

EFFICACY OF THROMBOLYTIC THERAPY IN THE TREATMENT OF ACUTE MYOCARDIAL INFARCTION (AMI)

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Abstract

Acute Myocardial Infarction (AMI) is the immediate cessation of the blood supply to the heart muscle and occurs due to lack of oxygen and is one of the most frequent medical emergencies. ST-Elevation Acute Myocardial Infarction (STEMI) is one of the major cardiological emergencies which is associated with complications of heart failure, arrhythmia, and high mortality. The main treatment is coronary artery recanalization of the involved artery in the shortest time possible. Percutaneous transluminal coronary angioplasty has shown the best results of AMI treatment. Reperfusion of the ischemic myocardium can be achieved by pharmacologic methods (thrombolysis) and PCI (Percutaneous Coronary-arteries Intervention).

Purpose of the study: The study is of cohort-prospective type. It is a study for the coronary-angiography evaluation of the current treatment of STEMI at the University Hospital Center in Tirana in patients undergoing thrombolysis with streptokinase or reteplase (choice is based on the specific case), and the effect of predisposing factors upon the mortality of STEMI.

Materials and methods: this study included all patients admitted to the department of cardiology resuscitation, from 01 Feb 2013, until 05 Jul 2013 (56 patients, of whom 26 were females and 30 were males, with an identical average age of 56.0 ± 10.0 years old) diagnosed with STEMI in whom thrombolysis with reteplase or streptokinase has been performed according to previously tested protocols, respecting the absolute contraindications for the application of reperfusion procedure. Thrombolysis was performed in patients who presented within 6 hours since the onset of pain. Follow-up includes days of hospitalization (cardiology resuscitation + cardiology clinic I or II).

Results: Data analysis showed Thrombolysis in Myocardial Infarction (TIMI) 3 in 82% of the total cases; The group of patients treated with streptokinase showed TIMI 3 of 70% and the group of patients treated with reteplase showed TIMI 3 of 91%. The total mortality rate was 6.9% (3 patients) and these were part of the group treated with reteplase. Predisposing factors for high mortality in patients undergoing thrombolysis such as age, sex, diabetes mellitus (DM) type II (prevalence of DM type II was 33.9% of all patients, of whom 41% of the patients treated with RP and 22% of patients treated with ST, $p=0.0001$) and TIMI had a statistical significantly higher risk factors in the group treated with reteplase.

Conclusion: Thrombolysis of STEMI patients presents an effective recanalizing alternative when the patient presents within the first few hours since the onset of pain onset, a conclusion achieved by TIMI-based coronary angiography assessment. Mortality in thrombolysis is related to factors such as: age, gender, high blood pressure (BP), DM, and other comorbid factors.

Keywords: Acute Myocardial Infarction (AMI), Coronarography, Thrombolytic therapy

1. Introduction

Acute myocardial infarction (AMI), i.e., heart attack, is the irreversible death or necrosis of the heart muscle because of prolonged lack of oxygen supply or prolonged ischemia. Treatment of AMI is based on thrombus dissolution by fibrinolysis. Fibrinolysis recanalizes thrombotic occlusion, which manifests as *ST-Elevation Myocardial Infarction* (STEMI), and restores coronary vessel continuity, thereby reducing infarction size, improving myocardial function, and short- and long-term survival. In most patients with STEMI thrombotic occlusion persists, however, in some patients spontaneous late reperfusion occurs. Timely reperfusion of the myocardium at risk is the best way to restore the balance between oxygen supply and demand (Rathore SS *et al.*: 2007; Gersh BJ *et al.*: 2005). The amount of myocardium that is saved depends on the time of onset of treatment of patients with fibrinolysis or PCI (White H. D. *et al.*: 2008, De Luca *et*

al.: 2004). A very important factor that influences fibrinolysis is the time of initiation of the reperfusion procedure because as time passes the thrombus matures leading to a decrease in the efficiency of thrombolytic drugs. Reliable experimental and clinical data have shown that re-establishment of coronary circulation as soon as possible increases the favourable outcome and improvement of the parameters such as improvement of the systolic function of the left ventricle (LV), the diastolic function of the LV and the reduction of mortality (Fibrinolytic Therapy Trialists (FTT) *Collaborative Group*: 1994; Boersma E, *et al.*: 1996; Levine G. N., *et al.*: 2016). The reperfusion process although beneficial in terms of myocardial salvage may be associated with reperfusion injury, which leads to other sequelae such as myocardial cell death, microvascular damage resulting in hemorrhagic infarction, stunned myocardium, and reperfusion arrhythmias (Majidi M, *et al.*: 2009; Ibanez B, *et al.*: 2018). Reperfusion-induced arrhythmias usually accompany successful reperfusion but have reduced specificity. Clinical data are generally poor markers of successful reperfusion as they are not reliable indicators for the presence of open coronary vessels on coronarography. A method used to assess coronary blood flow and compare different reperfusion regimens is TIMI which can be graded as 0, 1, 2, or 3. The effect of thrombolytic therapy on mortality in patients of the age group up to 56 years of age is of interest, and this group is associated with reduced mortality (Gershlick A. H. *et al.*: 2009; Schiele S, Meneveau N, *et al.*: 2009). Important clinical factors that affect mortality during fibrinolysis are the presence of DM type II, age, sex, and vital signs during hospitalization. Several models are used to assess mortality before fibrinolysis. One such model used in the InTIMI II study, “TIMI risk score”, predicts patients’ mortality up to one month before fibrinolysis (Morrow DA, *et al.*: 2000) The considered variables are age, systolicBP, heart rate, Killip class II-IV (the Killip Classification is frequently used during acute myocardial infarction; first published in 1967, this system focuses on physical examination and the development of heart failure to predict cardiac risk), anterior STEMI, left bundle branch block, DM, high BP, residual angina, Body Mass Index, and time since onset of treatment.

Purpose of Study: The study is of a cohort-prospective type. The decision whether the patient will be treated with streptokinase or reteplase is random, depending on the thrombolytics offered in the hospital service. For each patient, the obtained data were: age, gender, DM, high BP, smoking, STEMI localization, time of presentation, time of coronary angiography, residual angina, and heart blocks of various degrees.

Materials and Methods: This study included all patients admitted to the department of cardiologic resuscitation, from 01 Feb 2013, until 05 Jul 2013 (56 patients, of whom 26 were females and 30 were males, with an identical average age of 56.0 ± 10.0 years old) diagnosed with STEMI in whom thrombolysis with reteplase and streptokinase has been performed according to previously tested protocols, respecting the absolute contraindications for the application of reperfusion procedure. Thrombolysis was performed in patients who presented within 6 hours since the onset of pain. Follow-up includes days of hospitalization (cardiology resuscitation + cardiology clinic I or II). After thrombolysis, all patients were treated with heparin for the first 24-48 hours and subsequently with Low Molecular Weight Heparin (LMWH) – Enoxaparin. Also, immediately after thrombolysis, all patients were given aspirin 250 mg, clopidogrel 300 mg, and other therapeutic interventions as needed.

From the total of 56 patients, coronarography was performed in 40 patients, 13 did not undergo coronarography, and 3 patients died.

Table 1: Presentation of number and percentage of patients included in this study

Gender of patients	Number of patients and percentage of total number of patients (56 patients)	Average age
<i>Female</i>	26 (45 %)	56.0 ± 10.0
<i>Male</i>	30 (55 %)	56.0 ± 10.0

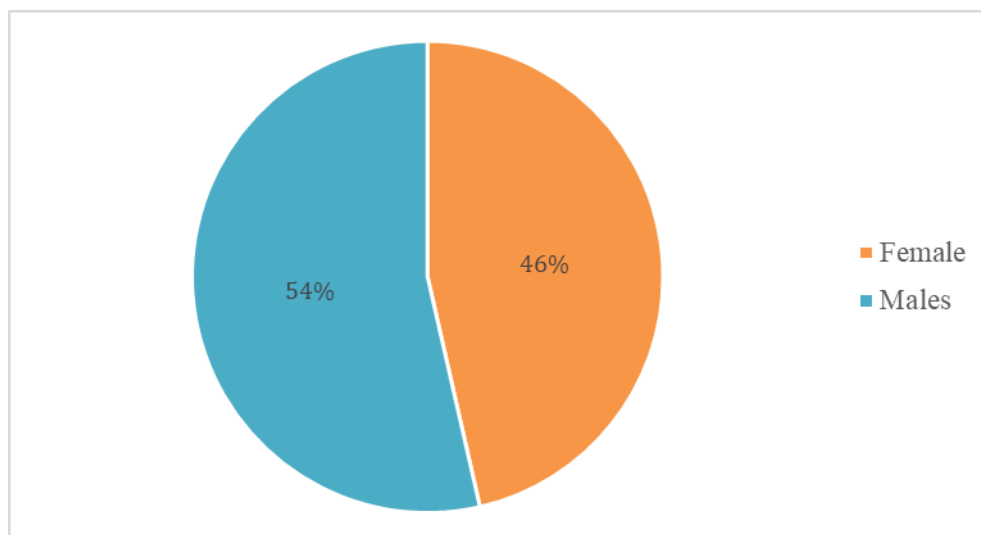


Chart 1: Number of patients included in the study

Table 2: Patients included in the study

Patients who underwent coronarography	40 patients	72 %
Patients who did not undergo coronarography	13 patients	23 %
Patients who died	3 patients	5 %
Total number of patients who presented with symptoms	56 patients	100 %

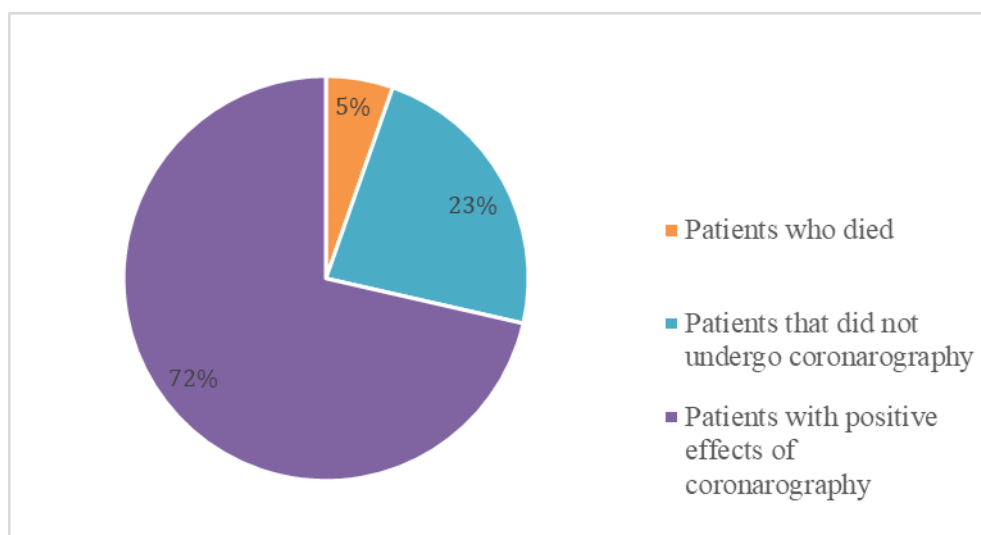


Chart 2: Patients undergoing coronarography

Results:

Table 3: Student's test for independent samples; ** Hi-square test

	STREPTOKINASE	RETEPLASE	TOTAL	P VALUE
NUMBER OF PATIENTS	22	34	56	0.0001*
DM	5 (22 %)	14 (41 %)	19 (40 %)	0.0001*
HTA	3 (13 %)	17 (50 %)	20 (36 %)	0.0001*
SMOKING	18 (82 %)	12 (35 %)	30 (35.7 %)	0.0001*
AMI-ANTERIOR	9 (41 %)	14 (41 %)	23 (41 %)	0.500**
AMI-INFERIOR	12 (54 %)	19 (55.8 %)	31 (55 %)	0.130**
AMI-POSTERO-LATERAL	1 (4.5 %)	1 (2.9 %)	2 (3.5 %)	0.040**
TIME OF THROMBOLYSIS INITIATION AFTER ONSET OF PAIN	2.8 ±1.0 h	3.0 ±1.0 h	2.7 ±1.6 h	0.130**
TIME OF CORONAROGRAPHY	13.5 ±1.6 days	10.0 ±1.5 days	12.0 ±8.0 days	0.040**
TIMI-0	1 (5.8 %)	0	1 (2.5 %)	0.050**
TIMI-I	1 (5.8 %)	1 (4.3 %)	2 (5 %)	0.050**
TIMI-II	3 (18 %)	1 (4.3 %)	4 (10 %)	0.050**
TIMI-III	12 (70 %)	21 (91 %)	33 (82 %)	0.050**

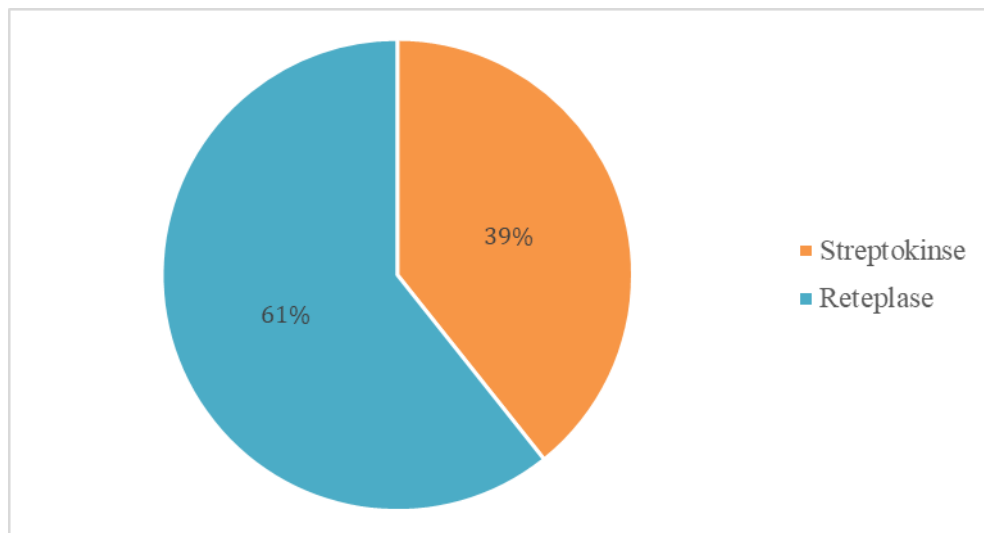


Chart 3: Number of patients treated with different thrombolytic agents

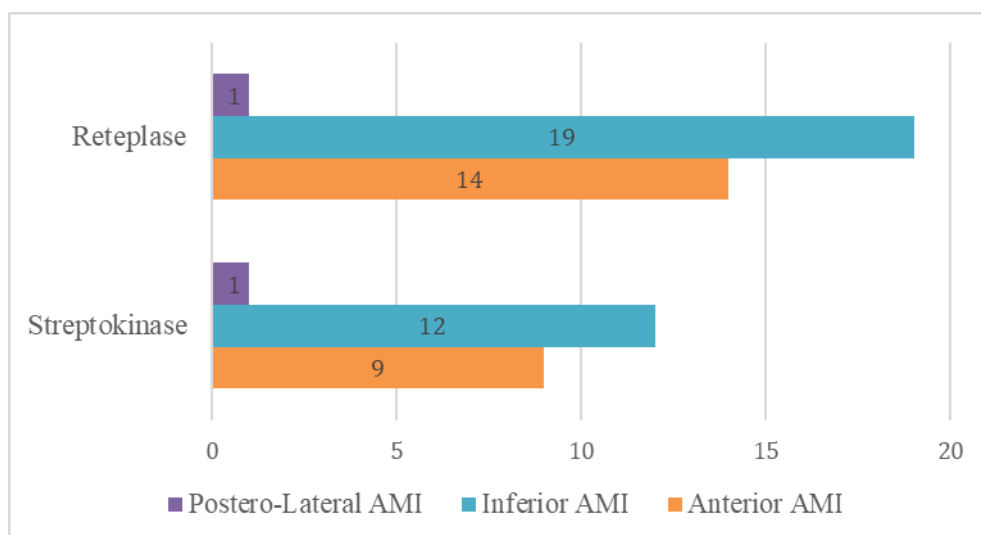


Chart 4: Treatment of choice for AMI of different locations

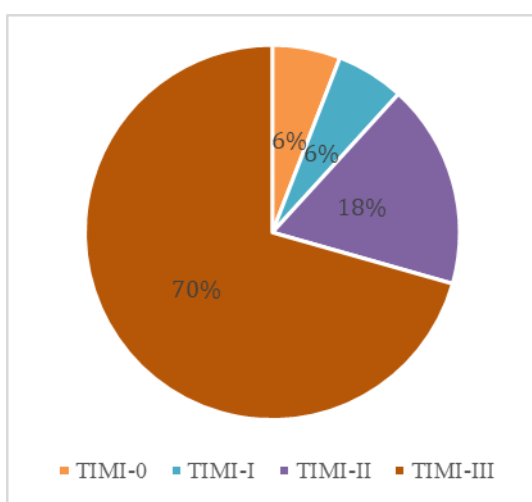


Chart 5: Percentage of TIMI, in patients treated with Streptokinase

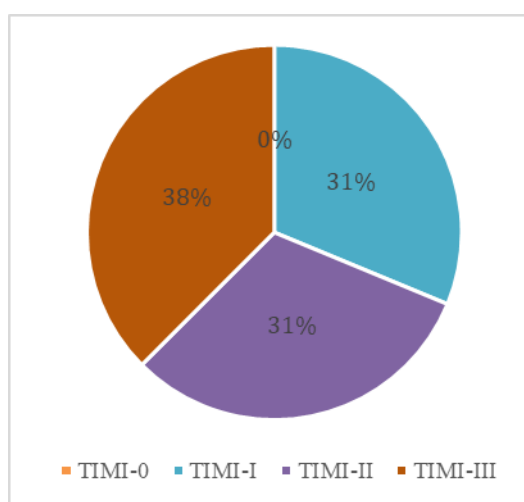


Chart 6: Percentage of TIMI, in patients treated with Reteplase

From the table above it is evident that between groups of patients treated with streptokinase and reteplase there is no significant statistical difference which means that the therapy has very high efficacy whether it is streptokinase or reteplase.

2. Discussion

AMI is manifested because of necrosis of a smaller or larger part of the heart muscle, occurring due to insufficient blood supply. The most common trigger for the onset of AMI is the occlusion of any of the coronary arteries by a blood clot. The arteries supply the heart with oxygen-rich blood so that it contracts and pumps blood to the rest of the body. When the heart muscle is not supplied with the appropriate necessary amount of oxygen, its function decreases. How can we identify and what are the forms of AMI manifestation? Generally, the symptoms of AMI are chest pain which also radiates towards the forearm accompanied by dyspnea, profuse or excessive diaphoresis and vomiting. Chest pain can be described as tightness, heaviness, pressure, or as typical pain. Some patients, however, do not have these typical signs. This study presents the current treatment of patients with STEMI at University Clinical Hospital of Tirana

and does not aim to compare thrombolytic agents, but to evaluate by coronary angiography the effectiveness of thrombolysis and the impact of predisposing factors on mortality in patients with STEMI who undergo thrombolysis with streptokinase or with reteplase by random choice. Reteplase is known to be more successful than streptokinase in terms of the percentage of coronary artery opened in 90 minutes (75 % vs. 90 %). (Data from Armstrong PW, et al.: D, Fibrinolysis for acute myocardial infarction: Current status and new horizons for pharmacological reperfusion, part 1. *Circulation* 103:2862,2001). The result achieved in our clinical experience regarding TIMI grade 3 flow is reteplase 91 % vs. 70% streptokinase, and the total for both groups combined is 82%. The reason why TIMI grade 3 flow differs greatly from the above is due to the fact of delayed coronary angiography where the average for the whole group is 11.89 ± 9.05 days, because as the days pass there is a probability of spontaneous opening of the specific coronary vessel and including treatment with aspirin and clopidogrel. Mortality is 6.9% (different thrombolysis studies show different results such as 6.5 % - 7.5 %). These deaths were observed only in the group with reteplase and this may be due to two reasons:

1. The number of cases in the study is very small,
2. The group of patients treated with reteplase compared to the group of patients randomly treated with streptokinase has a significantly higher percentage of precursor parameters for mortality in patients STEMI patients treated with thrombolysis. Thus, parameters such as age, sex, DM type II, TIMI (which includes parameters such as age, systolic BP, heart rate, Killip class II-IV, anterior STEMI, left bundle branch block, DM and/or HTA and/or residual angina, body mass, time until onset of a treatment since the time of presentation of the patient), are significantly higher in the group treated with reteplase. This conclusion reiterates the known facts regarding age, gender, DM type II, and high BP as the highest risk group for death in STEMI. There is also a significant correlation between the status of the patient on presentation (TIMI risk score) and mortality in patients who have undergone thrombolysis. Related to what we have discussed above in our study all three deaths were also Insulin-Dependent Diabetes Mellitus positive patients. Two patients suffered AMI of the inferior wall and one patient with anterior AMI. The prevalence of DM type II in total is 33.9%, of which in the group treated with reteplase was 41% whereas in the streptokinase group it was 22%. Concerning the hemorrhagic complications associated with the treatment of thrombolysis, there were 6 complications in total, of which two were minor complications in the group of streptokinase (bleeding from gums) and 4 complications in the group of reteplase of which one was major (needed blood transfusion).

3. Conclusion

Thrombolysis of patients presenting with STEMI. presents an effective recanalizing alternative when the patient presents within the first hour of the onset of symptoms, this is assessed by TIMI-based coronary angiography. Mortality in thrombolysis is associated with comorbidities such as age, gender, DM, high BP, sedentary lifestyle, stress, adiposity, and time to presentation in a hospital. In the end, we can suggest that treatment of AMI with thrombolysis or coronarography-assisted angioplasty since the early phases of the disease must be the main postulate of vascular cardiology.

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