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The effectiveness of resuscitation in patients with acute myocardial infarction according to the population register

Aim	To study clinical and anamnestic features and tactics of managing patients with acute myocardial infarction (MI) in groups with different effectiveness of resuscitation procedures.
Materials and methods	Patients were selected using the "Acute Myocardial Infarction Registry" epidemiological program. 219 cases of acute MI recorded from 2007 through 2017, which required emergency life support, were studied. Two groups were formed based on success of the resuscitation: group 1 consisted of patients with acute MI who survived due to the cardiovascular life support (n=61); group 2 included fatal cases after resuscitation failure (n=158). Quantitative variables were described as median and interquartile range, Me (Q1; Q3); comparison was performed in two independent samples using the Mann-Whitney test. Qualitative variables were presented as absolute and relative values (n (%)). Statistical significance of differences in nominal properties was determined with contingency tables (Pearson χ^2; two-tailed Fisher's exact test). Critical level of two-tailed significance was set equal to 0.05.
Results	The groups consisted of severe cases at baseline. The groups were sex- and age-matched. Mean age of patients in groups 1 and 2 was 63.5±13.1 and 60.9±14.8 years, respectively (p=0.2); in both groups, females were considerably older than males. Analysis of preceding drug therapy showed that comparable proportions of patients received antihypertensive and/or anti-ischemic treatment; however, the qualitative composition of the therapies was significantly different in these group. Thus, survived patients more frequently than deceased patients received drugs from vitally important groups, including β-blockers (93% and 13%, p<0.001), antiplatelets (97% and 13%, p<0.001), statins (84% and 5%, p<0.001), and angiotensin-converting enzyme (ACE) inhibitors (90% and 8%, p<0.001). In additions. success of resuscitation procedures was interrelated with the clinical picture. Thus, in atypical MI, the rate of fatal outcomes was higher (89% and 56.5%, p<0.001) despite the life support.
Conclusion	The patients who survived due to resuscitation procedures more frequently had a history of adequate drug therapy for ischemic heart disease and arterial hypertension with β-blockers, ACE inhibitors, antiplatelets, and statins. In this group, MI mostly had a clinical picture of a prolonged anginal attack. The long-term prediction for survivors after successful resuscitation presently remains important and requires further study.
Keywords	Myocardial infarction; acute myocardial infarction registry; resuscitation
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Coronary artery disease (CAD) is the most common cause of death in the general population, accounting for 20% of all deaths in Europe. Acute myocardial infarction (MI) is the main life-threatening condition in CAD; in turn, ventricular fibrillation (VF) is the direct cause of many fatal outcomes in MI [1]. Since VF often develops at the initial stages of MI, patients often die before reaching the hospital; this is especially true of working-age male patients [2]. For this reason, close attention has been paid to the various methods of resuscitation and life support for patients with cardiac pathology in recent years. However, acute MI is still characterized by high lethality. Survival rates for patients having suffered a circulatory arrest vary from 0 to 40%. Regardless of the cause, treatment of cardiac arrest remains a pressing challenge in emergency medicine, especially prior to hospital admission. Improvements in modern medical science and real-world practice have resulted in patients who were considered incurable a half-century ago now having a chance of survival through the use of various new critical care methods. However, despite the well-

coordinated work of emergency services, the percentage of survivors among successfully-resuscitated patients remains extremely low even in large US hospitals. Mainly due to the out-of-hospital development of circulation arrest, resuscitation procedures are often applied too late, which in turn increases the risk of unfavorable prognosis. According to several authors, survival significantly decreases by 2–3% per minute prior to the start of resuscitation procedures and by 1.1% per minute before defibrillation. In the absence of treatment, the survival rate decreases by 5.5% per minute. Approximately 20 minutes following cardiac arrest, resuscitation is no longer effective [3, 4]. Thus, the prevention of sudden cardiac death should be one of the main goals of cardiology science and practice. Investigations into this pathology should include findings concerning patients with cardiovascular diseases at higher risk, who require special attention in terms of the preventive care due to a high probability of sudden circulation arrest and the potentially low efficacy of resuscitation procedures.

Aim

To study clinical and anamnestic characteristics and management of patients with acute MI in groups having a varying efficacy rate of previously carried out resuscitation procedures.

Materials and methods

According to the study objective, patients were selected using the epidemiological population program «Register of Acute Myocardial Infarction» (RAMI) implemented at the Research Institute of Cardiology, Tomsk National Research Medical Center, since 1984. An objective analysis of the course of acute coronary pathology in different patient cohorts is carried out through the use of unified diagnosis criteria and a comprehensive investigation into clinical anamnestic, laboratory instrumental and pathoanatomical characteristics of MI, as well as peculiarities in the medical care of patients studied [5]. In the case of a lethal outcome, pathoanatomical protocols and medicolegal autopsy reports were analyzed and the patient's family members – as well as any witnesses of the clinical event – were interviewed.

Two hundred nineteen cases of acute MI registered between 2007 and 2017, which had required resuscitation, were studied. Depending on the success of the resuscitation procedures, two comparison groups were formed. Group 1 included patients with acute MI who survived after cardiopulmonary resuscitation (n=61), while Group 2 consisted of patients who had

died after unsuccessful resuscitation attempts (n=158). It should be noted that 86% of fatal cases in Group 2 occurred before reaching the hospital.

Statistical analysis. The normal distribution of quantitative data was verified using the Shapiro-Wilk test. Since the distribution of quantitative variables was different from normal, these were described as the median and interquartile range, Me (Q1; Q3). The qualitative data are presented as absolute and relative values (n (%)). The quantitative data in two independent samples were compared using the Mann-Whitney test. An analysis of contingency tables was performed to determine the statistical significance of differences in nominal characteristics (Pearson's χ^2 test and the two-tailed Fisher's exact test if the expected value was less than 5 in at least one cell of a contingency table). The critical level of bilateral significance in the tests of statistical hypotheses was 0.05 (p-value is the achieved level of significance).

Results

The sex and age composition of patients in compared groups was similar except for the fact that 70% of patients were male. The age of patients in Group 1 varied from 41 to 91 years, with a mean age of 63.5±13.1 years. The mean age of patients in Group 2 was 60.9±14.8 years (p=0.2). However, female patients were significantly older than males in both groups (Table 1). In the groupwise analysis of age gradient (according to the 2016 WHO age classification), the only trend was of a significantly higher number of young patients in the group of patients for which resuscitation had been unsuccessful.

Some peculiar qualities were revealed during the study of anamnestic characteristics. For example, the incidence of patients who had a history of MI and/or ischemic stroke and diabetes mellitus was comparable in both groups. At the same time, the number of patients with hypertension in Group 1 was significantly higher than in Group 2. The lower proportion of smokers found in the group of deceased patients (Group 2); may be attributed to the possible unwillingness of interviewed relatives to report the smoking status of the patient.

Angina pectoris required emergency medical care in 82% of patients in Group 1. At the same time, in Group 2, the first symptoms of coronary deficiency were the stereotyped prolonged attack of retrosternal pain (41%, p<0.001), as well as atypical localization of pain (2 and 5% in Groups 1 and 2, respectively, p=0.3), symptoms of acute left ventricular failure (1.6 and 10%; p=0.03), and an acute decrease in blood pressure (BP) with loss

Table 1. Clinical and anamnestic characteristics of patients and peculiarities
of the course of acute myocardial infarction in groups with different efficacy of resuscitation

Parameters	Group 1, n=61	Group 2, n=158	Significance of differences between the groups, p
Mean age, years	63.5 ± 13.1	60.9 ± 14.8	0.2
Male, n (%): mean age	42 (69) 59.2±11.5	108 (68) 56.9±13.3	>0.05 >0.05
Female, n (%): mean age	19 (31) 73.0±11.5*	50 (32) 69.5±14.4*	>0.05 >0.05
Age gradient, n (%): – <45 years old – 45–59 years old – 60–74 years old – 75–90 years old – >90 years old	3 (5) 25 (41) 22 (36) 10 (16) 1 (2)	22 (14) 69 (44) 37 (23) 27 (17) 3 (2)	0.06 >0.05 >0.05 >0.05 >0.05
Medical history, n (%): – History of MI – History of CVA – Hypertension – Type 2 DM – Smoking	13 (21) 3 (5) 46 (75) 8 (13) 34 (56)	37 (23) 11 (7) 83 (53) 19 (12) 63 (40)	>0.05 >0.05 0.002 >0.05 0.03
Atypical clinical picture, n (%)	11 (18)	93 (59)	<0.001
Time from the onset of the pain syndrome to health care encounter, min (Me [Q1; Q3])	87 (40; 185)	25 (9; 72.5)	0.03
Change of general state before MI, n (%)	37 (61)	43 (27)	<0.001
Including, n (%): – New-onset exertional angina – Changes in the nature of existing angina – Onset of resting angina – Onset / worsening of shortness of breath – Weakness	18 (49) 17 (46) 5 (14) 3 (8) 1 (3)	11 (26) 16 (38) 7 (17) 9 (21) 5 (12)	0.04 >0.05 >0.05 0.05 0.05
Therapy at the moment o MI, n (%): – Beta-blockers – Antiplatelets – Statins – ACE inhibitors	57 (93) 59 (97) 51 (84) 55 (90)	21 (13) 21 (13) 8 (5) 13 (8)	<0.001 <0.001 <0.001 <0.001
Management, n (%) – Thrombolytic therapy – coronary angiography – PCI	21 (34) 39 (64) 25 (41)	5 (3) 3 (2) 0	<0.001 <0.001 <0.001

* p, the significance of intragroup differences versus male patients <0.001, Me (Q1; Q3),
the median and interquartile range. MI, myocardial infarction; CVA, cerebrovascular accident;
DM, type 2 diabetes mellitus; ACE, angiotensin-converting enzyme; PCI, percutaneous coronary intervention.

of consciousness (6 and 31%; p<0.001). Moreover, acute MI debuted in 20 patients of Group 2 (13%) and 5 patients of Group 1 (8.4%) with the development of sudden arrest of circulation before reaching the hospital.

The clinical picture of MI was atypical and symptomatic in every tenth case in the group of survivors, as well as in half of the patients who died of acute MI despite resuscitation (p<0.001). The median time from the first symptoms of coronary failure to calling an ambulance in Group 1 was 87 (40; 185) minutes, which was significantly more than in Group 2–25 (9; 72.5) minutes (p=0.03). The time from seeking medical care to the first medical contact with the patient did not differ in Groups 1 and 2 (18 (10; 28) and 16 (10; 25) minutes, respectively; p=0.2).

Patients in both groups had episodes of changing or worsening of general condition prior to the vascular accident. More than half of the patients in Group 1 and every third patient in Group 2 reported poor health 3–4 days prior to the index event of MI (p<0.001). The main clinical manifestations of the altered general state were first-onset angina in 49 and 26% of patients in Groups 1 and 2, respectively (p=0.04); progressive increases in the functional class of angina and the onset of resting angina, which were reported equally often in both groups, as well as the onset/worsening of shortness of breath and weakness prevailing in Group 2 (Table 1). Thus, if there was a change in the patient's general state before the onset of acute MI, the clinical symptoms in every third deceased patient were non-specific and could be a manifestation of a developing hemodynamic instability.

Concerning this, ST elevation on the electro-cardiogram was registered in 55% of patients in Group 1 and 60% in Group 2 (of the cases in which the electrocardiographic examination was performed, p=0.3). Moreover, if possible, markers of myocardial damage (troponin I, creatine phosphokinase myocardial band) were determined. These appeared to be elevated in all subjects, forming one of the main criteria for the diagnosis of acute IM in RAMI.

According to our findings, 95% of patients who had survived prior to reaching the hospital were admitted to specialized medical facilities providing high-tech medical care or to the cardiology departments of city hospitals. However, 4 cases of hospitalization to other facilities and departments (gastroenterology department, stroke center, etc.) were registered in Group 2. The volume and depth of myocardial damage did not differ significantly. A similar number of patients in both groups had transmural damage involving all or some ventricular walls. The complicated course of MI was observed equally as often in both groups. However, the nature of complications varied. There were more severe and life-threatening conditions in Group 2 i.e. cardiogenic shock (63 and 32%, p<0.001) and left ventricular wall rupture (9 and 1%, p=0.04). The rate of Killip class I–III acute left ventricular failure did not differ significantly between the study groups (33 and 32%, p=0.8).

The analysis of the nature and intensity of the drug therapy preceding MI found that the survivors had been administered essential drugs more often than the deceased patients (p<0.001, such drugs comprising beta-blockers, antiplatelets, statins and anticoagulants (Table 1). The volume of interventions was significantly higher in Group 1. Intravascular revascularization was performed only in Group 1 (64% of those who underwent coronary angiography). These differences in the treatment strategy can be partly explained by the death of patients in Group 2 in some cases prior to the provision of high-tech medical care.

Discussion

The significant increased in the number of vascular centers in the Russian Federation in recent years (by 88.6% from 2012 to 2015) has led to the introduction of modern technologies for the diagnosis and treatment of CAD across much of the country, providing the population with affordable high-tech medical care. However, the main challenge in acute forms of CAD consist in the fact that patients, in most cases, live far away from health facilities, significantly reducing their chances of survival. For this reason, the priority is to actively identify high-risk patients, ensure the prevention of cardiovascular pathologies and apply preventive care principles in each particular situation. Epidemiological studies and clinical observations show that patients with fatal acute coronary insufficiency requiring resuscitation often have prodromal symptoms preceding the event. Prospective observations carried out in Scotland showed that 46% of patients reported changes in their general state and the onset of specific or nonspecific symptoms before the onset of acute MI [6]. The rate of prodromal events reported in our study varied from 27 to 61% and was lower in the group of patients with adverse outcomes.

Previous studies suggest that the patient's age does not determine the success of resuscitation [4]. Our findings are consistent with this data, demonstrating an absence of age-related differences between the groups. The investigation into the use of drug therapy for hypertension and/or exertional angina before the onset of MI in the compared groups revealed that a similar number of patients received antihypertensive and/or anti-ischemic treatment. However, the qualitative composition of the therapy in terms of the predominant classes of drugs used was significantly different in the compared groups. This data is confirmed by the studies carried out previously. According to some authors, the established cardioprotective action of beta-blockers is implemented through their ability to raise the threshold of VF [7–9]. According to the literature, a decrease in the rate of sudden cardiac death due to the use of angiotensin-converting enzyme (ACE) inhibitors varies from 30 to 50% [10, 11]. Previous studies have demonstrated the positive effect of antihypertensive drugs on cardiovascular mortality in patients with CAD, even if they are administered with normal blood

pressure [11]. Given this data, a decrease in the rate of sudden death has been observed over the past 30 years, even before the widespread use of implantable defibrillators, which emphasizes the relevance of evidence-based therapy, including reperfusion interventions and preventive measures [4]. Moreover, our work showed that the success of resuscitation procedures correlates the clinical picture of the disease. For example, the number of fatal outcomes was higher in the atypical course of acute MI despite resuscitation (p<0.001).

Study limitations

The study was based on population Register data, which allowed us to form representative groups of patients according to the study objective. However, due to the uniform nature of the criteria analyzed in the initial registration card of the Register, we were not able to use the individual characteristics of each patient (doses, degree of BP control, etc.). That would have required additional studies, which was not possible in that framework (most patients died of MI).

Moreover, we were not able to establish a Killip class of acute heart failure in all cases. According to the study design, the cause of the sudden arrest of circulation was the development of acute MI. A more detailed description of the causes (arrhythmic, non-arrhythmic) and the clarification of immediate manifestations of acute coronary insufficiency, which required

cardiopulmonary resuscitation in each individual case, is not possible in the framework of the population register, comprising an additional limitation to this study.

Conclusion

The analyzed groups of patients with MI and differing efficacies of resuscitation procedures were represented at baseline by severe clinical cases, as confirmed by the high rate of complicated MI and transmural damage of the myocardium in both groups.

At the same time, patients who survived following resuscitation more often had a history of adequate medical therapy of CAD and hypertension, including the use of beta-blockers, ACE inhibitors, antiplatelets and statins. Unlike the group of deceased patients, MI was primarily characterized in this group by a typical clinical picture in the form of a prolonged attack of angina and changes in the course of CAD preceding MI, such as the first-time exertional angina or changes in the nature of existing angina.

The long-term prognosis for patients who survived after successful resuscitation remains a significant issue requiring additional attention.

No conflict of interest is reported.

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