Effectiveness of t-PA in Patients with Acute Myocardial Infarction

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الخلاصة

خلفيـة الموضـوع: ان العـلاج بمحلـلات الخثـرة وباسـتخدام منشـط البلازمينـوجين النسـيجي قـد أحـدث ثـورة فـي عـلاج احتشـاء العضـلة القلبيـة الحـاد. حيـث ان الكثيـر مـن مؤشـرات الفعاليـة والأمـان حثـت البـاحثين لتقيـيم نسـبة تلـك المؤشرات.

الاهـداف: غايـة الدراسـة هـي تقـيم الأجابـة عنـد مرضـى أحتشـاء العضـلة القلبيـة الحـاد لمنشـط البلازمنـوجين مـن خـلال حسـاب نسـبة الانحسـار فـي مقطـع الـ(ST) المرتفـع خـلال (90) دقيقـة، تحسـن ألـم الصـدر وحـدوث لا نظميـة ال(AIVR) او اجابة موجبة لجميع المؤشرات المختارة.

الطـرق والمرضـى: هـذه دراسـة ملاحظـة اشـتملت علـى (62) مريضـا مصـابين باحتشـاء العضـلة القلبيـة الحـاد والـذين عولجـوا بمنشـط البلازمنـوجين (الالتبليـز) وريـديا كعـلاج مـذيب للخثـرة حيـث تـم اختيـارهم مـن الـذين تـم ادخـالهم لوحـدة انعاشـس القلـب فـي مستشـفى الديوانيـة التعليمـي للفتـرة مـن الاول مـن اذار 2014 ولغايـة 31 آب 2015 علمـا ان انحسـار مقطـع الـ(ST) المرتفـع قـد عـرف بانـه اختـزال لأرتفـاع المقطـع بنسـبة (50%) او اكثـر فـي غضـون (90) دقيقـة بعـد بدايـة العـلاج بمثـبط البلازمنـوجين وتحسـن ألـم الصـدر أعتمـادا علـى تقيـيم الـريض و حدوث لا نظمية ال(AIVR) او اجابة موجبة للثلاثة مؤشرات المختارة وفي نفس الوقت.

النتـائج: اوضـحت الدراسـة بـأن (59.6%) مـن المرضـى قـد انحسـر لـديهم مقطـع الـ(ST) المرتفـع و(56.4%) مـنهم قـد تحسـن لـديهم الـم الصـدر، لانظميـة ال(AIVR) بنسـبة 30.6%والأجابـة الموجبـةلجميع المؤشـرات كانـت 9.6%. 45.1% مـن المرضـى كـان لـديهم أنحسـار فـي مقطـع الـ(ST) المرتفـع، 30.6%مـن المرضـى تحسـن لـديهم ألـم الصـدر، 22.5% مـن المرضـى حـدثت لـديهم لانظميـة ال(AIVR) و9.6% مـن المرضـى كانـت لـديهم أجابـة موجبـة لجميـع الم}شـرات المختـارة وبـنفس الوقـت، علمـا ان جميـع هـؤلاء المرضـى كانـت أعمـارهم أقـل مـن 60 سـنة، (P.value هـي أقـل مـن 0.05). 61.3% مـن المرضـى امـا بـدينين او لـديهم زيـادة فـي الـوزن و 38.7% مـن المرضـى لـديهم دليـل كتلـة جسـم طبيعـي. المـدخنون كـان لـديهم أنحسـار فـي مقطـع الـ(ST) المرتفـع بنسـبة 41.3% مـن المرضـى، 38.7% مـنهم كـان لـديهم تحسـن فـي ألأم الصـدر، لا نظميـة ال(AIVR) حـدثت بنسـبة 16.12% مـن المرضـى وأجابـة موجبـة لجميـع المؤشـرات المختـارة بنسـبة 8.06% مـن المرضـى، (P.valueهـي أقـل مـن 0.05). 1.61% مـن المرضـى كـان لـديهم أنحسـار فـي مقطـع الـ(ST) المرتفـع و11.29% من المرضى كان لديهم تحسن في ألم الصدر عند أستخدام الأرواء في وقت أكثر من 6 ساعات.

الاسـتنتاجات: اشـرت هـذه الدراسـة بـأن زيـادة العمـر، السـمنة، داء السـكري والتـأخر فـي الوصـول الـى المستشـفى بعـد بدايـة الـم القصـور الـدموي (يعنـي وقـت اطـول لبدايـة اعـادة الافعـام) مـن الممكـن اعتبـارهم كمؤشـرات لأسـتجابة ضـعيفة لمنشـط البلازمنـوجين بـين المرضـى المصـابين بأحتشـاء العضـلة القلبيـة الحـاد. لايوجـد تـأثير لـدليل كتلـة الجسـم علـى الأسـتجابة لمنشـط البلازمنـوجين. المرضـى المـدخنون كانـت لـديهم أسـتجابة جيـدة لمنشـط البلازمنوجين.

Abstract

Tissue plasminogen activator (t-PA) had improve the treatment of ST elevation myocardial infarction (STEMI). The aims considered assessment the response of patients with STEMI to t-PA (Alteplase) infusion by estimate the frequency of selected parameters. This is study that included 62 patients with STEMI who had been treated with t-PA infusion as a thrombolytic therapy. They had been selected from those who had been admitted to the Coronary Care Unit at Al-Diwaniya Teaching Hospital, Diwaniya city, Iraq during the period between 1st of March 2014 to the 31st of August 2015. Specific selected parameters used to assess effectiveness of t-PA. Parameters including: resolution of ST segment elevation (reduction in the ST elevation ≥ 50%), relieve of chest pain, occurrence of accelerated idioventricular rhythm (AIVR) and positive response for three parameters (simultaneously), observe within 90 minutes after t-PA infusion. After t-PA infusion, 59.6% of the patients had resolution of ST segment elevation, 56.4% getting relieve of chest pain, AIVR occur in 30.6% and positive response of all parameters in 9.6%. Patients less than 60 years old age constitutes 45.1% of patients who had ST segment resolution, 30.6% of patients who had relieve of chest pain,

patients with AIVR in 22.5%, and patients with positive response of all three parameters in 9.6%, (significant p.value). Smokers patients getting ST segment resolution in 41.3% of patients, relieve of chest pain in 38.7%, AIVR in 16.12% and positive response for all selected parameters in 8.06% of patients, (significant p.value). 1.61% of patients with ST segment resolution and 11.29% of patients with relieve of chest pain seen with time to perfusion more than 6 hours. This study indicated that increasing age, obesity, diabetes mellitus (DM), and delay in reaching hospital after onset of ischemic chest pain considered as predictors for poor response to t-PA infusion among patients with STEMI. BMI has no significant consideration but smokers patients had been associated with better response to t-PA.

Introduction

The management of the patient with STEMI has been revolutionized by the development of modalities to reestablish blood flow in the occluded culprit coronary artery, specifically thrombolytic therapy and percutaneous revascularization[1]. Thrombolysis, defined as the dissolution of thrombus or, more specifically, the breakdown of fibrin (fibrinolysis), is a critical component of normal hemostasis. At the present time, thrombolytic agents are used most often in the early treatment of STEMI[2].

Plasminogen converted by t-PA to plasmin which is a serine protease with trypsin-like activity. It attacks fibrin at two principal sites, thrombolytic agents include first generation non fibrin-specific Streptokinase, second generation fibrin specific t-PA (Alteplase), third generation fibrin-specific Tinikteplase and Reteplase [3].

Recombinant t-PA is a naturally occurring enzyme (serine protease) produced by a number of tissues including endothelial cells [4]. The high affinity of t-PA for plasminogen in the presence of fibrin thus allows efficient activation on the fibrin clot, while no efficient plasminogen activation by t-PA occurs in plasma [5]. In contrast to streptokinase, t-PA (short half-life, 3-4 minutes) results in less fibrinogen depletion and it is not associated with allergic or hypotensive effects. Intravenous heparin (for at least 24 hours) is generally required as concomitant therapy to maintain vessel patency and to prevent reocclusion[6].

Several different dosing regimens have been designed for t-PA, but accelerated or "front loaded" regimen is currently most popular and appears to be superior to streptokinase as shown in the GUSTO trial (Global Utilization of Streptokinase or t-PA for Occluded Coronary Arteries) [7]. This regimen consists of a 15 mg intravenous bolus followed by 0.5 mg/kg (up to 50 mg) over the next 30 minutes and then by 0.5 mg/kg (up to 35 mg) over the following 60 minutes. The total dose is 100 mg over 90 minutes and should not exceeding this because it has been associated with an increase in intracranial hemorrhage[7].

There is a limited experience with readministration of t-PA, although there is no clinical relevant antibody formation has been reported after adminstration[8].

All currently available thrombolytic agents reduce mortality in acute STEMI[9].

Several markers had been selected as predictors for effectiveness of thrombolytic therapy[10]. These markers include:

1. TIMI flow:
2. TIMI frame count:
3. TIMI myocardial perfusion grade from (0 to3)
4. Biochemical markers : particularly CK-MB and troponin T
5. Presence of Q-wave or T-wave inversion on the presenting ECG is associated with a poorer result from thrombolysis.
6. Infarct size: by assessing global left ventricular function or ejection fraction, end systolic volume, regional wall motion, creatine kinase release, thallium infarct size, and QRS score based on evolutionary ST segment and T-wave change[s]
7. Reperfusion arrhythmias: an additional marker of successful reperfusion after thrombolytic (or mechanical) therapy is the development of "reperfusion arrhythmias". Such arrhythmias include AIVR, ventricular

tachycardia, and ventricular fibrillation. AIVR generally require close observation without pharmacologic management[11].

Risks of thrombolytic therapy particularly t-PA carry two major risks, including bleeding and hemorrhagic stroke. Bleeding divided into two types, superficial bleeding (from puncture or damaged blood vessels) and internal bleeding (into central nervous system, gastrointestinal tract, urogenital tract, retroperitoneal or bleeding into paranchymatous organs). The risk of moderate or severe bleeding appears to be greater in women than men with STEMI[12]. The most common site for spontaneous bleeding was the gastrointestinal tract. The risk of hemorrhage may be increased with the use of oral anticoagulant, platelets aggregation inhibitors, heparin and other agents influencing coagulation [12].

Hemorrhagic Stroke found in 1.4%, which is fatal in 41% and produced moderate or severe disability in 31% [13]. Risk factors include previous transient ischemic attack or stroke, older age, weight less than 70 kg, blood pressure above 170/95, and aggressive intravenous heparinization, and t-PA dose above 1.5 mg/kg [14]. Rarely t–PA may cause nausea, vomiting, drop in blood pressure and increase in temperature have been reported also, but these effects can also occur as concomitant symptom of acute myocardial infarction (AMI). In rare cases, anaphylactoid reaction (urticaria, bronchspasm) had been reported. There is very limited experience with the usage during pregnancy (although it has relative contraindication) and lactation [15].

Resolution of chest pain is an inaccurate measure of reperfusion, because the pain may be blunted by narcotic analgesia or the partial denervation that is known to occur among some patients with AMI. Serial assessment of 12-lead ECGs is a more reliable indicator of reperfusion, although it is also suboptimal. AIVR is fairly specific for reperfusion, but arrhythmias other than AIVRs are not reliable indicators because a variety of ventricular and supraventricular arrhythn1ias may be observed in patients with nonreperfused infarction-related artery. The complete resolution of chest pain and electrocardiographic changes, accompanied by a run of AIVR, is highly specific for successful reperfusion [16].

Aims of the study:

This study had been designed to:

1. Estimate the frequency of resolution of ST segment elevation, relieve from chest pain, and occurrence of AIVR as markers for effectiveness of t-PA.
2. Evaluate the effect of different demographic features and the time period between the onset of symptoms to the time of reperfusion therapy on the frequency of specific selected parameters.

Patients and methods:

This is an observational study, enrolled 85 patients with STEMI, were admitted to the Coronary Care Unit at Al-Diwanyia Teaching Hospital during the period between 1st of March 2014 to the 31st of August 2015. 23 patients were excluded for different causes (10 patients refuse participation and 13 patients cannot tolerate chest pain without using analgesia). 62 patients were included in this study. All patients received the standard t-PA infusion regimen (without using analgesia) subjected to thorough history taking and physical examination (patient`s height in meters and weight in Kg were recorded with body mass index, BMI). Three important parameters used to assess the response for t-PA infusion including ≥ 50% resolution of ST segment elevation compared to the baseline ECG at the time of diagnosis, relieve of chest pain (patient`s self assessment), occurrence of AIVR and positive response for all selected parameters (simultaneously) within 90 minutes post infusion.

Hyperlipidemia define as patients with positive history or lipid profile done within first day after AMI after fasting (for at least 12 hours) showing increase lipid levels.

Collected data had been summarized and arranged in tables in form of number and frequency (percentage). All of the patients included in this study were normotensive at time of thrombolysis with blood pressure

range of 110-150/ 60-80 mmHg. Statistical analysis had been done using chi-square test. P-value less than 0.05 had statistical significance. The consents of the patients and the official requirement were taken.

Results:

This an observational study had enrolled 62 patients with AMI, whose age ranged between 30-75 year old (53.45 ± 10.47 year old). 37 patients (59.7%) were younger than 60 years old. Regarding gender of patients who had been included in this study, male patients comprised 39 (62.9%) and female patients were 23 (37.1%), creating a male to female ratio of 1.7:1 as shown in table 1.

After administration of t-PA infusion, 37 patients (59.6%) had resolution of ST segment elevation post infusion, 35 patients (56.4%) felt relieve of chest pain, 19 patients had AIVR (30.6 %) and 6 patients (9.6%) had positive response for all parameters as shown in table 2. In males, 25 patients (40.3%) had ST segment resolution, 22 patients (35.5%) felt relieve of chest pain, AIVR occur in 15 patients (24.1%), and all parameter have positive response in 4 patients (6.4%). Otherwise in females, 12 patients (19.3%) had ST segment resolution, 13 patients (20.9%) felt relieve of chest pain, AIVR occur in 4 patients (6.4%), and all parameter have positive response in 2 patients (3.2%), as shown in table 2.

28 patients (45.1%) younger than 60 year had ST segment resolution. 19 patients (30.6%) had relieve of chest pain, AIVR occur in 14 patients (22.5%), and all parameters have positive response in 6 patients (9.6%), as shown in table 3 , p.value < 0.05.

Table 4 showing that 38 patients (61.3%) either obese or overweight and only 24 patients (38.7%) had normal BMI or even underweight. In patients with normal BMI or even underweight, 14 patients (22.5%) had ST segment resolution, 18 patients (29%) had relieve of chest pain, 14 patients (22.5%) had occurrence of AIVR and 4 patients (6.4%) had positive response for all parameters, p.value is 0.7,

As in table 5, our study revealed that hypertension (HT) was the commonest risk factor for developing AMI in this patients` sample, 32 patients (51.61%) were hypertensive, followed in frequency by 31 smokers patients (50%), 25 patients with hyperlipidemia (40.32%), 22 patients with previous history of ischemic heart disease, H_x of IHD (35.48%), 19 patients with positive family history, FH_x of IHD (30.64%)) and 16 patients with DM (25.8%) as shown in table 5. 15 patients (21.1% of patients) had 2 or more risk factors. The percentage of the risk factors for ST segment resolution were as follow: DM (16.12%), HT (20.96%), previous Hx of IHD (22,58%), hyperlipidemia (24.19%), positive FHx of IHD (25.8%), and smoking (41.33%). Chest pain relieve more frequently seen in smokers patients (38,7%), AIVR most commonly occur in smokers patients (16.12%) and combined positive response for all parameters also occur with smoking (8.06%), p.value < 0.05.

Table 6 shows patients' distribution according to their time to perfusion and frequency of selected parameters after t-PA infusion , p.value < 0.05. Patients included in this study spent 30 minutes to 7 hours to reach the hospital after the onset of ischemic chest pain. 54.8% of the sample (34 patients) had reached the hospital within the first 3 hours after the onset of chest pain. 1.61% of patients with ST segment resolution (1 out of 12 patients), and 11.29% of patients with chest pain relieve (7 out of 12 patients) seen with time to perfusion more than 6 hours. On the other hand, 29.03% of patients (18 out of 20 patients) presented to hospital within the first hour from onset of chest pain had resolution of ST segment elevation, and 19.35% of patients (12 out of 20) felt relieve of chest pain, 16.12% of patients (10 out of 20) have occurrence of AIVR, and 8.06% of patients (5 out of 20) have positive response to all parameters.

Table 1. Demographic features of the patients

Age group	Males		Females		Total no.		M:F
	No.	**%**	**No.**	**%**	**No.**	**%**	
30-39y	8	12.9	0	0	8	12.9	-------
40-49y	9	14.5	4	6.5	13	21.0	**2.2:1**
50-59y	9	14.5	7	11.3	16	25.8	**1.2:1**
60-69y	6	9.7	10	16.1	16	25.8	**1:1.6**
70-79y	7	11.3	2	3.2	9	14.5	**3.5:1**
Total	39	62.9	23	37.1	62	100	1.7:1

Table 2. Patient`s distribution according to gender and selected parameters after t-PA infusion

Gender	ST segment resolution		Chest pain relieve		AIVR		All parameters simultaneously	
	No.	%	No.	%	No.	%	No.	%
Males	25	40.3	22	35.5	15	24.19	4	6.4
Females	12	19.3	13	20.9	4	6.45	2	3.2
Total	37	59.6	35	56.4	19	30.6	6	9.6
P.value	0.7							

Table 3. Patients' distribution according to age and frequency of selected parameters after t-PA infusion

Age group	Total		ST segment resolution		Chest pain relieve		AVIR		All parameters simultaneously	
	No.	%	No.	%	No.	%	No.	%	No.	%
30-39y	8	12.9	6	9.67	4	6.45	7	11.29	3	4.83
40-40y	13	21.0	10	16.12	11	17.74	5	8.06	1	1.61
50-59y	16	25.8	12	19.35	4	6.45	2	3.22	2	3.22
60-69y	16	25.8	6	9.67	10	16.12	1	1.61	0	0
70-79y	9	14.5	3	4.83	6	9.67	4	6.45	0	0
Total	62	100	37	59.6	35	56.4	19	30.6	6	9.6
P.value	< 0.05									

Table 4. Patients' distribution according to BMI and frequency of selected parameters after t-PA infusion

BMI		Total		ST segment resolution		Chest pain relieve		AIVR		All parameters simultaneously	
		No.	%	No.	%	No.	%	No.	%	No.	%
Underweight	<20	8	12.9	5	8.06	6	9.67	5	8.06	1	1.61
Normal	20-25	16	25.8	9	14.5	12	19.35	9	14.5	3	4.83
Overweight	26-30	15	24.2	13	20.96	9	14.5	2	3.22	1	1.61
Obese **I**	31-35	9	14.5	6	9.67	4	6.45	2	3.22	0	0

	II	36-40	7	11.3	2	3.22	3	4.83	1	1.61	1	1.61
	III	>40	7	11.3	2	3.22	1	1.61	0	0	0	0
Total			62	100	37	59.6	35	56.4	19	30.6	6	9.6
P.value			0.7									

Table 5. Patients' distribution according to the risk factors and frequency of selected parameters after t-PA infusion

Risk factors	Total		ST segment resolution		Chest pain relieve		AIVR		All parameters simultaneously	
	No.	%	No.	%	No.	%	No.	%	No.	%
Smoking	31	50	26	41.33	24	38.70	10	16.12	5	8.06
DM	16	25.80	10	16.12	1	1.61	1	1.61	0	0
HT	32	51.61	13	20.96	14	22.58	4	6.45	2	3.22
Hyperlipidemia	25	40.32	15	24.19	9	14.51	3	4.83	3	4.83
Positive FH_x of IHD	19	30.64	16	25.80	10	16.12	2	3.22	1	1.61
Previous H_x of IHD	22	35.48	14	22.58	4	6.45	0	0	3	4.83
P.value	< 0.05									

Table 6. Patients' distribution according to (time to perfusion) and frequency of selected parameters after t-PA infusion

	Total		ST segment resolution		Chest pain relieve		AIVR		All parameters simultaneously	
	No.	%	No.	%	No.	%	No.	%	No.	%
<1h	20	32.2	18	29.03	12	19.35	10	16.12	5	8.06
1-3h	14	22.6	8	12.90	10	16.12	7	11.29	1	1.61
3-6h	16	25.8	10	16.12	6	9.67	2	3.22	0	0
>6h	12	19.4	1	1.61	7	11.29	0	0	0	0
Total	62	100	37	59.6	35	56.4	19	30.6	6	9.6
P.value	< 0.05									

Discussion

Thrombolysis by using t-PA is established therapy for AMI and fundamentals of thrombolytic therapy efficacy and safety limitations is the cornerstone in wise decision about who and when can be thrombolysed [17].

This study revealed that 75.7% of those patients with ST segment resolution at 90 minutes after t-PA infusion are younger than 60 year old and 24.3% are older than 60 year old. Furthermore, 54.3% of those patients with relieve of chest pain are younger than 60 year old, and 45.7% are older than 60 year old, with small difference. 73.7% of those patients with AIVR are younger than 60 year old, and 26.3% are older than 60 year old. 100% of patients with positive response to all parameters are younger than 60 year old.

Our study prove that ST segment resolution, occurrence of AIVR, and positive response to all selected parameters (9.6%) after t-PA infusion are more commonly seen in younger patients than 60 year old although there is no much difference in age group regarding relieve of chest pain and this can explained by autonomic disturbances that can occur in elderly patients inaddition to co-morbidity or

due to partial denervation that is known to occur among some patients with AMI.

The complete resolution of chest pain and electrocardiographic changes, accompanied by a run of AIVR, is highly specific for successful reperfusion, but it occurs in < 10% of patients receiving thrombolytic therapy as report by Brian P. and et al [18].

Theimann et al conclusion suggested that elderly patients have nothing to gain from thrombolysis, indeed they may be harmed [19]. Age appears not to affect any fundamental way the pathology of the culprit lesion of AMI. However, the extent of associated disease in the coronary arteries is likely to be greater and co-morbid conditions are common . Therefore, in the elderly only those with early presentation and clear cut new ST segment elevation, especially if in the anterior leads or new bundle branch block, should be thrombolysed [17].

61.3% of the patients who had been enrolled in this study were either obese or overweight. In this study, ST segment resolution mostly occur in overweight patients (20.96%), relieve of chest pain (19.35%), AIVR (14.5%), and positive response to all parameters (4.83%) occur mostly in patients with normal BMI but with no significance, although obese patient represent 37.1% of total patients, and the study not considered the absolute rate of patients with AMI that admitted to the coronary care unit.

Many studies have demonstrated a linear, longitudinal relationship between obesity and incidence of coronary heart disease [20]. As an example, the Munster Heart Study (PROCAM) followed 16,288 men and 7325 women for up to seven years [21]. There was a graded positive relationship between BMI and other coronary heart disease risk factors including age, total serum cholesterol, low density lipoprotein holesterol, and systolic and diastolic blood pressure [22].

This study indicated that diabetic patients are at higher risk of having persistent ST segment elevation and the resolution represent 16.12% of all patients, relieve of chest pain is 1.61%, AIVR occur in 1.61% of total patients and no recorded case for positive response of all selected parameters in diabetics.

DM is a risk factor for coronary artery disease and is associated with an increased mortality in the setting of an AMI. The GUSTO-I reported the results on almost 41,000 patients, 15 percent of whom were diabetic[23]. Despite a similar response to thrombolysis, the diabetic patients had a significantly higher mortality rate at 30 days (11.3 versus 5.9 percent) and one year (14.5 versus 8.9 percent) than nondiabetic patients[23].

Surprisingly, this study revealed that smokers patients who had been included in this study had high percentages of resolution of ST segment elevation at 90 minutes, relieve of chest pain, occurrence of AIVR, and positive response to all selected parameters. Despite the important role of cigarette smoking in the development of atherosclerosis, several studies have reported that smokers who receive a thrombolytic agent for an AMI have a better outcome than non-smokers [24]. This difference in outcome may be explained by the following factors:

- Smoker patients have a better risk profile than non smokers, particularly their tendency to be significantly younger [25].
- Qualitative angiographic analysis suggests that the mechanism of infarction in smoker patients are more often have thrombosis of a less critical atherosclerotic lesion compared with non smokers [25]. More active thombogenic mechanisms may be operative in smoker patients, leading to larger thrombus component that is more susceptible to thrombolytic therapy. This may explain that smoker patients have a higher patency rate and are more likely to have TIMI III flow in the infarct artery after thrombolysis than non-smokers [26].
- Smoker patients have variety of signs of a hypercoagulable state that may be responsive to pharmacologic intervention. These include increases in hematocrit and baseline plasma fibrinogen[25], enhanced platelets

thrombus formation, and reduced local fibrinolytic activity[26].

The earlier that fibrinolytic therapy is started after the onset of symptoms, the greater the benefit and greater degree of myocardial salvage that can be achieved. Thus the benefit is greater when t-PA agent is administered within the first four hours after the onset of symptoms[27], particularly within the first 70 minutes (the golden hour).

This study revealed that all the patients, who had reached the hospital within the first hour from the onset of their chest pain (32.2% of the patients), had resolution of ST segment (29.03%), felt relief of chest pain (19.35%), AIVR (16.12%), and positive response to all selected parameters (8.06%). While patients who had reached more than 6 hour had resolution of ST segment (1.61%), and felt relief of chest pain (11.29%) with no AIVR or positive response to all selected parameters.

It has been estimated that an approximate 1% reduction in mortality occurs for each hour of time saved within the first six hours [28].

References:

1. Awtry EH, Loscalzo J. Coronary heart disease. In: Andreoli TE, Carpenter CCJ, Griggs RC, Loscalzo J, eds. Cecil essentials of medicine. Philadelphia: W.B. Saunders company. 2010, 79-99.
2. Anderson, HV, Willerson, JT. Thrombolysis in acute myocardial infarction. N Engl J Med 2009; 329:703.
3. Robbins, KC, Summaria, L, Hsieh, B, et al. The peptide chains of human plasmin. Mechanism of activation of human plasminogen to plasmin. J Biol Chem 2005; 242:2333.
4. Anderson, HV, Willerson, JT. Thrombolysis in acute myocardial infarction. N Engl J Med 2006; 329:703.
5. van Zonneveld, AJ, Veerman, H, Pannekoek, H. Autonomous functions of structural domains on human tissue-type plasminogen activator. Proc Natl Acad Sci U S A 2009; 83:4670.
6. Califf, RM, White, HD, Van de Werk, F, et al for the GUSTO-I Investigators. One-year results from the Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries (GUSTO-I) Trial. Circulation 2008; 94:1233.
7. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. The GUSTO investigators. N Engl J Med 1993; 329:673.
8. The GUSTO Investigators. The effects of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival after acute myocardial infarction. N Engl J Med 1993; 329:1615.
9. Holmes, DR Jr, Califf, RM, Topol, EJ. Lessons we have learned from the GUSTO trial. J Am Coll Cardiol 2009; 25(Suppl):10S.
10. Adler, Y, Zafrir, N, Ben-Gal, T, et al. Relation between evolutionary ST segment and T-wave direction and electrocardiographic prediction of mycardial infarct size and left ventricular function among patients with anterior wall q-wave acute myocardial infarction who received reperfusion therapy. Am J Cardiol 2002; 85:927.
11. Berger, PB, Ruocco, NA, Ryan, TJ, Frederick, MM, Podrid, PJ. Incidence and significance of ventricular tachycardia and fibrillation in the absence of hypotension or heart failure in acute myocardial infarction treated with recombinant tissue-type plasminogen activator: results from the Thrombolysis in Myocardial Infarction (TIMI) Phase II trial. J Am Coll Cardiol 2008; 22:1773.
12. Hochman, JS, Tamis, JE, Thompson, TD, et al. Sex, clinical presentation, and outcome in patients with acute coronary syndromes. Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators [see comments]. N Engl J Med 2009; 341:226.
13. Gore, JM, Granger, CB, Simoons, ML, et al for the GUSTO-I Investigators. Stroke after thrombolysis: mortality and functional outcomes in the GUSTO-I trial. Circulation 2003; 92:2811.
14. Barron, HV, Rundle, AC, Gore, JM, et al. Intracranial hemorrhage rates and effect of immediate beta-blocker use in patients with acute myocardial infarction treated with tissue plasminogen activator. Participants in the National Registry of Myocardial Infarction-2. Am J Cardiol 2009; 85:294.
15. Muller, DWM, Topol, EJ. Selection of patients with acute myocardial infarction for thrombolytic therapy. Ann Intern Med 2010; 113:949.
16. Hennekens, CH, O'Donnell, CJ, Ridker, PM, Marder, VJ. Current issues concerning thrombolytic therapy for acute myocardial infarction. J Am Coll Cardiol 2011; 25(Suppl):18S.
17. Ball SG. Thormbolysis: too old and too young. Heart 2002; 87(4): 312-3.
18. Brian P. Griffin; manual of cardiovasculare medicine/editor, edition 4th , section I, ischemic

heart disease, part one, acute myocardial infarction,24; 2013.

19. Theimann DR, Coresh J, Schulman SP, et al. Lack of benefit for intravenous thrombolysis in patients with myocardial infarction who are older than 75 years. Circulation 2012; 101: 2239-46
20. 7th Bethesda Conference. Matching the Intensity of Risk Factor Management with the Hazard for Coronary Disease Events. September 14-15. Am Coll Cardiol 2014; 27:957.
21. Muller, DWM, Topol, EJ. Selection of patients with acute myocardial infarction for thrombolytic therapy. Ann Intern Med 2015; 113:949.
22. Schulte, H, Cullen, P, Assmann, G. Obesity, mortality and cardiovascular disease in the Munster Heart Study (PROCAM). Atherosclerosis 2010; 144:199
23. Mak, KH, Moliterno, DJ, Granger, CB, et al for the GUSTO-I Investigators. Influence of diabetes mellitus on clinical outcome in the thrombolytic era of acute myocardial infarction. J Am Coll Cardiol 1997; 30:171.
24. Barbash, GI, White, HD, Modan, M, et al. Significance of smoking in patients receiving thrombolytic therapy for acute myocardial infarction. Experience gleaned from the International Tissue Plasminogen Activator/Streptokinase Mortality Trial. Circulation 2009; 87:53.
25. Grines, CL, Topol, EJ, O'Neill, WW, et al. Effect of cigarette smoking on outcome after thrombolytic therapy for myocardial infarction. Circulation 2007; 91:298.
26. Newby, DE, McLeod, AL, Uren, NG, et al. Impaired coronary tissue plasminogen activator release is associated with coronary atherosclerosis and cigarette smoking: Direct link between endothelial dysfunction and atherothrombosis. Circulation 2009; 103:19.36
27. Chesebro, JH, Knatterud, G, Roberts, R, et al. Thrombolysis in myocardial infarction (TIMI) trial, phase I: A comparison between intravenous tissue plasminogen activator and streptokinase. Circulation 2006; 76:142.
28. Weaver, WD, Cerqueira, M, Hallstrom, AP, et al. Prehospital-initiated vs. hospital-initiated thrombolytic therapy: The Myocardial Infarction Triage and Intervention Trial. JAMA 2010; 270:1211.