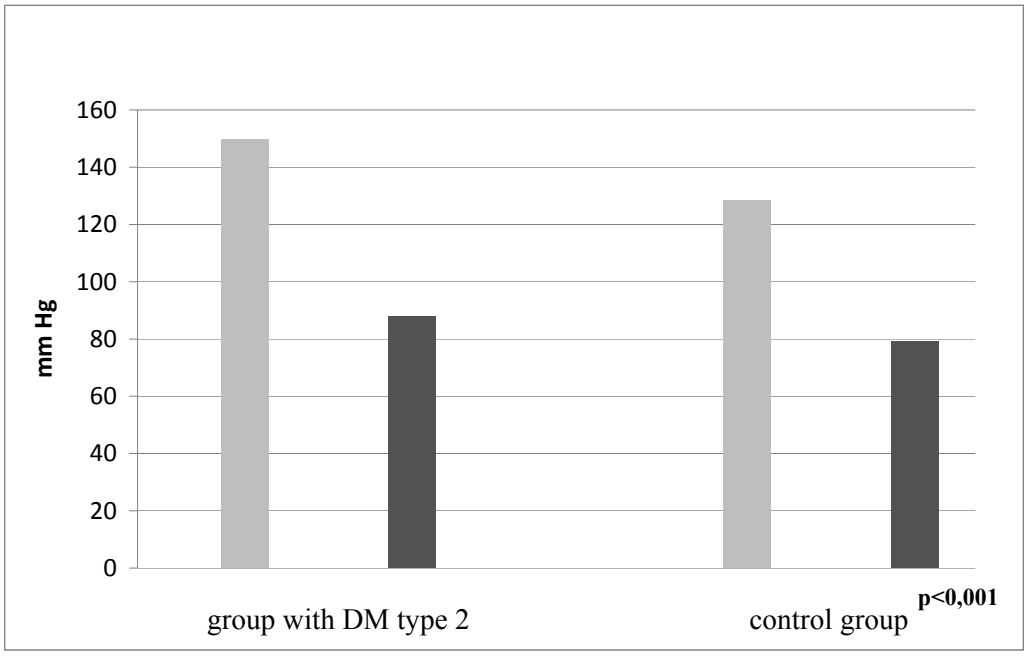

Figure 2. Mean values of systolic and diastolic blood pressure in the patients with type 2 diabetes mellitus and control group

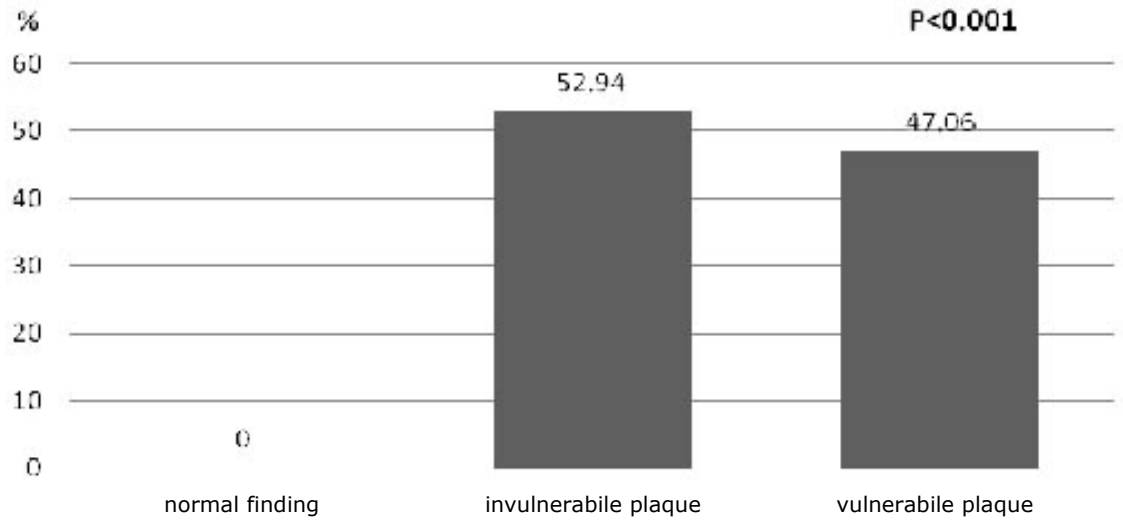

Figure 3. Distribution by the presence and classes of plaque in the group of patients with diabetes mellitus type 2

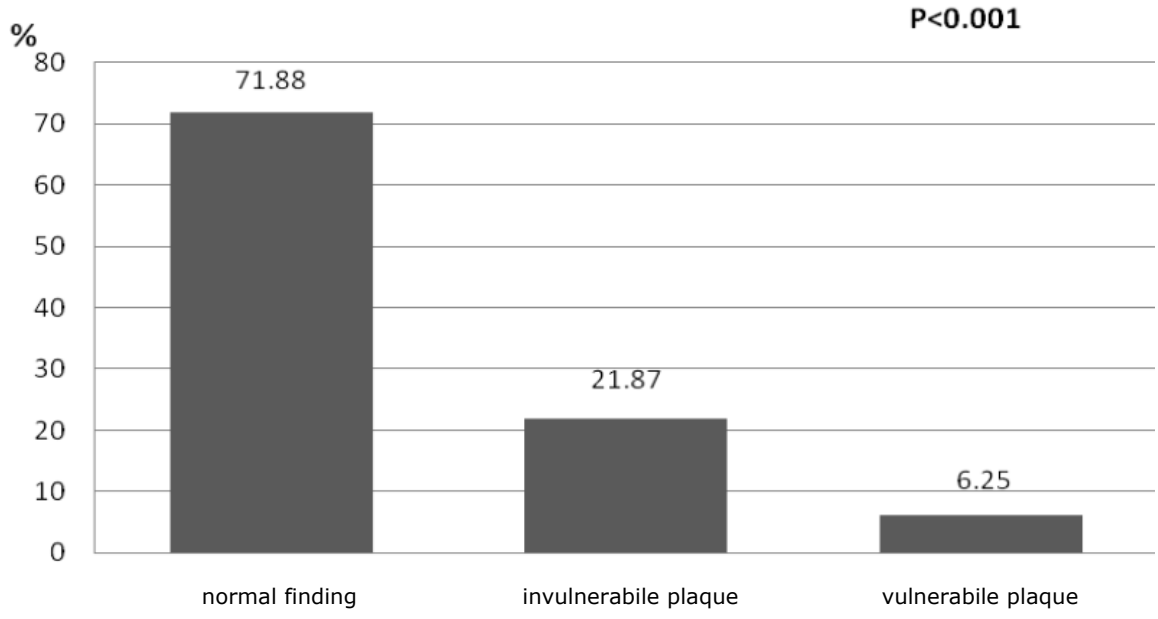

Figure 4. Distribution by the presence and classes of plaque in control group

Table 1. Statistically significant correlation between atherosclerotic plaque vulnerability and relevant research parameters

	Spearman's correlation coefficient	Statistical significance
Age	0,738	p<0,0001
Presence of diebetes	0.709	p<0,0001
Glycemia	0,692	p<0,0001
HbA1C	0,651	p<0,0001
Presence of hyperlipoproteinemia	0,164	p<0,01
Presence of hypertension	0,477	p<0,0001

Table 2. Statistically significant correlation between glycemia value and relevant research

	Spearman's correlation coefficient	Statistical significance
Age	0,988	p<0,0001
Presence of hypertension	0,242	p<0,045
Plaque vulnerability	0,692	p<0,0001

Table 3. Statistically significant correlation between presence of hypertension and relevant research parameters

	Spearman's correlation coefficient	Statistical significance
Age	-0,386	p<0,001
Presence of diebetes	0.54	p<0,0001
Glycemia	0,242	p<0,045
HbA1C	0,292	p<0,007
Presence of hyperlipoproteinemia	0,279	p<0,006
Presence of hypertension	0,477	p<0,0001

Table 4. Statistically significant correlation between presence of hyperlipoproteinemia and relevant research parameters

	Spearman's correlation coefficient	Statistical significance
Age	0,235	p<0,017
Presence of hypertension	0,279	p<0,006
Plaque vulnerability	0,364	p<0,01

Table 5. Statistically significant correlation between presence of diabetes mellitus and relevant research parameters

	Spearman's correlation coefficient	Statistical significance
Age	0,565	p<0,0001
Presence of hyperlipoproteinemia	0,235	p<0,02
Presence of hypertension	0,54	p<0,0001
Plaque vulnerability	0,709	p<0,0001

The results of a recent study (Long Term With Intervention With Pravastatin in Ischemic Disease Trial) with about 2.000 patients with coronary disease, who had DM or glucose intolerance, have shown that statin therapy lowers the risk of cardiovascular disease (CVD) and acute ischemic stroke. United HPS study (Heart Protection Study) in which simvastatin was used for cholesterol lowering has given the evidence of the efficacy of this treatment in the prevention of CVD and CVA. The patients with CVD and earlier acute ischemic stroke were under great risk of future vascular events and had the greatest benefit from taking statins. It is recommended that the statins are used routinely in primary and secondary prevention of acute ischemic stroke in diabetic patients, regardless of initial cholesterol values (10). The positive effect of statins is beyond their hypolipaemic effect, which is explained by non-lipid protective mechanisms such as plaque stabilization, recovery of endothel and anti-inflammatory effect.

The results of CARDS study (Collaborative Atorvastatin Diabetes Study) contribute to the effectiveness of statins in primary prevention of acute ischemic stroke in patients with DM. Suffering from acute ischemic stroke was lower by 48% in patients who received atorvastatin (10mg/dan) compared to the placebo group, with a total of 2.838 patients with type 2 DM (11).

ASCOT (Anglo Scandinavian Cardiac Outcomes Trial) study showed that the patients with high levels of blood pressure and normal cholesterol levels have a significant improvement during treatment with atorvastatin at the dose of 10 mg per day. The results showed that even before the deadline for completion of the study, the groups of subjects who took statins had a 36% reduction in heart attack and stroke than the control group (12).

MIRACL (Effect of Atrovastatin on early ischemic events in recurrent acute coronary syndromes) study showed that the early use of atorvastatin in acute coronary syndrome reduced the incidence of adverse ischemic events and reduced significantly the occurrence of cerebral infarction (50%)(17). ASAP (Effect of aggressive versus conventional lipid lowering on atherosclerosis progression in familiar hypercholesterolaemia) study is the first study that showed the regression of atherosclerotic plaque in the carotid arteries (14).

The latest experience with intravascular ultrasound examination of the coronary arteries showed that the hypoechoic, echolucent (lipid) plaque is vulnerable, can easily rupture when atheromatous content gets into the blood, acting immediately procoagulantly, forming a thrombus and occlusion of the coronary arteries with an acute myocardial infarction. These hypoechoic, eholucent plaques, which are unstable, are seen and have the same importance in the carotid arteries (11). There was a correlation between the presence of hypoechogenic (echolucent)

plaques and ischemic changes on brain CT (15). A longitudinal, prospective study found an association between hypoechogenic plaques and the subsequent occurrence of ischemic strokes in people who were asymptomatic at the time of ultrasound scan. The results of this study showed that hypoechoic plaques were a risk factor for stroke at the same level as the carotid stenosis of 50% or more (11). Unregulated diabetes and hypercholesterolaemia usually correlate with the appearance of hypoechogenic plaques. Quantitative and qualitative analysis of the plaque should be finished with the evaluation of plaque stability. Unstable plaque is potentially emboligenic or thrombogenic, and is directly linked with possible ischemic disorders of the brain. It is essential to assess the surface of plaque, which can be regular (smooth), irregular (ragged, but continuous) and exulcerated (ulcerated, with craterous hollows in places where the parts of lipid plaque were separated). Regular and irregular surfaces are seen in stable plaques and exulcerated surface in unstable or vulnerable plaques (8,16).

In the UKPDS study (United Kingdom Prospective Diabetes Study), 1.148 patients were randomized to achieve target blood pressure (144/82mmHg). After 9 years, patients with lower blood pressure achieved the 37% reduction in cardiovascular complications including microvascular ones, stroke by 44% and heart failure by 56%.The subsequent results of this study showed that lowering systolic pressure by 10mmHg reduces microvascular complications by 13% and myocardial infarct by 11%. (17).

HOT study (Hypertesion Optimal Treatment) showed that the incidence of ischemic heart disease and other vascular complications in diabetics were reduced by 50% if the diastolic pressure was below 80mmHg (18).

HOPE study (Heart Outcomes Prevention Evaluation) showed that a large number of patients, treated with ramipril, had a reduction in cardiovascular mortality by 37%, myocardial infarction by 22%, stroke by 33% (19). The results of the largest global study on hypertension so far - ALLHATstudy (Antihypertesive and Lipid Lowering treatment to Prevent Heart Attack Trial) showed a significant reduction in morbidity and mortality in diabetic and non-diabetic patients with a decrease in hypertension, whereas it showed that new groups of antihypertensive drugs are not better than diuretics (20).

The results of a meta-analysis of 38 studies that have examined the incidence and mortality due to cardiovascular diseases have shown that the risk for cardiovascular disease increases by 36% in patients with elevated HbA1c. It is also shown that the value of fasting glucose and HbA1c show a correlation with the appearance of fatal and nonfatal stroke (21). The mechanisms by which glycaemic control in type 2 diabetes accelerates the occurrence of atherosclerosis and cardiovascular events are complex and intertwined with each other. Hyperglycaemia is the cause of endothelial dysfunction, which is an important risk factor for cardiovascular disease in diabetes (22). Hyperglycaemia indirectly increases cardiovascular risk increasing the value of triglycerides, total cholesterol and LDL-cholesterol in serum; it is the cause of the glycation of lipoproteins, which become more atherogenic and also accelerates the oxidation of lipoproteins, the most important event in the pathogenesis of atherosclerosis (23). In IRAS study (Insulin Resistant Atherosclerosis Study), it was shown that CRP correlates not only with the appearance of coronary disease but it correlates with insulin sensitivity, glucose resistance, sex and age. Similar results have been obtained with interleukin 1 and interleukin 6. Also, PAI 1 (Plasminogen Activator Inhibitor) has increased in patients with diabetes type 2. Lp-PLA 2 (Lipoprotein-associated phospholipase A2) is a specific enzyme which indicates an inflammatory process in the vascular system. It is not an indicator of systemic inflammation but a proatherogenic enzyme which is produced by macrophage and lymphocytes. Lp-PLA 2 is present in two forms - as interleukins which circulate in plasma and 80% is binded to LDL. Lp-PLA2 indicates the presence of plaques which have tendency to rupture and it is significantly increased when rupture occurs. Many epidemiology studies have shown the association between high values of Lp-PLA2 and risk of cardiovascular disease. In ARIC (Atherosclerosis Risk in Communites Study), the mass of Lp-PLA2 was an independent risk predictor for coronary events in patients with valuesof LDL below the median (LDL-c 130mg/dl).

Conclusion

1. Hypertension and hyperlipidaemia, regardless of the type of disorder, were far more frequent in patients with diabetes mellitus type 2 than in the control group.

2. Hyperlipidaemia, hypertension, serum glucose level and duration of diabetes significantly correlated with the presence of atherosclerotic plaque vulnerability.

3. The incidence of vulnerable plaques was significantly higher in patients with diabetes mellitus than in the control group of healthy subjects. Also, the vulnerability of atherosclerotic plaque on carotid artery significantly correlates with age, hypertension, hyperlipidemia and glucose value.

4. Diabetes mellitus type 2 and the parameters of metabolic control were significantly associated with atherosclerotic changes in blood vessels. Ultrasound evaluation of plaque vulnerability in the carotid arteries is one of the important criteria for classification of patients at high risk for ischemic stroke.

References

1. Danaei G, Lawers C, Hoorn S, Murray C, Ezzati M. Global and regional mortality from ischaemic heart disese and stroke attributable to higher-than–optimum blood glucose concetracion :comparative risik assessment. The Lancet 2006; 368: 1651-9. [CrossRef]
2. Beckman J, Creager M, Libby P. Diabetes and Atherosclerosis: Epidemiology, pathophysiology, and Menagment. JAMA 2002; 287: 2570-81. [CrossRef] [PubMed]
3. Fonseca VA. Risk factors for coronary heart disease in diabetes. Ann intern Med 2000; 133: 154-6. [PubMed]
4. Laakso M. Lipids in type 2 diabetes. Semin Vasc Med 2002; 2(1): 59-66. [CrossRef] [PubMed]
5. Carroll MD, Kit BK, Lacher DA, Shero ST, Mussolino ME. Trends in lipids and lipoproteins in US adults, 1988-2010. JAMA 2012; 308(15):1545-54. [CrossRef] [PubMed]
6. Sowers JR, Epstein M, Frohlich ED. Diabetes, hypertesion and cardiovascular disease: an update. Hypertesion 2001; 37:1053. [CrossRef]
7. Sadiya A. Nutritional therapy for the management of diabetic gastroparesis: clinical review. Diabetes Metab Syndr Obes 2012; 5: 329-35. [CrossRef] [PubMed] [PubMedCentr]
8. Polak FJ. Carotid risk factors and carotid ultrasound. In: Alexandrov VA, editors. Cerebrovascular ultra sound in stroke prevention and treatment. 1st ed. Blackwell Publishing 2003. p. 141-61.
9. Tegeler HC. Carotid and vertebral duplex scanninng in secondary stroke preventionand stenting. In: Alexandrov VA, editors. Cardiovascular ultrasound in stroke prevention and treatment. 1st ed. Blackwell Publishing 2003. p. 161-70.
10. Collins R, Armitage J, Parish S, et al. MRC/BHF Heart protection Study of cholesterol –lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. Lancet 2003; 361: 2005-16. [CrossRef]
11. Colhoun HM, Betteridge DJ, Durrington PN et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet 2004; 364: 685-96. [CrossRef]
12. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin and fluvastatin in patients with hypercholesterolemia (The CURVES Study). the American Journal of Cardiology 1998; 81: 582-7.
13. Effects of atorvastatin on early recurrent ichemic events in acute coronary syndromes: The MIRACL Study: A randomized, controlled trial. JAMA 2001; 285:1711-8. [CrossRef] [PubMed]
14. Effect of aggressive versus cinvetional lipid lowering on aterisclerosis progresion in familiar hyperc holesterolemia (ASAP): a prospective, randomised, double-blind trial. The Lancet 2001; 357: 577-81. [CrossRef]
15. Geroulacos G, Ramaswami G, Nicolaides A, James K, Labropoulos N, Belcaro G et al. Characterisation of symptomatic and asymptomatic carotid plaques using ligh-resolution real-time ultrasonographi. Br J Surg 1993; 80(10): 1274-7. [CrossRef]
16. Zweibel JW. Ultrasound assessment of carotid plaque. In: Zwiebl JW, editor. Introduction to vascular ultrasonography. 4th ed. Philadelphia: W.B.Saunders Company 2004;
17. UKPDS Group: tight blood pressure control and riskof macrovascular and microvascular compli cations in type 2 diabetes; UKPDS 38.UK Prospective Diabetes Study Group. BMJ 1998: 317: 703. [CrossRef] [PubMed] [PubMedCentr]
18. Jönsson B, Hansson L, Ståhlhammar NO. Health economics in the Hypertension Optimal Treatment (HOT) study: costs and cost-effectiveness of intensive blood pressure lowering and low-dose aspirin in patients with hypertension. J Intern Med 2003; 253(4): 472-80. [CrossRef] [PubMed]
19. HOPE Investigatorss: Effects of ramipril on cardiovascular and microvascular outcomes in peolple with diabetes mellitus: Results of the HOPE study and MICRO-HOPE. Substudy Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000; 355: 253. [CrossRef]
20. The ALLHAT and Coordinators. Major outcomes in high-risc hypertensive patients randomised to ACE inhibitor or calcium channel blocker vs. diuretc. JAMA 2002; 288: 2981-97. [CrossRef]
21. Prior JO, Quiñones MJ, Hernandez-Pampaloni M, Facta AD, Schindler TH, Sayre JW et al. Coronary circulatory dysfunction in insulin resistance, impaired glucose tolerance, and type 2 diabetes mellitus. Circulation2005; 111(18): 2291-8. [CrossRef] [PubMed]
22. Kaplan M, Aviram M, Hayek T. Oxidative stress and macrophage foam cell formation during diabetes mellitus-induced atherogenesis: Role of insulin therapy. Pharmacol Ther. 2012; 136(2): 175-85. [CrossRef] [PubMed]
23. Vlassara H. In: Diabetes and Cardiovascular Disease. 2001. pp. 81-102. [CrossRef]

POVEZANOST METABOLIČKIH PARAMETARA I VULNERABILNOSTI PLAKOVA NA KAROTIDNIM ARTERIJAMA KOD OSOBA OBOLELIH OD DIJABTES MELITUSA TIP 2

Muamer Suljić i Aleksandar Jovanović

Kod većine bolesnika sa tipom 2 dijabetesa, uporedo sa prisustvom poremećaja glikoregulacije postoje i poremećaji metabolizma lipida i povišen arterijski krvni pritisak koji predstavljaju snažne faktore rizika za razvoj kasnih, posebno makrovaskularnih komplikacija, a u čijoj osnovi je vulnerabilni aterosklerotski plak.

U ispitivanju je učestvovala 101 osoba (51 sa dijabetes melitusom tip 2-DMT2 i 50 zdravih ispitanika). Bolesnici su analizirani u odnosu na hiperlipoproteinemije, kao i prema prisustvu vulnerabilnog i nevulnerabilnog aterosklerotskog plaka. Podaci su obrađeni odgovarajućim statističkim metodama.

Hiperlipidemija je zastupljenija kod bolesnika sa DMT2 nego u kontrolnoj grupi ($p<0.05$). Vrednosti holesterola u krvi bile su značajno više ($p<0.05$) kod ispitanika sa DMT2 (5.74±2.69 vs. 4.82±1.11 mmol/L) kao i triglicerida (1.94±2.2 vs. 1.14±1.6 mmol/L) ($p<0.001$). Srednje vrednosti glikemije u grupi ispitanika sa dijabetes melitusom tip 2 (10.54±3.75 mmol/L) i u kontrolnoj grupi (4.53±2.14mmol/L) značajno su različite ($p<0.001$). Vrednosti glikoziliranog hemoglobina HbA1c su značajno veće u grupi ispitanika sa dijabetes melitusom (9.30±2.26%) u odnosu na kontrolnu grupu (4,98±0,05%). Srednje vrednosti kako sistolnog tako i dijastolnog krvnog pritiska bile su znatno više kod ispitanika sa DMT2 (149.55±29.27 mmHg, odnosno 87.92±17.58 mmHg) u odnosu na kontrolnu grupu (128.32±25.77 mmHg, a srednji dijastolni pritisak 79.11±9.51 mmHg). Plak je nađen kod 100% bolesnika sa dijabetesom, nasuprot 28.12% u kontrolnoj grupi. Vulnerabilni plak nađen je kod 47.06% DMT2 bolesnika i 6.25% kontrolnih. Analiza Mann-Whitney-jevim testom pokazuje da je učestalosti pojave plaka i vulnerabilnog plaka značajno veća kod DMT2 bolesnika ($p<0.001$).

Hiperlipidemija, hipertenzija i dijabetes melitus tip 2 značajno su povezani sa aterosklerotskim promenama na krvnim sudovima. Ultrazvučno određivanje vulnerabilnosti plakova na karotidnim arterijama jedan je od značajnih kriterijuma za klasifikaciju bolesnika sa visokim rizikom za ishemijski moždani udar i pojavu DMT2. *Acta Medica Medianae 2012;51(3):29-37.*

***Ključne reči**: hiperlipidemija, hipertenzija, dijabetes melitus, plak, karotidne arterije*