Retrospective analysis of outcomes in patients with myocardial infarction in late admission to PCI center

Vorontsova S. A.[1,2], Pavlova T. V.[1,2], Avramenko A. A.[1,2], Khokhlunov S. M.[1,2]

Aim. This study aims to determine the impact of invasive treatment strategy on long-term outcomes in patients with ST-segment elevation myocardial infarction (STEMI) in late admission to PCI center (12-48 hours from the symptom onset) in comparison with conservative management.

Material and methods. The study population included 154 people with STEMI, admitted to V. P. Polyakov Samara Regional Clinical Cardiology Dispensary during 12-48 hours after onset of myocardial ischemia symptoms, for the period of inclusion (2013-2017). The mean age of the patients was 57,2±9,2 years old. The study evaluated two time periods: intrahospital and long-term (during 4 years from the index hospitalization). The primary end-point: cardiovascular death. The secondary combined end-point included: myocardial infarction recurrence, life-threatening rhythm disturbances, acute bleeding, heart failure NYHA III-IV functional class. The patients were divided into two groups depending on initially chosen management strategy: invasive (I) (n=113; 73,4%) or conservative (II) treatment (n=41; 26,6%).

Results. Comparing frequency of occurrence of cardiovascular death depending on chosen treatment tactics, we found that the probability of lethal outcome from cardiovascular causes in conservatively treated patients increased by 20,64 times (95% confidence interval (CI): 1,04-408,61), p=0,018 during intrahospital period of the study. The analysis performed using the Kaplan-Meier method showed the medians of the time of lethal outcome occurrence: in conservative group — 76,5 months (95% CI: 67,6-85 months), in invasive group — 92,1 months (95% CI: 88,9-95,3 months), p=0,014.

Conclusion. This study presented the results of our own retrospective study which confirms that revascularization in late-presenting patients with STEMI (12-48 hours from the symptom onset) results in improving the outcomes in both intrahospital and long-term periods.

Keywords: acute myocardial infarction, ST-segment elevation acute coronary syndrome, percutaneous coronary intervention, revascularization.

[1]Samara State Medical University of the Ministry of Health of the Russian Federation, Samara; [2]V. P. Polyakov Samara Regional Clinical Cardiology Dispensary, Samara, Russia.

Vorontsova S. A.* ORCID: 0000-0003-2080-7613, Pavlova T. V. ORCID: 0000-0003-3301-1577, Avramenko A. A. ORCID: 0000-0002-6284-8387, Khokhlunov S. M. ORCID: 0000-0001-6000-6200.

*Corresponding author:
leushkina.sonia@yandex.ru

Key messages

- The relevance of the present study is caused by the absence of complete clarity regarding the management tactics of patients with ST-segment elevation myocardial, admitted between 12 and 48 hours after onset of myocardial ischemia symptoms.
- To date, there has been little research on this issue, and the obtained results are contradictory.

Restoration of blood flow through infarct-related artery (IRA) in early stages of ST-elevation myocardial infarction (STEMI) is the basis for treatment of patients of this profile. That is why the vast majority of the patients immediately after verification of STEMI diagnosis (regardless of age and gender) should be considered as the candidates for reperfusion therapy. Currently, this type of treatment involves the use of two strategies: primary percutaneous coronary intervention (PCI) and pharmacoinvasive approach [1].

There are the clear indications for the performance of primary PCI and thrombolysis in patients admitted within 12 hours from the onset of ischemia symptoms. So, in clinical recommendations of the Ministry of Health of Russian Federation (MH RF) "Acute ST-elevation myocardial infarction", the level of reliability of evidences (LRE) and the level of persuasiveness of recommendations (LPR) reach the highest values — LRE A and LPR 1 [1]. In similar document of European Society of Cardiology (ESC), the class of recommendations and the level of reliability for this treatment tactics also correspond to the maximum — IA [2]. Besides, primary PCI is indicated to patients with STEMI, having the duration of the symptoms >12 hours and the signs of ongoing ischemia, the clinical picture of heart failure (HF), and the signs of shock or life-threatening rhythm disturbances (Ministry of Health of Russian Federation — LRE A; LPR 2; ESC — IA) [1, 2].

Currently there is no common opinion on the benefits of PCI performed in patients with STEMI beyond 12 hours from the onset of symptoms in the absence of the evidences of ongoing ischemia (Ministry of Health of Russian Federation — LRE A, LPR 2; ESC — IIA) [1, 2]. However, a certain number of patients with STEMI seek medical help quite late — for example, in countries with economies in transition and developing countries the number of such patients reaches 20% [3]. Accordingly, this influence the choice of the management strategy, and is directly related with the absence of reperfusion in patients [4].

By now, the register data have been published, proving that delayed revascularization (>12 hours from the onset of symptoms) performed in patients with STEMI, leads to improvement of their survival both in hospital and long-term periods [5-7].

Kim C and Braunwald E [8] proposed a hypothesis of "open artery", according to which even quite late blood flow restoration through IRA contributes to the reduction of severity of post-infarctional myocardial remodeling. On our opinion, it is this hypothesis that may explain the improvement of the life prognosis in patients who underwent PCI.

Taking into account the contradictory data on expediency of surgical reperfusion in patients with STEMI, who admitted during 12-48 hours after the onset of myocardial ischemia symptoms, we conducted a retrospective analysis of the outcomes in patients of this profile using the materials of Samara regional register of acute coronary syndrome. The analysis included patients admitted to V. P. Polyakov Samara Regional Clinical Cardiology Dispensary (SRCCD) in the period from 2013 to 2017. We assessed short-term and long-term (during 4 years) outcomes in patients of this profile depending on the management tactics.

The aim of the study: to determine the influence of invasive treatment strategy on immediate and long-term outcomes in patients with STEMI in late admission to PCI center (12-48 hours from the onset of symptoms), in comparison with conservative treatment tactics.

Material and methods

During 2013-2017 6368 patients with MI were admitted to V. P. Polyakov SRCCD, 4333 of them had STEMI. We selected the patients admitted within 12-48 hours after the onset of myocardial ischemia symptoms, the total number was 746 people. Then we assessed these patients according to the presence of the exclusion criteria such as: 1) the presence of indications to primary PCI performance (hemodynamic instability, life-threatening arrhythmias, signs of ongoing ischemia); 2) impossibility of PCI performance; 3) administration of a thrombolytic drug; 4) age ⩾75 years old; 5) taking of oral anticoagulants; 6) severe concomitant pathology (moderate and severe anemia (hemoglobin <90 g/l), malignant neoplasms, severe thrombocytopenia ($<75\times10^9$/l) or severe blood clotting disorders in the anamnesis, renal failure with glomerular filtration rate <30 ml/min/1,73 m^2 (CKD-EPI), aortic dissection). The criterion of exclusion from the analysis was also the use of ticagrelor or prasugrel as a component of double antiplatelet therapy for leveling of additional benefits for the outcomes obtained in patients who took these P2Y$_{12}$ blockers in the randomized controlled trials PLATO and TRITON-TIMI38 [9, 10].

Finally, the study population reached 154 people, that was 2,4% of the total number of patients with STEMI admitted to V. P. Polyakov SRCCD for the inclusion period (2013-2017). Of them men — 114 (74%), women — 40 (26%). The average age of the patients was 57,2±9,2 years old. The diagnosis of STEMI was made on the basis of the recommendations valid at the moment of admission to the hospital. All patients included into the study received optimal drug therapy (ODT) [11, 12]. At hospitalization,
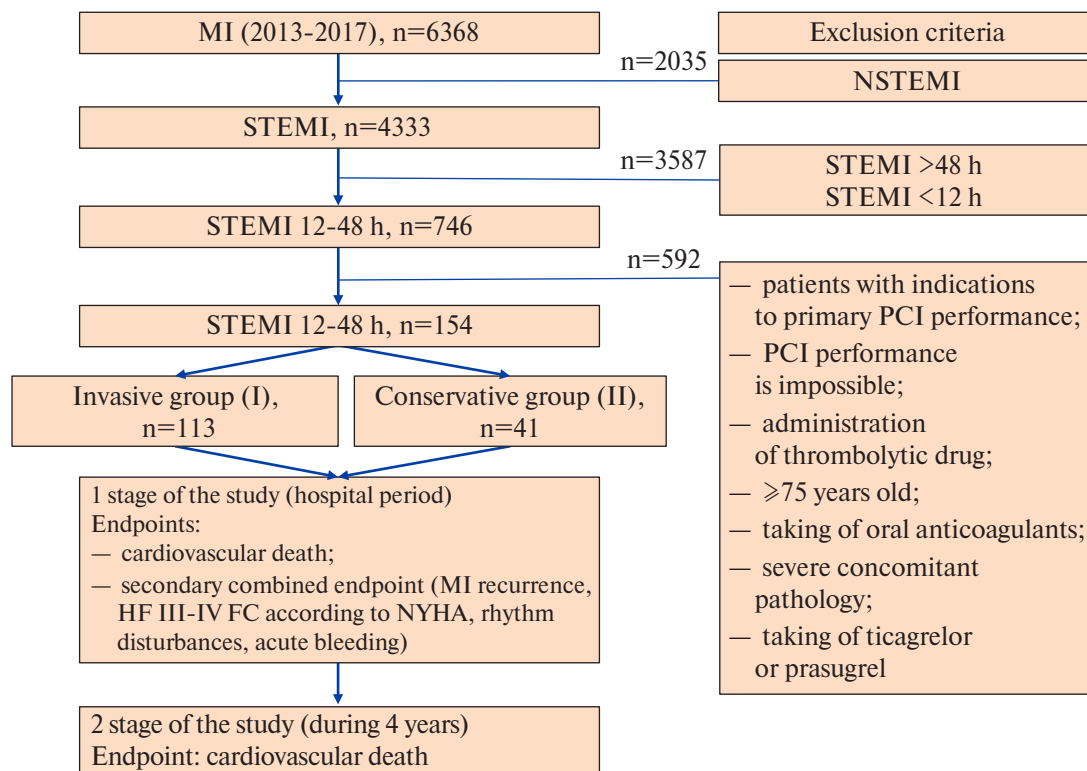
Figure 1. Study design.
Abbreviations: MI — myocardial infarction, NSTEMI — non-ST-elevation myocardial infarction, STEMI — ST-elevation myocardial infarction, HF — heart failure, FC — functional class, PCI — percutaneous coronary intervention.

the patients signed a standard form of informed voluntary consent to medical intervention and processing of personal data. The conduction of this study was approved by Local Ethics Committee.

Depending on the chosen management tactics, the patients were divided into two groups: invasive (I) or conservative (II) treatment. The group I patients underwent coronary angiography with revascularization of IRA (n=113; 73,4%), in addition to ODT. The group II received ODT only, and did not undergo PCI (n=41; 26,6%). We tried to analyze the reasons due to which the patients were managed conservatively. 8,1% of the patients signed the refusal of coronary angiography, 32,4% of this group were recommended to undergo planned coronary angiography, and 40,5% — to undergo load testing in 3-6 months followed by cardiologist consultation to determine the further management tactics. In 19% of the cases we could not find an obvious reason of choosing conservative management tactics. On our opinion, PCI was not performed exactly because of the time factor, i.e. late admission of patients.

The study design is presented in the Figure 1. The data given in the Table 1 show that the groups of conservative or invasive treatment were comparable for the basic statistical parameters.

The study estimated two time periods: hospital and long-term (during 4 years from the index hospitalization). Following the hospital period results, we accepted cardiovascular death as the primary endpoint; the secondary combined endpoint included: MI recurrence, life-threatening rhythm disturbances, acute bleeding developed during the index hospitalization period, and heart failure III-IV functional class according to NYHA at discharge. Following the long-term observation results, we accepted cardiovascular death as the primary endpoint. Taking into account the retrospective design of the present study, it was not possible to reliably establish the frequency of the occurrence of the secondary endpoints that is why they were excluded from this stage of the analysis.

The study materials were subjected to statistical processing using the parametric and nonparametric methods. Accumulation, correction and systematization of the initial information were carried out in spreadsheets Microsoft Office Excel 2019. Statistical analysis was performed using the program IBM SPSS Statistics v.26 (the software developer — IBM Corporation) and program MedCalc (the software developer — MedCalcSoftware Ltd).

The quantitative indicators were evaluated for compliance with the normal distribution using the

Table 1

Characteristics of groups at the moment of admission to hospital

Characteristics	Invasive tactics, Me [Q1; Q3] or n (%)	Conservative tactics, Me [Q1; Q3] or n (%)	p
Total number of patients	113	41	–
Male	88 (77,9)	26 (63,4)	0,071
Female	25 (22,1)	15 (36,6)	0,071
Age	56 [50; 64]	61 [51; 65,5]	0,150
MI in anamnesis	12 (10,6)	3 (7,3)	0,760
Anterior MI	56 (49,6)	16 (39,0)	0,247
Inferior MI	50 (44,2)	17 (41,5)	0,758
Another MI localization	4 (3,5)	4 (9,8)	0,210
Hypertensive disease	98 (86,7)	37 (90,2)	0,557
Obesity	29 (25,7)	10 (24,4)	0,872
Diabetes	15 (13,3)	11 (26,8)	0,055
Hyperlipidemia (total cholesterol >5 mmol/l)	83 (73,5)	27 (65,9)	0,356
Tobacco smoking	43 (38,1)	11 (26,8)	0,197
Diabetes mellitus	16 (14,1)	11 (26,8)	0,068
Acute cerebral circulatory disorder in the anamnesis	6 (5,3)	6 (14,6)	0,084
Chronic obstructive pulmonary disease in the anamnesis	7 (6,2)	3 (7,3)	0,726
Gastrointestinal diseases	4 (3,5)	1 (2,4)	0,724

Abbreviations: MI — myocardial infarction, Me — median, Q1; Q3 — lower and upper quartiles.

Kolmogorov-Smirnov criterion, as well as the indices of asymmetry and kurtosis. The sets of qualitative indicators, the distribution of which differed from normal, were described using the values of the median (Me), as well as the lower and upper quartiles [Q1-Q3]. Nominal data were described indicating the absolute values and percentages.

To compare the independent sets in the cases of the absence of normal data distribution signs, the Mann-Whitney U-test was used.

The comparison of the nominal data was performed using the Pearson χ^2 criterion. In the case of the analysis of four-field tables with the expected phenomenon in at least one cell less than 10, we calculated the criterion χ^2 with the Yates correction.

As a quantitative measure of the effect, when comparing relative indicators, the odds ratio indicator (OR) was used, defined as the ratio of the likelihood of an event occurrence in the group exposed to the factor to the likelihood of an event occurrence in the control group. With the purpose to project the obtained OR values onto the general set, we calculated the limits of the 95% confidence interval (CI). If zero values caused calculation problems, 0,5 was added to all cells. Based on the obtained data, the significance of the relationship between the outcome and the factor was considered proven if the CI was found outside the no-effect limit, taken as 1.

The survival function of patients was estimated using the Kaplan-Meier method, and the significance of the differences in survival between the groups — using the long-rank criterion of Mantel-Cox.

Results

When comparing the frequency of cardiovascular death occurrence depending on the chosen treatment tactics, it was established that the likelihood of lethal outcome from cardiovascular causes in the conservative group patients increased by 20,64 times (95% CI: 1,04-408,61), p=0,018 during hospital period of the study.

In addition, in the selected groups the frequency of the secondary combined endpoint during hospital period was analyzed. This indicator was statistically significantly higher in the conservative treatment group — 10 (24,4%) compared to group I of invasive treatment — 9 (7,96%) (OR 3,73; 95% CI: 1,39-9,99), p=0,006. The data obtained in the comparison of the frequency of different outcome occurrence during the index hospitalization, are shown in Table 2. During the study, we revealed that the patients in ODT group we more often prescribed additional medications (nitrate and diuretics) — 18 (43,9%) and 27 (23,9%), respectively (OR 2,49; 95% CI: 1,17-5,29), p=0,018, and this indirectly points to

Table 2

Hospital outcomes depending on chosen management tactics

Indicator	Invasive group, n (%)	Conservative group, n (%)	OR (95% CI)	p
Death during index hospitalization	0 (0)	3 (7,3)	20,64 (1,04-408,61)	0,018
Secondary combined point	9 (7,96)	10 (24,4)	3,73 (1,39-9,99)	0,006
CHF 3-4 according to NYHA	8 (7,1)	7 (17,1)	–	0,119
MI recurrence	0 (0)	2 (4,9)	–	0,070
Rhythm disturbance	0 (0)	1 (2,4)	–	0,266
Bleeding	1 (0,9)	0 (0)	–	1,000
Prescription of nitrates and diuretics at discharge	27 (23,9)	18 (43,9)	2,49 (1,17-5,29)	0,018

Abbreviations: CI — confidence interval, MI — myocardial infarction, OR — odds ratio, CHF — chronic heart failure.

Number of patients under observation

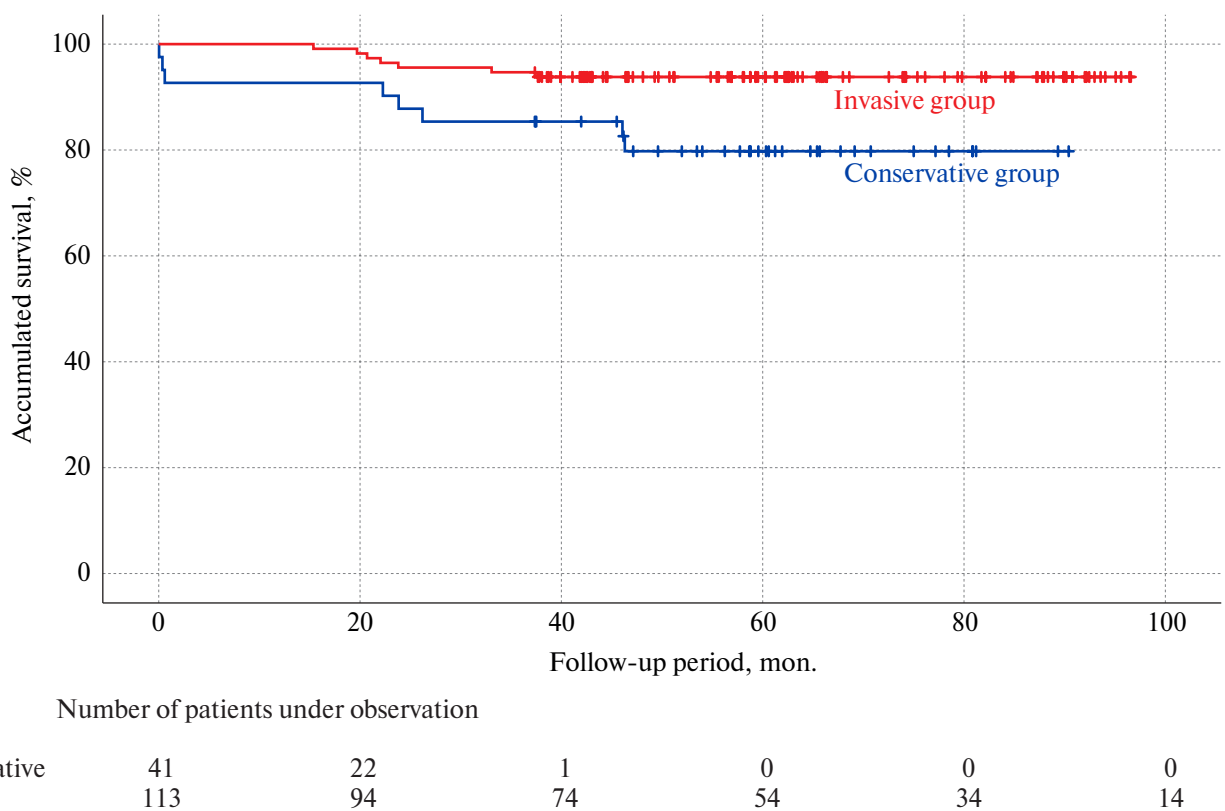|						
Conservative	41	22	1	0	0	0
Invasive	113	94	74	54	34	14

Figure 2. Chart of survival function of patients in conservative and invasive groups during 4 years.

the development of angina pectoris and HF in the patients of this group.

The Kaplan-Maier analysis showed that the medians of time of death occurrence were: in conservative group — 76,5 months (95% CI: 67,6-85 mon.), in invasive group — 92,1 mon. (95% CI: 88,9-95,3 mon.), p=0,014 (Figure 2).

Discussion

The relevance of this study is caused by the absence of complete clarity regarding the mana-gement tactics of patients with STEMI, admitted within the period of 12-48 hours after the onset of myocardial ischemia symptoms. It is known that patients of this profile have an adverse prognosis of life compared to patients admitted in more early time from the onset of myocardial infarction symptoms [13].

To date, there has been little research on this issue, and the obtained results are contradictory. For example, in the BRAVE-2 research (2005) the authors came to conclusion that the late PCI (12-

48 hours from the onset of ischemia symptoms) increase the volume of viable myocardium, improve the long-term outcomes decreasing frequency of cardiovascular complications and lethal cases. In the first research stage the primary endpoint was the final size of MI, measured using single-photon emission computed tomography with 99m technetium in 5-10 days after randomization. The results showed that the size of MI was reliably smaller in the surgical group patients compared to the ODT group — 8,0% (2,0-15,8) and 12% (3,2-25,0) of the left ventricular size; p=0,004. The index of myocardial viability was 0,44 (0,13-0,8) in the invasive group and 0,23 in the conservative group (0,0-0,5); p<0,001. In the long-term period of the BRAVE-2 research (during 4 years), the frequency of death from cardiovascular causes was estimated. In the invasive group, 20 patients died (11,1%; 95% CI: 7,3-16,7), and in the ODT group — 34 patients died (18,9%; 95% CI: 13,9-25,4) (adjusted risk ratio (RR) 0,55; 95% CI: 0,31-0,97); p=0,04 [5, 14].

The effect of reperfusion on the survival rate within 12 months in patients with STEMI, admitted during 12-24 hours from the onset of myocardial ischemia symptoms, was studied in Polish register of acute coronary syndromes in the period from June 2005 to August 2006. Total number of patients included into the analysis was 2036. The study results showed that mortality among patients with invasive treatment tactics in 12 months was lower than in patients with conservative strategy (9,3% vs 17,9%, p<0,0001) [15].

The meta-analysis performed by Hai-TaoYang, et al. (2019) investigated the results of 18 studies which were both randomized controlled and observational and cohort trials according to design. All the studies assessed the outcomes in patients with MI depending on the management tactics — only ODT or its combination with late reperfusion (>12 h). The results showed that late revascularization was associated with the decrease of mortality rate from all causes (RR 0,60; 95% CI: 0,44-0,83), p=0,002; main cardiovascular outcomes (RR 0,67; 95% CI: 0,50-0,89), p<0,001 and HF (RR 0,76; 95% CI: 0,60-0,97), p=0,03, compared to the ODT group. Besides, in the invasive treatment group, the frequency of MI recurrences tended to decrease (RR 0,70; 95% CI: 0,47-1,05), p=0,08. But late PCI significantly improved the prognoses, when performed in 12-48 hours, while revascularization performed between 2 and 60 days after the onset of ischemia symptoms, had no a positive effect [16]. The limitation of this meta-analysis was the inclusion of patients with non-ST elevation MI that might influence the final outcomes because such patients have initially more favorable prognosis compared to patients with STEMI [17].

In retrospective analysis conducted by Russian authors, they came to the results that PCI performed to patients with STEMI, admitted later than 12 hours from the onset of symptoms, may improve the long-time prognosis. This study analyzed the data of 178 patients admitted with STEMI later than 12 hours from the onset of angina attack, in period 2008-2009. The average time from the onset of symptoms was 96,6 hours. 83 patients underwent PCI with coronary stenting, — these patients were included into the invasive treatment group. 95 patients received conservative therapy only. According to the results of coronary angiography, 51 patients had initial IRA occlusion. During 3-year follow-up period, the mortality rate was 13,2% in the surgical treatment group and 35% — in the conservative therapy group (RR 0,23; 95% CI: 0,10-0,53), p=0,0004. And the survival rate was reliably higher in revascularized patients both with occluded and stenosed IRA compared to the conservative treatment group [18].

The importance of the time factor in performance of even late PCI was also confirmed in the OAT research (2006) which found no benefits regarding the outcomes in the invasive group in PCI performance during 3-28 days after the onset of myocardial ischemia symptoms. The primary endpoint of the research — death, MI, hospitalization with HF IV NYHA class, collectively. For 4 years the frequency of the primary endpoint has been 17,2% in the PCI group vs 15,6% in the OMT group (RR 1,16; 95% CI: 0,92-1,45), p=0,2 [19].

In 2022, the data of the retrospective register were published, that showed ambiguous results. The authors analyzed the medical histories of 274 patients with STEMI, admitted to hospital in ⩾12-48 hours after the onset of myocardial ischemia symptoms without the signs of ongoing ischemia, in period from October 2010 to December 2019. The proportion of men was 67,5%, the average age of the patients was 68±13 year old. The patients were divided into two groups depending on the management tactics (primary PCI or conservative approach). Statistical processing of the obtained data revealed the tendency to the decrease in the frequency of the occurrence of severe clinical outcomes such as recurrent MI (0 vs 0,4%, p=1,0), mechanical complications (0 vs 2,2%; p=1,0), stable ventricular tachycardia (0 vs 0,9%, p=1,0) and hospital death (0 vs 4,4%, p=0,37) in the primary PCI group, in contrast to the patients with conservative management. However, none of the differences reached statistical significance [20].

In our study we came to conclusion that the surgical strategy improves the survival rate in patients

with STEMI, admitted in 12-48 hours from the onset of ischemia symptoms. These results are consistent with the conclusions of a number of studies described above [5, 14-16, 18], along with that for the first time in our work it was shown that in the conservative management group, patients more often needed the prescription of drugs such as nitrates and diuretics. The additional therapy was required because of the persistence of the morphological substrate — atherosclerotic plaque in the coronary artery as well as HF progression.

Pathophysiological basis of the expediency of the intervention within 12-48 hours can be the fact that in 12 hours from the onset of myocardial ischemia symptoms, the viable myocardium may be saved in the IRA bed. Accordingly, even late restoration of blood flow through IRA, beyond the standard time limit for saving the myocardium from necrosis, has a positive effect of "hibernating" cardiomyocytes [8]. Reperfusion performed in a late phase of MI, contributes to acceleration of the tissue repair process due to the increase in population of infiltrating cells which play significant role in the lysis of necrotized myocardium and in collagen synthesis. Myocardial revascularization in the zone of infarction contributes to proliferation of cardiomyocytes and protects from apoptosis [21]. Collateral circulation is one more factor that preserves coronary blood flow necessary to maintain myocardial viability after coronary artery occlusion. Due to this, in late mechanical reperfusion, the left ventricle has the possibility of functional recovery [22].

Our study shows that invasive tactics in patients with STEMI in late admission improves the hospital outcomes and also has a positive effect on the long-term prognosis of life. The monitoring of patients is continuing.

Limitations of the study. The limitations of the present study are the retrospective design and participation of patients from one medical center.

Conclusion

Thus, currently there is no common opinion about the time period during which PCI has a positive effect on the prognosis of patients with STEMI in their late admission to PCI center (>12 hours from the onset of the disease). The clinical studies and meta-analyses published to date have shown contradictory results regarding to the prognosis of patients with STEMI, who underwent late PCI. According to the results of our retrospective analysis, statistically significant increase of the survival rate in the invasive treatment group was revealed, both during hospital and long-term period. We also observed the tendency to the decrease in the frequency of MI complications during the index hospitalization. Besides, the conservative group patients were more often prescribed additional medications necessary for treatment and correction of HF and angina attacks, and this most likely indicates to the presence of a substrate for the development of these pathologies in patients who did not undergo PCI. To definitively determine the effect of delayed PCI on patient outcomes and determine the time period during which invasive treatment statistically significantly increases survival in patients of this profile, it is advisable to perform a clinical trial with a prospective design and randomization procedure at the moment of admission of patients to hospital.

Relationships and Activities: none.

References

1. Russian Society of Cardiology. 2020 Clinical practice guidelines for Acute ST-segment elevation myocardial infarction. Russian Journal of Cardiology. 2020;25(11):4103. (In Russ.) doi:10.15829/29/1560-4071-2020-4103.
2. ESC/EACTS Guidelines on myocardial revascularization (2018). J European Heart. 2019;40:87-165. doi:10.1093/eurheartj/ehy394.
3. Guan W, Venkatesh A, Bai X, et al. Time to hospital arrival among patients with acute myocardial infarction in China: a report from China PEACE prospective study. Eur Heart J Qual Care Clin Outcomes. 2019;5(1):63-71. doi:10.1093/ehjqcco/qcy022.
4. Cenko E, Ricci B, Kedev S, et al. Reperfusion therapy for ST-elevation acute myocardial infarction in Eastern Europe: the ISACS-TC registry. Eur Heart J Qual Care ClinOutcomes. 2016;2(1):45-51. doi:10.1093/ehjqcco/qcv025.
5. Ndrepepa G, Kastrati A, Mehilli J, et al. Mechanical reperfusion and long-term mortality in patients with acute myocardial infarction presenting 12 to 48 hours from onset of symptoms. JAMA. 2009;301(5):487-8. doi:10.1001/jama.2009.32.
6. Fan Y, Bai X, Chen Y, et al. Late percutaneous coronary intervention prevents left ventricular remodeling and improves clinical outcomes in patients with ST-elevation myocardial infarction. Clin. Cardiol. 2015;38(2):82-91. doi:10.1002/clc.22356.
7. Bouisset F, Gerbaud E, Bataille V, et al. Percutaneous myocardial revascularization in late-presenting patients with STEMI. J Am Coll Cardiol. 2021;78(13):1291-305. doi:10.1016/j.jacc.2021.07.039.
8. Kim C, Braunwald E. Potential benefits of late reperfusion of infarcted myocardium. Theopen-arteryhypothesis. Circulation. 2003;88(5):2426-36. doi:10.1161/01.cir.88.5.2426.
9. Wiviott S, Braunwald E, McCabe C, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2007;357:2001-15. doi:10.1056/NEJMoa0706482.
10. Wallentin L, Becker R, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2009;361:1045-57. doi:10.1056/NEJMoa0904327.
11. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (2012). J European Heart. 2012;33:2569-619. doi:10.1093/eurheartj/ehs215.
12. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology

(2017). J European Heart. 2018;39(2):119-77. doi:10.1093/eurheartj/ehx393.

13. Cerratoa E, Forno D, Ferro S, et al. Characteristics, in-hospital management and outcome of late acute ST-elevation myocardial infarction presenters. J Cardiovasc Med. 2017;18(8):567-71. doi:10.2459/JCM.0000000000000527.

14. Schömig A, Mehilli J, Antoniucci D, et al. Beyond 12 hours Reperfusion Alternative Evaluation (BRAVE-2) Trial Investigators. JAMA. 2005;293(23):2865-72. doi:10.1001/jama.293.23.2865.

15. Gierlotka M, Gasior M, Wilczek K, et al. Reperfusion by primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction within 12 to 24 hours of the onset of symptoms (from a prospective national observational study [PL-ACS]). Am. J. Cardiol. 2011;107(4):501-8. doi:10.1016/j.amjcard.2010.10.008.

16. Hai-TaoYang, Wen-JuanXiu, Ying-YingZheng, et al. Invasive reperfusion after 12 hours of the symptom onset remains beneficial in patients with ST-segment elevation myocardial infarction: Evidence from a meta-analysis of published data. Cardiology Journal. 2019;26(4):333-42. doi:10.5603/CJ.a2018.0034.

17. Stiermaier T, Eitel I, Waha S, et al. Myocardial salvage after primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction presenting early versus late after symptom onset. Int J Cardiovasc Imaging. 2017;33(10):1571-9. doi:10.1007/s10554-017-1143-x.

18. Konovalov E, Luk'yanova Yu, Skrypnik D, et al. Mechanical reperfusion and long-term survival in latecomers with ST-elevation myocardial infarction. Creative Cardiology. 2014;3:13-23. (In Russ.)

19. Hochman J, Lamas G, Buller C, et al. Occluded Artery Trial Investigators. Coronary intervention for persistent occlusion after myocardial infarction. NEngl. J Med. 2006;355(23):2395-407. doi:10.1056/NEJMoa066139.

20. Moura A, Castilho B, Saraiva M, et al. Outcome following late reperfusion with PCI in stable patients with ST-segment elevation myocardial infarction presenting more than 12 hours from onset of symptoms. Eur Heart J Acute Cardiovascular Care. 2022;11(1). doi:10.1093/ehjacc/zuac041.032.

21. Abbate A, Bussani R, Biondi-Zoccai G, et al. Persistent infarct-related artery occlusion is associated with an increased myocardial apoptosis at postmortem examination in humans late after an acute myocardial infarction. Circulation. 2002;106(9):1051-4. doi:10.1161/01.cir.0000030936.97158.c4.

22. Sabia P, Powers E, Ragosta M, et al. An association between collateral blood flow and myocardial viability in patients with recent myocardial infarction. N. Engl. J. Med. 1992;327:1825-31. doi:10.1056/NEJM199212243272601.