AMERICAN JOURNAL OF SOCIAL AND HUMANITARIAN RESEARCH

ISSN: 2690-9626
Vol.3, No 2, 2022

Advantage of Prehospital Thrombolysis in Acute Coronary Syndrome

Sh. H. Pulatova, Kenjaev M. L., Sharopov U. R.
Bukhara Medical Institute

ABSTRACT: The review describes the features of thrombolytic therapy in patients with acute myocardial infarction in detail. Thrombolytic therapy helps to reduce 30-day mortality in myocardial infarction from 17-18% to 5-8%. The issues of the optimal period of thrombolysis from the onset of the clinical manifestations of a heart attack, alternative methods for restoring coronary blood flow, indications and contraindications, complications and side effects, and methods for evaluating the effectiveness of thrombolysis are highlighted. The main fibrin-selective and fibrin-non-selective fibrinolytic drugs: streptokinase, alteplase, tenecteplase are listed. The results of large randomized clinical trials on fibrinolytic therapy of myocardial infarction are presented. The possibilities of increasing the effectiveness and safety of fibrinolytics by combining them with acetylsalicylic acid and heparins are discussed.

KEYWORD: myocardial infarction, thrombolysis, fibrinolytics

Acute myocardial infarction (AMI) in most cases develops as a result of intracoronary thrombosis formed over damaged atherosclerotic plaque [12]. Thrombolytic drugs began to be used in patients with acute myocardial infarction more than 50 years ago . Over the years, it has been shown that emergency restoration of coronary blood flow leads to a decrease in the focus of necrosis, makes the process of its formation reversible, and prevents the deterioration of the function of the affected myocardium . The use of thrombolytic therapy led to a decrease in 30-day mortality in patients with myocardial infarction to 5-8% , while in the "pre-fibrinolytic era" it reached 17-18%.But it is obvious that even now myocardial infarction remains one of the most prognostic formidable diseases, with the largest number of deaths observed in the first hours of the disease: 28% of patients die during the first hour of the disease, 38% within 4 hours and 46% in the first hours. 24 hours [6,7,9,10]. In this connection, one of the main tasks of treating a patient with myocardial infarction is the earliest possible, complete and sustainable restoration of coronary blood flow [12].

All available guidelines are based on the results of RCTs comparing primary PCV and TLT, as well as data from registries [1, 13]. Since most of the guidelines were published several years ago, the most recent results have obviously not been taken into account. All experts agree that the time factor is key and reperfusion therapy should be started as early as possible. The American Heart Association (AHA) and the American College of Cardiology (ACC) favor pre-hospital thrombolysis over PCI, emphasizing that the timing of therapy is more important than the method of reperfusion. The ACC and ACC guidelines state that prehospital thrombolysis can be performed if there is confirmation of MI with 8T segment elevation on the ECG, interpreted by the on-site physician or referred to a specialist. Further, it is advisable to complete a reperfusion checklist to ensure that the

ISSN 2690-9626 (online), Published by "Global Research Network LLC"
under Volume: 3 Issue: 2 in February-2022 https://grnjournals.us/index.php/AJSHR

patient has no contraindications to such therapy and to identify high-risk patients who will benefit more from primary PCI. Pre-hospital thrombolysis should be performed within 30 minutes from the arrival of the ambulance to the patient. If a fibrinolytic agent cannot be administered prehospital and If the patient is transported to a hospital where PCI is not possible, the door-to-needle time (from arrival to the hospital to thrombolytic administration) should not exceed 30 minutes. However, if the hospital has facilities for under leather intervention V, the door-to-balloon time (from arrival at the hospital to balloon inflation at the catheter lab) should not exceed 90 min [4].If a patient is admitted to a center that is not equipped to perform under leather intervention and cannot be transferred to another hospital and is unable to perform under leather intervention within 90 minutes of the first medical contact, thrombolytic therapy should be started no later than 30 minutes from admission to the hospital if no contraindications (level of evidence B). The goal of organizing the patient care system is the interval of the total "ischemic time" at the stages of care, not exceeding 120 minutes. The goal for each treatment step is to:

- the time from the onset of symptoms to the call of an ambulance - 5 minutes;
- transfer of the call by the EMS dispatcher to the EMS team - 1 min;
- arrival of the ambulance crew at the place of call - 8 minutes,
- conducting an ECG and deciding on prehospital fibrinolytic therapy, if possible, and the time before TLT will be less than 30 minutes;
- if it is decided to take the patient to the hospital without the possibility of PCV, the “door-to-needle” time should be less than 30 minutes;
- if it is decided to deliver the patient to the hospital with the possibility of PCV, the time from calling the ambulance to the start of the balloon insertion should be less than 90 minutes (if the patient is delivered by his own transport
- the “door-balloon” time should not exceed 90 minutes).

The latest guideline of the European Society of Cardiology [13] recommends reperfusion by PCI if the intervention is performed by an experienced surgeon.within 120 minutes from the first medical contact (call for the EMS) or within 90 minutes from the first medical contact if the patient applied within 2 hours from the onset of symptoms and has a significant myocardial area at risk and a low risk of bleeding. Primary PCI is reasonable in patients with contraindications to TLT, and this method of reperfusion is preferred in patients with cardiogenic shock. In other cases, TLT should be done as quickly as possible.

If TLT was unsuccessful, a rescue PCV with a reasonable time delay (up to 12 hours from the onset of symptoms) is recommended. If thrombolysis was successful (more than 70% ST-segment decrease after 60-90 min, reperfusion arrhythmias, disappearance of chest pain), coronary angiography and under leather intervention are recommended in the absence of contraindications in a time period of 3-24 hours in order to avoid bleeding risk and minimize the risk of coronary vessel reocclusion [13]. On the contrary, the use of “facilitated” under leather intervention (the use of fibrinolysis or Ilb-IIIa glycoprotein receptor blockers before angioplasty is not recommended). The NICE Institute in the UK supports reperfusion through TLT, recommending the latest agents, reteplase and tenecteplase, for pre-hospital thrombolysis. Administration of thrombolytics by bolus facilitates their use, but none of them has been shown to be superior to alteplase in terms of long-term prognosis. In the GUSTO III study, which included 15,060 patients, reteplase compared with tenek-teplase did not differ in effect on 30-day mortality (7.47% versus 7.24%) and the cumulative incidence of death and disabling stroke (7.89% in compared to 7.91%). In the ASSENT II study, which included more than 17,000

ISSN 2690-9626 (online), Published by “Global Research Network LLC"
under Volume: 3 Issue: 2 in February-2022 https://grnjournals.us/index.php/AJSHR

patients, tenecteplase had a comparable effect on 30-day mortality (6.18% vs. 6.15%) and the combined end point of death and non-fatal stroke (7.11% vs. 04%) and the incidence of hemorrhagic strokes (0.93% versus 0.94%). The time factor is also decisive here and therapy should be started within 12 hours of the onset of symptoms.

European Institute for Resuscitation states: thrombolysis is indicated in the absence of contraindications if PCV is not possible hold within 90 minutes, or if the duration of symptoms is less than 3 hours and the time before PCV is more than 60 minutes. Under leather intervention is indicated if it can be performed within 90 min, if thrombolysis is contraindicated, in patients with cardiogenic shock, severe heart failure, or in patients presenting later than 3 hours from the onset of symptoms [2].

Comparison of thrombolysis with percutaneous coronary interventions in patients according to randomized clinical trials. RCTs have shown that primary Subcutaneous Invasion is more effective than fibrinolysis in patients with T-segment Elevation MI when performed by an experienced team within 90 min from the first medical contact [7]. Kelyu et al. evaluated 23 studies comparing primary Subcutaneous Incision with TLT using streptokinase or a fibrin-specific agent. Regardless of the thrombolytic drug, primary under leather intervention was more effective [7]. However, as noted in a meta-analysis of 6 randomized trials, prehospital thrombolysis had an advantage over in-hospital thrombolysis in terms of hospital mortality and could be performed up to 45 min earlier, potentially saving more myocardial volume and improving outcomes. the use is associated with a significant 17% reduction in hospital mortality compared with treatment initiated in the hospital [9]. This is especially important for countries and regions where there is no possibility at all to carry out under the skin accommodation or there is no possibility of invasive interventions around the clock. Only one CART1M study directly compared prehospital thrombolysis with primary under leather intervention. Patients who received thrombolysis within 2 hours of onset of symptoms showed a strong trend towards a reduction in 30-day mortality compared to those who underwent primary dermal insertion. In the time interval over 2 hours from the onset of symptoms, the difference between the groups changed towards the advantage of the primary skin placement. [11].The results of the CART1M study are consistent with the data of RNAA&E-2. which showed that if treatment was started within 3 hours from the onset of symptoms, the incidence of deaths was identical, but if patients were randomized later than 3 hours from the onset of symptoms, the mortality in the thrombolysis group was significantly higher [14]. The investigators concluded that if patients with ST-segment elevation MI could be transported to a hospital with the possibility of being placed under a skin pouch for 20-30 min, they should be placed under a leather pouch. If Under the Skin Insertion cannot be performed within 60 minutes, thrombolytic therapy should be given up to 3 hours from the onset of symptoms. TLT should not be used if more than 3 hours have passed since the onset of the pain syndrome and then the patient must be referred to the hospital for Under the Skin Surgery. Interestingly, in a meta-analysis of PCAT studies, 30-day mortality was twice as high in the fibrinolysis group if the delay in treatment was increased from 1 hour to more than 6 hours [4]. The frequency of reinfarctions was also higher in this group in proportion to the time of delay in therapy; in the group under the skin insertion, this dependence was not recorded. Thus, the time delay before reperfusion remains the central point in the choice of reperfusion strategy [4].

Another important key point is the role of the follow-up group under skin placement after prehospital thrombolysis. In the CAPTIM study, 70% of the patients in the thrombolysis group underwent a skin grafting group for a month, and 26% of patients underwent a skin graft rescue group. Therefore, this study actually compared the administration of primary DUT and pre-hospital thrombolysis with subsequent DUT if thrombolysis was unsuccessful [11]. Moreover, the role of under-skin insertion

ISSN 2690-9626 (online), Published by "Global Research Network LLC"
under Volume: 3 Issue: 2 in February-2022 https://grnjournals.us/index.php/AJSHR

within 24 hours of fibrinolysis has been tested in the GRACIA-1 [6] and CARES S-in-AMI [6] studies. In both examples, the use of Under the Skin Insertion after thrombolysis gives better results than conservative treatment. The WEST study extended this concept and compared the use of tenecteplase with the administration of tenecteplase followed by a mandatory 24-hour Subcutaneous Intervention and an initial Subcutaneous Intervention with a loading dose of clopidogrel.

Based on the results of the study, it was concluded that rapid pharmacological reperfusion followed by salvage or routine subcutaneous insertion within 24 hours is comparable to primary subcutaneous insertion [2].

Largeregisterdata

Inclusion and exclusion criteria in drug RCTs imply that only ideal cases are presented. Registry data provide a more realistic view of treatment strategy and outcomes in the general population. Therefore, the results of the registersand RCTs often do not match. B_]ogk1aps1 e1 a1. demonstrated that one-year mortality in patients with T-segment elevation MI treated with thrombolytics in RCTs was 8.8% compared with 20.3% in patients not included in RCTs but treated in a hospital where RCTs were conducted and 19.0 % for patients treated in a hospital that does not conduct RCTs ($p<0.001$ for both cases). Thus, it is clear that "lighter" patients are selected for RCTs [3]. The success of reperfusion therapy in MI with ST segment elevation depends on the time of administration [8]. However, register data have shown that 30 min door-to-needle and 90 min door-to-balloon times are incredibly difficult to achieve [4]. Door-to-balloon time is often significantly longer in real clinical practice than in RCTs, due to, for example, transport of patients to a hospital with the possibility of carrying under skin placement, local factors (weather, remoteness, availability of staff.) [10] Analysis 75% of the NRMI registry data indicate that only 4.2% of patients undergoing skin insertion achieve a “door-to-balloon” time of less than 90 min [10]. This fact indicates that there is room for improvement in the care of such patients, but this task looks extremely difficult in the light of the recent results of the GRACE registry study: the time before the start of PCV in the period from 2000 to 2005 did not change [6]. Prehospital thrombolysis: advantages and limitations.

Prehospital thrombolysis is one of the main factors to reduce the time delay in the appointment of reperfusion therapy. However, its implementation poses several organizational problems, which can be solved in different ways in different countries and regions. A significant number of barriers may limit the actual use of prehospital thrombolysis. The question of the optimal organization of prehospital care for a patient with myocardial infarction, when it is provided by a team with a doctor or by paramedics without the participation of a doctor, remains debatable. In a Finnish study of 641 MI patients, clinical outcomes were found to be better when the patient was seen by a physician in the primary care phase compared to similar outcomes when the patient was attended to by paramedics.

Clearly, the system of care chosen is likely related to the percentage of patients who can receive prehospital thrombolysis. According to the French MI registry in 2005, prehospital thrombolysis was performed in 19% of patients, accounting for 2/3 of all cases of thrombolytic therapy [5]. Therefore, from a practical point of view, emergency care teams in France are staffed by doctors and the decision to prescribe fibrinolytics is made by the doctor after assessing the clinical picture and ECG data.

Conclusion

If we consider the issue as a whole, there are not so many unclear moments in the conduct of reperfusion therapy at present, there are clear time limits for the implementation of one or another

ISSN 2690-9626 (online), Published by “Global Research Network LLC"
under Volume: 3 Issue: 2 in February-2022 https://grnjournals.us/index.php/AJSHR

type of therapy. Although primary PCA is the strategy of choice, this procedure is often not available in the required time window. In this case, thrombolysis should be considered as the first step of treatment, with the possibility of systemic or salvage PCI. In countries and regions where PCV is not available around the clock, thrombolysis remains the only option and should be performed as soon as possible, preferably in the prehospital setting. The most recent data from both registries and RCTs suggest that a pharmaco-invasive strategy is probably the preferred strategy in patients treated with TLT. In this regard, it is necessary to establish an organized network of clinical evaluation, treatment and transportation and adapt it to local conditions for optimal management of patients with T-segment MI with subsequent monitoring of clinical results.

List of references

1. Antman E.M. 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/ Antman E.M., Hand M., Armstrong P.W, [et al] // Circulation. - 2008. -Vol. 117. - P.296-329
2. Armstrong P., WEST Steering Committee. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study/ Armstrong P. // Eur Heart J. -2006. - Vol.27. -P.1530-1538.
3. Bjorklund E. Prehospital thrombolysis delivered by paramedics is associated with reduced time delay and mortality in ambulance-transported real-life patents with ST-elevation myocardial infarction / Bjorklund E., Stenestrand U., Lindback J., et al on behalf of the RIKS-HIA Investigators // Eur Heart J. - 2006. -Vol.27 - P.1146-1152.
4. Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction / Boersma E., the PCAT-2 Trialists' Collaborative Group //Eur Heart J. - 2006 - Vol.27 - P.779-788.
5. Danchin N. 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) / Danchin N., Coste P., Fejrieres J., [et al], for the FAST-MI Investigators. // Circulation. - 2008 - Vol.118 - P. 268276.
6. Eagle K.A. Global Registry of Acute Coronary Events (GRACE) InvestigatorsTrends in acute reperfusion therapy for ST-segment elevation myocardial infarction from 1999 to 2006: we are getting better but we have got a long way to go / Eagle K.A., Nallamothu B.K., Mehta R.H., [et al]. // Eur Heart J. - 2008.
7. Keeley E. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials / Keeley E., Boura J., Grines C. // Lancet. - 2003.-Vol.361 -P.13-20.

ISSN 2690-9626 (online), Published by "Global Research Network LLC"
under Volume: 3 Issue: 2 in February-2022 https://grnjournals.us/index.php/AJSHR

8. McNamara R. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction / McNamara R., Wang Y., Herrin J., [et al], for the NRMI Investigators. // J Am CollCardiol. - 2006. - Vol.47 - P.45-51.
9. Morrison L. Mortality and prehospital thrombolysis for acute myocardial infarction. A meta-analysis / Morrison L., Verbeek P., McDonald A., [et al]. // JAMA. -Vol. 2000. -Vol.283 - P.2686-2692.
10. Nallamothu B. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States. National Registry of Myocardial Infarction (NRMI)-3/4 Analysis / Nallamothu B., Bates E., Herrin J., [et al], for the NRMI Investigators. // Circulation. - 2005. - Vol.111 -P.761-767.
11. lmpact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty / Steg G., Bonnefoy E., Chabaud S., [et al], for the Comparison of Angioplasty Prehospital Thrombolysis In acute Myocardial infarction (CAPTIM) Investigators // Circulation. - 2003. - Vol.108 -P.2851-2856.
12. S.H.Pulatova .TROMBOLYTIC THERAPY IN ACUTE MYOCARDIAL INFARCTION// herald of emergency medicineю – 2019.- Vol.6.- P. 88-91.
13. Van de Werf F. The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation / Van de Werf F., Bax J., Betriu A., [et al]. //EHJ.- 2008. -Vol.29. -P.2909-2945.
14. Widimsky P. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial—PRAGUE-2 / Widimsky P., Budesmsky T., Vorac D., [et al], on behalf of the PRAGUE Study Group Investigators // Eur Heart J. -2003. - Vol.24. - P.94-104.

ISSN 2690-9626 (online), Published by "Global Research Network LLC"
under Volume: 3 Issue: 2 in February-2022 https://grnjournals.us/index.php/AJSHR