Early in hospital outcome of thrombolytic therapy for myocardial infarction

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Background
In Erbil city we till now using fibrinolytics as first reperfusion strategy more than primary percutaneous coronary intervention especially when facilities are not available or the transfer times are too long.
Aim of study
To evaluate and assess benefit versus drawback of thrombolytic therapy and its early outcome for patients with STEMI acute myocardial infarction.
Methodology
A cross sectional study carried out in Coronary Care Unit (CCU) of three Teaching Hospitals in Hawler city (Rozhalat, Hawler, and Rzgari Teaching Hospitals) for period from 1st of June, 2015 to 30th of February, 2016 on convenient sample of one hundred acute myocardial infarction patients. The data was collected by the researcher by direct interview and filling a prepared questionnaire. The patients were subsequently divided into three groups depending upon the resolution of ST-segment.
Results
Mean age of studied patients was 53.6±12.6 years and males were more than females. Thrombolysis response was complete among 15% of patients, partial response present among 56% of them, and response was poor among 29% of them,. There was a significant association between poor response to thrombolysis and long symptoms duration ($p<0.001$), hypertensive AMI ($p=0.009$), diabetic AMI patients ($p=0.002$) and obese AMI patients ($p=0.01$). Patients with poor response to thrombolysis developed significant complications like atrial fibrillation, bleeding, mitral regurgitation (MR) and regional wall motion abnormality (RWA) more than other patients.
Conclusions
Thrombolysis response among AMI patients in Erbil hospitals is within acceptable range in comparison to nearby countries.
Key words: Thrombolytic therapy, MI, early in hospital outcome

Introduction

Cardiovascular disease is the single most common cause of death worldwide and is commonly associated with myocardial infarction, Around 30% of global mortality and 10% of global morbidity is due to cardiovascular diseases.[1] In 2008 according to WHO around 17.3 million of worldwide mortality were attributable to cardiovascular diseases with 42% of all cardiovascular deaths being due to myocardial infarction.[1] Coronary heart disease and resulting death rates are decreasing in many developed countries, especially North America and western European countries. This decrease is the result of improved prevention, diagnosis and treatment, particularly reductions in cigarette smoking, control of blood cholesterol and blood pressures.[1,2] In developing and transitional countries, coronary heart disease is increasing, partly as a result of increasing longevity of life, urbanization, and lifestyle changes. More than 60% of the global burden of coronary heart disease occurs in developing countries. [1,3]Nationally, despite limitations in the mortality statistics available in Iraq,

CVDs rank first as a cause of death in Iraq. Coronary heart disease (CHD) and stroke are the predominant types of CVD encountered in clinical practice. Hospital morbidity data provided by the MOH indicates a 65% increase in hospital admissions due to CHD between 1989 and 1999. The average age of persons hospitalized with acute myocardial infarction seems to have shifted towards younger age groups.[4] Prompt restoration of blood flow in coronary arteries before the heart muscle is irreversibly damaged is the primary treatment goal in acute myocardial infarction.[5] coronary arteries Reperfusion is accomplished either: mechanically, by primary percutaneous coronary intervention (PPCI); or pharmacologically, by administration of a thrombolytic agent as soon as possible after diagnosis of MI.[6] The recognition of the time-dependent progression of necrosis in the heart muscle, constitutes the basis for the international guidelines stating that MI patients' treatment time should not extend beyond 45 minutes and that reperfusion therapy, with fibrinolysis or PCI, should be performed as soon as possible, i.e. < 90 minutes after the onset of symptoms.[7] Regardless of mode of reperfusion, early treatment, especially within the first 'golden hour', has a significant mortality benefit.[8] For patients with the clinical presentation of MI within 12 hours after symptom onset with persistent ST- elevation or new LBBB, reperfusion therapy should be given.[9] There is also a general agreement to consider primary PCI even if more than 12 hours have passed since symptom onset, if there is clinical evidence of on-going ischemia.[9] Fibrinolytic therapy is still an important reperfusion strategy where PCI facilities are not available or the transfer times are too long. The benefit of fibrinolysis is well established with approximately 30 early deaths prevented per 1000 patients treated.[10] Pre-hospital administration is proven to be superior of hospital administration with 17% relative risk reduction.[11]

Aim of study

The aim of this study is to evaluate and assess benefit versus drawback of thrombolytic therapy and its early hospital outcome for patients with ST segment elevation acute myocardial infarction in Erbil city.

Patients & Methods

Study design and setting: A cross sectional study carried out from a convenient sample of 100 patients with AMI admitted to CCU of three Teaching Hospitals in Hawler city was selected. for period from 1st of June/ 2015 to 30th of February/ 2016.

Inclusion criteria:

1. First attack acute myocardial infarction (AMI).
2. Duration 0-12 hours.

Exclusion criteria:

1. Previous MI.
2. Any cases with absolute contraindications for thrombolysis.
3. Previous coronary intervention (PCI, CABG).
4. Previous bundle branch block.
5. Active malignancy, ESRD, or severe disabling comorbidities.
6. Patients put on warfarin for any reason.
7. Patients with bleeding tendency.

The diagnosis of acute STEMI relied on the revised criteria established by the WHO. The ST-segment elevation resolution was calculated as the initial sum of ST-segment elevation on admission before thrombolytic therapy minus the sum of remaining ST segment elevation at 90 minutes after thrombolytic therapy divided by the initial sum of ST-segment elevation expressed as percentage. The patients were subsequently divided into three groups depending upon the resolution of ST-segment which is stratified by Schroder et al:

Group A: complete resolution (≥70% reduction of ST-segment).

Group B: partial resolution (<70% to 30% reduction of ST-segment).

Group C: no resolution (<30% reduction of ST-segment).

Results

A total of 100 acute myocardial infarction (AMI) patients were included in present study with mean age 53.6±12.6 years, 32% of them were elderly (≥ 60 years). Males with MI were more than females with male to female ratio as 2.7:1. All these findings were shown in figures 1, 2.

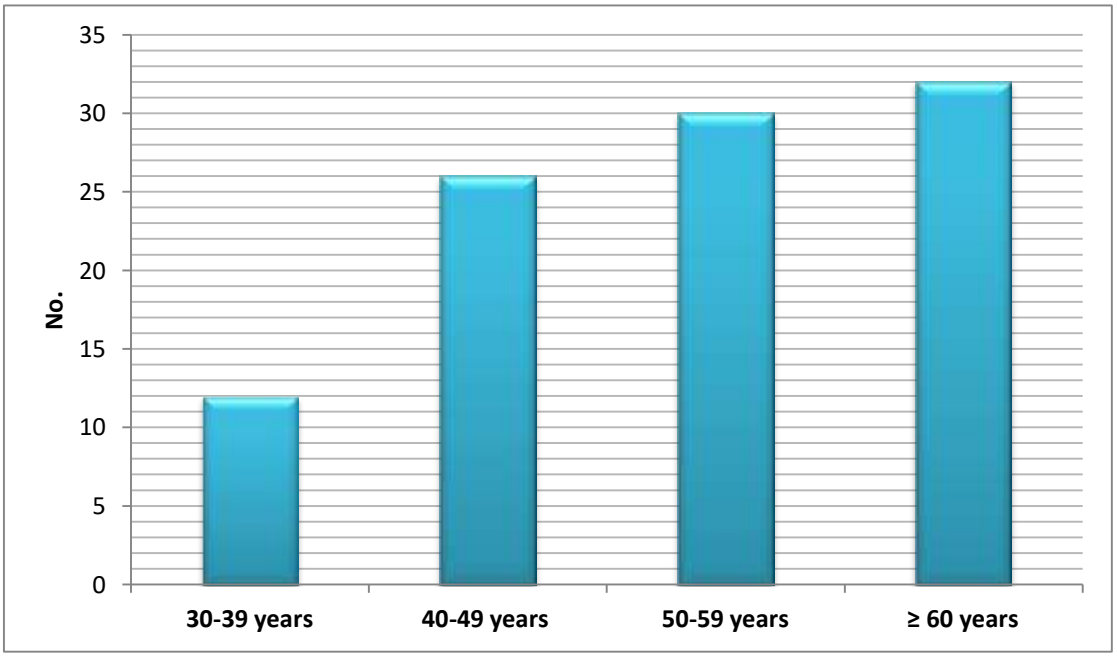

Figure 1: Age distribution of MI patients.

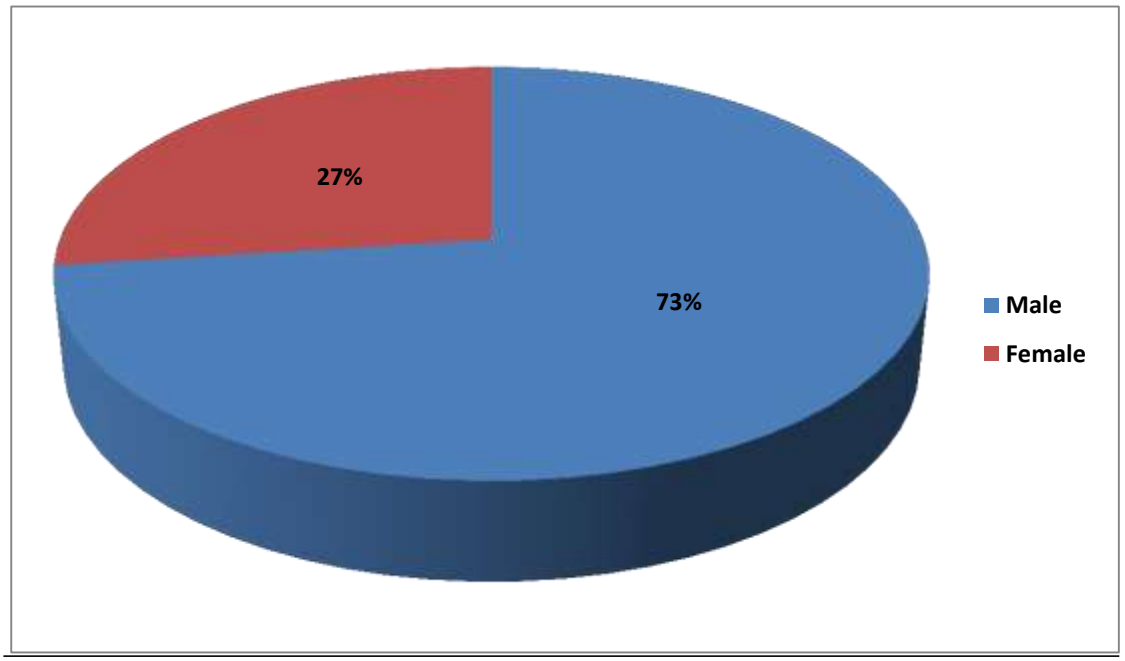

Figure 2: Gender distribution of MI patients.

More than half (55%) of AMI patients had 1-6 hours symptoms duration, 25% of them 7-12 hours and 20% of them <1 hour symptom duration. All these findings were shown in figure 3.

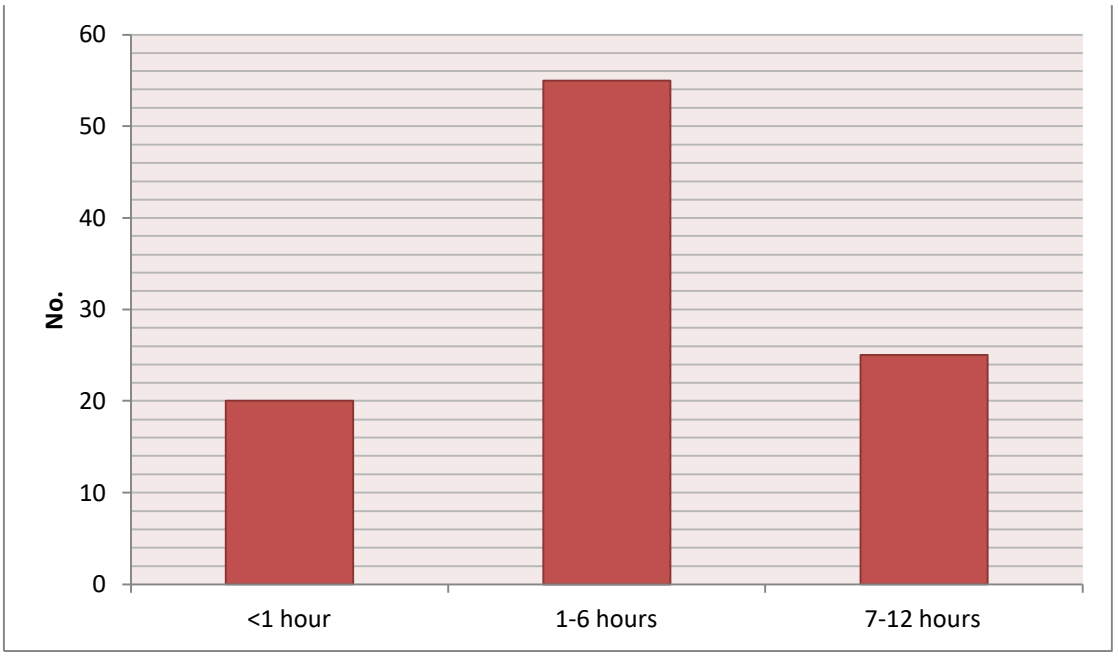

Figure 3: Symptoms duration distribution of AMI patients.

About one third of AMI patients were hypertensives, 32% of them were diabetics, 32% of them were obese, 60% of them had smoking history, 26% of them had positive family history of heart diseases and 19% of them had history of alcohol consumption, figure 4.

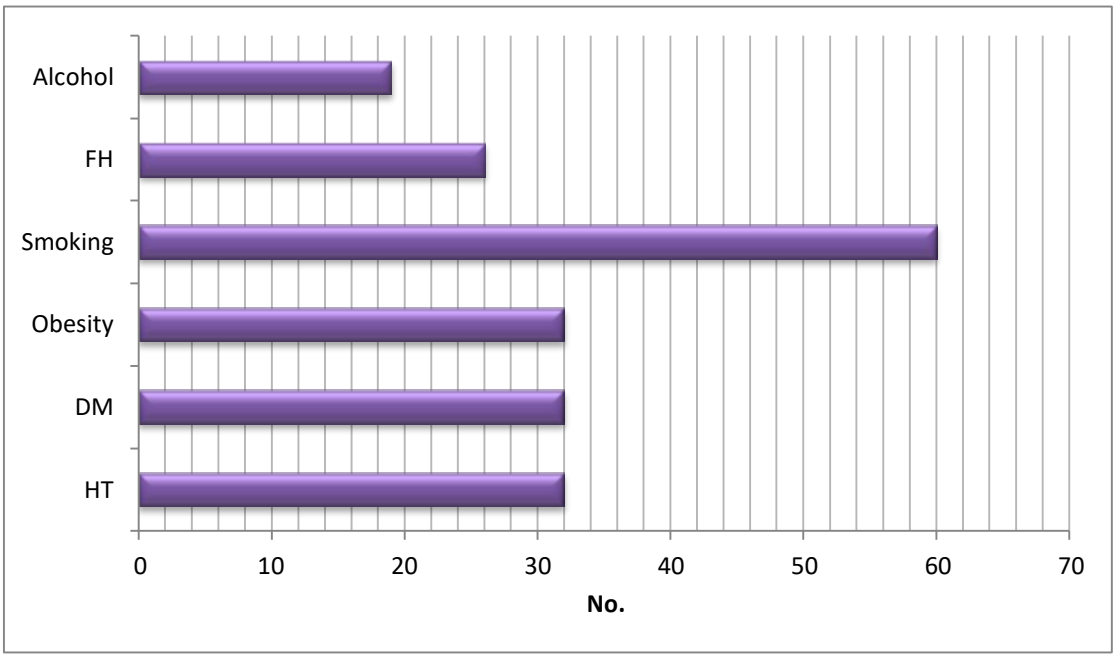

Figure 4: Cardiac risk factors.

Normal heart rate was record among 66% of studied AMI patients, sinus tachycardia found among 16%, sinus bradycardia 12%, AF 3% and VT 3%. Cardiogenic shock was present among 7% of AMI patients. ST-segment deviation was distributed as followings; 54% moderate, 40% severe and 6% mild. All these findings were shown in figures 5, 6.

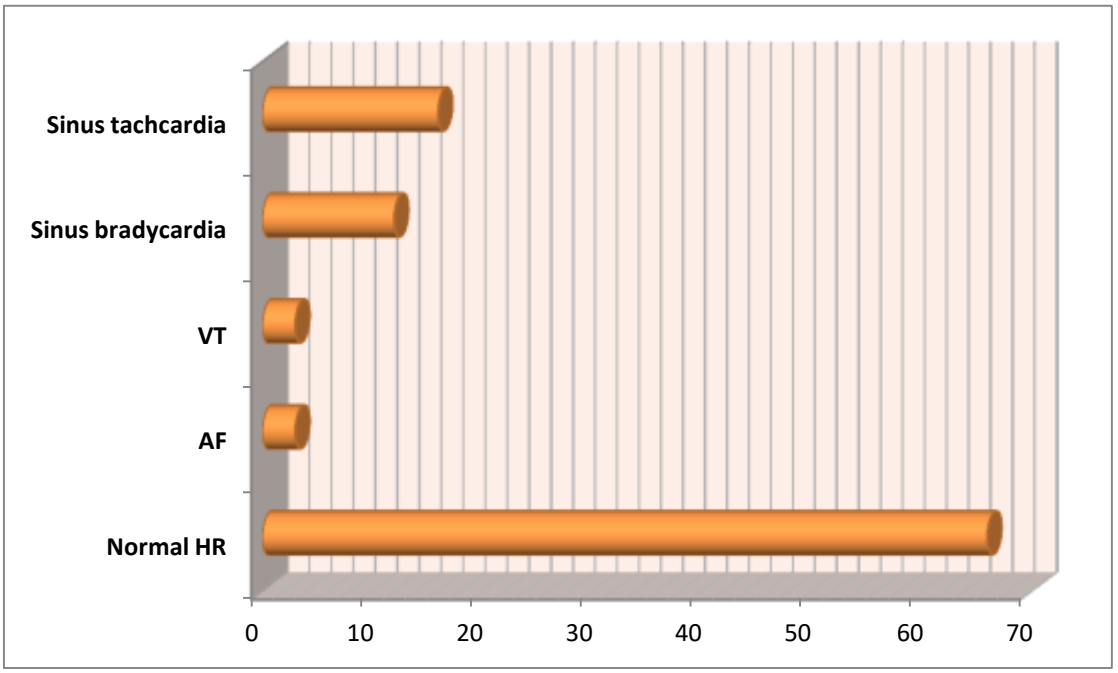

Figure 5: AMI patients' arrhythmias.

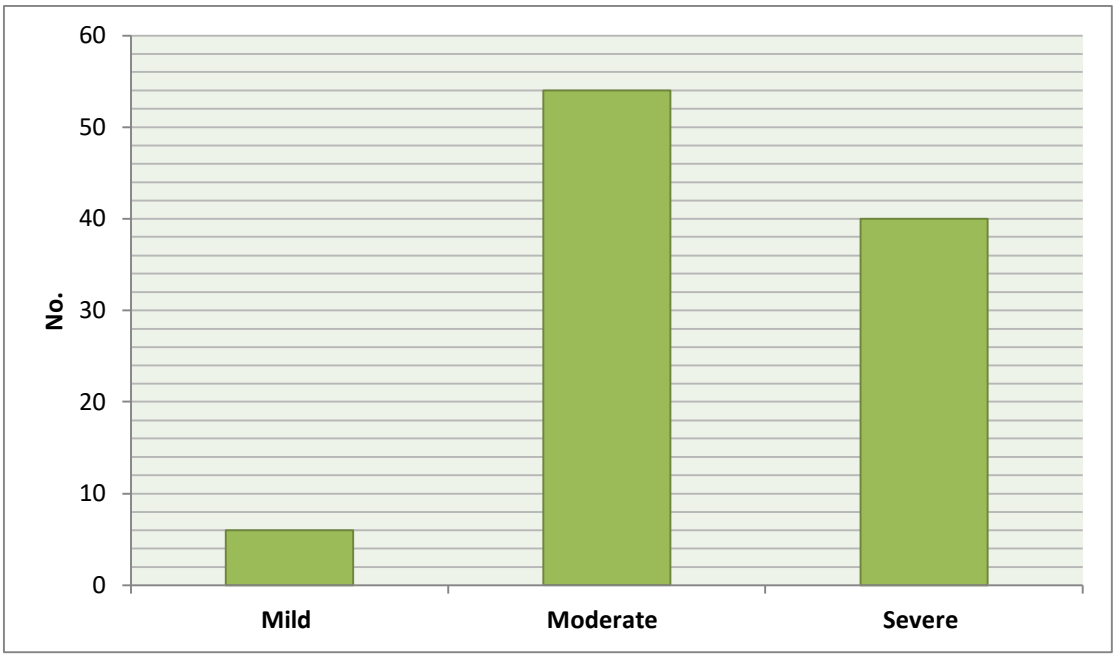

Figure 6: ST-segment deviation distribution AMI patients.

Bleeding was presented as minor bleeding among 20% of AMI patients, MR present among 31% of them, pericardial effusion present among 11% of them RWA detected among 47% of them. All these findings were shown in figure 7.

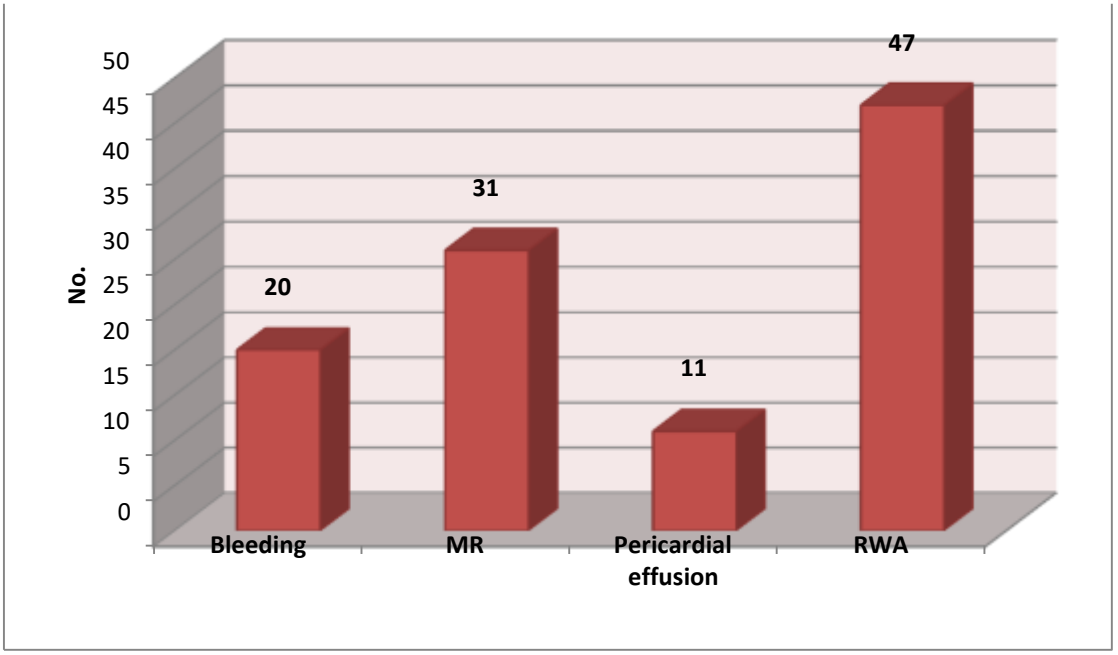

Figure 7: Complications.

Mean grace score was 2, EF% 30.9, FS% 15.5, LVSD 32.4 and LVDD 49.7, table 1.

Table 1: Outcome score means of MI patients.

Variable	Mean	SD
Grace score	2	1
EF%	30.9	31.5
FS%	15.5	15.9
LVSD	32.4	6.2
LVDD	49.7	8.8

Thrombolysis response was absent among 29% of AMI patients, partial response present among 56% of them and complete response present among 15% of them, figure 8.

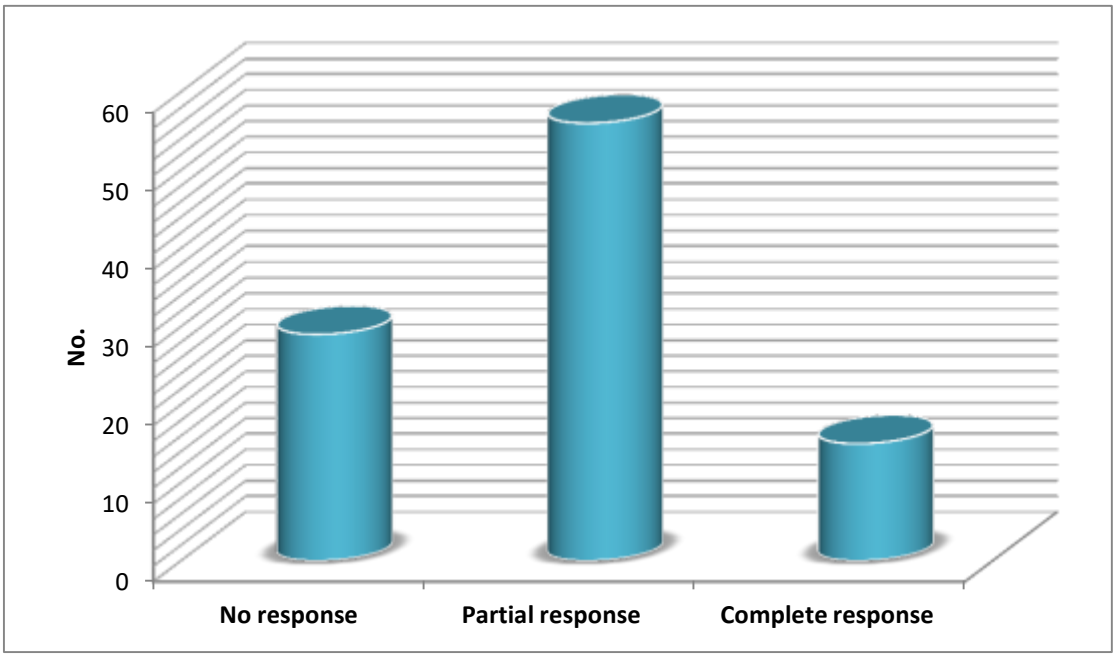

Figure 8: AMI patients' response to thrombolysis.

No significant differences were observed between AMI patients with different response to thrombolysis regarding their age and gender. All these findings were shown in table 2.

Table 2: Distribution of demographic characteristics according to response to thrombolysis.

Variable	No		Partial		Complete		χ^2	P
	No.	%	No.	%	No.	%		
Age							9.9*	0.1
30-39 years	6	50.0	6	50.0	0	-		
40-49 years	4	15.4	16	61.5	6	23.1		
50-59 years	11	36.7	13	43.3	6	20.0		
>60 years	8	25.0	21	65.6	3	9.4		

Gender							0.9	0.6
Male	20	27.4	43	58.9	10	13.7		
Female	9	33.3	13	48.1	5	18.5		

**Fishers exact test.*

There was a significant association between long symptoms duration and no response to thrombolysis ($p<0.001$). A significant association was observed between hypertensive AMI patients and partial response to thrombolysis ($p=0.009$). There was a significant association between diabetic AMI patients and no response to thrombolysis ($p=0.002$). A significant association was observed between obese AMI patients and partial response to thrombolysis ($p=0.01$). No significant differences were observed between AMI patients with different response to thrombolysis regarding their age and gender. All these findings were shown in table 3 and figure 9.

Table 3: Distribution of duration and risk factors according to response to thrombolysis.

Variable	**No**		**Partial**		**Complete**		χ^2	**P**
	No.	**%**	**No.**	**%**	**No.**	**%**		
Duration o symptoms							21.9*	**<0.001**
<1 hour	5	25.0	13	65.0	2	10.0		
1-6 hours	8	14.5	37	67.3	10	18.2		
7-12 hours	16	64.0	6	24.0	3	12.0		
HT							9.3	**0.009**
No	16	23.5	37	54.4	15	22.1		
Yes	13	40.6	19	59.4	0	-		
DM							12.9	**0.002**
No	16	20.5	50	64.1	12	15.4		
Yes	13	59.1	6	27.3	3	13.6		
Obesity							8.3	**0.01**
No	18	26.5	35	51.5	15	22.1		
Yes	11	34.4	21	65.6	0	-		
Smoking							2.2	0.3
No	9	22.5	26	65.0	5	12.5		
Yes	20	33.3	30	50.0	10	16.7		
Family history							2.3	0.3
No	19	25.7	42	56.8	13	17.6		
Yes	10	38.5	14	53.8	2	7.7		
Alcohol consumption							0.3	0.8
No	23	28.4	45	55.6	13	16.0		

Yes	6	31.6	11	57.9	2	10.5		

**Fishers exact test.*

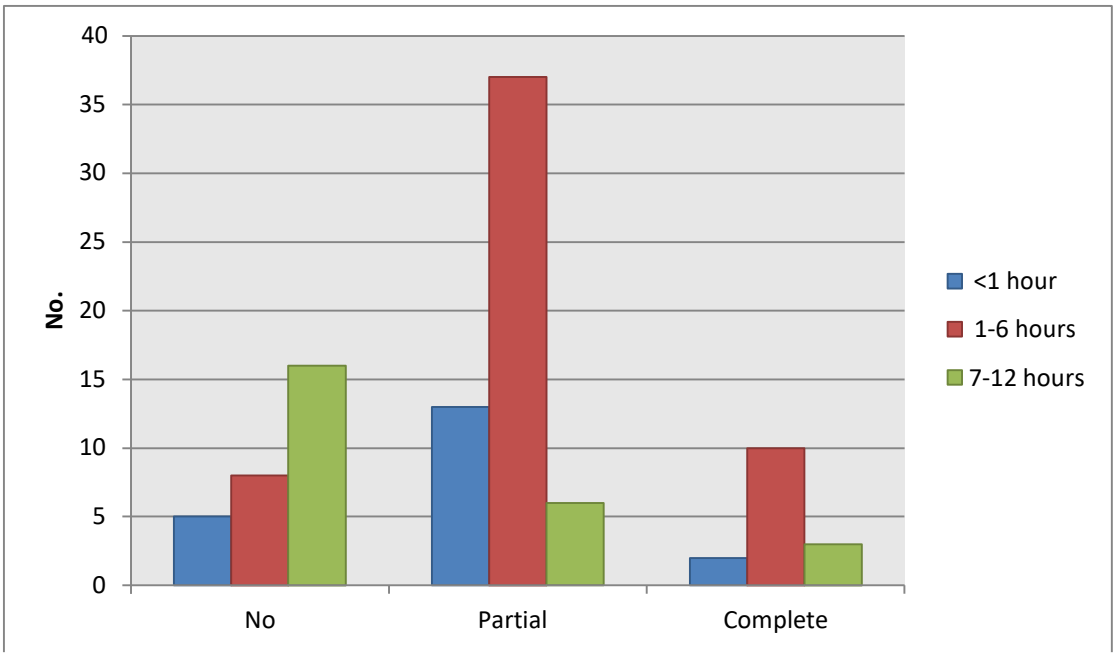

Figure 9: Symptoms duration distribution according to response to thrombolysis.

There was a significant association between AMI patients with AF and no response to thrombolysis ($p<0.001$). A significant association was observed between AMI patients with severe ST-segment deviation and partial response to thrombolysis ($p<0.001$). There was a significant association between MI patients with cardiogenic shock and no response to thrombolysis ($p<0.001$). A significant association was observed between AMI patients with bleeding, MR and pericardial effusion and no response to thrombolysis ($p<0.05$). There was a significant association between recorded RWA among AMI patients and no response to thrombolysis ($p<0.001$). All these findings were shown in table 4 and figures 10, 11.

Table 4: Distribution of complications according to response to thrombolysis.

Variable	**No**		**Partial**		**Complete**		**χ^2**	**P**
	No.	**%**	**No.**	**%**	**No.**	**%**		
Arrhythmias							29.5*	**<0.001**
Normal HR	15	22.7	41	62.1	10	15.2		
AF	3	100.0	0	-	0	-		
VT	0	-	0	-	3	100.0		
Sinus bradycardia	4	33.3	8	66.7	0	-		
Sinus tachycardia	7	43.8	7	43.8	2	12.5		
ST-segment deviation							11.1*	**0.02**
Mild	3	50.0	0	-	3	50.0		
Moderate	16	29.6	33	61.1	5	9.3		
Severe	10	25.0	23	57.5	7	17.5		
Cardiogenic shock							18.4*	**<0.001**

No	22	23.7	56	60.2	15	16.1		
Yes	7	100.0	0	-	0	-		
Bleeding							11.0*	**0.002**
No	17	21.3	51	63.7	12	15.0		
Minor	12	60.0	5	25.0	3	15.0		
MR							8.5	**0.01**
No	14	20.3	43	62.3	12	17.4		
Yes	15	48.4	13	41.9	3	9.7		
Pericardial effusion							15.5*	**<0.001**
No	21	24.4	53	61.6	12	14.0		
Yes	8	72.7	0	-	3	27.3		
RWA							17.4	**<0.001**
Negative	6	11.3	38	71.7	9	17.0		
Positive	23	48.9	18	38.3	6	12.8		

**Fishers exact test.*

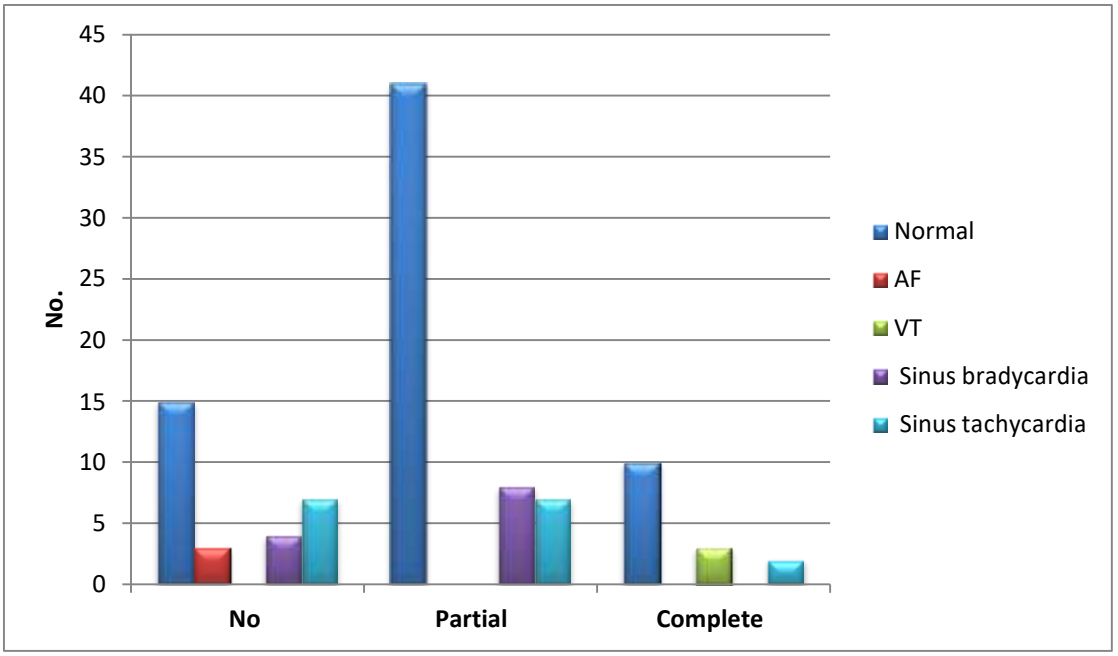

Figure 10: ST-segment deviation distribution according to response to thrombolysis.

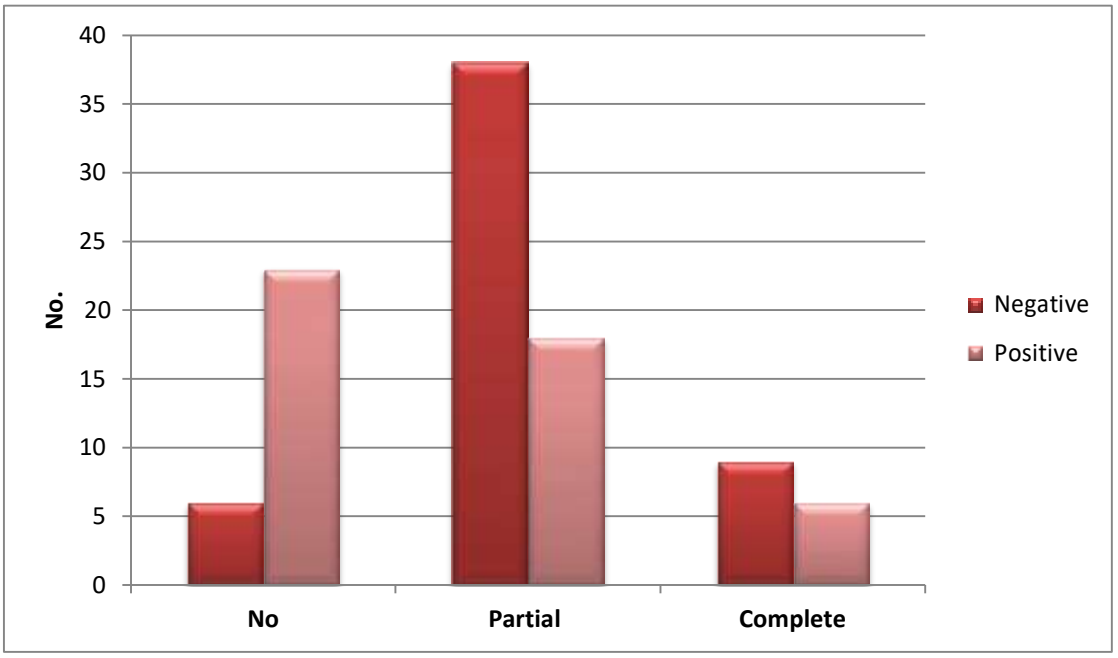

Figure 11: RWA distribution according to response to thrombolysis.

There was a significant association between higher means of grace score and LVDD among AMI patients with no response to thrombolysis (p<0.001), table 5 and figure 12.

Table 5: Distribution of outcome scores means according to response to thrombolysis.

Response	**Grace sc.**	**EF%**	**FS%**	**LVSD**	**LVDD**
	Mean±SD	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**
No	2.1±0.7	29.5±30.9	14.7±15.6	33.6±7	55.8±7.5
Partial	1.3±0.5	33.6±31.5	16.9±15.8	31.6±6.1	46.5±8.6
Complete	1.2±0.4	23.3±33.2	11.6±16.3	33±4.5	49.4±5.3
P value*	**<0.001**	0.5	0.5	0.3	**<0.001**

**ANOVA*.

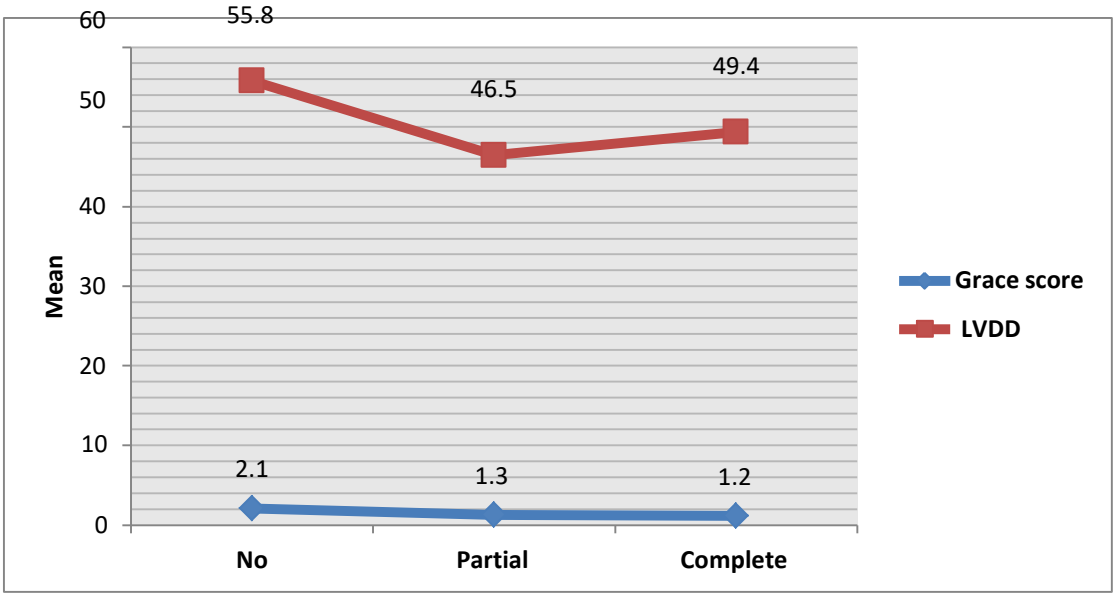

Figure 12: Grace score and LVDD means distribution according to response to thrombolysis.

Discussion

Reperfusion therapy in acute MI attempts to reduce mortality and morbidity. Therefore, it is necessary to obtain complete and sustained patency of the infarct-related coronary artery as early as possible.[56] Closer collaboration between disciplines handling various life-threatening complications of atherosclerosis has the potential to improve our understanding of ways of improving treatment. The literature about the early treatment of stroke has mainly appeared during the last decade, whereas similar literature about the heart often appeared 10 years earlier.[57]

In present study, only 15% of AMI patients had complete response to thrombolysis therapy after follow up, 56% of them had partial response and 29% of them had no response to thrombolytic therapy. These findings are better than results of Al-Selaimy and Al-Missari study in Iraq [58] which found that 7.3% of AMI patients had complete response after treatment with thrombolysis, 41% of them had partial response and 51.7% of them had no response. This difference is attributed to highly qualified cardiac centers in Kurdistan in comparison to Diyala province.

Our findings regarding thrombolysis outcome are lower than that reported by Schofield study in UK [59] which revealed that 42% of AMI patients treated within 1st hour with thrombolytics had complete response. Another study in UK [60] reported that shortening prehospital delay in acute myocardial infarction will tend to increase the risk profile of patients presenting to emergency departments. Memon et al [61] study in Pakistan found that not only mortality was improved by thrombolysis but also patients had less complications, early pain relief and shorter hospital stay. The Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) trial suggested that early fibrinolysis could lead to comparable results such as those of primary angioplasty.[62] Patients with cardiac arrest due to MI are seen very early after the onset of ischemia because most of the time the collapse is only preceded by a short duration of symptoms. A further advantage of thrombolysis in these patients could be a positive effect on the microcirculatory reperfusion of the brain.[63]

Our study found no significant association between demographic characteristics of AMI patients and response to thrompolysis therapy. This finding is inconsistent with results of Ghadimi et al [64] study in Iran and Herlitz et al [57] study in Sweden which stated that younger age females had good in-hospital outcome after thrombolysis treatment. This difference might be due to difference in sample size and inclusion criteria between studies.

Current study showed that AMI patients with long duration of symptoms had significantly no response to thrombolysis ($p<0.001$). This is consistent with results of McGinn et al [65] studywhich found that long symptoms duration and delay in thrombolysis treatment associated with high mortality of AMI patients. Despite large-scale efforts to reduce the delay between the onset of symptoms and the patient's decision time and admission to hospital respectively, the results have not been particularly impressive. In Sweden, the prehospital delay in AMI has not changed much during the last 10 years.[57]

AMI patients in present study with HT and obesity had significantly partial response to thrombolysis than others ($p<0.05$). This is similar to results of Mousa and Sherhan study in Iraq [66]. Diabetic AMI patients in this study had significantly no response to thrompolysis than others ($p=0.002$). This finding is in agreement with results of Gurm et al [67] study in UK which concluded as compared to nondiabetics, diabetics continue to have a worse outcome with MI. Although combination therapy did not provide a survival benefit, nonfatal ischemic outcomes, including reinfarction, recurrent ischemia, and urgent revascularization, were substantially reduced. Diabetics have evidence of increased platelet activation, adhesiveness and aggregability, and greater expression of platelet GP IIb/IIIa, thrombospondin, and P selectin.[67]

Other studied cardiac risk factors as smoking, alcohol and family history had no significant effect on thrombolysis response of AMI patients ($p>0.05$). These findings are similar to results of Goldman and Eisenberg study in Canada[68]. Survival following thrombolytic therapy for AMI is closely related to the early restoration of coronary blood flow in the infarct-related artery. Numerous studies have demonstrated a consistent relationship between mortality rates and TIMI flow grade at 90 minutes. The in-hospital mortality rate after MI is 3.9% for TIMI 3, 6.7% for TIMI 2, and 9.9% for TIMI 0 or 1 flow. [69] Since thrombolysis achieves TIMI 3 flow in less than 60% of patients, coronary angioplasty performed early after thrombolytic therapy may improve coronary patency rates and thereby improve clinical outcomes.[70]

The main associated cardiac characteristics that significantly associated with no response of AMI patients to thrombolysis were AF (p<0.001), moderate to severe ST segment deviation (p=0.02), cardiogenic shock (p<0.001), bleeding (p=0.002), MR (p=0.01), pericardial effusion (p<0.001) and positive RWA (p<0.001). These findings are consistent with results of Ghadimi et al [64] study in Iran. Other studies reported incidence of 1% for asystole and 4.5% for ventricular fibrillation among AMI patients in Western countries.[71] On the other hand, other arrhythmias were as frequent as, or less common than, the rates mentioned in large series [71], reporting 10, 5 and 10–15% frequencies for paroxysmal supraventricular tachycardia, atrial flutter and fibrillation, respectively. First-degree atrioventricular block, Mobitz type I and II and complete atrioventricular block have a global incidence of 15, 10, 1 and 5–15%, respectively.[71] Cardiogenic shock was seen in 7.5% of patients in a large study of 4762 American patients.[72] Recurrent angina pectoris was encountered in 29% of STEMI and 37% of non-STEMI cases in GRACE.[73] Reinfarction was reported in 4.6% and extension of infarct in 3% of Indian STEMI patients.[74] Stroke (4.3%) was more common, however, than Western studies like GRACE [73] and of others who reported an incidence of 1–2%. Nevertheless, a 5% incidence for stroke among AMI patients has been observed in previous study.[64]

In this study, Mean LVDD was significantly higher among AMI patients with no response to thrombolysis (p<0.001). This is similar to results of Al-Othman and Al-Tawil study in Erbil [75] which concluded that early reperfusion therapy in acute anterior myocardial infarction can decrease the incidence of early left ventricular infarct expansion, preserve left ventricular systolic function and decrease in-hospital mortality.

Limitations of the study

1. Loss to follow up.
2. Single center study.
3. Selection bias.
4. Interference with PCI.

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