

## **Study of Indicators of Endothelium Dysfunction in Young Patients with Myocardial Infarction**

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### **ABSTRACT**

The aim of this study was to study indicators of endothelial dysfunction - platelet aggregation activity, a humoral marker of von Willebrand factor, indicators of oxidative stress in young patients with myocardial infarction. 74 patients with acute myocardial infarction (AMI) were examined. The patients were divided into 2 groups: 38 AMI patients of young age made up group 1 and 36 patients with AMI over the age of 60 years made up group 2. The analysis of the obtained data showed that among the risk factors in young AMI patients, smoking was reliably frequent, there was an increase in the aggregation ability of platelets and the level of VWF in the blood plasma, an increase in the processes of oxidative stress, characterized by an increase in the MDA content and a decrease in the activity of the antioxidant system. At the same time, high MDA indices were associated with the anterior localization of AMI compared with the group of AMI patients over the age of 60 years.

### **Keywords**

Myocardial infarction; endothelial dysfunction; young age

### **Introduction**

One of the most socially significant problems of modern medicine is the treatment and prevention of acute myocardial infarction (AMI). This is determined by both the high mortality directly during this disease, and the subsequent development of severe heart failure, which leads to the disability of patients [1,4]. The development of thrombosis in the coronary artery is one of the main causes of myocardial infarction [8]. According to angiographic and pathological studies, coronary artery thrombosis is observed in myocardial infarction in 80-90% of cases, especially in myocardial infarction with ST segment elevation and the presence of a Q wave. The development of coronary artery thrombosis is preceded by rupture or rupture of an atherosclerotic plaque or its superficial erosion, since adhesion and aggregation of platelets occurs in the area of the damaged atherosclerotic plaque with the release of a large amount of biologically active substances, the accumulation of which contributes to increased platelet aggregation [6,7].

In the genesis of myocardial infarction, undoubtedly, disorders of the coagulation and anticoagulation systems of the blood are of particular importance. An important role in the development of thrombosis is assigned to the marker of endothelial dysfunction - von Willebrand factor (VWF), which is involved in the process of platelet adhesion and aggregation, and also VWF is involved in the binding and stabilization of factor VIII [13], to enhance oxidative stress processes[5,9]. In recent years, there has been an increase in the frequency of myocardial infarction in young people, which is possibly associated with an increase in the number of stressful situations, a decrease in physical activity [3,10]. Difficult and controversial for clinical study is the question of the causes of myocardial infarction in young people.

### Purpose

Study of indicators of platelet aggregation activity, oxidative stress and von Willebrand factor in young patients with myocardial infarction.

### Methods

74 patients with acute myocardial infarction (AMI) were examined. The study included male patients with primary Q-wave myocardial infarction no more than 6 hours from the onset of angina pain. The diagnosis was established based on the WHO criteria in the presence of the following signs: a characteristic attack of angina pain or its equivalent lasting at least 30 minutes; the appearance of pathological Q or QS waves in two or more ECG leads. The patients were divided into 2 groups: 38 AMI patients of young age made up group 1 and 36 patients with AMI over the age of 60 years made up group 2. The control group consisted of 16 healthy volunteers. Platelet aggregation activity (AAT) was determined by the method of G.V. Born. ADP was used as an inductor. The platelet aggregation activity (AAT), the rate and maximum amplitude of aggregation were determined. The level of VWF was determined using a quantitative enzyme-linked immunosorbent assay using RPA «RENAM» (research and production association of the Russian society of patients with hemophilia) reagents. The indicators of oxidative stress were assessed: malondialdehyde (MDA), diene conjugates; the state of the antioxidant enzymatic system was judged by the activity of the enzymes catalase and superoxide dismutase (SOD).

### Data Analysis

Statistical processing of the research results was carried out on an IBM PC / AT personal computer using the ECXEL 6.0 Windows-95 spreadsheet package. The parameters were described as: arithmetic mean  $\pm$  standard deviation ( $M \pm SD$ ).

### Results

The analysis of the obtained results showed that MI of the anterior localization occurred in 43 (41.9%) patients, MI of the posterior wall was observed in 31 (72.9%) patients (Table 1). Arterial hypertension (AH) had a history of 54 (72.9%), angina pectoris before myocardial infarction had 38 (51.3%) patients (Table 1).

Table 1  
Clinical characteristics of patients

Indicators	Number of patients n=74	%
Average age (years)	52.34 $\pm$ 11.31	
Men	74	100%
Posterior MI	31	41.9%
Anterior MI	43	58.1%
History of hypertension	54	78.8%
Obesity	49	66.2%
Smoking	31	41.9%
Angina in anamnesis	38	51.3%

Acute heart failure (Killip II-IV)	13	17.5%
Early post-infarction angina	24	32.4%
LV aneurysm	12	16.2%
Group 1 (age<45)	38	51.4%
Group 2 (age> 60)	36	48.6%

When analyzing the occurrence of risk factors (RF) depending on age, it was revealed that in patients the occurrence of such RF as smoking was significantly more frequent in the group of young patients in 64.5% of cases. AH in this group of patients was found in 21 (38.8%), and obesity - in 20 (40.8%). A comparative analysis of the significance of risk factors for coronary artery disease in patients under 40 years of age who have had myocardial infarction revealed that obesity, hyperlipidemia, smoking, diabetes mellitus, atherosclerosis in relatives are more common in young people, and in patients over 40 years of age - arterial hypertension. A combination of several risk factors is especially typical for young people who have had myocardial infarction.

Analysis of the data obtained in the study of platelet aggregation capacity in patients of group 1 and in patients of group 2, the initial indicators of platelet aggregation activity (AAT) were significantly higher than in healthy individuals, amounting to  $1.75 \pm 0.72 \mu\text{mol ADP}$  and  $2.78 \pm 1.28 \mu\text{mol ADP}$  versus  $4.78 \pm 0.22 \mu\text{mol ADP}$  in healthy individuals ( $P < 0.001$ ) and  $P < 0.05$ ). In patients of group 1, the rates of platelet aggregation (Vagr) were also significantly high. In group I they were  $2.9 \pm 0.36 \text{ cm / min}$  and in group 2  $1.83 \pm 0.41 \text{ cm / min}$  versus  $0.34 \pm 0.5 \text{ cm / min}$  in healthy individuals, respectively,  $P < 0.01$ . In patients with MI, the maximum amplitude of aggregation (Amax) was also significantly higher than in healthy and was  $3.6 \pm 0.55 \text{ cm}$  in group I,  $2.94 \pm 0.55 \text{ cm}$  in group II versus  $0.5 \pm 0.07 \text{ cm}$  in healthy individuals, respectively ( $P < 0.001$ ) (Table 2).

The study of platelet aggregation capacity depending on age revealed that the rates of aggregation by 22.4% and AAT by 37% were significantly higher in patients of group 1 compared with these indicators of group 2 ( $P < 0.05$ ).

Table 2.

Baseline ADP-induced platelet aggregation in AMI patients, ( $M \pm SD$ )

Patient groups	Vagr, cm / min	Amax, cm	AAT, $\mu\text{molADP}$
Control	$0.34 \pm 0.5$	$0.5 \pm 0.07$	$4.78 \pm 0.22$
1st group	$2.9 \pm 0.36^{**}$	$3.6 \pm 0.25^{***}$	$1.75 \pm 0.72^{***}$
2nd group	$1.98 \pm 0.20^{***}$	$2.94 \pm 0.55^{**}$	$2.78 \pm 1.28^{**}$

Note:\*\*  $P < 0.005$

\*\*\*  $P < 0.001$

The initial level of VWF in the examined AMI patients was 1.6 times higher than in the control group: in patients of group 1 it was  $178.6 \pm 5.30\%$  versus  $112 \pm 6.9\%$  in healthy individuals and

1.2 times in patients compared with the indicator of patients in group 2 -  $158 \pm 6.8\%$ , while a significant difference was noted between the indicators of patients in groups 1 and 2 ( $P < 0.001$ ).

An integral marker in the formation of endothelial dysfunction, the triggering mechanism for the formation of platelet thrombus and its first stage - platelet adhesion is VWF [7]. Its initial level in the examined AMI patients was 1.6 times higher than in the control group: in patients of group 1 it was  $125.6 \pm 5.30\%$  versus  $112 \pm 13.9\%$  in healthy individuals and 1.4 times in patients of group 2 it was  $158 \pm 3.46\%$ , while a significant difference was also noted between the indicators of patients in groups 1 and 2.

The study of indicators of oxidative stress in AMI patients of young age showed an increase in the level of MDA by 32.4% higher than in the group of AMI patients over the age of 60 years, which was accompanied by an increase in the level of DC by 21.5%.

In young patients with AMI, the indicators of the antioxidant system were significantly lower than those in the group of AMI patients over the age of 60: the SOD indicator was reduced by 33.5% ( $P < 0.001$ ). There was also a decrease in the level of catalase by 27.4% ( $P < 0.05$ ) compared with the group of AMI patients over the age of 60, which indicates a decrease in AOS activity and is possibly associated with the participation of SOD and catalase to suppress  $O_2$ -hyperexcretion, which used in tissues to react with NO and form ONOO-. The study of indicators of oxidative stress revealed the dependence of these indicators on the localization of MI. In patients with anterior myocardial infarction, both in young and elderly patients, the MDA indicator was significantly higher compared with these parameters in patients with posterior MI by 13.6 and 10.4%, respectively. The analysis of complications in the early postinfarction period among patients revealed the following: the incidence of such complications as the development of acute heart failure, LV aneurysm and potentially dangerous ventricular arrhythmias is statistically significantly associated with baseline high MDA values (Table 3).

Table 3.  
 Baseline indicators of oxidative stress and AOS of the system in patients with AMI

Indicator	Control n = 18	The first group up to 45 years old n = 38	Second group over 60 years old n = 36
Malondialdehyde -MDA, nmol / ml	$8.1 \pm 0.78$	$20.9 \pm 1.42$	$15.8 \pm 1.25^{**}$
Conjugated dienes -CD, $\mu\text{mol/L}$	$1.61 \pm 0.78$	$4.19 \pm 0.12$	$3.45 \pm 0.22$
Superoxide dismutase - SOD, EU / ml	$17.3 \pm 1.8$	$5.3 \pm 0.13^*$	$8.86 \pm 0.65^*$
Catalase, $\mu\text{mol / L}$	$4.95 \pm 0.33$	$1,48 \pm 0.21^*$	$2.04 \pm 0.154^{**}$

\*  $P < 0.05$

\*\*  $P < 0.001$  - reliable compared with the control group

Thus, smoking is a significant risk factor in AMI patients of young age; there is an increase in platelet aggregation and the level of VWF in blood plasma, which is more pronounced in AMI patients of a young age.

### Discussions

Long-term study of the cardiovascular system in health and disease has shown that vascular homeostasis is largely due to the normal functioning of the vascular endothelium. Violation of its work reduces the vasomotor tone of the vessel, causes local and systemic spastic reactions, thrombosis, vascular remodeling. The main functions of the vascular endothelium are the release of such vasoactive agents as nitric oxide, endothelin, angiotensin I-AI (and possibly angiotensin II), prostacyclin, thromboxane [12]. The high content of ONOO- as a result of increased lipid peroxidation processes contributes to the delay in tissue structures of many enzyme systems, including enzymes of the antioxidant system - SOD and catalase. In young patients with AMI, the indicators of the antioxidant system were significantly lower than those in the group of AMI patients over the age of 60 years: the SOD indicator was reduced by 33.5% ( $P < 0.001$ ).

The thrombotic-resistant surface of the endothelium (the same charge of the surface of the endothelium and platelets) prevents "sticking" - the adhesion of platelets to the vessel wall [2]. In young patients with MI, the rate of platelet aggregation (Vagr) was also reliably high, being  $2.9 \pm 0.3.6$  cm / min in group I and  $1.83 \pm 0.41$  cm / min in group 2 versus  $0.34 \pm 0.5$  cm / min /.

VWF is a recognized marker of endothelial dysfunction. The relationship between an increase in the concentration of VWF in the blood with the degree of damage to the vascular endothelium has been proven in many experimental studies. An integral marker in the formation of endothelial dysfunction, the triggering mechanism for the formation of a platelet thrombus and its first stage - platelet adhesion is also VWF [11]. In patients of group 1, the EFV index was 1.6 times higher than in the control group.

### Conclusion

Among the risk factors in young AMI patients, smoking was reliably frequent; there was an increase in platelet aggregation capacity and the level of VWF in blood plasma. Strengthening the processes of oxidative stress, characterized by an increase in the content of MDA and a decrease in the activity of the antioxidant system. At the same time, high MDA indices were associated with the anterior localization of AMI compared with the group of AMI patients over the age of 60 years.

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