PROBLEMS OF REVASCULARIZATION IN ACUTE MYOCARDIAL INFARCTION WITH ST SEGMENT ELEVATION

V.A. Ryabinin, P.Y. Lopotovsky, E.V. Migunova, A.P. Golikov, N.E. Kudryashova
N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Healthcare Department, Moscow, Russian Federation

SUMMARY	Based on the data of 370 patients with acute myocardial infarction with ST segment elevation, problems affecting the efficiency of revascularization treatment by PCI have been analyzed. It has been considered difficult to achieve further reduction in the timing of PCI compared to the available. The acceleration dynamics of ST segment on the electrocardiogram during PCI compared to thrombolysis and limitations of ECG monitoring during reperfusion in assessing myocardial perfusion have been specified. The necessity and appropriateness of PCI in different periods from the onset of MI have been reasoned. The prospects of using perfusion myocardial SPECT in assessing hypoperfusion and prognosis of restoration of myocardial function have been mentioned.
Keywords:	myocardial infarction, percutaneous coronary intervention, single photon emission computed tomography.

ECG – electrocardiogram

MI – myocardial infarction

PCI – percutaneous coronary intervention

RP – radiopharmaceutical

SPECT – single photon emission computed tomography

STEMI – myocardial infarction with ST segment elevation

TLT – thrombolytic therapy

INTRODUCTION

Restoration of blood circulation in the infarct-related artery is the main treatment for myocardial infarction with *ST* segment elevation (STEMI), affecting the prognosis of the disease. Percutaneous coronary intervention (PCI) is recognized to be the most effective procedure. The introduction of PCI in our country and its results differ from the overseas experience. For example, in Russia, 80% of patients do not undergo PCI, while in other developed countries – only 30%. One of the main reasons for this difference is the lack of angiographic laboratories. As a result, the combined pharmacoinvasive strategy is considered reasonable. When PCI cannot be performed, thrombolytic therapy (TLT) is a possible first stage of revascularization. Then, transfer to the patient department with PCI capability is provided.

However, pharmacoinvasive strategy has not led to significant reduction in mortality in Moscow hospitals. In 2013, it was 17.7% versus 4.7% in the European countries [1–3]. Unsatisfactory results of treatment were the basis of issuance of the order by the Department of Healthcare in Moscow "On the further improvement of medical care for patients with acute myocardial infarction with *ST* segment elevation" in 2013. The order designated the main objective – providing primary PCI to vast majority of patients with myocardial infarction (MI), and reduction of the procedure duration. The purpose of the study is to clarify the results of reperfusion therapy introduction in STEMI.

MATERIAL AND METHODS

The observations are based on the analysis of cardiology department databases in 2009–2013. There were 370 patients in the STEMI group. The diagnosis was based on clinical, electrocardiographic (ECG), enzymatic (cardiospecific myocardial fraction of creatine phosphokinase, troponin) data considering the results of echocardiographic examination. All the patients underwent coronary angiography and PCI of the infarct-related artery. ECG was performed before and after PCI and also 24 hours after the onset of MI and was analyzed by a fivefold magnification on the display of a computer. The degree of stenosis was assessed by Y.S. Petrosian and L.S. Zingerman grades [4]. The degree of the main coronary flow restoration was evaluated using *TIMI* classification [5]. In order to assess myocardial perfusion after intervention, single photon emission computed tomography (SPECT) with Technetril ^{99m}Tc was performed 2–3 days after the onset. The analysis of the violation degree of perfusion was performed with a 17-segmental model of the left ventricle using a scale (normal perfusion was designated as 0, a slight decrease in perfusion – 1, moderate – 2, significant – 3, no accumulation of a tracer – 4). For each degree of impaired perfusion, the percentage of the total area of the left ventricle was calculated [6].

RESULTS AND DISCUSSION

The purpose designated in the order of the Department of Healthcare, is going to be achieved by reducing the time gaps before PCI: "pain - calling the ambulance" – 30 minutes, "calling the ambulance - admission to the department with the possibility of PCI performance" – 90 minutes, "door - balloon" – less than 60 minutes.

Achieving the target terms in the near future is questionable. Thus, the interval "pain-calling the ambulance" may be reduced by health education in the media, conducted by the doctors and scientists. It has not been implemented yet.

It is doubtful whether further reduction of the interval "ambulance call – hospitalization" is possible because of existing traffic problems. Thus, the time of arrival of an ambulance team to a patient reduced in 2013 by 0.2 minutes in Moscow compared to 2012.

The influence of the interval "door-balloon" on the results of treatment can be assessed according to *CathPCI Registry*, in which reduced time of "door-balloon" gap by 16 minutes for 3 years has not been accompanied by reduction in mortality in patients with myocardial infarction and primary PCI [2].

Despite the location in the city center and close to the ambulance stations, average time between PCI and the onset of MI is 15 hours in the cardiology department of the Institute with 24h angiographic service. The proportion of patients with PCI performed within the first 6 hours after the onset of STEMI is 49%. Despite this, the mortality rate in patients with MI is 5.4%, which is close to the European level.

The most available method to monitor the clinical efficacy of PCI in *STEMI* is ECG and the rate of return of the *ST* segment to the isoline in particular. It was found that after the early PCI, the *ST* segment decreased 24 hours after the onset of the disease more intensively than in successful thrombolytic therapy (Fig. 1). Acceleration of the ST segment decrease has not been observed in the performance of PCI after 6 h. The results confirm the importance of both time and method of reperfusion.

Full main artery blood flow was not restored in all cases. The reason for this was PCI complications, such as intimal dissection, thrombosis in the stent, peripheral embolization, accompanied by myocardial ischemia, observed in 8% of cases. In addition to them, in 12% of cases, the blood flow in the infarct-related artery did not reach the degree of *TIMI* 3 due to technical difficulties. Furthermore, in 56% of cases with the bloodstream regarded as *TIMI* 3 in the early stages of the disease there was no acceleration of the *ST* segment decrease. Presumably, the reason for this was the violation of myocardial perfusion due to the depth of myocardial ischemia, dependant from the initial degree of arterial occlusion, condition of the collateral circulation zone, areas remote from ischemia as well as myocardial stunning during reperfusion. These conditions affecting the evolution of the ECG in STEMI were presented in earlier publications [7].

In this regard, it should be emphasized that the degree of deviation of the *ST* segment from the isoline does not reflect the amount of infarction. As we know, the basis of this phenomenon is uneven repolarization of the myocardium in its different areas and the presence of the electric field which vector is directed to the recording electrodes (Fig. 2a). In the subacute and scarring stages of myocardial infarction the area of ischemic damage can be transformed into scar tissue or viable myocardium. The proportion depends on the conditions listed above. As the unevenness of repolarization decreases, the *ST* segment approaches to the isoline (Fig. 2b).

Thus, acceleration of the *ST* segment return to the isoline is a result of acceleration of two processes –formation of necrosis and restoration of myocardial viability.

Defining the depth of ischemic myocardial injury is advisable for studying the prospects for restoration of myocardial function after PCI. For this, all patients underwent perfusion SPECT of the myocardium after the restoration of blood flow on days 2–3. In this study, the capture of the radiopharmaceutical (RP) (Technetril ^{99m}Tc) by cardiomyocytes is proportional to blood flow and depends on the depth of the ischemic cell damage. The results of the survey of 56 patients of similar age and degree of stenosis showed that after early PCI (no more than 6 h), 60% of patients (18 patients out of 30) had a significant violation of perfusion (grade 2–4) in the system of the infarct related artery, whereas after the late PCI violation of perfusion of the same grade was revealed in 46% of cases (12 patients out of 26), indicating a lack of reperfusion. The ratio of the degree of damage to the myocardium of the left ventricle and its area after early and late PCI is shown on Fig. 3.

At first glance, this fact seems to be paradoxical. However, temporary deepening of ischemic damage in conditions of oxidative stress during reperfusion accounts for the phenomenon. It is known from clinical observations that in deep myocardial ischemia reperfusion may be accompanied by rhythm disturbances, transient hypotension, angina, which is reflected in the concept of "reperfusion syndrome" [8]. These observations are confirmed by the data of morphological studies of the area of infarction when hemorrhagic changes are revealed after successful reperfusion. In the long-term period, this factor can accelerate regenerative processes [9]. In this regard, methods of drug myocardial protection have been proposed. Beta-blockers, antioxidants, antihypoxants, phosphocreatine were among them [10–12]. Their effect is based on reduced myocardial demand in oxygen, and damaging effects of free radicals on cell membranes.

In the current guidelines PCI after 24 hours is not considered to be appropriate to conduct due to the absence of the reduced mortality evidence. However, this does not preclude positive effect of reperfusion on the myocardial function in the long-term period. This assumption is confirmed by the comparative prospective study of D.G. Ioseliani [13], as well as the results of research carried out at the Institute, where reduction in the rate of deaths in the long-term period is observed in addition to surgical improvements [14].

The obtained results are the basis for the study of the reperfusion reasonability not only in the early, but in the long-term period from the onset of MI as well. This leaves a number of questions and the calculation of the minimum time of thrombolysis before PCI within pharmacoinvasive strategy in particular.

The trend of increase in number of patients with acute coronary syndromes who previously underwent coronary intervention has become noticeable recently. While the need for repeated PCI among patients admitted to the Institute was in 18% of cases in 2009, it was 27% in 2013. The corresponding figures for patients undergoing coronary artery bypass surgery is significantly lower – 1.7% and 6.1%, respectively, but the trend is the same.

Several possible reasons underline this. The first reason is an increase in the number of patients with ischemic heart disease undergoing PCI, second – the lack of effectiveness of methods of secondary prevention of atherosclerosis, third – the limitations of PCI.

CONCLUSION

The presented data suggest that, in addition to the importance of reducing the time of PCI in STEMI, interest in conducting PCI does not lower in a long-term period. According to findings given above, organizational difficulties of timing reduction, the diversity of processes occurring in the ischemic myocardium under reperfusion, and their influence on the reparative processes are the basis for the continuation of the long-term observations.

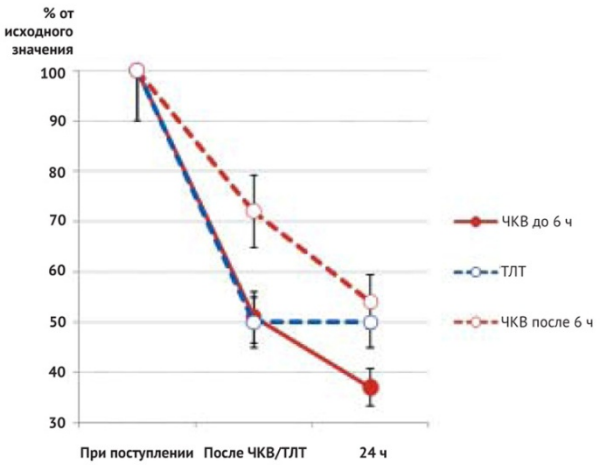

Fig. 1. Changes in the degree of *ST segment* elevation during PCI in various periods of time compared to TLT.
Notes: TLT – thrombolytic therapy; PCI – percutaneous coronary intervention

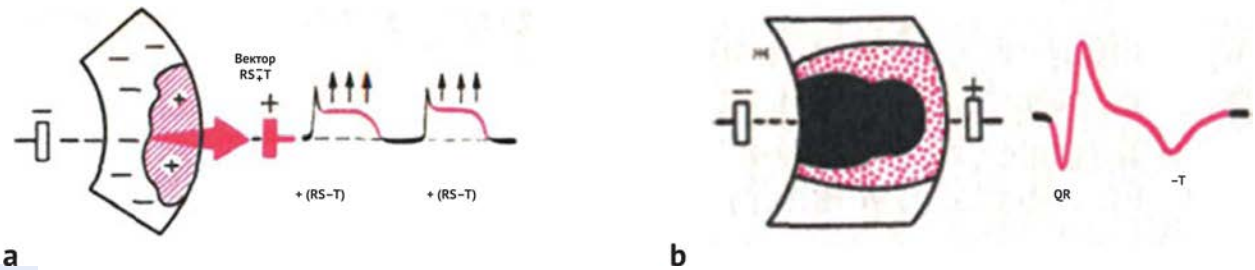

Fig. 2. The origin of the *ST segment* elevation on the electrocardiogram in myocardial infarction

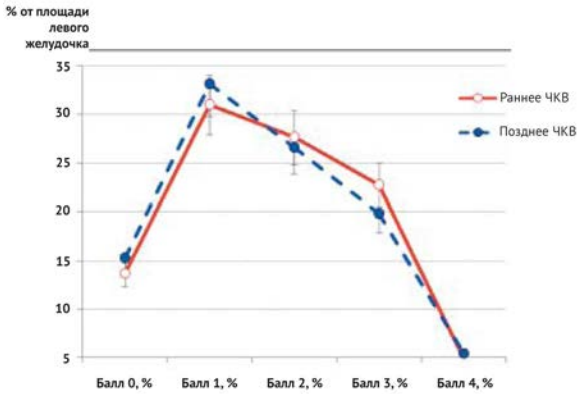

Fig. 3. The ratio extent / area of impaired perfusion of the left ventricle (in points) after PCI according to SPECT data.
Notes: SPECT – single photon emission computed tomography; PCI – percutaneous coronary intervention

REFERENCES

1. *Sbornik srednemoskovskikh osnovnykh pokazateley deyatel'nosti meditsinskikh organizatsiy Departamenta zdravookhraneniya goroda Moskvy za 2012-2013 gg*. [A collection of medium-Moscow main indicators of activity of medical institutions of the Department of Healthcare of Moscow in 2012-2013]. State institution of health, Bureau of medical statistics HD. Moscow, 2014. Ex. No. 99/1-14. 25.03.2014. (In Russian).
2. Menees D.S., Peterson E.D., Wang Y., et al. Door-to-balloon time and mortality among patients undergoing primary PCI. *N Engl J Med.* 2013; 369 (10): 901–909.
3. NCDR study shows D2B times for STEMI have improved, in-hospital mortality rates remain unchanged. *Additional Strategies Needed to Reduce In-hospital Mortality September 4, 2013.* Available at: http://www.cardiosource.org/
4. Petrosyan Yu.S., Zingerman L.S. *Koronarografiya* [Coronary Angiography]. Moscow: Meditsina Publ., 1974. 115–125. (In Russian).
5. TIMI-III B Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-ST elevation myocardial infarction. Results of the TIMI IIIB trial. Thrombolysis in Myocardial Ischemia. *Circulation*. 1994; 89 (4): 1545–1556.
6. Trufanov G.E., Dekan V.S., Romanov G.G., Ryzhkova D.V. *Perfuzionnaya stsintigrafiya miokarda* [Perfusion scintigraphy of the myocardium].Saint-Peterburg: ELBI-SPb. Publ., 2012. 69. (In Russian).
7. Golikov A.P., Ryabinin V.A., Lopotovsky P.Yu. et al. Otsenka elektrokardiograficheskikh priznakov reperfuzii miokarda u bol'nykh s ostrym infarktom miokarda s pod'emom segmenta ST [Evaluation of electrocardiographic signs of myocardial reperfusion in patients with acute myocardial infarction with ST segment elevation]. *Zhurnal im. N.V. Sklifosovskogo Neotlozhnaya meditsinskaya pomoshch'*. 2012; 1: 20–23. (In Russian).

8. Braunwald E., Kloner R.A. The stunned myocardium: prolonged postischemic ventricular dysfunction. *Circulation*. 1982; 66 (6): 1146–1149.
9. Galankina I.E. Morfologicheskiye osobennosti evolyutsii infarkta miokarda posle effektivnoy trombolitycheskoy terapii [The morphological features of the evolution of myocardial infarction after successful thrombolytic therapy]. *Arkhiv patologii*. 1988; 7: 63–70. (In Russian).
10. Polumiskov V.Yu. *Vliyaniye beta-adrenoblokatora propranolola i antioksidanta dibunola na formirovaniye ochaga nekroza u bol'nykh infarktom miokarda: avtoref. dis. … kand. med. nauk* [Effect of beta-blocker propranolol and antioxidant dibunolum on the formation of necrosis in patients with myocardial infarction. Abstract cand. med. sci. diss.]. Moscow, 1983. (In Russian).
11. Vaniyev S.B. *Gemodinamicheskiye effekty preparatov adrenoblokiruyushchego deystviya pri arterial'noy gipertenzii v ostrom periode infarkta miokarda: avtoref. dis. … kand. med. nauk* [Hemodynamic effects of drugs with adrenergic blocking activity in hypertension in acute phase of myocardial infarction. Abstract cand. med. sci. diss.]. Moscow, 1981. (In Russian).
12. Kryzhanovskiy S.A., Vititnova M.B., Ryabinin V.A. *Fosfokreatin (neoton) kak predstavitel'novogo klassa membranoprotektorov (Teoriya, eksperiment, klinika)* [Phosphocreatine (Neoton) as the representative of a new class of membranoprotectors (Theory, experiment, clinical picture)]. Voronezh: Istoki Publ., 2000. 230–237. (In Russian).
13. Ioseliani D.G., Rogan S.V., Semitko S.P., et al. Sravnitel'nye rezul'taty rannego (do 24 chasov) i otsrochennogo (do 21 dnya) stentirovaniya u patsientov s ostrym infarktom miokarda [The comparative results of early (within 24 hours) and delayed (up to 21 days) stenting in patients with acute myocardial infarction]. *Interventsionnaya kardiologiya*. 2005; 8: 25–29. (In Russian).
14. Khubutiya M.Sh., Gazaryan G.A., Zakharov I.V. *Reperfuzionnaya terapiya v ostrom periode infarkta miokarda* [Reperfusion therapy in acute phase of myocardial infarction]. Moscow: GEOTAR-MEDIA, 2010. 168 p. (In Russian).

Article received: 25 June, 2014

For correspondence:
Ryabinin Vladimir Aleksandrovich, Dr. Sc. Med.,
Leading Researcher of the Department of Emergency Clinical Cardiology
N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Healthcare Department, Moscow, Russian Federation
e-mail: ryabinin_va@mail.ru

Перевод: А.П. Богопольская