Journal of Clinical and Experimental Cardiology

Elesily et al., J Clin Exp Cardiolog 2018, 9:6
DOI: 10.4172/2155-9880.1000592

Research Article Open Access

Correlation between Grace Risk Score and Cardiovascular Event Rate in Patients with ST Segment Elevation Myocardial Infarction with Successful Fibrinolysis and Delayed Coronary Intervention

Ahmed H. Elesily[1*], Mohammed A. Mandour[2], Mahmoud A. Hashish[3], Mohy M. Samy[2] and Mohammed S. Elbaz[2]

[1]*Department of Cardiology, El Matareya Teaching Hospital, Cairo, Egypt*

[2]*Department of Cardiology, Faculty of Medicine, Al-Azhar University, Egypt*

[3]*Department of Clinical Pathology, Faculty of Medicine, Al-Azhar University, Egypt*

[*]**Corresponding author:** Ahmed H Elesily, El Matareya Teaching Hospital, Cairo Elmatareya Squere, Cairo- 02, Egypt, Tel: 020453174413; E-mail: ahmedhassan6387@gmail.com

Received date: June 10, 2018; **Accepted date:** June 19, 2018; **Published date:** June 22, 2018

Abstract

Background: In several countries, fibrinolytic therapy represents the current reperfusion therapy for most patients with STEMI due to decrease of PCI-capable centers. Current guidelines recommended routine early revascularization (within 2-24 h) after successful thrombolysis but, it cannot be performed in timely fashion due to limitation of PCI-capable centers

Aim of the work: To assess the utility of the GRACE risk score as prognostic factor in patients receiving delayed coronary intervention after successful thrombolysis in non-PCI-capable hospitals.

Methods: This was a prospective observation study that was done from March 2017 to February 2018 and included 120 patients presented to the coronary care unit at Al-Azhar University Hospital and Al Mataryia Teaching Hospital with acute STEMI and treated successfully with thrombolytic therapy. All patients were subjected to full clinical examination, ECGs, Echocardiography, full labs. The patients who had successfully thrombolysis and received delayed PCI (during 48 h to 14 days) were included. Follow up was done on outpatient basis monthly after delayed PCI for three months.

Results: There were 70 patients (58.3%) with low GRACE score and 50 patients (41.7%) with high GRACE score. This study showed that more than three quarters of the studied cases had no follow up complications and the most frequent complication was ACS. The percentage of cases which had ACS was 13.3% (number of patients 16), the percentage of cases with HF was 9.2% (number of patients 11), the percentage of cases with stroke was 1.7% (2 patients) and only one case died. During 3 months, the cardiovascular complications occurred in 8 patients in low GRACE group and 20 patients in high GRACE group (P<0.001). Cases with cardiovascular complications had significantly higher time from successful fibrinolysis to PCI (P<0.001).

Conclusion: The delayed pharmacoinvasive strategy in patients with intermediate to high GRACE score after successful thrombolysis in non PCI-capable centers was associated with bad cardiovascular outcomes (death, rehospitalization with ACS, rehospitalization with heart failure and cerebrovascular stroke) than the patients with low GRACE score within three months

Keywords: Myocardial injury; GRACE score; Successful fibrinolysis; Complications; ST segment elevation myocardial infarction

Introduction

Primary Percutaneous coronary intervention (PPCI) is reperfusion therapy of choice for STEMI patients. However, the PCI-capable centers are still limited in many countries including Egypt.

So, fibrinolytic therapy is the main reperfusion therapy for most STEMI patients in Egypt [1]. Even more, early pharmacoinvasive (within 2-24 h after successful thrombolysis) cannot be performed in a timely fashion due to decrease of PCI- capable hospitals. Therefore, risk stratification is a crucial issue in planning management in non-PCI capable hospitals. Patients with intermediate to high GRACE risk should be transferred for coronary angiogram as early as possible [2].

Although several risk scores for acute coronary syndrome (ACS) have been developed to stratify the risk of ACS patients, GRACE (Global Registry of Acute Coronary Events) score is applied to assess the clinical risk and the selection of patients for clinical and interventional procedures following an ACS episode [3].

Many studies and meta-analysis demonstrated the accuracy and the usefulness of the GRACE score on the mortality, morbidity of ACS patients in hospital and follow-up after hospital discharged [4].

Patients and Methods:

This prospective observational study involved 120 patients from the patients coming to the emergency department at Al-Azhar University Hospital and Al-Matarya Teaching Hospital (MTH) who were admitted with the diagnosis of ST segment elevation myocardial infarction (STEMI) and received streptokinase 1.5 MU as per the institutional protocol, during the period from March 2017 to February 2018 [5-7].

Patients were treated and observed in the coronary care unit for at least five days. All patients presented, within 6 h from symptom onset with ECG showing ST-segment elevation at the J point, in at least 2 contiguous leads, ≥ 2 mm (0.2 mV) in men ≥ 40 years, 2.5 mm (0.25 mV) in men <40 years or ≥ 1.5 mm (0.15 mV) in women in leads V2-V3 and/or ≥ 1 mm (0.1 mV) in other contiguous chest leads or the limb leads [8].

Exclusion criteria were patients with unsuccessful fibrinolysis (ST-segment decrease in elevation less than 50% at 90 min after the start of thrombolysis), those receiving early coronary intervention (<24 h after thrombolysis).

Also, Patients receiving very delayed coronary intervention (two weeks after thrombolytic therapy) and those who refused further interventions after fibrinolysis.

Patients received primary PCI or rescue PCI were excluded.

Also, Patients with previous history of coronary artery bypass surgery (CABG) were excluded. The study protocol was approved by the Faculty of Medicine of Al-Azhar University. A chart review was performed, and data were collected including patient demographics, medical history, clinical examination, laboratory tests, ECG, echocardiography.

History was taken including age, sex, smoking was recognized as a long history of >100 cigarettes in their life and had continued smoking in the last 6 months was considered a positive smoking history, while ex-smoker was defined as having history of smoking at least 100 cigarettes in their life and had completely stopped smoking for at least 6 months [5]. Current diabetes mellitus was defined as having history of DM on admission with the use of oral anti-hyperglycemic full medications or any extended release insulin and confirmed by laboratory HbA1c on admission if more than 6.5% [6], dyslipidemia was defined by total cholesterol level ≥ 220 mg/dl, triglyceride level ≥ 150 mg/dl, high-density lipoprotein (HDL cholesterol) ≤ 40 mg/dl or current use of anti-hyperlipdemic drug [7], hypertension was defined as systolic/diastolic blood pressure ≥ 140/90 mmHg or patients having history of hypertension and current use of any antihypertensive medications [8]. Family history of premature coronary artery disease was defined as fatal or non-fatal events in first degree relatives men<55-years-old or women <60-years-old [9].

We did full clinical examination including vital data, full cardiac examination to know the Killip classification for each patient. Heart failure included advanced congestive heart failure (New York Heart Association functional class III/IV) or acute heart failure (Killip class II-IV).

Twelve leads ECG were obtained to confirm the diagnosis. M-mode, two-dimensional echocardiography and doppler examination was performed for all patients in the left decubitus position during normal breathing using a GE Vivid 5 Ultrasound Machine (Echo Pac; GE Vingmed, Horten, Norway) according to the recommendations of American Society of Echocardiography to assess the left ventricle size, the left atrium size, the left ventricular ejection fraction, any wall motion abnormalities or ischemic complications and to detect any morbidities during the in-hospital follow up.

Laboratory tests were done including routine labs that include liver and kidney functions. Serum cardiac markers that include Serial measurement of cardiac troponin I (CTnI), myocardial band of creatine kinase (CK-MB) and creatine kinase (CK). Measured hormones and their respective reference values are: CK (up to 195 U/L), CK-MB (up to 25 U/L), Troponin I (0-0.1 ng/ml).

The STEMI patients who had successfully fibrinolysis and received delayed PCI (during 24 hours to 14 days) were included. Follow up was done within the clinic every 21 days after delayed PCI for three months. The end point for this study was the total outcomes, which included all-causes of mortality, hospital admission with acute coronary syndrome (ACS), with heart failure (HF) and stroke at 1 and 3-month.

Rehospitalization with ACS is defined as readmission after discharge from hospital with ACS including clinical chest pain or discomfort, rising of cardiac enzymes and dynamic ST-segment change.

Rehospitalization with heart failure is defined as readmission after discharge from hospital with clinical symptoms of decompensated heart failure or received intravenous diuretic therapy (Table 1).

Variables		Mean ± SD	Range
Onset (hours)		5.1 ± 2.1	1.0-12.0
HR (Beat/minute)		97.9 ± 21.7	40.0-150.0
SBP (mmHg)		126.6 ± 28.5	80.0-190.0
DBP (mmHg)		77.2 ± 17.7	50.0-120.0
Serum creatinine (mg/dl)		1.23 ± 0.51	0.40-2.30
Serum urea (mg/dl)		38.0 ± 11.9	20.0-80.0
Hb (gm/dl)		13.6 ± 1.4	10.0-16.0
RBS (mg/dl)		284.7 ± 97.6	100.0-500.0
EF%		51.7 ± 8.1	30.0-68.0
		N	%
Killip Class	I	87	72.5
	II	28	23.3
	III	5	4.2
DKA		9	7.5
Crepitaion		67	55.8
Tachyarythmia		21	17.5
Bradyarrythmia		10	8.3
Cardiac Arrest		11	10.8
Site (ECG)	Anterior	69	57.5
	Inferior	46	38.3

	Both	5	4.2

Table 1: Clinical condition and laboratory findings of the studied cases at presentation

All patients received a loading dose of 300 mg of clopidogrel in combination with 300 mg of acetylsalicylic acid. Streptokinase was given in coronary care unit under strict observation and monitoring during hospital stay. Patients with ST elevation myocardial infarction were observed for evidence of both in-hospital morbidity and mortality (Table 2 and Figure 1).

Variables		Mean ± SD	Range
Age (years)		56.3 ± 9.3	34.0-80.0
		N	%
Sex	Male	84	70
	Female	36	30
Smoking		67	55.8
HTN		69	57.5
DM		64	53.3
Dyslipidemia		18	15
Family history for IHD		13	10.8
Previous PCI		7	5.8
Previous MI		30	25

Table 2: Baseline characteristics of the study group

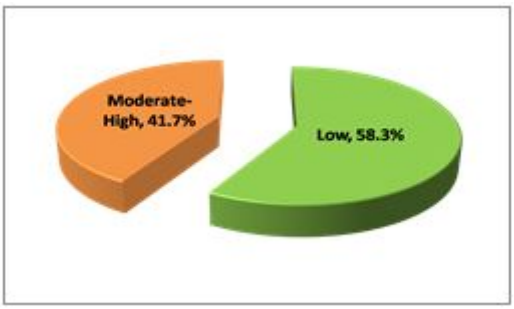

Figure 1: GRACE score among the studied cases

Data were analyzed *via* Statistical program for social science (SPSS) version 20.0. Quantitative data were expressed as mean ± standard deviation (SD) while qualitative data were expressed as and percentage frequency. Independent samples t-test of significance was used when comparing between two means. Chi-square (χ^2) test of significance was used in order to compare proportions between two qualitative parameters.

Results

This was a prospective cross sectional observational study that involved 120 patients who presented to the emergency rooms of Al-Azhar University Hospital and Al Matareya Teaching Hospital (MTH) with acute STEMI and treated with fibrinolytic therapy, within the period between March 2017 to February 2018.

The Mean age was 56.3 ± 9.3 years (ranged from 34-80 years). Males represented 70% (84 patients) of the study population while females represented 30% (36 patients). Fifty seven percent (69 patients) were hypertensive while fifty three percent (64 patients) were diabetic and fifty five percent (67 patients) were smokers. Fifteen percent of study group (18 patients) had history of dyslipidemia. Ten percent (13 patients) have positive family history of ischemic heart disease. Twenty five percent of the study group (30 patients) (Table 3).

Variables		Mean ± SD	Range
Total score		113.1 ± 26.0	56.0-165.0
		N	%
Risk	Low	70	58.3
	Moderate-High	50	41.7

Table 3: GRACE score among the studied cases.

In our study group, the mean GRACE score was 113.1 ± 26 ranged from 56.0-165.0. The percentage of the patients with low GRACE score was 58.3% (70 patients) while the percentage of the patients with moderate to high GRACE score was 41.7% (50 patients) (Figure 2).

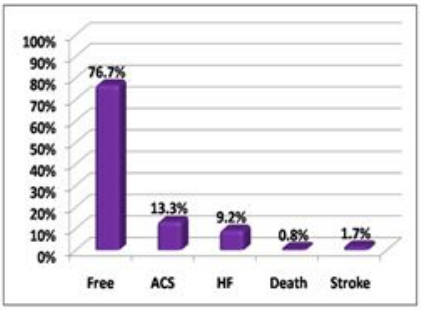

Figure 2: Follow up complications among the studied cases.

Among the study group, the mean time from fibrinolysis to PCI is 7.8 ± 3.5 with 94 patients had culprit PCI and 26 patients had multi-vessel PCI. Among those patients, 86 patients had one stent and 29 patients had two stents and 2 patients had more than two stents while 3 patients had only PTCA. Also, 65 patients had single vessel disease, 44 patients had two vessel disease and 11 patients had more than two vessel disease (Table 4).

		Mean ± SD	Range
Time from fibrinolysis to PCI (days)		7.8 ± 3.5	2.0-14.0
		N	%
PCI	Culprit	94	78.3
	Multi-vessel	26	21.7
Number	Single	65	54.2

	Two	44	36.7
	Multiple	11	9.2
Stent	None	3	2.5
	One	86	71.7
	Two	29	24.2
	Multiple	2	1.7
Complications during PCI	None	114	95
	Thrombus	4	3.3
	Slow flow	1	0.8
	Dissection	1	0.8

Table 4: Procedural data among the studied cases

This study showed that more than three quarters of the studied cases had no follow up complications and the most frequent complication was ACS. The percentage of cases which had ACS was 13.3% (number of patients 16), the percentage of cases with HF was 9.2% (number of patients 11), the percentage of cases with stroke was 1.7% (2 patients) and only one case died.

There was no statistically significant difference between the two groups regarding demographic characteristics and comorbidities.

Cases with complication had statistically significant higher HR (p value=0.027), killip classification (p=0.004), history of cardiac arrest (p=0.012) and total GRACE score (p=0.001) and statistically significant lower ejection fraction (p=0.016) (Figure 3).

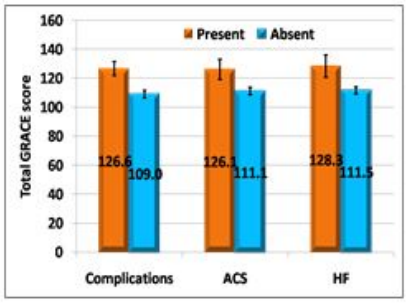

Figure 3: GRACE score among different complications

Cases with cardiovascular complications had significantly higher time from successful fibrinolysis to PCI (p value<0.001) (Figure 4).

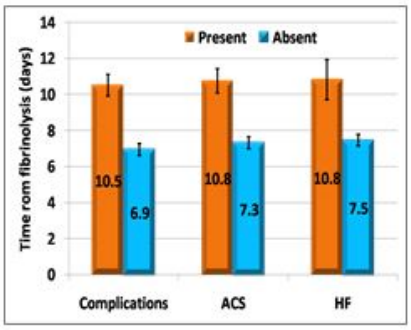

Figure 4: Time from fibrinolysis to PCI among different complications.

There was statistically significant positive correlation between rate of complication and HR (p=0.027), Killip classification (p= 0.004), cardiac arrest on hospital admission (p=0.001) and total GRACE score (p<0.001) and negative correlations with ejection fraction (p=0.016). Cases with cardiovascular complications had significantly higher time from successful fibrinolysis to PCI (p<0.001). Cases with ACS had significantly higher total GRACE Score (p value=0.031) and lower hemoglobin level (p=0.013). Also, cases with ACS had significantly higher time from fibrinolysis and more frequent procedural complications (p<0.011). There was statistically significant positive correlation between rate of HF and Killip classification (p=0.011), cardiac arrest on hospital admission (p=0.018) and total GRACE score (p=0.041) and negative correlations with ejection fraction (p=0.006). Cases with HF had significantly higher time from fibrinolysis to revascularization (p=0.002).

GRACE and time from fibrinolysis to PCI were significant factors that affect complications, ACS and HF, while EF was a significant factor that affects complications and HF (Figures 5-7).

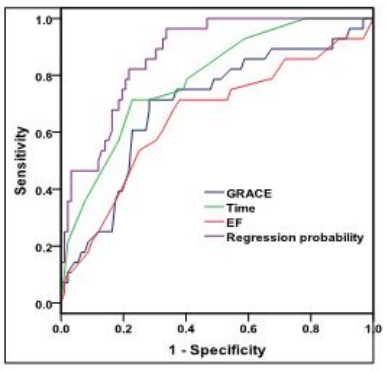

Figure 5: ROC curve for GRACE, time from fibrinolysis, EF and regression probability in prediction of complications.

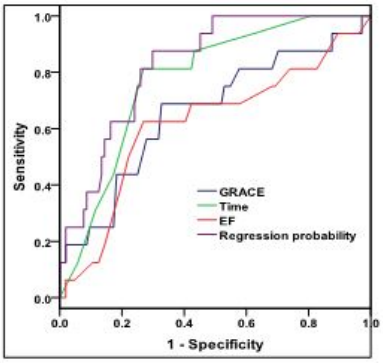

Figure 6: ROC curve for GRACE, time from fibrinolysis, EF and regression probability in prediction of ACS.

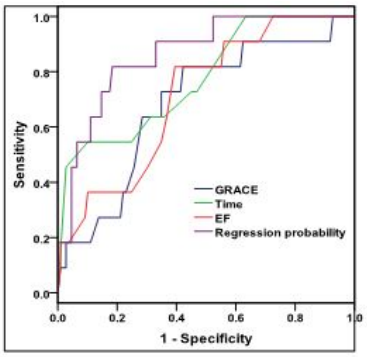

Figure 7: ROC curve for GRACE, time from fibrinolysis to PCI, EF and regression probability in prediction of HF.

Predicting probability for any complication:

Exp(-6.933+(0.047×GRACE)+(0.419×Time)+(-0.070×EF))/(1+(Exp(6.933+(0.047×GRACE)+(0.419×Time))))

Predicting probability for any ACS:

Exp(-9.140+(0.033×GRACE)+(0.360+Time))/(1+(Exp(-9.140+(0.033×GRACE)+(0.360+Time))))

Predicting probability for any HF:

Exp((0.019×GRACE)+(0.242×Time)+(-0.137×EF))/(1+(Exp((0.019×GRACE)+(0.242×Time)+(-0.137×EF))))

Discussion

Early pharmacoinvasive strategy (within 2-24 h) after successful reperfusion by fibrinolysis is recommended by recent guidelines [10], timely fashion coronary intervention is not widely available in countries with limited PCI capable hospitals including Egypt. Several randomized trials have shown that early routine post fibrinolysis angiography with subsequent PCI reduced the rates of recurrent ischemia and re-infarction compared with a waiting strategy, in which angiography and revascularization were indicated only in the patients with spontaneous or induced severe ischemia or left ventricular (LV) dysfunction. The benefits of early routine PCI after thrombolysis were noted in the absence of increased risk of adverse complications in many studies [11].

Many studies and meta-analysis demonstrated the accuracy and the usefulness of the GRACE score on the mortality of ACS patients in hospital and follow-up after hospital discharged [12].

Because of the long and geographic distance of transfer and few of number of interventional cardiologists, primary PCI and routine PCI after successful thrombolysis were very difficult to be done early. Several studies demonstrated the worst cardiovascular outcomes occur in patients who received delay coronary revascularization after thrombolytic therapy [13].

Risk assessment and stratification of STEMI patients is very important for the physicians in non-PCI capable hospital to guide selection of for early invasive strategy. GRACE risk score, one of clinical risk scores, has been shown to be a good risk stratification score in population with NSTE-ACS and STEMI.

The current study aimed to evaluate the prognostic utility of the GRACE score among an Egyptian cohort in a prospective cross sectional observational study conducted at Al-Azhar University Hospital and EL-Matarya Teaching Hospital (MTH) and involved 120 patients who presented with (STEMI) and received successful fibrinolysis, from March 2017 to February 2018.

This study showed that more than three quarters of the studied cases had no follow up complications and the most frequent complication was ACS. The percentage of cases which had ACS was 13.3% (number of patients 16), the percentage of cases with HF was 9.2% (number of patients 11).

Our study demonstrated that the long delay in patients with intermediate to high GRACE score after successful thrombolysis in non PCI-capable hospitals was associated with worse cardiovascular complications (death, rehospitalization with ACS, rehospitalization with HF and stroke) than the patients with low GRACE score ($P<0.001$) and this was concordant with the Southwest German Interventional Study in Acute Myocardial infarction (SIAM III) which has evaluated the effects of transfer and early PCI (within 6h after fibrinolysis) in comparison with delay PCI strategy (elective PCI 2 weeks after fibrinolysis). Early PCI has showed significant reduction of primary end point (death, reinfarction, target lesion revascularization (TLR) and ischemic events) ($p = 0.008$) and higher long term survival than delayed PCI ($p=0.057$) [14].

Similarly, The Trial of Routine Angioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI) trial showed that the patients who were transferred from non-PCI hospitals within 6 h after thrombolysis had fewer ischemic events than standard treatment (delayed PCI) with no increase of major bleeding rates [15].

Also, the Norwegian study on District treatment of ST-Elevation Myocardial infarction (NORDISTEMI) study also demonstrated a significant reduction in the total cardiovascular complications (stroke, reinfarction, death, or recurrent ischemia) at 1 year in the patients with immediate transferred to PCI following with thrombolysis as compared with the patients in conservative arm treatment (6% *vs.* 16%, $p=0.01$) [7].

The Combined Abciximab RE-teplase Stent Study in Acute Myocardial Infarction (CARESS-AMI) study, a more conservative

strategy (i.e. angiogram only in cases of failed fibrinolysis) was associated with a worse clinical outcome than the strategy of angiogram and PCI (if indicated) in all cases following fibrinolysis (composite of death, re-infarction and refractory ischemia at 30-day, 11% *vs.* 4%, p=0.004) [16].

On the data from CARESS-AMI [16] and TRANSFER-AMI [15], The American College of Cardiology (ACC) and the American heart association (AHA) a class IIa recommendations were given for high risk features (such as Kilip class>2, extensive ST-elevation, left ventricular systolic ejection fraction (LVEF) <35 %, or hypotension) and should be immediately transferred to PCI-capable facilities [17]. The transfer of low and moderate risk STEMI patients to PCI-capable hospital received a class IIb recommendation (Tables 5-14).

		Complication (N=28)	No (N=92)	P
Onset (h)		5.1 ± 1.9	5.1 ± 2.2	0.984
HR (Beat/minute)		105.8 ± 18.5	95.5 ± 22.1	0.027*
SBP (mmHg)		126.3 ± 30.3	126.7 ± 28.1	0.944
DBP (mmHg)		74.8 ± 20.7	77.9 ± 16.7	0.424
Serum creatinine (mg/dL)		1.36 ± 0.51	1.20 ± 0.51	0.146
Serum urea (mg/dL)		40.2 ± 13.0	37.3 ± 11.5	0.261
Hb (gm/dL)		13.2 ± 1.3	13.7 ± 1.5	0.107
FBG (gm/dL)		278.2 ± 108.9	286.7 ± 94.5	0.689
EF%		48.5 ± 9.3	52.6 ± 7.5	0.016*
Killip Class	I	14 (50.0%)	73 (79.3%)	0.004*
	II	13 (46.4%)	15 (16.3%)	
	III	1 (3.6%)	4 (4.3%)	
DKA		3 (10.7%)	6 (6.5%)	0.434
Crepitation		19 (67.9%)	48 (52.2%)	0.143
Tachyarythmia		7 (25.0%)	14 (15.2%)	0.260
Bradyarrythmia		1 (3.6%)	9 (9.8%)	0.450
Cardiac arrest		7 (25.0%)	4 (4.3%)	0.012*
Site (ECG)	Anterior	18 (64.3%)	51 (55.4%)	0.290
	Inferior	8 (28.6%)	38 (41.3%)	
	Both	2 (7.1%)	3 (3.3%)	
Total grace score		126.6 ± 25.2	109.0 ± 24.9	0.001*
Risk	Low	8 (28.6%)	62 (67.4%)	<0.001*
	Moderate-High	20 (71.4%)	30 (32.6%)	

Table 5: Comparison between cases with and without complications regarding clinical condition and laboratory findings at presentation

	Complication (N=28)	N (N=92)	P value
Time from fibrinolysis (days)	10.5 ± 3.1	6.9 ± 3.2	<0.001*
PCI	Culprit	22 (78.6%)	72 (78.3%)	1
	Multivessel	6 (21.4%)	20 (21.7%)	
Affection	Single	12 (42.9%)	53 (57.6%)	0.247
	Two	14 (50.0%)	30 (32.6%)	
	Multiple	2 (7.1%)	9 (9.8%)	
Stent	None	0 (0.0%)	3 (3.3%)	0.365
	One	18 (64.3%)	68 (73.9%)	
	Two	9 (32.1%)	20 (21.7%)	
	Multiple	1 (3.6%)	1 (1.1%)	
Complications		3 (10.7%)	3 (3.3%)	0.139

Table 6: Comparison between cases with and without complications regarding procedural data

Variables		ACS (N=16)	No (N=104)	P
Onset (hours)		5.7 ± 1.5	5.0 ± 2.2	0.128
HR (Beat/minute)		101.6 ± 21.2	97.4 ± 21.8	0.466
SBP (mmHg)		135.6 ± 33.7	125.2 ± 27.5	0.174
DBP (mmHg)		79.1 ± 23.1	76.9 ± 16.8	0.720
Serum creatinine (mg/dL)		1.40 ± 0.55	1.21 ± 0.51	0.165
Serum urea (mg/dL)		43.0 ± 13.4	37.2 ± 11.5	0.068
Hb (gm/dL)		12.9 ± 1.0	13.7 ± 1.5	0.013*
FBG (mgm/dL)		276.6 ± 95.8	286.0 ± 98.3	0.721
EF%		49.2 ± 8.9	52.0 ± 7.9	0.189
KillipClass	I	10 (62.5%)	77 (74.0%)	0.435
	II	5 (31.3%)	23 (22.1%)	
	III	1 (6.3%)	4 (3.8%)	
DKA		0 (0.0%)	9 (8.7%)	0.606
Basal Crepitaion		10 (62.5%)	57 (54.8%)	0.564
Tachyarythmia		4 (25.0%)	17 (16.3%)	0.478
Bradyarrythmia		1 (6.3%)	9 (8.7%)	1.000
Cardiac Arrest		3 (18.8%)	10 (9.6%)	0.379
Site (ECG)	Anterior	10 (62.5%)	59 (56.7%)	0.634
	Inferior	5 (31.3%)	41 (39.4%)	
	Both	1 (6.3%)	4 (3.8%)	
Total grace score		126.1 ± 28.0	111.1 ± 25.2	0.031*
Risk	Low	5 (31.3%)	65 (62.5%)	0.018*

	Moderate-High	11 (68.8%)	39 (37.5%)	

Table 7: Comparison between cases with and without ACS regarding clinical condition and laboratory findings at presentation

		ACS (N=16)	No (N=104)	P
Time from fibrinolysis (days)		10.8 ± 2.7	7.3 ± 3.4	0.001*
PCI	Culprit	13 (81.3%)	81 (77.9%)	1
	Multi-vessel	3 (18.8%)	23 (22.1%)	
Affection	Single	8 (50.0%)	57 (54.8%)	0.226
	Two	8 (50.0%)	36 (34.6%)	
	Multi	0 (0.0%)	11 (10.6%)	
Stent	None	3 (2.9%)	0 (0.0%)	0.571
	One	76 (73.1%)	10 (62.5%)	
	Two	23 (22.1%)	6 (37.5%)	
	Multiple	2 (1.9%)	0 (0.0%)	
Complications		3 (18.8%)	3 (2.9%)	0.031*

Table 8: Comparison between cases with and without ACS regarding procedural data

		HF (N=11)	No (N=109)	P
Onset (hours)		4.7 ± 2.0	5.1 ± 2.1	0.543
HR (Beat/minute)		108.4 ± 15.6	96.9 ± 22.0	0.094
SBP (mmHg)		121.4 ± 29.7	127.1 ± 28.4	0.526
DBP (mmHg)		74.5 ± 23.0	77.4 ± 17.1	0.607
Serum creatinine (mg/dL)		1.35 ± 0.46	1.22 ± 0.52	0.450
Serum urea (mg/dL)		36.5 ± 12.5	38.1 ± 11.8	0.659
Hb (gm/dL)		13.2 ± 1.3	13.6 ± 1.5	0.316
FBG (gm/dL)		286.7 ± 135.1	284.5 ± 93.9	0.943
EF %		45.4 ± 8.5	52.3 ± 7.8	0.006*
Kilib Class	I	4 (36.4%)	83 (76.1%)	0.011*
	II	7 (63.6%)	21 (19.3%)	
	III	0 (0.0%)	5 (4.6%)	
DKA		2 (18.2%)	7 (6.4%)	0.193
Crepitaion		8 (72.7%)	59 (54.1%)	0.343
Tachyarythmia		3 (27.3%)	18 (16.5%)	0.405
Bradyarrythmia		0 (0.0%)	10 (9.2%)	0.596
Cardiac arrest		4 (36.4%)	9 (8.3%)	0.018*
Site (ECG)	Anterior	9 (81.8%)	60 (55.0%)	0.286
	Inferior	2 (18.2%)	44 (40.4%)	
	Both	0 (0.0%)	5 (4.6%)	
Total grace score		128.3 ± 25.1	111.5 ± 25.7	0.041*
Risk	Low	3 (27.3%)	67 (61.5%)	0.049*
	Moderate-High	8 (72.7%)	42 (38.5%)	

Table 9: Comparison between cases with and without HF regarding clinical condition and laboratory findings at presentation

		HF (N=11)	No (N=109)	P
Time from fibrinolysis (days)		10.8 ± 3.7	7.5 ± 3.4	0.002*
PCI	Culprit	9 (81.8%)	85 (78.0%)	1.000
	Multivessel	2 (18.2%)	24 (22.0%)	
Affection	Single	5 (45.5%)	60 (55.0%)	0.505
	Two	4 (36.4%)	40 (36.7%)	
	Multi	2 (18.2%)	9 (8.3%)	
Stent	None	0 (0.0%)	3 (2.8%)	0.319
	One	8 (72.7%)	78 (71.6%)	
	Two	2 (18.2%)	27 (24.8%)	
	Multiple	1 (9.1%)	1 (0.9%)	
Complications		0 (0.0%)	6 (5.5%)	1.000

Table 10: Comparison between cases with and without HF regarding procedural data

Factors	AUC	SE	P	95% CI	Cut off
Complications					
GRACE	0.696	0.058	0.002*	0.582-0.810	≥ 127.0
Time	0.787	0.047	<0.001*	0.696-0.879	≥ 9.0
EF	0.653	0.063	0.014*	0.530-0.776	≤ 51.0
Regression probability	0.872	0.032	<0.001*	0.809-0.936	≥ 0.135
ACS					
GRACE	0.66	0.078	0.040*	0.508-0.812	≥ 127.0
Time	0.775	0.054	<0.001*	0.669-0.880	≥ 9.0
EF	0.619	0.081	0.127	0.459-0.778	--
Regression probability	0.844	0.038	<0.001*	0.769-0.919	≥ 0.135
HF					

GRACE	0.685	0.082	0.043*	0.525-0.845	≥ 116.0
Time	0.776	0.074	0.003*	0.630-0.921	≥ 13.0
EF	0.714	0.071	0.020*	0.574-0.853	≤ 51.0
Regression probability	0.844	0.054	<0.001*	0.739-0.950	≥ 0.109

Table 11: Diagnostic performance of GRACE, time from fibrinolysis, EF and regression probability in prediction of complications

Characters	Value	95% CI	Value	95% CI
	GRACE ≥ 127.0		Time ≥ 9.0	
Sensitivity	71.40%	51.3%-86.8%	71.40%	51.3%-86.8%
Specificity	68.50%	58.0%-77.8%	72.80%	62.6%-81.6%
DA	69.20%	60.1%-77.3%	72.50%	63.6%-80.3%
Youden's index	39.90%	20.7%-59.1%	44.30%	25.2%-63.3%
PPV	40.80%	27.0%-55.8%	44.40%	29.6%-60.0%
NPV	88.70%	79.0%-95.0%	89.30%	80.1%-95.3%
LR+	2.27	1.55-3.32	2.63	1.75-3.95
LR-	0.42	0.23-0.76	0.39	0.22-0.71
LR	5.43	2.14-13.77	6.7	2.62-17.15
Kappa	0.317	0.152-0.481	0.365	0.197-0.534
	EF ≤ 51.0%		Regression ≥ 0.135	
Sensitivity	71.40%	51.3%-86.8%	96.40%	81.7%-99.9%
Specificity	62.00%	51.2%-71.9%	66.30%	55.7%-75.8%
DA	64.20%	54.9%-72.7%	73.30%	64.5%-81.0%
Youden's index	33.40%	13.9%-52.8%	62.70%	50.9%-74.6%
PPV	36.40%	23.8%-50.4%	46.60%	33.3%-60.1%
NPV	87.70%	77.2%-94.5%	98.40%	91.3%-100.0%
LR+	1.88	1.32-2.67	2.86	2.13-3.85
LR-	0.46	0.25-0.85	0.05	0.01-0.37
LR	4.07	1.62-10.23	53.13	6.89-409.50
Kappa	0.25	0.094-0.406	0.457	0.318-0.596

Table 12: Diagnostic characteristics of GRACE, time from fibrinolysis, EF and regression probability in prediction of complications

Characters	Value	95% CI	Value	95% CI
	GRACE ≥ 127.0		Time ≥ 9.0	
Sensitivity	68.80%	41.3%-89.0%	81.30%	54.4%-96.0%
Specificity	63.50%	53.4%-72.7%	69.20%	59.4%-77.9%
DA	64.20%	54.9%-72.7%	70.80%	61.8%-78.8%
Youden's index	32.20%	7.7%-56.7%	50.50%	29.4%-71.6%
PPV	22.40%	11.8%-36.6%	28.90%	16.4%-44.3%
NPV	93.00%	84.3%-97.7%	96.00%	88.8%-99.2%
LR+	1.88	1.24-2.85	2.64	1.82-3.83
LR-	0.49	0.23-1.03	0.27	0.10-0.76
LR	3.82	1.23-11.83	9.75	2.60-36.59
Kappa	0.172	0.027-0.317	0.286	0.130-0.441
	Regression ≤ 0.135			
Sensitivity	81.30%	54.4%-96.0%		
Specificity	73.10%	63.5%-81.3%		
DA	74.20%	65.4%-81.7%		
Youden's index	54.30%	33.4%-75.3%		
PPV	31.70%	18.1%-48.1%		
NPV	96.20%	89.3%-99.2%		
LR+	3.02	2.03-4.48		
LR-	0.26	0.09-0.72		
LR	11.76	3.12-44.39		
Kappa	0.327	0.162-0.492		

Table 13: Diagnostic characteristics of GRACE, time from fibrinolysis, EF and regression probability in prediction of HF

Characters	Value	95% CI	Value	95% CI
	GRACE ≥ 116.0		Time ≥ 13.0	
Sensitivity	72.70%	39.0%-94.0%	54.50%	23.4%-83.3%
Specificity	57.80%	48.0%-67.2%	89.90%	82.7%-94.9%
DA	59.20%	49.8%-68.0%	86.70%	79.3%-92.2%
Youden's index	30.50%	2.6%-58.4%	44.50%	14.5%-74.4%
PPV	14.80%	6.6%-27.1%	35.30%	14.2%-61.7%
NPV	95.50%	87.3%-99.1%	95.10%	89.0%-98.4%
LR+	1.72	1.13-2.63	5.4	2.48-11.77
LR-	0.47	0.18-1.26	0.51	0.26-0.97
LR	3.65	0.92-14.52	10.69	2.80-40.85
Kappa	0.111	-0.005-0.227	0.357	0.111-0.603
	EF≤51.0		Regression ≥ 0.109	
Sensitivity	81.80%	48.2%-97.7%	81.80%	48.2%-97.7%
Specificity	57.80%	48.0%-67.2%	81.70%	73.1%-88.4%
DA	60.00%	50.7%-68.8%	81.70%	73.6%-88.1%

Youden's index	39.60%	15.0%-64.2%	63.50%	39.5%-87.4%
PPV	16.40%	7.8%-28.8%	31.00%	15.3%-50.8%
NPV	96.90%	89.3%-99.6%	97.80%	92.3%-99.7%
LR+	1.94	1.36-2.76	4.46	2.75-7.24
LR-	0.31	0.09-1.11	0.22	0.06-0.78
LR	6.16	1.27-29.88	20.03	4.01-99.89
Kappa	0.142	0.028-0.256	0.366	0.171-0.561

Table 14: Diagnostic characteristics of GRACE, time from fibrinolysis, EF and regression probability in prediction of HF

Conclusion

The excessive delay pharmacoinvasive strategy in patients with intermediate to high GRACE score after successful thrombolysis in non PCI-capable centers were associated with worse cardiovascular complications (death, readmission with ACS, readmission with HF and stroke) than the patients with low GRACE score at short term follow up. The GRACE score, the time from thrombolysis to PCI and regression probability were significant factors that predict complications, ACS and HF, while EF was a significant factor that predicts complications and HF.

Recommendations

- GRACE risk score is helpful for guiding the physicians in non PCI-capable centers to select those patients who need early intervention in STEMI patients after thrombolytic therapy

- Early transfer for early PCI after successful fibrinolysis to decrease the rate of ischemic complications after myocardial infarction.

- High GRACE score is a very helpful predictor for poor cardiovascular outcomes in STEMI patients.

- High GRACE score mandates early intervention in the pharmacoinvasive pathway.

- A bigger scale study is recommended to set the cut off values of GRACE score in guiding early intervention in the pharmacoinvasive strategy.

Limitations

There were some limitations in our study that may affect the clinical implication. The huge number of excluded patients reflected the limited facilities to coronary intervention within 2 weeks. The mortality was decreased because the small number of patients with high GRACE risk was included in our study. The GRACE score modality which we are validating in this study is the one that enables us to estimate risk of death 6 months after discharge following an ACS episode but we follow our patients for 3 months only. The precise assessment of the duration and nature of cardiac arrest during hospital admission couldn't be achieved accurately. The results were obtained from only two centers (Al-Azhar University hospital and El-Matareya Teaching Hospital).

References

1. Danchin N, Di Mario C, Falk V, Folliguet T, Garg S, et al. (2014) Guidelines on myocardial revascularization, Eur Heart J.
2. Srimahachota S, Boonyaratavej S, Kanjanavanit R, Sritara P, Krittayaphong R, et al. (2012) Thai Registry in Acute Coronary Syndrome (TRACS)-An Extension of Thai Acute Coronary Syndrome Registry (TACS) Group: Lower In-hospital but still high mortality at one-year. J Med Assoc Thai 95: 508-518.
3. GRACE Investigators (2001) Rationale and design of the GRACE (Global Registry of Acute Coronary Events) project: a multinational registry of patients hospitalized with acute coronary syndromes. Am Heart J 141: 190-199.
4. Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, et al. (2004) GRACE Investigators, et al. A validated prediction model for all forms of acute coronary syndromes in an international registry. JAMA 291: 2727-2733.
5. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, et al. (2012) Third universal definition of myocardial infarction. Circulation 126: 2020-2035.
6. Leung Y, Kaplan GG, Rioux KP, Hubbard J, Kamhawi S, et al. (2012) Assessment of variables associated with smoking cessation in Crohn's disease. Dig Dis Sci 57: 1026-1032.
7. Catapano A, Graham I, De Backer G, Wiklund O, Chapman MJ, et al. (2016): 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. Eur Heart J 37: 2999-3058.
8. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, et al. (2013) 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 34: 2159-2219.
9. Vanderpump MPJ (2005) The epidemiology of thyroid diseases. In: Braverman LE, Utiger RD, editors. Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text. 9th edn. Philadelphia: JB Lippincott-Raven p. 398-496.
10. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, et al. (2014) ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 35: 2541-2619.
11. D'Souza SP, Mamas MA, Fraser DG, Fath-Ordoubadi F (2011) Routine early coronary angioplasty vs. ischaemia-guided angioplasty after thrombolysis in acute ST elevation myocardial infarction: a meta-analysis. Eur Heart J. 32: 972-978.
12. Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, et al. (2004) A validated prediction model for all forms of acute coronary syndromes in aninternational registry. JAMA 291: 2727-2733.
13. D'Ascenzo F, Biondi-Zoccai G, Moretti C, Bollati M, Omede P, et al. (2012) TIMI, GRACE and alternative risk scores in acute coronary syndromes: a metaanalysis of 40 derivation studies on 216,552 patients and of 42 validation studies on 31,625 patients. Contemp Clin Trials 33: 507-514.
14. Scheller B, Hennen B, Hammer B, Walle J, Hofer C, et al. (2003) SIAM III Study Group. Beneficial effects of immediate stenting after thrombolysis in acute myocardial infarction. J Am Coll Cardiol 42: 634-641.
15. Cantor W, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, et al. (2009) Routine early angioplasty after fibrinolysis for acute myocardial infarction. N Engl J Med 360: 2705-2718.
16. Bøhmer E, Hoffmann P, Abdelnoor M, Arnesen H, Halvorsen S (2010) Efficacy and safety of immediate angioplasty versus ischemia-guided management after thrombolysis in acute myocardial infarction in areas with very long transfer distances results of the NORDISTEMI (NORwegian study on DIstrict treatment of ST-elevation myocardial infarction). J Am Coll Cardiol 55: 102-110.

17. Di Mario C, Dudek D, Piscione F, Mielecki W, Savonitto S, et al. (2008) Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI: an open, prospective, randomised, multicentre trial. Lancet 371: 559-568.