Thrombolytic therapy and indirect reperfusion signs in ST segment elevation myocardial infarction

دراسة علاج مذيب الخثرة والعلامات الغير مباشرة لإعادة الإرواء للشرايين القلبية في احتشاء العضلة القلبية المصاحب لارتفاع قطعة أس- تي

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Key words: Thrombolytic therapy, reperfusion signs, myocardial infarction

ABSTRACT

OBJECTIVE: To study the value of some indirect reperfusion signs as markers of coronary artery patency in patients with acute myocardial infarction submitted for intravenous thrombolytic therapy.

DESIGN: A cross sectional study, with analysis of the predictive value (PV) of four indirect reperfusion signs (IRS): 1-chest Pain 2-ST segment resolution in the first three hours; 2. Peak CK in 4-6 hours; 3. Cardiac arrhythmia in the first three hours.post thrombolytic therapy

SETTING: Coronary Care Unit of the AL-Mawani Hospital in Basrah(south of Iraq)

Methods : 200 Patients with ST segment elevation myocardial infarction (STEMI) were studied between June 2009 and August 2010, their ages ranged between 38-74 year(mean age 53.4+/-10.6 years) 156 males and 44females , 122 with anterior infarction and 78 with inferior infarction. All patients received Intravenous thrombolytic agent, followed by oral 300 mg acetilsalicylic acid, and IV heparin therapy with continuous electrocardiographic monitoring. The indirect reperfusion signs were recorded which include ST segment reduction by 50% or more recorded at the start and 30, 60,90 minutes and 3 hours of thrombolytic therapy , reperfusion arrhythmia ,elevation of Cardiac enzyme the relief of chest pain ,

RESULTS: The response to thrombolytic therapy in STEMI was much better as the patients received the therapy in the early periods (0-6 hours) than the later periods (more than 6 hours). One or more of the IRS were present in 156(78%) patients with STEMI; the relieve of chest pain and ECG ST segment decrement in elevation were more frequent than elevation of cardiac enzymes and reperfusion arrhythmia . there was no difference in response to thrombolytic therapy with regard to location of myocardial infarction whether anterior or inferior .

CONCLUSIONS: patients with STEMI should receive thrombolytic therapy as early as possible in order to get better reperfusion to save the myocardium. The analysis of IRS are useful to assess the successful of thrombolytic therapy especially in areas where the coronary angiography is not available.

الخلاصة

تم دراسة قيمة العلامات الغير مباشرة لإعادة الإرواء كعلامة لانفتاح الشرايين القلبية في المرضى الذين يعانون من أحتشاء العضلة القلبية بعد الحقن الوريدي للادوية المذيبة للتخثر، حيث تم دراسة مائتان مريض يعانون من احتشاء العضلة القلبية المصاحب لارتفاع قطعة أس-تي مع تحديد العلامات الغير مباشرة لإعادة الإرواء لكل مريض والتي تشمل الام الصدر، أنخفاض قطعة أس-تي في الساعات الثلاث بعد العلاج، ارتفاع نسبة انزايم القلب سي-كي في الثلاث عشر ساعة بعد العلاج و عدم انتظام ضربات القلب في الساعات الثلاث بعد العلاج. جميع المرضى كانوا يرقدون في انعاش القلب لمستشفى الموانئ العام في البصرة جنوب العراق.

تمت الدراسة للفترة من حزيران 2009 ولغاية آب 2010 ، تتراوح أعمار المرضى بين 38-74 ، 156 من الذكور و 44 من الاناث، 122 يعانون من أحتشاء العضلة القلبية الامامية و 78 من السفلية. كل المرضى استلموا العقار المذيب الخثرة مع الادوية المساعدة الضرورية. العلامات الغير مباشرة لإعادة الإرواء للشرايين القلبية سجلت أيجابا أو سلبا لكل مريض.

أظهرت النتائج ان الاستجابة لمذيبات الخثرة كانت افضل عند المرضى اللذين وصلوا مبكرا الى المستشفى ، حيث أن واحد أو أكثر من العلامات الاروائية كانت موجودة في 156 مريض وخاصة أختفاء الام الصدر و تحسن تخطيط القلب أكثر من العوامل الاخرى.

Introduction

Acute myocardial infarction (AMI) is caused by blockage of a coronary artery by a thrombus or clot (rupture of an atherosclerotic plaque).(1,2) .Thrombolytic drugs break down the thrombus so that the blood flow to the heart muscle can be restored to prevent further damage and assist healing. Thrombolytic therapy(TT) can reduce the relative risk of in-hospital death by up to 50% when administered within the first hour of the onset of symptoms of AMI, and much of this benefit is maintained for at least 10 years.(2,3,4). Appropriately used thrombolytic therapy appears to reduce infarct size, limit left ventricular dysfunction, and reduce the incidence of serious complications such as septal rupture, cardiogenic shock, and malignant ventricular arrhythmias (5,6). Since myocardium can be salvaged only before it has been irreversibly injured, the timing of reperfusion therapy, by thrombolysis or a catheter-based approach, is of extreme importance in achieving maximum benefit (7,8,9). While the upper time limit depends on specific factors in individual patients, it is clear that "every minute counts" and that patients treated within 1 to 3 h of the onset of symptoms generally benefit most. The median "door-to-needle time" - the delay between hospital admission and injection in most hospitals is in the range of 30 to 90 minutes (9,10,11). Although reduction of the mortality rate is more modest, the therapy remains of benefit for many patients seen 3 to 6 h after the onset of infarction, and some benefit appears to be possible up to 12 h, especially if chest discomfort is still present and ST segments remain elevated in electrocardiographic (ECG) leads that do not yet demonstrate new Q waves (12,13,14). In addition to the possibility of early treatment, clinical factors that favor proceeding with thrombolytic therapy include anterior wall injury, hemodynamically complicated infarction, and widespread ECG evidence of myocardial jeopardy. Although patients (younger than 65 years) achieve a greater relative reduction in the mortality rate than elderly patients, the higher *absolute* mortality rate (15 to 25%) in elderly patients results in similar absolute reductions in the mortality rates for both age groups(15,16).Intriguing data are accumulating to indicate that improved ventricular function and reduced mortality may also be achieved by *late coronary reperfusion*. The benefits of late reperfusion cannot be attributed to a reduction of infarct size but appear to result from improvement of tissue healing in the infarct zone with prevention of infarct expansion, enhancement of collateral flow, improvement of myocardial contractile performance, and reduction in the tendency to electrical instability(17,18,19). In addition, *hibernating myocardium* (i.e., poorly contractile myocardium in a zone that is supplied by a stenotic infarct-related coronary artery with slow antegrade perfusion), can benefit from reperfusion by improving the myocardial contraction and cardiac performance (20,21)

Coronary angiography remains the "gold standard" for assessment of coronary patency. However, because it is associated with high cost, limited availability, and increased morbidity when performed acutely, this invasive procedure is not practical or prudent for all patients receiving TT, accordingly patency can be assessed by indirect reperfusion signs . (22,23).

The aims of this study to asses the values of some indirect reperfusion signs as markers of coronary artery patency in patients with acute myocardial infarction submitted for intravenous thrombolytic therapy.

Methods :

This study was a cross-sectional performed in CCU of al-mawanee hospital in Basrah ,south of Iraq. 200 Patients with acute ST segment elevation myocardial infarction(STEMI) who were hospitalized in the CCU between June 2009 and August 2010 were studied.The patients were classified according to age group (young group less than 45 years, middle aged group between 45—65 years and elderly aged group more than 65 years), to the location of STEMI anterior(including anterior,septal and lateral MI) and inferior MI,and to the time of arrival to the hospital from the start of chest pain, within 3 hours, 3—6 hours, 6—12 hours and more than 12 hours of chest pain. All patients treated with thrombolytic therapy (Alteplase) was given over 90 minutes (bolus dose of 15 mg, followed by 0.75 mg/kg body weight , but not exceeding 50 mg, over 30 minutes and then 0.5 mg /kg body weight, but not exceeding 35 mg, over 60 minutes. concomitant therapy in the form of oral 300 mg acetylsalicylic acid, and IV heparin therapy were also given . The indirect reperfusion signs were assessed, a Serial ECG recording at start and after 30, 60,90 minutes and 3 hours to assess the ST segment reduction were under taken. ST segment reduction by 50% or more was consider as a good response to TT. The reperfusion arrhythmias were observed by continuous ECG monitoring immediately after TT. Cardiac enzyme (creatinin phosphokinase) was measure within 4-6 hours of TT . History of chest pain relief was also asked. The responded patients to one or more of IRS were distributed according to the site of MI and the time of starting the therapy from the onset of chest pain

RESULTS:

Table-1- Shows the age and sex distribution of 200 patients with ST segment elevation myocardial infarction(STEMI) treated by TT. 71.5% males and 28.5% females. most patients 83.5% aged 45-65 years . There is a male predominance in all age group affected by STEMI.

Table -2- shows the distribution of the patients with anterior and inferior myocardial infarction(MI) according to response to TT. 80% of anterior STEMI responded to TT by one of the indirect reperfusion signs , while 69% of the inferior STEMI respond .As illustrated in the Bar chart-1- No significant statistical difference can be observed between response to thrombolytic therapy in relation to the site of MI. (P value = 0.093)

Table-3- Shows the distribution of the response to thrombolytic therapy according to the time of receiving the drug from the onset of chest pain . The response to TT was 93% in those who arrived before 3 hours , had decreased to 86% in those who arrived between 3-6 hours , While 56% of patients responded to TT if they had arrived between 6-12 hours. No response in those who arrived more than 12 hours As observed in Bar chart -2-. There was a strong association exists between the time factor and the response to thrombolytic therapy. (p value =0.0001)

Table -4- Shows the distribution of indirect reperfusion signs among all patients, 78% had their chest pain relieved after receiving TT , there was slight difference between anterior MI 80% and inferior MI 69% in reliving of their chest pain. 62% had significant reduction in ST segment elevation, 72% of anterior MI and 34% of inferior MI. while reperfusion arrhythmis and increased cardiac enzyme occurred less commonly (15% and 5% respectively) As illustrated in the Bar chart—3- .This was statistically significant(p value =o.oo4)

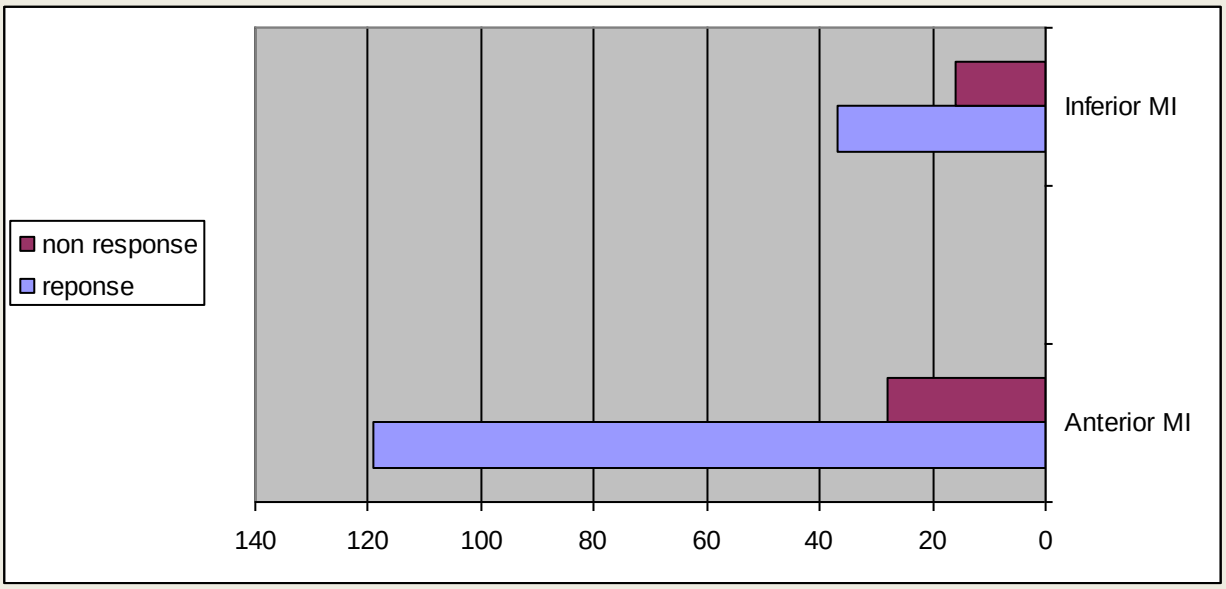
Table -1- Incidence of myocardial infarction among all studied adult patients according to the age and sex:

Age	Female	Male	Total (%)
Less than 45	4	13	17 (8.5%)
45---- 65	46	121	167 (83.5%)
More than 65	7	9	16 (8%)
Total	57	143	200 (100%)

Chi-squared value =2.1 df = 2 p value = 0.350

Table -2- Distribution of the response to thrombolytic therapy according to the site of infarction

	RESPONSE to TT	NON-RESPONSE to TT	TOTAL	P- Value
Anterior MI	119	28	147	Chi squared value = 2.1 Df = 1 P value = 0.093
Inferior MI	37	16	53	
TOTAL	156 (78%)	44 (22%)	200	

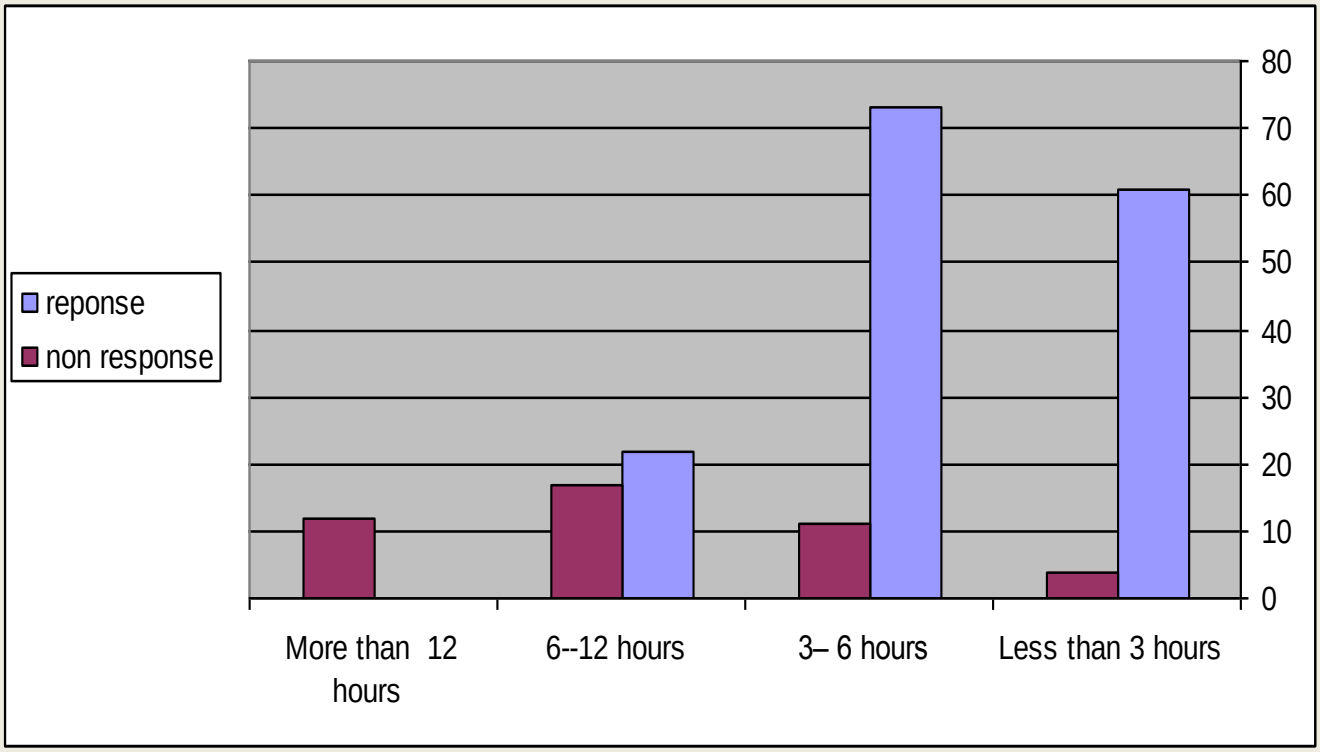


Bar chart -1- showing the distribution of STEMI according to the site of infarction in response to TT

Table -3 - Distribution of the response to thrombolytic therapy according to the time of arrival

	Responded	Non-response	TOTAL	P value*
Gr.1 Less than 3 hours	**61**	**4**	**65**	**0.005**
Gr.2 3– 6 hours	**73**	**11**	**84**	**0.005**
Gr.3 6--12 hours	**22**	**17**	**39**	**0.0001**
Gr.4 More than 12 hours	**0**	**12**	**12**	
Total	**156**	**44**	**200**	

***Chi-squared test**
Overall Chi-squared test value= 66.5 df=3 p value =0.0001

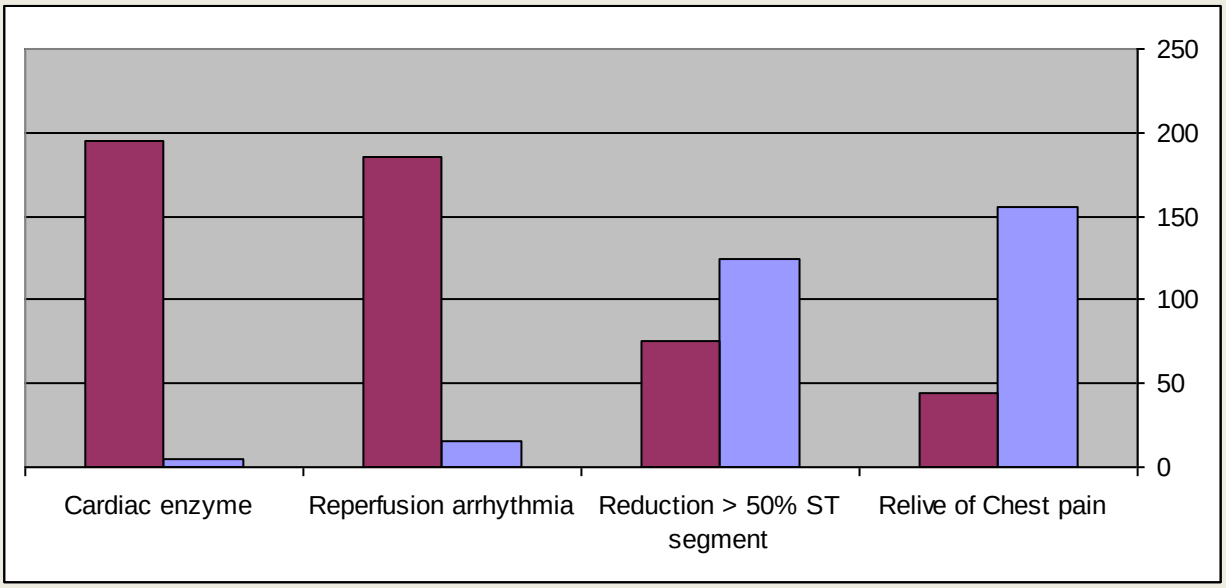


Bar chart -2-ddistribution of the response to thrombolytic therapy according to the time of arrival

Table -4- indirect reperfusion signs according to the type of MI

	Anterior MI (147) Response	Non-response	Inferior MI (53) Response	Non-response	Total(200) Response	Non-response	P value
Relive of Chest pain	119	28	37	16	156	44	**0.001**
Reduction > 50% ST segment	107	49	18	35	125	75	**0.001**
Reperfusion arrhythmia	7	140	8	45	15	185	**0.001**
Increase Cardiac enzyme	5	142	0	53	5	195	**0.001**

Overall Chi-squared value= 15.5 df=3 p value =0.004



Bar chart the distribution of indirect reperfusion signs in STEMI in response to TT

Discussion

In this cross-sectional study, It was observed that most of the cases of STEMI were in middle age group (45-65 years) 167(83.5%) as compared to elderly 16(8%) and young 17 (8.5%), with male predominance in middle and young age groups and less sex difference in elderly age group in the incidence of STEMI.These can be explained by high incidence of risk factors of IHD as hypertension , diabetes , smoking , hyperlipidemia , obesity and psychological stresses among middle age individual. This was similar to other studies (24,25,26)

This study showed high response rate of STEMI to thrombolytic therapy, but there was no significant difference of response to TT between anterior and inferior MI . other studies (27,28,29), showed similar results

A significant high response rate was found to TT in those who have arrived before six hours of chest pain , as to lesser degree in those who have arrived between 6-12 hours. No response was found in those who have received TT after 12 hours of arrival, this is because irreversible myocardial damage has occurred and an over view of large randomized trials confirms that TT significantly reduces short term mortality in patients with STEMI if it is given within 12 hour of the onset of the symptoms (30,31,33,34,35).

A good indicator for successful thrombolysis was shown by indirect reperfusion signs, as significant ST segment reduction, the relieving of chest pain in most of patients and to lesser degree reperfusion arrhythmias and cardiac enzymes ,which were agreed with other studies (36,37,38,39,40,41) .

Conclusion and recommendations:

1. Reperfusion therapy should be given as early as possible in patients with STEMI.
2. Indirect reperfusion signs as a successful thrombolysis remain a useful indicator in place where coronary angiography in not available

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