Original Article

CURRENT STATUS OF PREHOSPITAL SYSTEMIC THROMBOLYSIS PROBLEMS IN ST-ELEVATION MYOCARDIAL INFARCTION

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Abstract

This review article analyzes the results of modern, recent studies on the current status of pre-hospital thrombolysis, one of the treatment methods for STEMI, which is considered to be one of the serious forms of IHD. The article presents the pathogenesis of vascular occlusion in STEMI, mechanisms of action of thrombolytic drugs. At the same time, the results of pre-hospital TLT studies conducted around the world are presented. In conclusion, prehospital thrombolysis can be used as an alternative to primary PCI in STEMI if there are no contraindications.

Keywords: acute myocardial infarction, reperfusion, prehospital thrombolysis.

Introduction

Ischemic heart disease (IHD) remains the leading cause of death and disability worldwide and in Uzbekistan. ST-segment elevation acute myocardial infarction (STEMI) is a major cause of morbidity and mortality in patients with IHD. Despite early reperfusion with primary percutaneous coronary intervention (PCI), mortality (7% mortality per year) and disability (rehospitalization for heart failure 22% after 1 year) are significant. If STEMI is complicated by cardiogenic shock, the 1-year mortality rate is even higher, reaching 12% after 1 year. Thus, to reduce the size of myocardial infarction (MI), it is important to study effective methods of reperfusion, to optimize treatment methods. In order to preserve left ventricular (LV) systolic function, improve the efficiency of emergency medical services to prevent heart failure and improve the life of STEMI patients, minimizing the total ischemic time of reperfusion is the main factor in the formation of MI volume (1).

In order to improve the short- and long-term outcome of patients with STEMI, the timely diagnosis and recognition of symptoms of reperfusion syndrome in the management of patients with MI requiring emergency medical care require further study and implementation in the practice of emergency cardiology of the emergency medical system. Their implementation improved the quality and outcome of treatment in acute myocardial infarction (2).

Myocardial infarction develops when the surface of the atheromatous plaque in the coronary artery is damaged, which opens the subendothelial layer, platelet activation and aggregation factors are released, and a thrombus is formed on the destroyed plaque. When a thrombus bound by fibrin threads completely blocks an artery, the focus of myocardial necrosis grows rapidly. Myocardial infarction caused by complete occlusion of the coronary artery develops 15-30 minutes after severe ischemia, and if it lasts more than 30 minutes, irreversible damage to the myocardium occurs. In the case of infarct-related arterial occlusion, the rate of recovery of blood flow has been

shown to be the main factor determining the final size of the myocardial infarction and the development of complications. To a much lesser extent, these indicators affect the development of collateral blood flow. This determines the therapeutic tactics in case of complete occlusion of the coronary artery - to achieve early and stable reperfusion of the occlusive vessel, which saves the myocardium or reduces the spread of the necrosis zone and prevents the development of heart failure (4).

There are two methods of myocardial reperfusion - thrombolytic therapy (TLT) and angioplasty followed by coronary artery stenting. Today, these methods are not mutually exclusive and can complement each other. In French registries, they found that patients who underwent early thrombolysis in the prehospital phase had comparable outcomes to primary angioplasty and stenting.

Therefore, the decisive factor of reperfusion is not the method, but the time. The earlier the reperfusion therapy is started, the more effective the result can be. Angioplasty and stenting require significant technical equipment and professional training, this method is possible only in specialized centers. There are data that allow us to say if every 10 minutes primary percutaneous coronary intervention (PPCI) has an advantage over TLT under conditions of equal time. Delays in PCI reduce survival benefits by 1%. Thus, survival after late PPCI is comparable to survival after early TLT. A 1-hour reduction in initiation of TLT was associated with a 17% reduction in 30-day mortality. Pharmacological reperfusion - the use of thrombolytic drugs - is the simplest and fastest way to restore blood flow in myocardial infarction. The possibility of its use at the pre-hospital stage gives the method additional value. In the conditions of active development of invasive cardiology, pre-hospital thrombolysis (PHTLT) takes on a new color and is the first step towards complete myocardial reperfusion or limitation of the infarct zone. Coronary stenting should be performed within 3-24 hours after the start of PHTLT, according to the results of coronary angiography, if the blood flow is not completely restored in the hospital.(2,4).

With this approach, PHTLT can reduce the nonviable myocardial zone, prevent the development of life-threatening complications, and reduce mortality. A meta-analysis of 22 thrombolysis studies (Boersma et al., 1996), including 50,246 patients, showed a clear need for early treatment of myocardial infarction. The relative reduction in 35-day mortality was greatest (by 48%) with thrombolytic therapy 1 hour after symptom onset. Thrombolysis at hour 2 reduced mortality by 44%, and subsequent thrombus dissolution reduced mortality by only 20%. The number of lives per 1000 patients treated with TLT was 6580 in the first 30-60 minutes from the onset of symptoms, TLT saved 37 patients by the end of the 2nd hour and 26 patients by the end of the 3rd hour. According to the French National Registry of Acute Myocardial Infarction FAST-MI (p=1713), early PHTLT reduced 30-day mortality from myocardial infarction to 3.0%. In-hospital thrombolysis and PPCI mortality rates were 7.3 and 5.0%, respectively. 3-24 hours after PHTLT, PCI reduced mortality to a record 1.4% (3).

The advantage of this pharmacoinvasive approach is the long-term results: a significant difference in the reduction of the risk of death remains after 6 months and after 1 year of follow-up (USIC 2000 registry). The FAST-IM and USIC 2000 registries showed that early ambulance thrombolysis and in-patient PCI also reduced and in-hospital mortality was up to 3.0%, which was 1.5-2.5 times higher than in-hospital thrombolysis or PCI. Obviously, after initial early thrombolysis associated with angioplasty, stenting was performed in a group of patients with fewer complications and a smaller non-viable zone of the myocardium, and an interval of at least 3 hours between procedures would prevent hemorrhagic complications. (10).

The results of European studies show that the average delay time between pre-hospital and hospital reperfusion is about 1 hour. According to the VIENNA registry in Vienna, only 14.6% of patients receive PCI within the first 2 hours, and 50.5% of patients can receive prehospital systemic thrombolysis. In the French FAST-MI registry, the incidence of PCI within the first 2-3 hours after the onset of symptoms was 8-22%, hospital thrombolysis 24-47%, and pre-hospital thrombolysis 59-82%. A large American NRMI registry demonstrated the effect of a delay of only 40 min on mortality in different categories of patients. Delayed reperfusion and onset of symptoms less than 2 hours earlier in patients younger than 65 years of age with recurrent myocardial infarction increase the risk of death. Every 10-minute delay in PCI reduces survival by 1%, and every 60-minute delay in reperfusion increases the risk of death by 17% .(5, 6, 7).

In actual uzbek practice, it is difficult to achieve reperfusion in the hospital with PCI or TLT within the first 2 hours due to delays related to trasport, road conditions, weather conditions, traffic during peak hours, lack of free

X-ray. The number of patients in the first 90 minutes. after the development of symptoms, it is possible to open the artery through angioplasty, even according to western registers, it does not exceed 15%. Early pre-hospital thrombolysis is becoming an integral part of the patient care algorithm both abroad and in the healthcare system of Uzbekistan within the first 3-4 hours after the onset of symptoms. With the advent of fibrin-specific thrombolytics and the desire to shorten reperfusion time, the concept of "arrested myocardial infarction" - complete restoration of blood flow - entered medical practice. In patients treated with thrombolytics within 1 hour, this indicator was 25%, in the 2nd hour it was 17-20%, and by the end of the 3rd hour it decreased to 10%. These thrombolysis at the pre-hospital stage lead to an abortive course of myocardial infarction in every 4-5 patients. Death in such patients within 30 days is 5-6 times less than in all other patients. (11).

Signs of restoration of blood flow include direct signs of coronary angiography and indirect signs of restoration of blood flow. Assess the patency of the coronary arteries during coronary angiography from 0 to III according to the TIMI classification. TIMI II-III should restore coronary blood flow. The simplest and most effective of the indirect methods of assessing myocardial perfusion is monitoring the dynamics of the QRST complex. A rapid decrease in the ST segment indicates myocardial reperfusion. Evaluate the dynamics of the ST segment after 90 and 180 minutes. The degree of coronary reperfusion can be assessed by the rate and severity of ST segment depression of 30%, 50%, or 70%. Other indirect signs of blood flow restoration, such as reperfusion arrhythmias, the dynamics of biochemical signs of myocardial necrosis, give a less reliable idea about reperfusion. (11).

In some patients, restoration of blood flow through the large main artery supplying the injured area can be observed, but the microcirculation remains impaired and ST segment depression is not observed. This is because during reperfusion therapy (TLT or PCI), microemboli close the peripheral vascular bed, increase spastic reactions of small vessels, and ongoing ischemia increases interstitial edema, nonspecific inflammation, and contributes to the formation of many small myocardium, necrosis. This phenomenon, called no-reflow, is observed in the absence of a decrease in the ST segment with satisfactory blood flow through the main artery supplying the injured area (TIMI II-III). The complication and mortality rates of these patients are almost identical to those of non-reperfused patients. The phenomenon of no-reflow is noted to occur less often and to be less pronounced with early restoration of coronary blood flow.

Each hour of reperfusion delay increases the risk of myocardial "blockage" at the capillary level by 16% ($p=0.0005$), even if the artery is successfully opened. This is further evidence in favor of early thrombolysis in emergency care. Because the PCI performed after 2-4 hours in the hospital can restore blood flow to the great artery, but if the myocardium is blocked by edema, inflammation and necrosis by this time, it will not lead to clinical improvement.

Prehospital systemic thrombolysis: benefit-risk ratio. To decide on the use of thrombolytics, it is necessary to make a diagnosis of myocardial infarction with ST segment elevation on an ECG lasting 6-12 hours and to evaluate the absolute and relative contraindications for TLT. The possibility of remote ECG transmission for qualified consultation greatly facilitates the diagnosis at the emergency stage and removes obstacles before thrombolysis by the emergency team at any level, including the cardiobrigade and paramedic teams. Absolute contraindications to thrombolysis: intracranial hemorrhage or stroke of unknown etiology at any age, diagnosed MNS tumor, changes in intracranial vessels or ischemic stroke in the last six months, traumatic brain injury, serious trauma or surgery in the last 3 weeks, bleeding of the gastrointestinal tract leaving suspicion of aortic dissection and diseases of the blood coagulation system in the last month. Relative contraindications - refractory arterial hypertension (systolic blood pressure above 180 mm Hg, diastolic blood pressure above 110 mm Hg), transient ischemic attack in the brain in the last six months, traumatic resuscitation lasting more than 10 minutes and resuscitation, continuous use of indirect anticoagulants, pregnancy or the first week after childbirth, ulcer of the stomach or duodenum, infective endocarditis, serious liver disease. Sometimes the relative contraindications to thrombolysis can be overlooked in the hospital setting, where the benefits outweigh the risks and there are more options for intensive care in bleeding. At the stage of hospitalization, there is less chance of getting out of an emergency situation, and you should be more careful, for relative contraindications. When making a decision on thrombolysis, specially designed questionnaires to assess absolute and relative contraindications help to remember a number of factors affecting the risk of bleeding and make the right decision for both the doctor and the paramedic. A second limitation to performing thrombolysis in an ambulance is the fear of reperfusion arrhythmias

often expressed by health care providers. Because such arrhythmias are often short-term, self-resolved, do not significantly affect hemodynamics, and are not a reason to limit the method (12).

Arrhythmia caused by severe myocardial ischemia with complete closure of the coronary artery is more dangerous, often life-threatening, has a significant impact on hemodynamics, does not stop on its own, and increases the severity of the situation. Thus, time is the most important evaluation criterion for all patients with myocardial infarction, emphasizing the need for reperfusion as early as possible. Therefore, the discussion about the possibility of performing thrombolysis at the stage of hospitalization by the cardio team and paramedic teams should turn into work on the technical and material equipment of the ambulance: electrocardiographs, a remote ECG transmission system, emergency drugs, including the safest and simplest thrombolytics and improving the training of all emergency personnel. (2).

Every emergency medical team, including paramedics, should be ready for thrombolysis in myocardial infarction. These rules are included in the international recommendations of cardiologists (ACC / AHA, European Society of Cardiology) (2).

Each emergency team (specialized cardiology, medical, paramedic) that diagnoses acute coronary syndrome should be ready to actively treat a patient with myocardial infarction: stop pain, start antithrombotic treatment, if necessary, introduce thrombolytics; with developmental complications - cardiac arrhythmias or acute heart failure - taking cardiopulmonary resuscitation measures. These are. any emergency team must provide the full range of care specified in the ambulance standard for the relevant illnesses. Regardless of the composition of the team, the principle of fully ensuring the performance of all emergency medical and diagnostic measures with a reserve for two patients should be maintained. In the pre-hospital stage, after thrombolysis and admission to a specialized hospital, the patient should undergo coronary angiography within the first day, and a decision should be made about the need and possibility of angioplasty and stent placement.

Mechanism of action of thrombolytics. Dissolution of intravascular thrombi occurs under the influence of plasmin, which breaks down unstable fibrin into soluble products. Plasmin is formed when plasminogen is activated by plasminogen activators. There are 2 ways to activate plasminogen - intrinsic and extrinsic. The intrinsic pathway is triggered by the same factors that initiate blood clotting, namely factor XIIa, which converts plasminogen to plasmin throughout the systemic circulation. Activation through the external pathway is carried out by tissue plasminogen activator (TPA), which is synthesized in vascular endothelial cells. TPA has a strong affinity for fibrin and binds to it to form a fibrin-plasminogen-TPA ternary complex. The formation of the complex leads to the direct conversion of plasminogen to plasmin in the thrombus and proteolytic degradation of fibrin. The second plasminogen activator through the extrinsic pathway is the urokinase-type activator, which, unlike TPA, has no affinity for fibrin. Plasminogen activation occurs on the surface of endothelial cells and blood cells. The resulting plasmin lives in the blood for 0.1 seconds, and during this time it leads to the proteolysis of not only fibrin, but also fibrinogen, coagulation factors V, VIII and other plasma proteins (3, 4).

Circulating plasmin in the bloodstream is inactivated by α2-antiplasmin. An additional mechanism to limit fibrinolysis is to block plasminogen activators. Physiologically, the most important is endothelial type plasminogen activator inhibitor, which is synthesized in endothelial cells, platelets and monocytes. Pharmacologic dissolution of blood clots can be achieved by intravenous administration of plasminogen activators, of which there are currently 5 generations. Representatives of the first generation - urokinase and streptokinase - do not have a significant affinity for fibrin and lead to systemic activation of plasminogen.

Representatives of the second generation - TPA and prourokinase - have affinity for fibrin and activate plasminogen directly in the thrombus. Representatives of the third generation are obtained by the methods of creating recombinant DNK and chemical synthesis of biomacromolecules and differ from the natural forms of plasminogen activators. These include modified urokinase-fibrinogen, tenecteplase, reteplase and lanoteplase (mutant forms of TPA), saruplase (mutant form of prourokinase), chimeric forms of fibrinogen activators, in which the catalytic parts of plasminogen activators are combined with fragments of other reproductive proteins. thrombosis zone, binding and accumulated thrombolytic in the area of thrombosis. Representatives of the fourth generation were obtained using a combination of biological and chemical synthesis. Representatives of the fifth

generation are compositions of different plasminogen activators with complementary mechanisms of action and different pharmacokinetic profiles. (13).

Streptokinase is the first thrombolytic used to treat myocardial infarction. One of the first studies of thrombolytic therapy was the GISSI I (n =11,806) study [12]. In the example of using streptokinase, compared with its absence, the effectiveness of TLT was proven, the reduction in the risk of death was 18% (p=0.0002, 10.7% and 12%, respectively). Restoring the patency of the damaged vessel improves the residual function of the left ventricle, reduces myocardial infarction complications, mortality, and prolongs life after myocardial infarction. Late reperfusion of the ischemic area (within 6-12 hours after an anginal attack) also leads to a decrease in myocardial necrosis, preservation of contractile function and a decrease in the risk of complications. As a result of the clear positive effects of thrombolysis, further studies and improvements of TLT have occurred compared to streptokinase. Along with the advantages, a number of disadvantages of streptokinase are well known, which limit its use in clinical practice today. Because streptokinase is obtained from β-hemolytic group C streptococcus, it has antigenic properties. Repeated administration of streptokinase can cause immune reactions ranging from mild endotoxic to severe anaphylactic shock, manifested by hypotension, tremors, nausea. Preparedness for an allergic reaction develops after 5 days and can last a lifetime. Even with mild allergic manifestations, the presence of antigens can be accompanied by a decrease in the effectiveness of streptokinase. Antigens can be present even in the blood of a person who has not previously taken drugs, which is associated with a high prevalence of streptococcal infection in the population. The European Society of Cardiology recommends that streptokinase be used only once in a lifetime [12]. This fact is a serious obstacle to the widespread use of thrombolytics, since the frequency of repeated myocardial infarction is about 70% of all heart attacks. In addition to myocardial infarction, the history of the patient may include thromboembolism of the pulmonary artery and deep vein thrombosis treated with streptokinase.

One of the largest studies investigating the effectiveness of thrombolytic therapy in cardiology is the GUSTO-1 study among 41,000 patients. In the alteplase group, the frequency of recanalization of the infarct-related artery increased significantly in the most critical time interval - 90 minutes (81.3 and 59%, respectively). By the 180th minute, the efficiency was almost the same. However, faster restoration of blood flow led to a significant reduction in mortality in patients receiving alteplase (by 14% overall). According to other controlled studies, the use of alteplase confirms an increase in survival on the 30th day of the disease, an increase in the left ventricular ejection fraction on the 10-22nd day of the development of myocardial infarction, and a decrease in the risk of the development of myocardial infarction. complications such as cardiogenic shock, arrhythmia, pericarditis. (2).

Further research on thrombolytics led to the development of reteplase, a genetically modified TPA with a longer half-life than alteplase, allowing it to be administered as a bolus. In the INJECT study, comparing reteplase with streptokinase showed no benefit in reducing mortality. A comparison of replacement with alteplase showed no clinical superiority over alteplase. Reteplaza is not yet registered in Uzbekistan. With the advent of single-bolus tenecteplase, a thrombolytic agent equal to alteplase in reducing mortality, but superior in terms of safety profile and ease of use in the prehospital setting.

ASSENT-2 - a large study evaluating the safety and efficacy of tenectoplase and alteplase included 16,949 patients with acute myocardial infarction, who were prescribed 100 mg of alteplase or 30-50 mg of tenecteplase depending on body weight - 0.50-0.55 mg/kg. This dosing regimen is the same as that studied in the TIMI 10B and ASSENT-1 studies and recommended in the tenecteplase prescribing information. The results of the study showed equivalence between the two thrombolytics in terms of 30-day mortality and the overall endpoint of death and non-fatal stroke in all patient groups. However, tenecteplase had a significantly lower mortality rate in patients treated 4 hours after symptom onset: a significant (p= 0.018) reduction in mortality was 24% compared to the alteplase group (7.0% vs. 9.2%, respectively). Thus, in the case of late thrombolysis, tenectoplase may be the drug of choice. This study was also notable for having the lowest 30-day mortality rate of any large TLT study, which may reflect the more effective use of concurrent antithrombotic therapy (aspirin, clopidogrel, glycoprotein receptor Iia/IIIb blockers). Significantly fewer patients (p = 0.026) experienced complications after tenecteplase therapy.(14)

Predictors of risk of major bleeding in response to TLT include older age, low body weight, and female gender. The safety of tenecteplase was adequate and clear in all patient subgroups. It is noteworthy that this difference was especially true for a subgroup with a high risk of bleeding - women over 67 years old, weighing less than 67 kg. Two factors may be responsible: high specificity and dosing regimen based on patient weight. A new analysis of the ASSENT-3 and ASSENT-PLUS studies investigated the effect of PHTLT on the rate of termination of the pathological process in myocardial infarction. In the ASSENT-3 study, treatment with tenecteplase was administered in the hospital, and the average time of treatment was 162 minutes, and the overall rate of interruption of the pathologic process in myocardial infarction was 13.3%. Up to 25% of heart attacks were reversed in patients treated within 60 minutes of symptom onset. In the ASSENT-PLUS study, tenecteplase treatment was administered in an inpatient setting, and the median time to treatment was 115 minutes, and the overall rate of myocardial infarction was 20%. Thus, out of every 4-5 patients with myocardial infarction, myocardial necrosis did not develop in patients treated with tenecteplase in the first 1-2 hours. In the ASSENY-3 PLUS study, 53 percent of patients received therapy within two hours of hospital admission, a significant improvement compared to ASSENT-3, in which only 29 percent of hospitalized patients received therapy within the same time frame. Early initiation of treatment was associated with better outcomes. In ASSENT-PLUS, 30-day mortality was 4.4% among those treated for 0-2 hours, 6.2% among those treated for 2-4 hours, and 10.4% among those treated for 4-6 hours. Additionally, in the ASSENT-3 PLUS study, there were no significant differences in outcomes or complications between physician- or paramedic-staffed emergency teams. Treatment with tenecteplase in the prehospital setting is safe and shortens the duration of treatment. The 4.4% mortality rate in patients treated within 0-2 hours of the onset of a pain attack set a new record for reducing mortality in clinical trials with thrombolytics. (8, 9).

The fourth thrombolytic is recombinant prourokinase. Prourokinase is a single-chain proenzyme of urokinase isolated in 1977 from urine and kidney cultures of human embryos. For industrial production, the drug is obtained by DNK recombinant genetic engineering. Prourokinase has more fibrin specificity than streptokinase and urokinase, but this indicator is inferior to alteplase and even more so to tenecteplase. The systemic effect of prourokinase is explained by the fact that fibrin in the body is converted into two-chain urokinase, which has no specific properties. In the following years, a number of comparative studies of prourokinase with streptokinase and alteplase were conducted. The PRIMI study (n=402, 1989) compared the efficacy of prourokinase and streptokinase. After 24 and 36 hours, the opening of vessels for 90 minutes compared with more intracranial bleeding in prourokinase. Similar results were obtained in the larger COMPASS study (n = 3089, 1998), comparing 30-day mortality between the prourokinase and streptokinase groups, with intracranial hemorrhage rates 3 times higher in prourokinase (0.9 vs. 0.3%, respectively). The SESAM study (n = 473, 1997) compared the rate of blood flow recovery, reocclusion rate, and mortality between prourokinase and alteplase. However, the risk of death in the prourokinase group was 23.7% higher compared to alteplase (4.7% and 3.8%, respectively). After one year of follow-up, this difference increased to 43.8% relative risk (6.9 and 4.8%, respectively). Prourokinase has not been further clinically tested and due to its inferior safety compared to streptokinase, the EMEA has not approved prourokinase for clinical use in the treatment of MI. Prourokinase was also excluded from the ACC/AHA recommendations.

An interventional strategy is preferred if: an X-ray operating room with an experienced team is available; Severe myocardial infarction with heart failure of III degree according to Killip; there are indications against thrombolysis; more than 3 hours have passed since the onset of symptoms; if the diagnosis of myocardial infarction is unclear before coronary angiography.

The choice of pharmacological reperfusion does not exclude an invasive strategy. Coronary angiography and, if necessary, PCI should be performed within the first 3-24 hours after TLT. This tactic is called pharmaco-invasive strategy and is widely used in the world. The pharmaco-invasive approach was positively evaluated by the results of CAPTIM, WEST, GRACIA-2, NORDISTEMI studies and registries. A combination of two reperfusion modalities has been shown to additively reduce the risk of death in patients with myocardial infarction. (9).

Conclusion

The choice of the reperfusion method, the desire for early reperfusion is the most important component of the prehospital thrombolysis treatment algorithm for patients with myocardial infarction. Death, disability and quality of life of patients depend on the correctness of this decision. Coronary angiography and, if indicated, PCI should be performed within the first 3-24 hours after prehospital thrombolysis. In the pre-hospital stage, the recommended selection criteria for the primary PCI are that it can be performed within the first 2 hours from the time of seeking medical help, if there are contraindications to TLT, and if more than 3 hours have passed since the onset of symptoms of myocardial infarction, it is appropriate to conduct the PCI.

References

1. Khan M.A., Hashim M.J., Mustafa H., Baniyas M.Y., Al Suwaidi S.K.B.M., AlKatheeri R., Alblooshi F.M.K., Almatrooshi M.E.A.H., Alzaabi M.E.H., Al Darmaki R.S., Lootah S.N.A.H. Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study // Cureus. – 2020 – Vol. 12, №7. – P. e9349.
2. 2017 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 (ESC), European Heart Journal, Volume 39, Issue 2, 07 January 2018, Pages 119–177.
3. Boersma E. et al. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour Lancet 1996; 348: 771
4. Braunwald's Heart Disease. A Textbook of Cardiovascular Medicine. 8th Edition. Eds. P. Libby, R. O. Bonow, D. Mann, D. P. Zipes, E. Braunwald. Elsevier Saunders, 2008. — P. 1167-1318.
5. Danchin N., Coste P., Ferrieres J. et al. Comparison of thrombolysis followed by broad use of percutaneous coronary intervention with primary percutaneous coronary intervention for ST-segment — elevation acute myocardial infarction: data from the french registry on acute ST-elevation myocardial infarction (FAST-MI). Circulation. 2008; 118: 268-276.
6. Kalla K., Christ G., Karnik R. et al. Implementation of guidelines improves the standard of care: the Viennese registry on reperfusion strategies in ST-elevation myocardial infarction (Vienna STEMI registry). Circulation. 2006; 113: 2398-2405.
7. Nallamothu B.K., Bates E.R., Herrin J., Wang Y., Bradley E.H., Krumholz H.M. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. Circulation. 2005; 111: 761-767.
8. Kaul P., Armstrong P.W., Cowper P.A. et al. Economic analysis of the Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT-3) study: costs of reperfusion strategies in acute myocardial infarction. Am Heart J. 2005; 149: 637-644.
9. Wallentin L., Goldstein P., Armstrong P.W. et al. Efficacy and safety of tenecteplase in combination with the low-molecular-weight heparin enoxaparin or unfractionated heparin in the prehospital setting: the Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT)-3 PLUS randomized trial in acute myocardial infarction. Circulation. 2003; 108: 135-142.
10. Danchin N, Blanchard D, Steg PG, Sauval P, Hanania G, Goldstein P, Cambou JP, Guéret P, Vaur L, Boutalbi Y, Genès N, Lablanche JM., USIC 2000 Investigators. Impact of prehospital thrombolysis for acute myocardial infarction on 1-year outcome: results from the French Nationwide USIC 2000 Registry. Circulation. 2004 Oct 05;110(14):1909-15
11. Antman E.M., Hand M., Armstrong P.W. et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology/American Heart association Task Force on Practice Guidelines: Developed in Collaboration With the Canadian Cardiovascular Society Endorsed by the American Academy of Family Physicians: 2007 Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction, Writing on Behalf of the 2004, Writing Committee. Circulation. 2008; 117: 296-329.
12. Gruppo Italiano per lo Studio della Streptochinasi nell`Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986; 1: 397-402.
13. Crowder JS, Hubble MW, Gandhi S, McGinnis H, Zelman S, Bozeman W, Winslow J. Prehospital administration of tenecteplase for ST-segment elevation myocardial infarction in a rural EMS system. Prehosp Emerg Care. 2011 Oct-Dec;15(4):499-505. [PubMed]
14. Sinnaeve P.A., Alexander J.B., Belmans A.C. et al. One-year follow-up of the ASSENT-2 trial: A double-blind, randomized comparison of single — bolus tenecteplase and front-loaded alteplase in 16,949 patients with ST — elevation acute myocardial infarction. Am Heart J. 2003; 146: 27-32. 19.