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Morphology of intracoronary thrombi and its prognosis in young and older patients after STEMI

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The article presents the features of the morphologic structure of intracoronary thrombi and the prognosis of acute ST segment elevation myocardial infarction (STEMI) in patients of different age groups.

Methods: Histological analysis of the aspirated intracoronary clots was performed in 97 patients with STEMI. The patients were divided into two groups: 11 patients aged under 44 (young group) and the remaining older than 45 (older group). The short-term prognosis was determined by: ST-segment resolution, achievement of good coronary flow, myocardial blush, indices of myocardial contractility, and QS wave formation on ECG. The study's endpoints determined the long-term prognosis: The onset or worsening of angina symptoms, coronary revascularization (PCI or CABG), AMI, and death.

Results: Elderly patients were substantially more likely to have a history of coronary artery disease, as well as angina attacks, or their equivalents, at rest a few days before the onset of STEMI and arterial hypertension. Dyslipidemia was significantly more common in young patients. Formation of microchannels within the thrombi was significantly more common among older patients. Achieving the target quality of microcirculation was substantially more frequent among young patients (p=0.007). The long-term prognosis was better in young patients due to the lower prevalence of the combined endpoint.

Conclusions: Elderly patients were more likely to have intracoronary thrombi with microchannel formation, indicating a longer duration of the thrombotic process. The long-term prognosis after STEMI was significantly better in young patients.

Keywords: Myocardial infarction, coronary reperfusion, coronary occlusion, blood clot, cardiovascular risk factors.

Introduction

Coronary artery disease (CAD) causes about 1.8 million deaths annually in Europe. This is 20% of the overall mortality [1]. Acute myocardial infarction (AMI) is the leading cause of death. The frequency of AMI in Ukraine in 2017 was 1,189 per 1 million population per year [2]. The most comprehensive European registry is found in Sweden, where the incidence rate of acute myocardial infarction with persistent ST-segment elevation (STEMI) was 580 per 1,000,000 per year in 2015 [3]. In other European countries, the incidence rate ranged from 430 to 1,440 per 1 million per year [3]. There are different variants of AMI, and its clinical, laboratory and functional characteristics are described in medical publications, thus greatly simplifying the diagnostic algorithm. The highest mortality rates among patients with CAD are due to acute myocardial infarction with persistent ST-segment elevation (STEMI) [3].

The rupture of an atherosclerotic plaque is the leading cause of coronary artery thrombosis in STEMI patients. The main treatment element is timely percutaneous coronary revascularization (PCI) of the infarct-related coronary artery [3]. At the same time, some publications show that even with timely intervention, adequate reperfusion is not always possible [4]. The main reason for this no-reflow phenomenon is the development of distal embolization, which results in microvascular obstruction, leading to an increase in early post-infarction complications [4]. In recent years, some measures have been proposed to prevent distal embolization during PCI, including mechanical thrombus aspiration [5].

There is a steady increase in the incidence of AMI in Ukraine, just like in all European countries [1,2]. In elderly patients, changes in the coronary arteries are more pronounced, diffuse, and such patients have a higher incidence of comorbidities, which leads to a worse prognosis [6]. Noaman studied the consequences of PCI in 27,869 patients. Age over 65 years was a reliable, independent predictor of prognosis in patients with AMI. [6]. Thus, the increased mortality of STEMI in all age groups was the reason for further study of the structure of intracoronary thrombi and the effectiveness of different therapeutic methods in treating patients of different ages.

Materials and Methods

The research used patient data from three medical institutions: National Scientific Center "Institute of Cardiology n.a. M. D. Strazhesko," Kyiv, Clinical Municipal Communal Emergency Hospital, Lviv, and Lviv Regional Cardiological Clinic. The study included 100 patients with STEMI who underwent coronary angiography and primary PCI using manual thrombus aspiration within the first 12 (mean 7.00 [range 4.75-10.00]) hours from the onset of symptoms. There were 22 women (22%) in the study ranging in age from 35 to 85 (mean 57.81 ± 10.26) years. Informed consent to participate in the study was obtained from each patient. The study was approved by the National Scientific Center ethics committee "Institute of Cardiology n.a. M. D. Strazhesko" (protocol #25 from 2 Dec 2019).

Occlusion of the infarct-related coronary artery was seen in each patient on initial coronary angiography (Figure 1a). Sufficient aspiration material for histological examination was obtained in 97 patients (Figure 1b). The aspirated thrombi were analyzed macroscopically and divided into three groups: White, red, and mixed. Subsequently, they were fixed in a neutral solution of formalin, then filled with resin and stained by the standard method of hematoxylin-eosin and by the method of orange-red-blue (Zerbino-Lukasevych method). The latter allows estimating the age of fibrin by color. If the color of the fibrin is red or pink, its age is less than 24 hours, and a blue or purple color indicates the age of the fibrin to be greater than 24 hours. The thrombus was classified as "old" when the fraction of such fibrin was more than 30%.

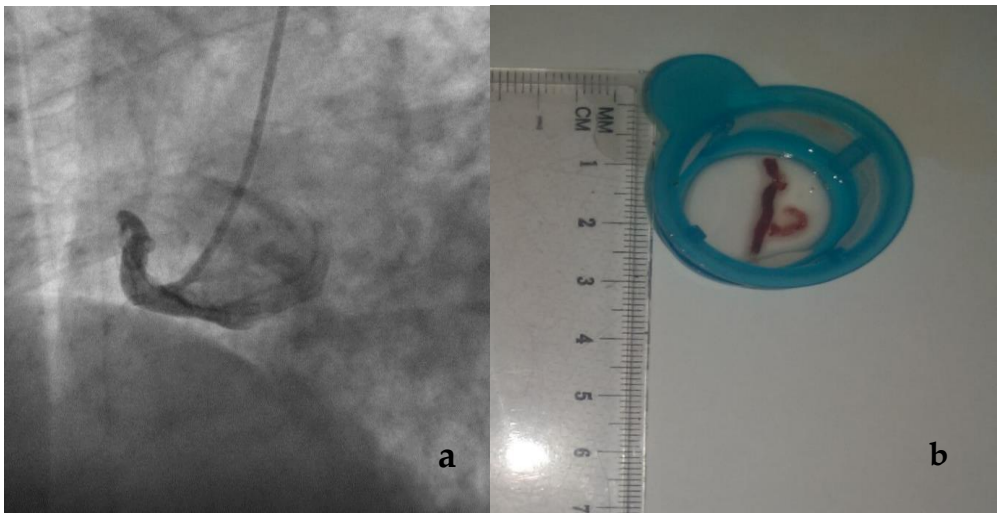


Figure 1. Occluded right coronary artery (a), and intracoronary thrombi aspirated from it (b)

Thrombi were classified as follows:

- Old or fresh (clot age)
- The presence or absence of a layered structure
- Microchannel presence
- Neutrophilic infiltration at the thrombus periphery
- Presence of eosinophilic leukocytes
- Presence of atherosclerotic plaque components (Figure 2).

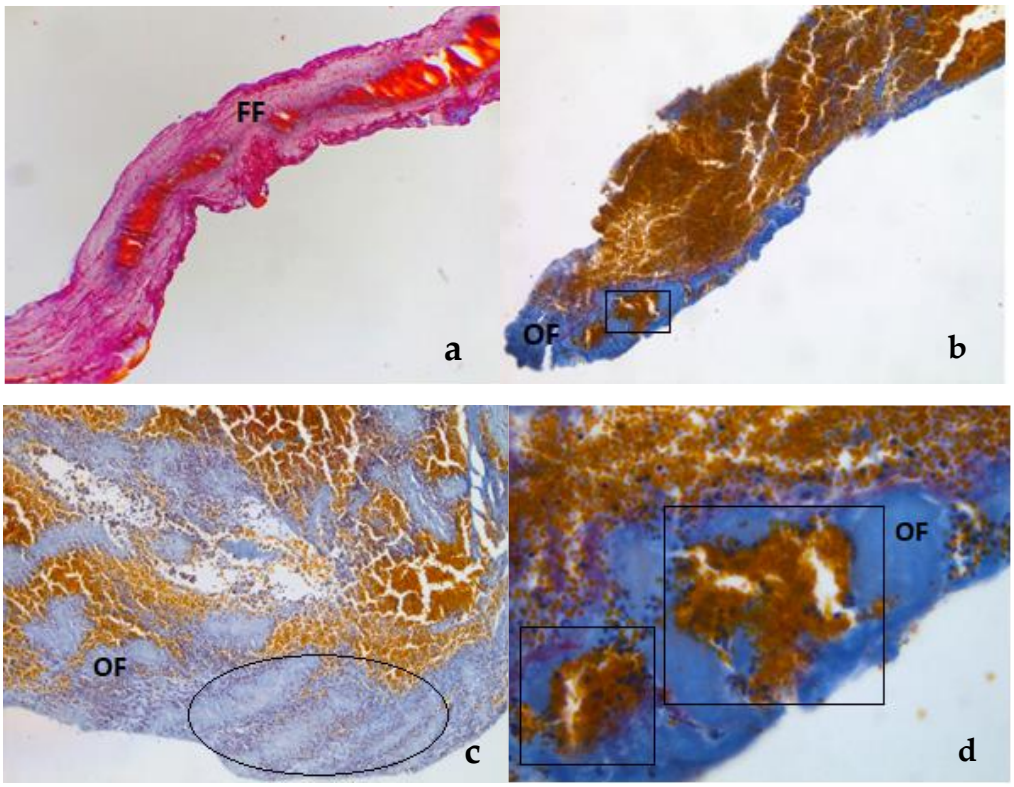


Figure 2. Different thrombi groups: "fresh" (a) (x40), "old" (b) (x100), with layered structure (c) (x200), with microchannel (d) (x400). FF- fresh fibrin, OF – old fibrin, ⬭ layered structure, ▭ microchannel

We compared the short and long-term consequences for the patients. The following indicators determined the short-term prognosis: ST-segment resolution by at least 50% in one hour after the intervention, achievement of thrombolysis in myocardial infarction (TIMI) grade 3 flow, and myocardial blush (MBG) 3, ejection fraction of the left ventricle (EFLV), myocardial contractility index, signs of postinfarction aneurysm of the left ventricle, and QS wave formation on discharge from the hospital. The study's endpoints determined the long-term prognosis: The onset or worsening of angina symptoms, coronary revascularization (PCI or CABG), AMI, and death. In addition, each of the elements was compared separately. Long-term consequences were determined 6, 12, and 24 months after primary.

We divided patients into two age groups to evaluate age-related differences in prognosis. We used the classification of age proposed by the WHO, where the young age is up to 44 [7]. Our study includes 11 such patients (young group), and the remaining 89 patients of our study were included in the elder group.

Results

Initial characteristics. The young group had a mean age of 39.64 ± 3.38, and the elder group 60.44 ± 9.76 ($p < 0.001$). Clinical and anamnestic characteristics are listed in Table 1. There was a significant difference in the frequency of coronary heart disease and chest pain a day before hospitalization among young individuals (1 [9.1%]) and in elder ones (41 [46.1%]) ($p = 0.019$). When comparing the frequency of risk factors for CAD, there was a significantly higher incidence of hypertension in elderly patients (3 young patients [27.3%] vs. 55 elder patients [61.8%]; ($p = 0.029$). Dyslipidemia was significantly more common in young people (7 [63.6%]) vs. elderly (26 [30.2]) ($p = 0.028$). Other risk factors did not differ significantly between groups (Table 1).

Table 1

Clinical and anamnestic characteristics of patients at presentation

Indices	Young		Elder		p
	number	%	number	%	
Males	10	90.9	72	80.9	0.41
CAD in anamnesis	1	9,1	41	46.1	0.019
Diabetes mellitus	3	27.3	20	22.5	0.72
Hyperglycemia on admission	7	63.6	37	42	0.174
Arterial hypertension	3	27.3	55	61.8	0.029
Smoking	9	81.8	48	53.9	0.078
Obesity	6	54.5	35	39.3	0.333
Dyslipidemia	7	63.6	26	30.2	0.028
Anemia	2	18.2	15	17	0.92
Leukocytosis	7	63.6	49	55.1	0.589
Chronic kidney failure	1	9.1	19	21.3	0.338
Exposure to chemical compounds	7	63.7	30	33.7	0.052
Exposure to metals	2	18.2	26	29.2	0.442
Dilation of the left ventricle	3	27.3	42	47.7	0.199
Cardiogenic shock on admission	0	0	12	13.5	0.19
Thrombolytic therapy prior to primary percutaneous coronary intervention	0	0	8	9	0.3

Table 2

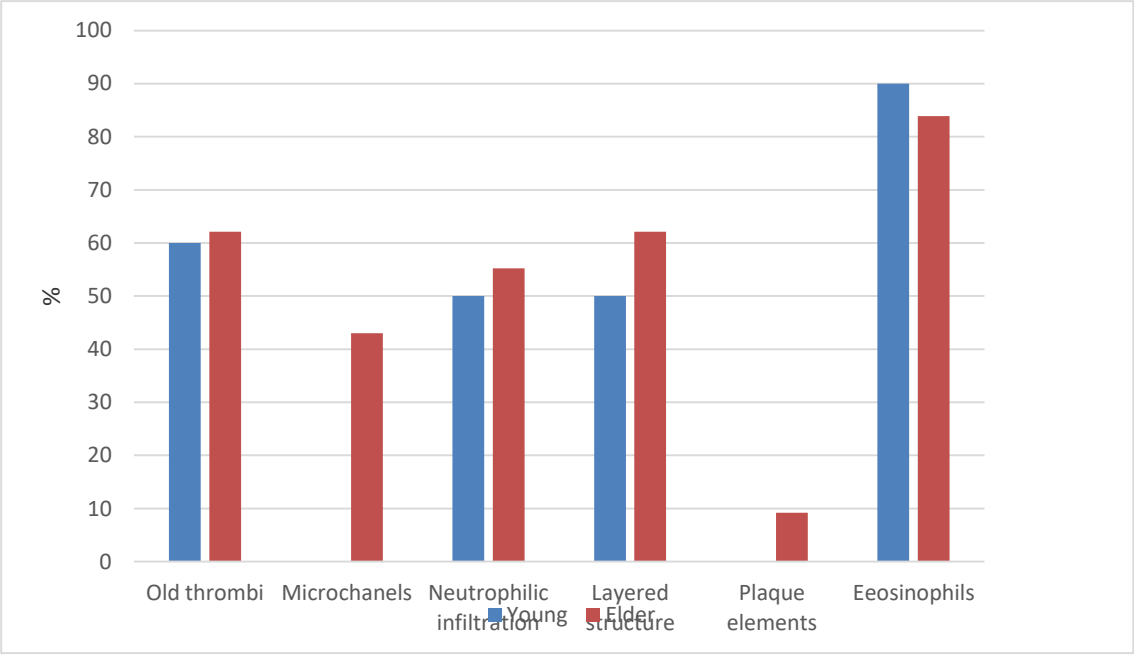
Angiographic and interventional features of patients at presentation

Indices	Young		Elder		P
	number	%	number	%	
Left coronary artery culprit vessel	4	36.4	37	41.6	0.74
Multi-vessel involvement	5	44.5	35	39.3	0.696
TIMI 0 blood flow before intervention	9	81.8	73	82	0.987
MBG 0 before intervention	10	90.9	78	87.6	0.753
Balloon used	4	36.4	45	50.6	0.372

Analysis of the morphological structure of blood clots showed that old blood clots were found in 6 (60%) young patients and 54 (62.1%) elder patients (p = 0.899). The layered structure was recorded in 5 (50%) and 54 (62.1%) patients, respectively (p = 0.459). The presence of microchannels, which indicates an old age of blood clots, was not found in any young patient, while among the elderly, there were 38 (43.7%) cases (p = 0.007). Inflammatory infiltration of the thrombus circumference was present in 5 (50%) young and 48 (55.2%) elder (p = 0.756) individuals. Elements of atherosclerotic plaque were rare, with none in young and 8 [9.2%] in older individuals, p = 0.317). Eosinophils were found in 9 (90%) intracoronary thrombi of young patients and 83 (83.9%) of older patients (p = 0.613) (Table 3).

Table 3

Morphological features of intracoronary thrombus in patients with STEMI

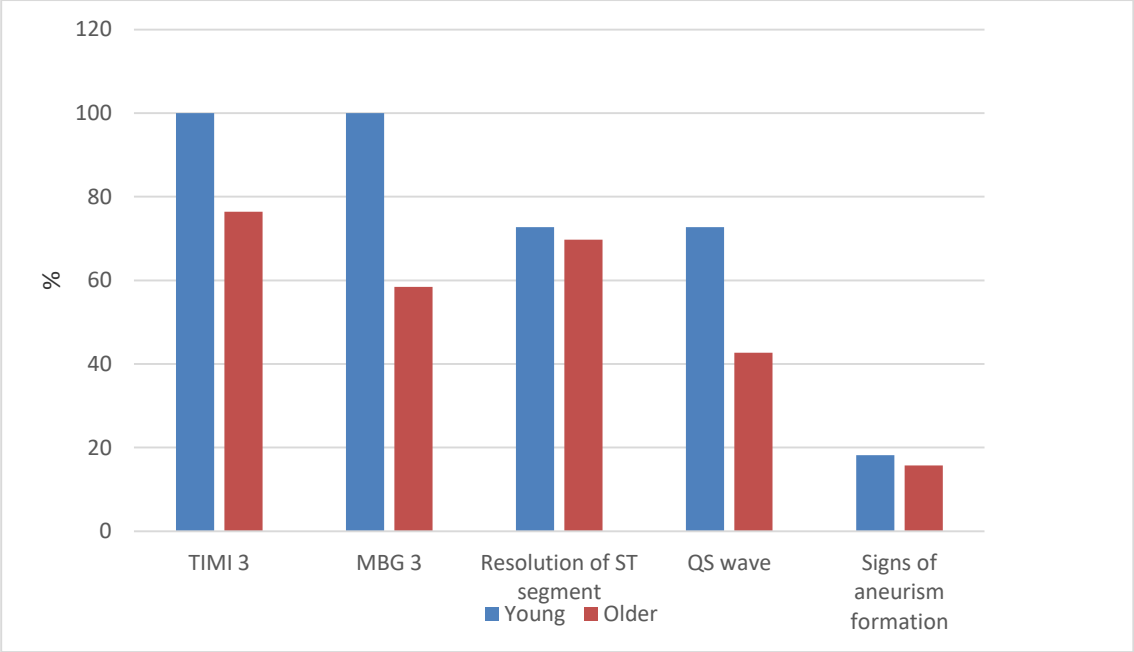


After the intervention, post-intervention blood flow was assessed by the incidence of TIMI 3 and MBG 3. TIMI 3 was achieved in 11 (100%) young and 68 (76.4%) older individuals (p = 0.07), and MBG 3 in 11 (100%) and 52 (58.4%), respectively (p = 0.007) (Table 4).

Resolution of ST-segment elevation by at least 50% one hour after the intervention occurred in 8 (72.7%) young and 62 (69.7%) older patients (p = 0.834). The QS wave on the ECG on discharge from the hospital was observed in 8 (72.7%) and 38 (42.7) patients, respectively (p = 0.059). Signs of LV aneurysm formation were recorded in 2 (18.2%) young and 14 (15.7%) older patients (p = 0.834) (Table 4).

Table 4

Post-intervention results for patients with STEMI of different ages

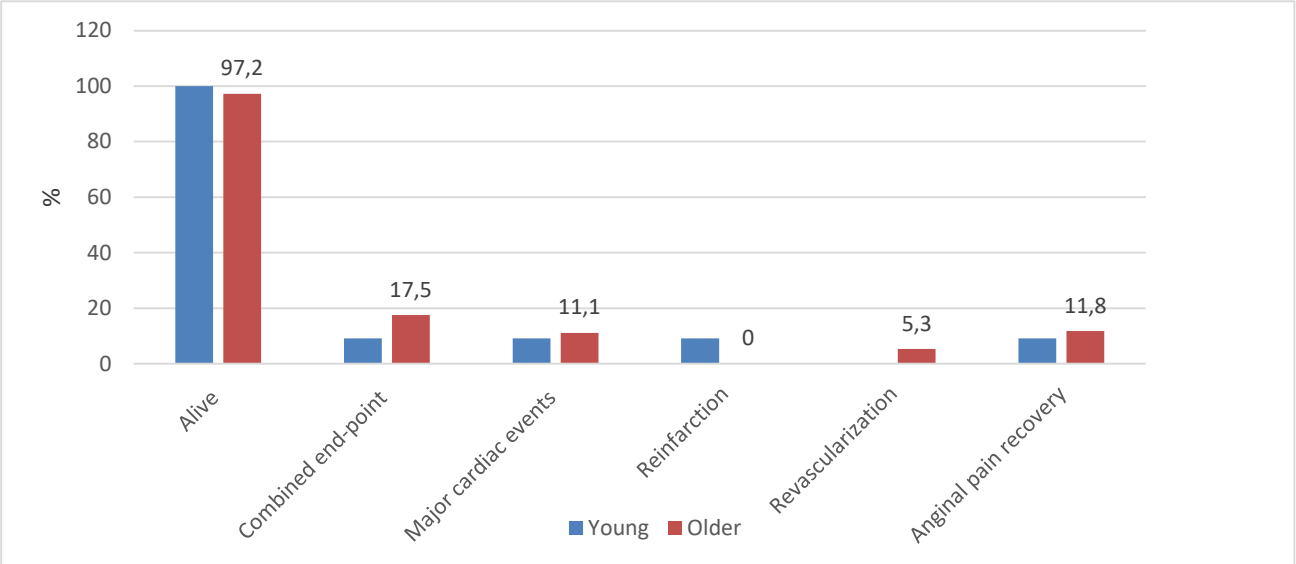


Prior to hospital discharge, echocardiographic data showed the EFLV in the young group to average 50.82 % ±6.37 and in the older group 48.03 % ±9.69 (p = 0.219). Total contractility was 1.25 [1.22; 1.44] and 1.38 [1.25; 1.63], respectively (p = 0.371). Long-term follow-up at 6, 12, and 24 months after the intervention. Information was obtained in 11 (100%) young and 81 (91.0%) older patients.

At six months, 11 (100%) young and 76 (92.7% of those who were contacted) older were alive (p = 0.354). The combined consequences (death, myocardial revascularization, myocardial infarction, or recurrence of chest pain), major cardiac events (death, myocardial revascularization, or myocardial infarction), and individual endpoint components were investigated for living patients who were contacted. These results are tabulated in Table 5. None were statistically significant. High adherence to drug treatment was found in 10 (90.9%) young and 67 (88.2%) older patients, p = 0.789.

Table 5

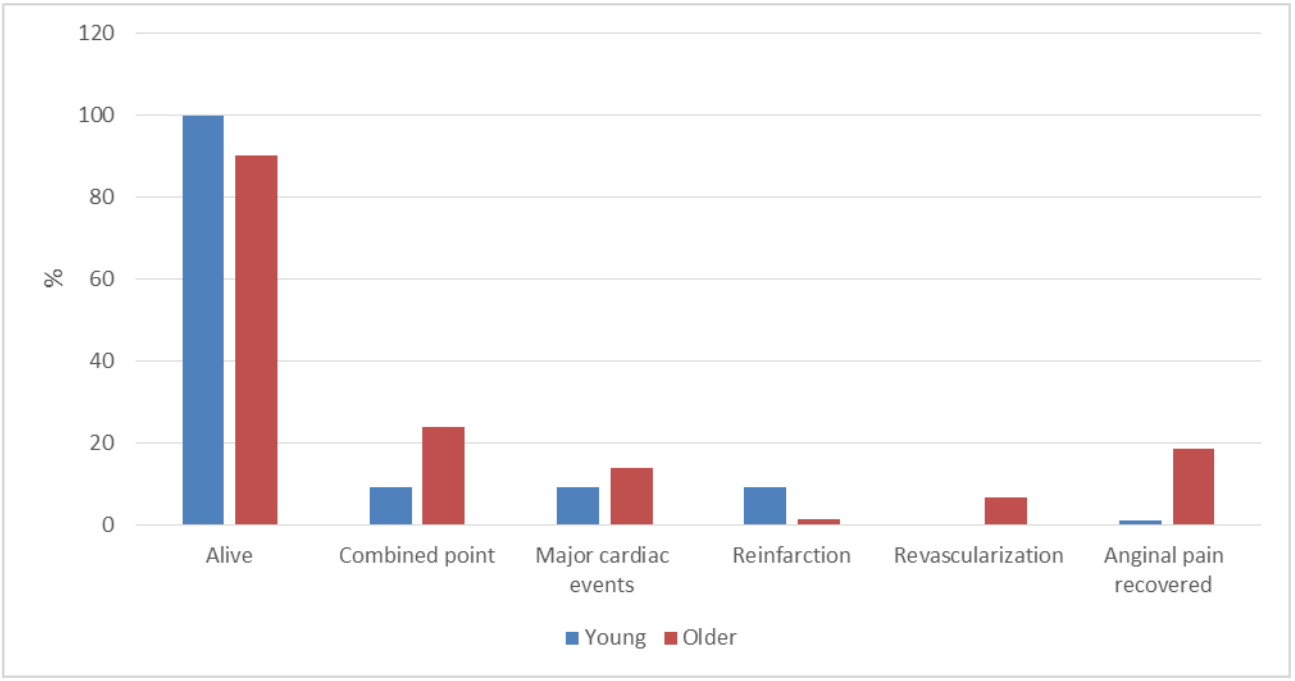
Results of patients with STEMI of different ages at six months after the intervention



At 12 months of follow-up, 11 (100%) young and 74 older (90.2% of those contacted) were alive (p = 0.279). The results are tabulated in Table 6. There were no statistically significant differences between the two groups. High adherence to drug treatment was in 10 (90.9%) young and 56 (73.7%) older patients, p = 0.212 (Table 6).

Table 6

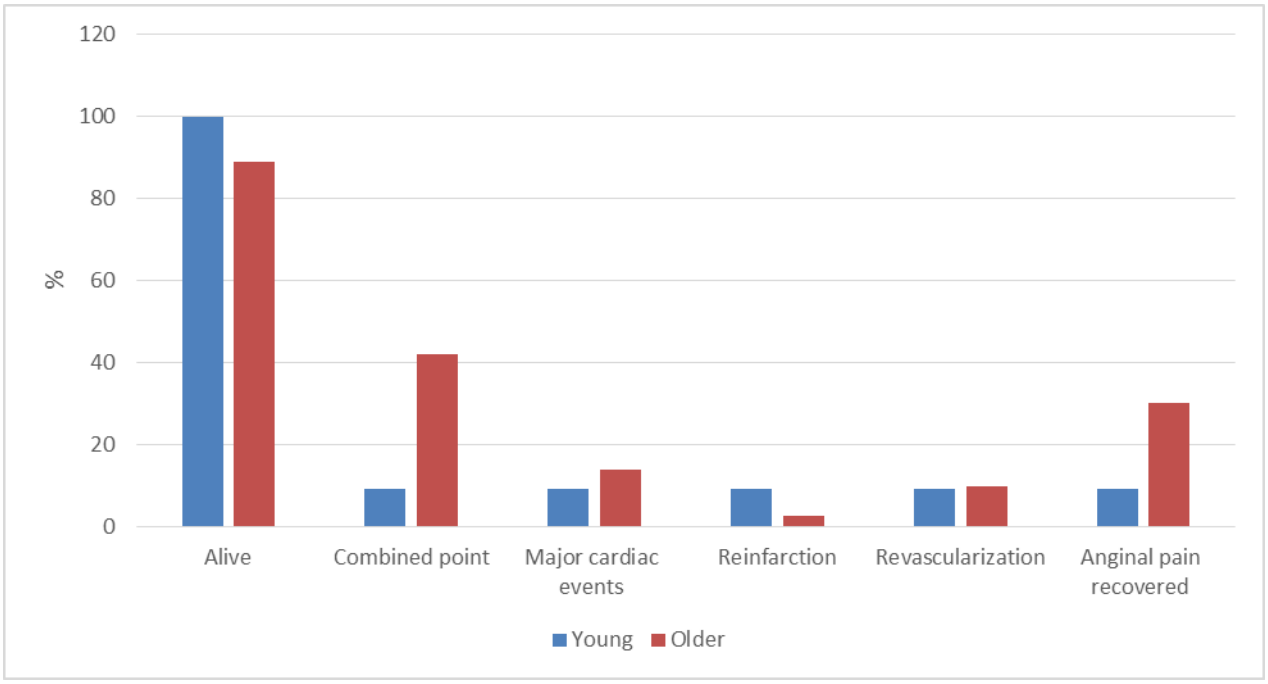
Results of patients with STEMI of different ages at 12 months after the intervention



After 24 months of follow-up, 11 (100%) young and 72 older (88.9% of those contacted) were alive, p = 0.244. The results are tabulated in Table 7. There were no statistically significant differences between the two groups except for the combined group of events (p = 0.035). High adherence to drug treatment was in 9 (81.8%) young and 53 (72.6%) older patients, p = 0.517 (Table 7).

Table 7

Results of patients with STEMI of different ages at 24 months after the intervention



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Discussion

Analyzing the clinical picture of patients who suffer from STEMI, older patients tend to have a more severe condition, but the difference is not statistically significant. Older patients in our study more have a history of CAD, as well as attacks of anginal pain, or their equivalents, a few days before the clinical manifestation of STEMI. It may be related to the higher prevalence of atherosclerosis in older persons [8].

Dyslipidemia, a risk factor for myocardial infarction, was more common in young people. This is consistent with the role of familial dyslipidemia in the development of STEMI [9]. The incidence of hypertension, another risk factor in CAD, also increased with age in our study cohort.

The morphological evidence of the formation of microchannels within the intracoronary thrombus indicates its age. This process begins on the fifth day after the occurrence of a thrombus [10]. This is consistent with our results regarding the greater prevalence of signs of atherosclerotic process destabilization in coronary arteries (anginal chest pain or its equivalents at rest) a few days before STEMI. Ischemic myocardial preconditioning also may play an important role in the outcome of CAD.

The discrepancy between the angiographic criteria for the effectiveness of PCI versus echocardiographic and ECG criteria is interesting. Achieving optimal blood flow through the infarct-related coronary artery was more common in young vs. older patients ($p = 0.07$). Achieving the target microcirculation (MGB) quality was significantly more common in the younger cohort ($p = 0.007$). However, this was not reflected in ST-segment resolution and echocardiography data resultsAuthors should discuss the results and how they can be interpreted from the perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible. Future research directions may also be highlighted. The last paragraph should include conclusions (2-3 sentences) in the research type of manuscript.

In conclusions: Analyzing the long-term prognosis, better results are expected in young patients. Two years of follow-up show a significantly higher incidence of combined endpoints in older patients, mainly higher mortality and recurrence of anginal pain or equivalents.

Summing up study results, it should be noted that older patients are more likely to have blood clots with signs of microchannel formation, which is morphologic evidence of a longer duration of the thrombotic process. Study results suggest lower tolerance to myocardial ischemia in young patients.

This study is limited by the small number of patients in the younger group.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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