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MULTIFOCAL ATHEROSCLEROSIS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND ITS COMBINATION WITH METABOLIC SYNDROME

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In this article, the results of the frequency of registered cases of multifocal atherosclerosis and plural atherosclerotic plaques in the different vessels of patients with diabetes mellitus type 2 and its combination with metabolic syndrome are presented. It is shown, that in patients with type 2 diabetes mellitus with and without metabolic syndrome, more often both multifocal atherosclerosis and plural atherosclerotic plaques are determined. The incidence of multifocal atherosclerosis was significantly higher in patients with diabetes mellitus (regardless of the presence of concomitant metabolic syndrome) compared to patients without diabetes and metabolic syndrome of similar age and sex composition. Only in patients with diabetes mellitus type 2 and its combination with metabolic syndrome plural atherosclerotic plaques in the same vessels in contrast to patients without diabetes and metabolic syndrome were discovered. Thus, a significant effect of diabetes mellitus on the rapid development and progression of atherosclerosis, which is exacerbated with the accession of the metabolic syndrome, has been demonstrated.

Key words: type 2 diabetes mellitus, metabolic syndrome, atherosclerosis, atherosclerotic plaques, large vessels.

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МУЛЬТИФОКАЛЬНИЙ АТЕРОСКЛЕРОЗ У ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ 2 ТИПУ У ПОЄДНАННІ З МЕТАБОЛІЧНИМ СИНДРОМОМ

У статті представлені результати частоти реєстрації випадків мультифокального атеросклерозу та множинних атеросклеротичних бляшок у різних судинах у хворих на цукровий діабет 2-го типу у поєднанні з метаболічним синдромом. Показано, що у хворих на цукровий діабет 2-го типу як з метаболічним синдромом, так і без нього, частіше визначаються як мультифокальний атеросклероз, так і множинні атеросклеротичні бляшки. Частота мультифокального атеросклерозу була достовірно вищою у хворих на цукровий діабет (незалежно від наявності супутнього метаболічного синдрому) порівняно з пацієнтами без діабету та метаболічного синдрому аналогічного віково-статевого складу. Тільки у хворих на цукровий діабет 2 типу у поєднанні з метаболічним синдромом були виявлені множинні атеросклеротичні бляшки в одних і тих же судинах на відміну від пацієнтів без діабету та метаболічного синдрому. Таким чином, було продемонстровано суттєвий вплив цукрового діабету на швидкий розвиток та прогресування атеросклерозу, який посилюється при ускладненні метаболічним синдромом.

Ключові слова: цукровий діабет 2 типу, метаболічний синдром, атеросклероз, атеросклеротичні бляшки, великі судини.

It is known that atherosclerotic lesions of the vascular bed often complicate the clinical course of type 2 diabetes mellitus (DM-2) [6]. On the other hand, the pathogenic effect of all components of the metabolic syndrome (MS) (arterial hypertension, hyperglycemia, obesity, lipid metabolism disorders) is also mainly directed to the vascular system [7, 10, 11].

In recent years, ultrasonic methods of vascular examination have been increasingly used to assess the functional and structural changes in the vessels, making it possible to visualize intravascular atherosclerotic plaques (AP), which directly indicate the development of an atherosclerotic lesion [8].

In this study, we presented the results obtained from a comparative analysis of the number of detected APs in patients with DM-2 and its combination with MS compared to persons without DM-2 and MS of similar age and sex composition.

The purpose of the study was to assess the frequency of registered cases of multifocal atherosclerosis and plural atherosclerotic plaques in the different vessels of patients with diabetes mellitus type 2 and its combination with metabolic syndrome.

Material and methods. 233 patients were examined: 139 (63.5 %) men and 94 (36.4 %) women, aged 27 to 81 years, with a mean age of 59.72±8.4 years. In 77 patients (49 men and 24 women), isolated DM-2 was diagnosed. In 74 patients (38 men and 36 women), DM-2 was in combination with MS, 84 patients (52 men and 35 women) made up the comparison group (CG) – without DM-2 and MS.

The diagnosis of DM-2 was established based on the recommendations of the American Diabetes Association (ADA) and the World Health Organization (WHO) [5]. The diagnosis of MS was established according to the WHO criteria in the presence of two additional of three diagnostic factors [1].

The compared groups were approximately the same in age, and the percentile of the age range equal to 50 years and younger was approximately the same in all compared groups of patients.

In the group of patients with isolated DM-2, 32 (20.12 %) patients had mild DM, and 41 (25.79 %) had moderate DM-2. In 49 (30.82 %) patients, DM-2 was in the compensation phase, in 24 (15.09 %) – in the subcompensation phase.

Table 1

Number, mean age (M+m), and percentile of the age range less than 50 years (pc<50) in 3 groups of patients: with DM-2 without MS, with a combination of DM-2+MS and hypertension syndrome (HS), depending on gender

Mean age	Total 233 (100 %)					
	Men: n=139 (59.6 %)			Women: n=94 (40.4 %)		
	DM-2 without MS (n=73)		DM-2+MS (n=74)		HS (n=86)	
	Men (n=49)	Women (n=24)	Men (n=38)	Women (n=36)	Men (n=52)	Women (n=34)
	58.53±9.03 (2–71)	61.54±9.18 (46–75)	59.71±9.02 (35–75)	64.31±8.93 (47–76)	58.94±6.95 (44–77)	59.05±7.58 (44–81)
	59.52±9.13 (27–75)		61.38±9.16 (35–76)		58.99±7.23 (44–81)	
pc<50	16.3		14.3		11.5	

In the group of patients with a combination of DM-2+MS, 28 (37.84 %) patients had mild DM-2, 46 (62.16 %) patients had moderate DM-2. In 31 (41.89 %) patients, DM-2 was in the compensation phase. In 43 (58.11 %) patients, it was in the subcompensation phase.

The degree of arterial hypertension (AH) was established by the recommendations of the European Society of Hypertension and the European Society of Cardiology [9]. In contrast, the percentage of patients with various degrees of AH in the groups of patients, regardless of the presence of DM-2 and MS, did not differ significantly. All compared groups of patients were comparable in age (p=0.3) and sex (according to Fisher's test, p=0.2).

All patients in 3 compared groups had concomitant diseases: arterial hypertension in 39 (53.42 %) with DM-2, in all 74 with DM-2+MS and in 44 (51.16 %) in HS; ischemic heart disease (IHD)–in 38 (52.05 %) with DM-2, in all 46 (62.16 %) with DM-2+MS and in 34 (39.53 %) in HS; angina pectoris–in 28 (38.35 %) with DM-2, in 33 (44.59 %) with DM-2+MS and 21 (24.42 %) in HS; CHF II–III– in 3 (4.11 %) with DM-2, in 8 (10.81 %) with DM-2+MS and 1 (1.16 %) in HS; postinfarction cardiosclerosis (PICS) – in 1 (1.37 %) with DM-2; in 7 (9.46 %) with DM-2+MS.

Laboratory research methods included the determination of the level of glucose and insulin in the blood on an empty stomach. All patients underwent ultrasound examination of the main arteries of the neck, upper and lower extremities using the PHILIPS–HD 11 ultrasound machine (Germany) according to the standard technique using a linear probe with a frequency of 7.5 MHz.

Statistical processing of the results of the study was carried out using the statistical computer program Statistica 6.0 from StatSoft. Spearman's nonparametric rank correlation test (method $\chi 2$) was used when comparing quantitative data. Differences were considered statistically significant at p<0.01.

Results of the study and their discussion. In 88 (37.77 %) patients out of the total number of patients examined, multifocal atherosclerosis was noted with simultaneous damage to several vascular beds.

The combined lesions, reflecting the presence of multifocal atherosclerosis, were significantly more often detected in patients with a combination of DM-2+MS, significantly exceeding the same index both in the group of patients with DM-2 without MS, and in CG: 53 (22.75 %) versus 28 (12.02 %) and 9 (3.86 %) (p<0.001), respectively. In the group of patients with DM-2+MS, the studied parameter was also significantly higher in comparison with DM-2 without MS (p<0.001). In the compared groups of men, multifocal atherosclerosis in the compared groups of patients was detected more often, although the differences did not reach significance.

According to the results obtained:

– significance of differences between patients with DM-2+MS and HS (chi-square test=36.018; chi-square test with Yates correction=34.399; chi-square test with likelihood adjustment=–39.388; p<0.001).

– significance of differences between patients with DM-2 without MS and HS (chi-square test=10.604 (p<0.01); chi-square test with Yates correction=8.911 (p<0.01); chi-square test with plausibility adjustment =–12.522; p<0.001).

– significance of differences between patients with DM-2 without MS and HS (chi-square test=10.598 (p<0.01); chi-square test with Yates correction=9.512 (p<0.01); chi-square test with plausibility adjustment =–11.080; p<0.001).

In the examined patients, vascular damage (VD) were represented by the following main combinations: common carotid arteries (CCA)+external carotid artery (ECA) – in 7 (3.0 %) patients in the DM-2 group without MS, in 13 (5.57 %) in the DM-2+MS group, and in 1 (0.43 %) in HS; CCA+ internal carotid artery (ICA) – in 7 (3.0 %) in the DM-2 group without MS, in 9 (3.9 %) in the DM-2+MS group and in 3 (1.29 %) in the CG; CCA+vertebral artery (VA) – in 4 (1.72 %) patients in the DM-2 group without MS, in 5 (2.1 %) patients in the DM-2+MS group, in 1 (0.43 %) patient in the HS; CCA+common femoral

artery (CFA) – in 4 (1.72%) in the DM-2 group without MS, in 9 (3.9 %) in the DM-2+MS group and in 2 (0.86 %) in the CG; CFA+deep femoral artery (DFA)/superficial femoral artery (SFA) – in 4 (1.72 %) in the DM-2 group without MS, in 5 (2.15 %) in the DM-2+MS group, and in 1 (0.43 %) in the CG; CFA+SA – in 3 (1.29 %) patients in the group of patients with DM-2 without MS, in 4 (1.72 %) in the group of patients with DM-2+MS and in 1 (0.43 %) in the HS. VD of 3 or more vascular beds were represented by a combination of CCA+CFA+SA–in 4 (1.72 %) and CCA+CFA+BA–0 – in 4 (1.72 %) patients in the DM-2+MS group. In the DM-2 group, VD was not detected without MS and CG.

Our data indicate a significant increase in the frequency of detection of combined atherosclerotic changes in the main arteries of various vascular beds in people with DM-2+MS, even in comparison with patients with DM-2 without MS. So, in the group of patients with DM-2 without MS, out of 73 people, 28 (12.02 %) of the total number of patients) had multifocal atherosclerosis with simultaneous damage to 2 vessels. In patients with a combination of DM-2+MS, such lesions were detected in 53 (22.75 %) of 74 patients. The differences reached statistical significance ($p<0.001$). At the same time, in the group without DM-2+MS, only 9 patients (3.86 % of the total number of patients) had SP, which was a significantly lower value compared to the first two groups ($p<0.001$).

Table 2

The frequency of detection of multiple APs in various main arteries in patients with DM-2 without and with MS

The number of vessels affected multiple plaques		Number of AP: A–2; B–3; C–4; G–5; D–6; E–7
DM-2 without MS		DM-2+MS
External carotid artery (ECA)		
right	1 (0.43 %) (A)	0 (0.0 %)
left	1 (0.43 %) (A)	0 (0.0 %)
generally	2 (0.86 %) (A)	0 (0.0 %)
Internal carotid artery (ICA)		
right	1 (0.43 %) (A)	0 (0.0 %)
left	1 (0.43 %) (A)	0 (0.0 %)
generally	2 (0.86 %) (A)	0 (0.0 %)
Vertebral artery (VVA)		
right	3 (1.29 %) (B–3)	1 (0.43 %) (B–1)
left	1 (0.43 %) (B–1)	1 (0.43 %) (B–1)
generally	4 (1.72 %) (B–4)	2 (0.86 %) (B–2)
Axillary artery (AA)		
right	1 (0.43 %) (A–1)	0 (0.0 %)
left	0 (0.0 %)	0 (0.0 %)
generally	1 (0.43 %) (A–1)	0 (0.0 %)
Common femoral artery (CFA)		
right	11 (4.72 %) (A–1, B–3)	1 (0.43 %) (B–1)
left	9 (3.86 %) (B–3)	2 (0.86 %) (A–1)
generally	20 (8.58 %) (A–1, B–3, B–3)	3 (1.29 %) (A–1, B–1)
Deep femoral artery (DFA)		
right	3 (1.29 %) (A–1, B–2)	2 (0.86 %) (A–2, B–1)
left	4 (1.72 %) (A–2, B–1, B–4)	2 (0.86 %) (A–1, B–1)
generally	7 (3.0 %) (A–3, B–1, B–6)	4 (1.72 %) (A–3, B–2)
Superficial femoral artery (SFA)		
right	4 (1.72 %) (A–2, B–2)	3 (1.29 %) (A–2, B–1, D–1)
left	2 (0.86 %) (B–2)	3 (1.29 %) (A–1, B–1, D–1)
generally	6 (2.58 %) (A–2, B–4)	6 (2.58 %) (A–3, B–2, D–2)
Popliteal artery (PA)		
right	3 (1.29 %) (B–2, D–1)	5 (2.15 %) (A–2, B–2)
left	4 (1.72 %) (B–1, B–1, E–1)	4 (1.72 %) (A–2, B–3)
generally	7 (3.0 %) (B–3, B–1, D–1, E–1)	9 (3.86 %) (A–4, B–3, B–2)
Posterior tibial artery (PTA)		
right	1 (0.43 %) (A–1)	2 (0.86 %) (A–2)
left	0 (0.0 %)	0 (0.0 %)
generally	1 (0.43 %) (A–1)	2 (0.86 %) (A–2)

In most cases, during ultrasound examination of blood vessels, we were able to visualize one intravascular AB of various shapes and sizes. However, often more than 1 AB was visualized in the same vessel, the so-called “multiple” AB.

Multiple ABs were not detected in the CG, only in the groups of patients with DM-2 without MS and DM-2+MS. The frequency of detection of multiple AP in the main arteries on the right and left were as follows (Table 2).

When several AP were found in one large vessel, their number in most cases did not exceed 2–3 relatively small, hemodynamically insignificant AP. In a few patients, however, the number of AP reached 6–7, particularly in the SA in 2 patients.

To assess the effect of elevated BP on this factor, we divided the total number of examined patients with DM-2 into 2 subgroups with high and normal BP.

The number of detected multiple AP was significantly higher in the subgroup with concomitant hypertension, which was confirmed by significant differences in the occurrence of multiple plaques in the DFA and DFA with a relatively more frequent, but not reaching statistical significance, detection in other main arteries of the lower extremities – SA and SFA. Based on the fact that not a single case of detection of multiple AP was noted in the CG, we concluded that the presence of DM-2 in patients, especially in cases of combination with AH and MS, led to an increase in the frequency of detection of more extensive and rapidly progressive atherosclerotic changes in the walls of the main arteries.

Thus, significantly more frequent detection of cases of multifocal atherosclerosis with simultaneous involvement of several vascular beds in groups of patients with DM-2 without MS and with a combination of DM-2+MS is consistent with the results of other studies that have demonstrated a significant contribution of DM-2 to the rapid development and progression of atherosclerosis [2, 3, 4, 6]. All this once again confirms that the presence of DM-2 plays the role of its own very significant risk factor in the development of atherosclerosis, the influence of which exceeds the influence of many traditional risk factors.

Conclusions

1. In 88 (37.77 %) patients out of the total number of patients examined, multifocal atherosclerosis was noted with simultaneous damage to several vascular beds.

2. The incidence of multifocal atherosclerosis was significantly higher in patients with diabetes mellitus (regardless of the presence of concomitant metabolic syndrome) compared to patients without diabetes and metabolic syndrome of similar age and sex composition. In the group of patients with DM-2+MS, the studied parameter was also significantly higher in comparison with DM-2 without MS ($p<0.001$). In the compared groups in men, multifocal atherosclerosis in the compared groups of patients was detected more often, although the differences did not reach significance.

Thus, a significant effect of diabetes mellitus on the rapid development and progression of atherosclerosis, which is exacerbated with the accession of the metabolic syndrome, has been demonstrated.

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