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Coronary "slow-flow" phenomenon in young males with STEMI: clinical features and follow-up

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Abstract

Objective of this study was to identify clinical and angiographic characteristics and evaluate long-term treatment outcomes in young male patients with STEMI.

Materials and methods

Depending on the coronary angiography results we formed two groups of patients aged 25-44 years: the first consisted of 44 men with the angiographic "Y-phenomenon" and the second of 25 men with the typical pattern of a coronary artery occlusion. We analyzed risk factors, laboratory parameters, echocardiographic findings, the severity of depression according to The Beck Depression Inventory (BDI) and the level of androgenic dysfunction according to the Aging Males' Symptoms (AMS) and International Index of Erectile Function (ICEF-5) questionnaires. Survival rates repeated acute coronary events and the prevalence of surgical revascularization after a year of the primary event were evaluated.

Results

There were more men with the higher body mass index (BMI) in the first group. No significant differences in lipid profile were identified. Patients in the second group had higher rates of myolysis (MB-CPK, AST, ALT) and a lower left ventricular ejection fraction at discharge — 52.8% [36; 63] versus 58.1% [20; 69]. These findings were statistically significant. There were no significant differences in the level of the androgen deficiency symptoms according to the AMS scale between the two groups. Depressive symptoms were present in 77.3% of the respondents in the

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first group and in 68% of the respondents in the second group. After 365 days from the indexed event all patients are alive and no large coronary events happened.

Conclusion

Young male patients with STEMI have different risk factor profiles and comparable annual survival rates depending on the angiographic picture. The intensity of the pathological process and inflammatory reaction are more pronounced in the classical MI. Depression, as one of the possible risk factors, turned out to be insignificant in groups with Y-syndrome and with atherothrombosis. Erectile dysfunction was less pronounced with distal coronary blood flow disorders than with proximal occlusions.

Key words: *Y-phenomenon, STEMI, males, risk factors.*

Conflict of interests: none declared.

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Introduction

Myocardial infarction (MI) was traditionally considered a disease of middle aged and older people, but recently MI started to develop more frequently in people under 45 y.o. The potential risk factors (RF) of coronary and myocardial damage vary and often represent a complicated clinical problem. Coronary slow-flow phenomenon, or Y-phenomenon, is one of the poorly understood coronary angiographic characteristics in patients with angina, including those with various types of acute coronary syndrome (ACS). The Y-phenomenon is seen in 1–7% of angiographies performed in patients with stable angina and reflects the presence of microvascular arterial damage caused by increased blood flow resistance [1]. Moreover, it increases the risk of myocardial infarction (MI). The Y-phenomenon is also seen in 1–5% of patients with ACS — typically in young men who are often smokers and obese [1]. As this phenomenon is still poorly recognized and mostly presents in men, the aim of our study is to determine the clinical and angiographical characteristics to evaluate long-term treatment results in young men with a history of ST-elevation myocardial infarction (STEMI) registered on an ECG.

Materials and methods

This study was conducted in the Clinical Cardiologic Healthcare Centre in Perm, Russia in 2019-2020. Male patients who were 25-44 years old, had a history of ST-elevation myocardial infarction less then 12 hours before admission and signed and informed consent for coronary angiography were included. Those with a history of any ACS episodes, prehospital thrombolysis, diabetes, congenital and acquired heart defects, atrial fibrillation or total left bundle branch block (LBBB), implanted pacemaker, genitourinary pathologies, pituitary diseases or cognitive disorders were included. The study was performed in accordance with the Good Clinical Practice guidelines and Helsinki Declaration. Study protocol was approved by E. A. Wagner Perm State Medical University Ethics Committee. Informed consents were obtained prior to participation in the study. Depending on the coronary angiography results two groups of patients were formed: the first consisted of 44 men with the angiographic Y-phenomenon and the second of 25 men with the typical pattern of coronary artery occlusion. Y-phenomenon was determined as slow antegrade progression of contrast agent to normal epicardial coronary arteries. We analyzed the risk factors, laboratory values, echocardiography findings in both groups. We also assessed the presence of depression using The Beck Depression Inventory (BDI) and the level of androgenic dysfunction according to the Aging Males' Symptoms (AMS) and and International Index of Erectile Function (ICEF-5) questionnaires on the 3d day after admission. At one-year follow-up we assessed survival rates, the recurrence of acute coronary events and the frequency of surgical revascularization via phone interviews. Statistical analysis was performed with Statistica 6.0 software. We carried out comparative and correlation analysis. As the data followed non-normal distribution, we used nonparametric tests to compare two groups: Mann-Whitney U test and Kolmogorov-Smirnov two-sample test. We also used Spearman's correlation test (R) to evaluate the associations between two variables. Descriptive statistics for numerical variables are presented as median and interquartile range (Me [25; 75]; for categorical variables — absolute frequencies

and percentages (%). p<0.05 was considered to be statistically significant.

Results

Clinical and demographic characteristics of the participants are presented in Table 1. Men in the first group had higher BMI (p=0.02), but other coronary artery disease (CAD) risk factors (smoking, family history) were more commonly present in the second group. The mean number of the affected coronary arteries (clinically significant stenosis >50%) was 0.3 [0;2] and 2.9 [1; 6] in the first and second groups, respectively. Myocardial bridges were found in 2 patients in the first group. Although the age distribution was similar in two groups, men with classical atherothrombosis had more coronary damage and longer stable angina that explains the differences in the pharmacological treatment before MI. MI localization was similar in both groups.

During the hospital stay apart from standard laboratory and instrumental workup patients filled out the questionaries for additional evaluation of erectile dysfunction and the presence and level of depression. We hypothesized that androgen deficit may cause earlier development of CAD and we also were interested in evaluating the possible differences in men with various MI etiology. Our findings are presented in Table 2. There were no significant differences in lipid profiles although the prevalence of statin therapy differed between the two groups. Moreover, the levels of myocardial necrosis markers (CPK-MB, AST, ALT) were significantly higher in patients from the second group. Left ventricular ejection fraction (LVEF) was also lower in the second group: 52.8% [36, 63] vs 58.1% [20; 69]. The analysis of ICEF-5 questionnaires showed mild erectile dysfunction was present in the majority of patients in the first group (52.3%) and 36.3% of patients didn't have any complaints. In the second group erectile dysfunction was absent in 28% of patients, 64% had only mild symptoms and 8% — moderate symptoms. The level of androgen deficiency assessed by AMS scale didn't differ significantly in the two groups of this age group. Most patients either had mild androgen deficiency symptoms or had none of them. 77.3% of respondents in the first and 68% in the second group didn't have any symptoms of depression and the difference wasn't statistically significant. Somatic and cognitive-affective scales scores were also similar in the two groups of patients.

Table 1. **Clinical and demographic characteristics of patients in the two comparison**

Clinical and demographic characteristics	Group "Y-phenomenon", N=44	Group "Coronary artery thrombosis", N=25	p1–2
Age, years (mean)	42.4 [32; 45]	43.9 [36; 45]	0.4
BMI, kg/m^2	29.8[21.3; 37.9]	26.7 [17.7; 36.1]	0.02
Smoking, absolute number (%)	19 (43.2)	25 (100)	0.001
Regular alcohol consumption, absolute number (%)	6 (13.6)	8 (32)	0.002
Family history of CVD, absolute number (%)	15 (34.1)	19 (76)	0.000
Hemodynamically significant (>50%) coronary stenosis, absolute number	0.3 [0;2]	2.9 [1; 6]	0.01
CAD present> 1 year, absolute number (%)	16 (36.4)	19 (76)	0.000
Statins, absolute number (%)	12 (27.3)	17 (68)	0.00002
ACEi, absolute number (%)	9 (20.5)	18 (72)	0.000
Aspirin, absolute number (%)	12 (27.3)	18 (72)	0.000

Note. CAD — coronary artery disease, CVD — cardiovascular disease, ACEi — Angiotensin-converting enzyme (ACE) inhibitors.

Table 2. **Laboratory and instrumental findings and the survey results**

Values	Group "Y-phenomenon", N=44	Group "Coronary artery thrombosis", N=25	p1–2
Total cholesterol, mmol/l	4.72 [3.9; 6.4]	4.85 [3.7; 6.8]	0.07
HDL cholesterol, mmol/l	1.03 [0.78; 1.12]	1.28 [0.9; 1.3]	0.05
LDL cholesterol, mmol/l	2.90 [2.11; 3.54]	2.96 [2.18; 3.67]	0.4
Triglycerides, mmol/l	1.64 [1.4; 2.1]	1.48 [1.47; 2.08]	0.07
LVEF, (%, Simpson)	58.1% [20; 69]	52.8% [36; 63]	0.02
No erectile dysfunction, absolute number (%)	16 (36.3)	16 (64)	0.01
Mild erectile dysfunction, absolute number (%)	23 (52.3)	7 (28)	0.01
Moderate erectile dysfunction, absolute number (%)	0 (0)	2 (8)	0.3
Depression (BDI)	34 (77.3)	17 (68)	0.08

Note. HDL — low-density lipoprotein, HDL — high-density lipoprotein, LVEF — left ventricular ejection fraction, BDI — The Beck Depression Inventory.

Correlation analysis in patients with Y-phenomenon revealed moderate inverse correlation between the levels of HDL (high-density lipoprotein) cholesterol and band neutrophils (R=0.48, p=0.004) and direct correlation between the number of lymphocytes, BMI and glucose levels (R=0.44; p=0.02; R=0.39; p=0.04 respectively). However, stronger correlations between inflammation markers and lipid profile were found in the second group. The level of total cholesterol and LDL (low-density lipoprotein) strongly correlated with the number of band neutrophils (R=0.84; p=0.00; R=0.69; p=0.00), lymphocytes (R=0.95, p=0.00; R=0.85, p=0.00) and monocytes ((R=0.76, p=0.00; R=0.71, p=0.00 respectively).

Telephone interviews showed that in 365 days after the event all patients were alive and none of all the patients in both groups requires surgical revascularization. None of the patients developed any cardiac rhythm disorders as well. However, unstable angina that stabilized on the II functional class was diagnosed in 3 patients in the second group.

Discussion

Coronary slow flow phenomenon was first described by Tambe et al. in 1972 and termed "cardiac syndrome Y" because of the probable role of neuropeptide Y in the pathophysiology of this condition. This angiographic phenomenon, which is rarely identified, can cause both recurrent chest pain episodes and myocardial infarction [1]. The estimated prevalence of syndrome Y in patients with STEMI who were admitted to Clinical cardiologic Healthcare Centre in 2019-2020 is 3.7% of all angiography studies performed in young men, which is similar to 1%-5.5% in ACS patients worldwide [2]. Recently a number of new studies explored the Y-phenomenon risk factors but data on clinical characteristics and long-term outcomes in such patients is still very sparse. The results of our study are very similar to those described in the majority of works that explore the possible connection between Y-phenomenon development with increased BMI and specific characteristics of chest pain that develops not during physical activity but after it [3]. There is a study that compares the patients with Y-phenomenon and the cardiac syndrome X and those with Y-phenomenon had a significantly lower LVEF [4, 5]. Echocardiography with speckle-tracking detects significant changes in longitudinal and circumferential strain in patients with Y-phenomenon [6]. We performed echocardiography without strain assessment. We couldn't find direct comparisons with classical MI but we determined that LVEF reduction was more prominent in the second group. In general, according to the markers of cardiac myocyte necrosis, LVEF and the levels of neutrophils and lymphocytes, the pathological process seemed to be more severe in patients with classical atherothrombotic MI. The association between the inflammatory markers and lipid profile values was also stronger in the second group.

It is thought today that the Y-phenomenon is caused by increased coronary microvascular resistance that happens at rest, which, in turn, develops due to endothelial dysfunction [1]. At the same time, endothelial dysfunction can be an early sign of CAD and its development can be considered a potential signal of cardiovascular disease.

We didn't find any works on erectile dysfunction in Y-phenomenon and in our study it was less prevalent in this patient group compared with the classical MI. Depression is considered to be one of the risk factors of erectile dysfunction development but its prevalence was low in both groups.

As the pathophysiological process that leads to Y-phenomenon is still not clearly understood, choice of treatment that would improve distal perfusion is also quite challenging. Current data show that dipyridamole and mibefradil improve perfusion in Y-syndrome bur mibefradil was pulled from the market in 1998 [1]. Sparse research explores intracoronary calcium antagonists (nifedipine) infusion followed by oral forms [8, 9]. Nevertheless, it is recommended to use standard pharmacological agents in patients with confirmed MI during acute event and for secondary prevention. Our study showed that the period of in-patient treatment had no significant differences between the two groups. Stenting was more frequently performed in the second group and the difference was statistically significant. Pharmacological treatment recommended at the discharge was similar in both groups. The described clinical observation period ended with a telephone follow-up interview that didn't explore the predictors of benign CAD. We will continue to collect data in order to increase statistical power of various laboratory and instrumental predictors of negative coronary outcomes. According to the available data, the following parameters are the predictors of negative coronary outcomes in patients with Y syndrome: the presence of arterial hypertension at baseline, age>50 years old, hyperhomocysteinemia and dyslipidemia [3, 10]. We suppose that this fact should be taken into consideration in regular follow-ups of this group of patients.

Conclusion

ounger men with STEMI have different risk factors and similar one-year survival depending on the angiography results. Traditional risk factors play a major role in patients with atherothrombosis. Pathological process and inflammatory reaction are more severe in patients with classical MI. Lipid profiles were similar in the two groups but atherosclerosis was significantly different in the two groups that probably explains increased relapses of angina in the second group. Depression, which is one of the probable risk factors, was uncommon in both the Y syndrome group and the classical atherosclerosis group. Erectile dysfunction was less prominent in patients with distal coronary occlusions compared with the proximal occlusions.

Conflict of interest: None declared.

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