Diyala Journal of Medicine

ORIGINAL RESEARCH
published: 23 June 2022
Doi: https://doi:10.26505/DJM.22026330109

The prediction role of TIMI score in correlation with coronary angiogram to determine the coronary artery disease severity and extent in patients presenting with Non-ST Elevation Acute Coronary Syndrome

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Abstract

Background: Accurate risk stratification in patient clinically presented as a case of Non-ST Elevation acute coronary syndrome (NSTE-ACS) is important to assess the prognosis as well as to estimate the possible adverse event especially in those patient who are at high risk. Of these scoring risk; Thrombolysis In Myocardial Infarction (TIMI) risk score have been well corroborated to predict the possible prognosis for patients with NSTE-ACS. However, their value in estimation the severity of coronary artery disease (CAD) has been less studied.

Objective: To determine the role of TIMI score in prediction the severity of CAD and its extent by correlate the TIMI score with coronary angiography in patients have NSTE-ACS.

Patients and Methods: A cross section study, conducted on 264 successive patients admitted with Non-ST Elevation acute coronary syndrome at Ibn-Albitar cardiac center, Baghdad, Iraq, from the 1st of October 2017 to the 1st of October 2018. Patients were rearranging into three groups according to the seven standard variables of TIMI score. The extent of CAD was examined on coronary angiography; a lesion defined significant if stenosis ≥70% in any artery of three major coronary arteries or ≥50% of left main coronary artery.

Results: The total number of was 246 patients, mean age was 62.5±2.3 years. There were 67 (27.2%) of them belong to group 1 (low risk group), 142 (57.7%) of them belong to group 2 (intermediate risk group), and 37 (15.1%) of them belong to group 3 (high risk group). 54.1% of patients in group 3 had significant three-vessels coronary artery disease on comparing with 17.6% of group 2 patients and only 7.5% of group 1 patients had these lesions on coronary angiography (P-value <0.01). On the other hand, one-vessel coronary artery disease occurs more commonly and significant statistically (P-value <0.01) in group 2 (31.7%) than in patients in group 1 (26.9%) and group 3 (10.8%).

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Website:https://djm.uodiyala.edu.iq/index.php/djm

Received: 9 January 2022
Accepted: 10 April 2022
Published: 23 June 2022

ORIGINAL RESEARCH
published: 23 June 2022
Doi: https://doi:10.26505/DJM.22026330109

Conclusion: High TIMI risk score patients were more probably to have significant multi-vessels coronary lesions in comparison with those with TIMI risk score in intermediate or low range which lead to help in stratify the risk and possibility of early intervention.

Keywords: Coronary Angiography, Non-ST Elevation Acute Coronary Syndrome, Acute Coronary Syndrome risk stratification, TIMI score.

Introduction

Ischemic heart disease (IHD) is a condition in which there is decrease blood and oxygen supply to the myocardium; it take place when there is an inequality between oxygen supply and demand to the myocardial muscles. The commonest cause of myocardial ischemia is atherosclerosis of coronary artery (s) adequate to cause diminish in myocardial blood flow and reduce perfusion of the myocardial blood supply by that involved artery[1]. IHD may manifest clinically as either Chronic Coronary Syndrome (CCS) or ACS. The spectrum of ACS includes ST-elevation myocardial infarction (STEMI), and the non-ST elevation acute coronary syndrome (NSTE-ACS). The latter consist of unstable angina (UA) and non-ST elevation myocardial infarction (NSTEMI). Which have indistinguishable clinical presentation at the initial evaluation [2].Patients with NSTE-ACS are a hybrid group of population with variable risk for morbidity and mortality[3]. Stratification of the risk is important to decide suitable decisions regarding management of these patients[4].Patients with elevated risk will receive more effective treatment strategy (Coronary intervention or medication)[5],[6].Besides the prognostic assessment, predicting the extension of coronary artery disease (CAD) lesions is beneficial for making decision clinically[5]. CAD accounts for 30% of all global deaths, representing the commonest cause of adult mortality[7].Although there is a drop in cardiovascular disease (CVD) mortality over the last three decades, cardio-vascular and circulatory diseases still the main causes of the death worldwide, responsible for more than 54 million deaths in 2013 [8],[9],[10].

Estimation of short term cardiovascular risk is a key component for the initial assessment for patients with ACS, cardiovascular risk in this setting refers to death or a further cardiovascular event (new or recurrent) STEMI, or acute recurrent ischemia need revascularization) within 30 days if the patient is managed medically[11].In Thrombolysis In Myocardial Infarction (TIMI) III Registry, the rate of (re)infarction and death were 2.9% and 2.5%, respectively. In many trials, which attend to enlist patients at increasing risk who reveal presence of ischemia on presentation, the rates are relatively higher ranging from 5% to 12% for (re)infarction and 3.5% to 4.5% for death. Therefore, Risk stratification is important in UA/NSTEMI in delivering a proper assessment of patients' prognosis[12]. "The American College of Cardiology (ACC)/American Heart Association (AHA) 2014 Guideline" update for the management of patients with UA/NSTEMI and "The 2015 European Society of Cardiology (ESC) Guidelines for the management of ACSs in patients presenting without ST-segment elevation" recommend (Class I, Level Of Evidence [LOE] B) using risk stratification scores such as Thrombolysis In Myocardial Infarction (TIMI)(5) or Global Registry of Acute Coronary Events (GRACE) risk scores

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to assess prognosis[13],[14],[15],[16].Risk scores estimate a likelihood for unfavorable outcomes based on combinations of clinical assessment, electrocardiographic (ECG), and laboratory information provided at presentation. These tools integrate multiple predictors and thus provide a more comprehensive risk assessment than does focus on a single variable. The short-term outcomes of UA/NSTEMI can be predicted by variety of methods, and the GRACE and TIMI risk scores are the most systematic and widely used approaches. The most important elements of these scores are the patient's age, clinical presentation, and co-morbidities; ECG finding; elevated troponin concentrations; and continuing episodes of pain despite medical therapy[16].The TIMI score is commonly used tool to predict the short-term risk for death and nonfatal myocardial infarction in NSTE-ACS patients.[11] This simple, rapid assessment at the initial evaluation identified patients at high-risk who can derive advantage from an early interventional strategy and more intensive antithrombotic therapy. The main benefit of the TIMI risk score is that is a simple numeric sum that can be calculated without calculator at the bedside; while GRACE risk score use the averages of multiple risk factors and may needed a computer to calculate.[16] Important variables were chosen from baseline characteristics that could be detected at presentation and that had been described and reported previously by several studies to be an important variable to predict outcome. Using logistic regression of multivariable, seven independent and statistically significant variables were identified of the composite end point at 14 days Table (1). Because the value of the prognostic significance for each variable were similar, the TIMI score for UA/NSTEMI was made up as a simple numeric total of the number of the variables. Thus, the risk score is determined by giving 1 point for each variable that exist[17]. Studies have found a number of the following variables as markers of increasing risk for cardiac ischemic events and death:

1- Severity of angina (≥ 2 anginal chest pain events within 24 hours); The importance of this variable has been approved in multiple studies, in which recurrent anginal episodes in last 24 hours, anginal chest pain at rest, and post-MI angina, each have been demonstrated to conduct a worse prognosis[18].

2- Age ≥65 years; increasing age has been demonstrated to be a risk factor in patients with ACS. For the purpose of simplicity, age is often deal with it as a dichotomous variable (e.g., younger than 64 years versus 65 years or older). In both UA/NSTEMI patients, appoint of inflection is nearly evident at 65 years, thus confirming the use of 65 years as a cut point when desired a binary approach.[17].

3- ≥3 Risk factors for CAD; the major four modifiable risk factors for CAD are hypercholesterolemia, hypertension, diabetes mellitus (DM), and cigarette smoking- have been shown to strongly predict prevalence and incidence of CAD in a large number of studies. Family history CAD prematurely "age <55 years for 1st degree male relative and <65 years for 1st degree female relative" considered as a no-modifiable risk factor [19].

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4- Prior use of aspirin; many studies have confirmed that there are increasing risk among patients with previous aspirin use.[20] This may be due to the presence of resistance to aspirin, platelet-rich thrombi or to the high probability for severe CAD in patients who present with UA/NSTEMI while taking aspirin[21].

5- ST-segment deviation on ECG; ST-segment depression on the ECG at presentation may indicate acute severe ischemia and is associated with a bad in-hospital prognosis[22]. The finding of ST-segment depression is also correlated with more culprit lesion complexity and hence a more probability of needing for revascularization[23].Depression of ST-segment regarded as a predictor of more extensive CAD and is correlated with bad outcomes at 6 months and 1, 4, and 10 years, ST-depression had an nearly two-fold increase risk of death or MI at 30 days and at 1 year [23].

6- Elevated serum cardiac markers; Patients with evidence of myocardial muscles necrosis (as documented by biochemical tests) have increase mortality rates than patients without such elevations[24].High sensitivity troponin test with their higher sensitivity and specificity, have arisen as the biomarker of choice for determining myocardial muscles necrosis [25].There is a clear correlation between the elevation of serum level of troponin and mortality[26].With higher clinical sensitivity, troponins have an ability to detect micro-infarction in nearly 30% of patients who diagnosed as having UA[26].

7-Known CAD (≥50% STENOSIS);among patients with stable CCS, there is an increasing risk in correlation to the number of vessels with diameter more than 50% stenosis and the presence and severity of left ventricular (LV) dysfunction. However, in patients with ACS; the relative prognosis impact of extent of CAD is probably less because the risk of short-term events is dominant by culprit lesion features, such as whether it induces ST-segment depression or increase troponin level [16].

The aim is to determine the role of TIMI score in prediction the coronary artery lesion(s) severity and extent in correlation with coronary angiographic finding during hospital admission in patients presented with NSTE-ACS.

Table (1): Timi Risk Score

Characteristics	points
Age ≥ 65 years	**1**
≥ 3 Risk factors for CAD “Family history of CAD, Hypertension, DM, Hypercholesterolemia, or being a current smoker”	**1**
Known CAD (stenosis ≥ 50%)	**1**
Aspirin use in last 7 days	**1**
≥ 2 anginal events within the prior 24 hours	**1**
≥ 0.5 mm ST-segment deviation on ECG	**1**
Elevated serum cardiac markers	**1**
Risk Score = Total Points	**(0 – 7)**

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Patients and Methods

A cross-sectional, single hospital based study was conducted on 264 successive patients in the department of cardiology of Ibn Al-Bitar Specialized center for cardiac surgery, during the period from October 2017 till October 2018. Patients who completed the criteria of NST-ACS (UA or NSTEMI) were selected and undergo coronary angiography during the hospitalization period after agreement. All patients were evaluated by use of an ordered questionnaire regarding main risk factors and past medical history. Detailed clinical examination, 12 lead surface ECG, biochemical tests including lipid profile, serum cardiac biomarker and echocardiography were conducted to all patients. Inclusion criteria was patients older than 20 years admitted with history of recent chest pain, resting chest pain or chest pain with minimal exertion or with symptoms suggestive of angina equivalent, with the last episode occurring during 24hours of admission. Any ST-segment deviation on ECG or elevated level of cardiac biomarkers were also recorded.

Exclusion criteria was any patients with ST-segment elevation on their admission ECG, new onset of LBBB, prior history of percutaneous coronary intervention (PCI), contraindications to coronary angiography, or coronary artery bypass grafting (CABG) because our aim to compare with the extent of native coronary artery disease.

The diagnosis of patients with NSTE-ACS was based on history and physical examination, ECG finding, and cardiac biomarkers. All registered patients receive standardized medical therapy and they admitted in the coronary care unit (CCU). The chest pain of ACS described heaviness or pressure usually lasting > 20 minutes, the pain may be exacerbated by minimal exertion and can be new-onset or increased in severity and frequency or triggered with minimum effort than previous angina. The chest pain of NSTE-ACS is more severe and protracted (as compared with stable angina), often requiring multiple doses of sublingual nitroglycerine or extended times of rest to relief chest pain. All patients underwent 12 lead ECG, patients with ST-segment changes (i.e. ST-segment depression ≥0.5, T-Wave inversion >3mm, or transient ST-segment elevation≥ 0.5 mm) on the initial ECG can help risk-stratify patients with NSTE-ACS. Blood samples for cardiac troponin I were drown on presentation to (CCU). Serum cardiac troponin I was determined using On SiteTM Troponin I Combo Rapid test (CTK BIOTECH), this test is a lateral flow chromatography immune-assay for qualitative detection of cardiac Troponin I and its complex in human serum, plasma or whole blood at a level ≥ 1 ng/ml. All tests were done by lab staff uninformed of the clinical and angiographic data. Lipid profile, fasting blood sugar and/or HbA1C were obtaining. Dyslipidemia is often referred to as an elevation of total cholesterol in the blood to > 200 mg/dl.

For all patients; calculation of TIMI risk score was done. TIMI risk score is the sum total of seven variables, each variable takes one point; I. Age ≥65 years. II. ≥3 risk factors for CAD [Hypertension, DM, hypercholesterolemia, family history of premature CAD, current smoker]. III. known CAD (stenosis ≥50%). IV. use of aspirin in previous 7 days. V. ≥ two episodes of rest chest pain in the last 24 hours. VI. deviation

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of ST-segment ≥ 0.5mm. V Elevated serum cardiac troponin. According to this score, the patients were classified into three groups; group 1 (the low risk group); TIMI risk score between 0- 2; group 2 (the intermediate risk group); TIMI risk score between 3 - 4; group 3(the high risk score group); TIMI risk score between 5 – 7.

Diagnostic coronary angiography done for all patients through radial or femoral access using Judkins approach. The procedure was carried out within 72 hours of admission to hospital. All significant lesions were examined in multiple views. Interpretation of Coronary Angiography and assessment of angiographic lesion was done by visual estimation of experienced cardiologist. In each case we tried to distinguish the ischemia related artery and a culprit lesion with a visual stenosis diameter of ≥ 70 % on the anatomical basis [Left Anterior Descending artery (LAD), Left Circumflex artery (LCX), Right Coronary artery (RCA) lesions], and ≥50% for Left Main coronary artery (LMCA) lesions which was taken as significant anatomical stenosis. According to coronary angiographic results; the degree of coronary artery disease was categorized as:

1-Normal (no lesion on coronary angiogram).

2-Non-significant coronary lesion "< 70% stenosis in one or more Coronary artery(s) and < 50% stenosis of left main coronary artery".

3-Significant one-vessel disease "≥ 70% stenosis in 1 major Coronary artery".

4-Significant two-vessels disease "≥ 70% stenosis in 2 major Coronary arteries".

5-Significant three-vessels disease "≥ 70% stenosis in all 3 major Coronary arteries".

6-Significant left main CAD "≥ 50% stenosis of left main coronary artery".

Statistical Analysis

All collected data were recorded and analyzed by the Statistical Package for Social Science version 19.0 Software (IBM SPSS Statistics). Continuous variables like age were shown as means ± standard deviation (SD); categorical variables were displayed as absolute numbers and percentage and they were compared by use of one-way Analysis Of Variance (ANOVA). Chi-square test was implemented to demonstrate the difference in proportions between the TIMI groups. A P-value of less than 0.05 was regarded to indicate significance for all factors. After the determination of the scores significant differences between the groups with and without coronary lesion, the predictive power (regardless of scores) was estimated using the C statistic [area under the Receiver Operating Characteristics (ROC) curve], area under curve (AUC) ≤ 0.69 considered as poor performance of the test [27].

Results

A total of 246 patients with NSTE-ACS (Unstable Angina or Non ST-Elevation Myocardial Infarction) were enrolled from 1st October 2017 to 1st October 2018. Table (2) shows the baseline characteristics of patients according to the status of TIMI risk score, the patients were arranged into three groups; 67 (27.2%) of them belong to group 1 (low risk group), 142 (57.7%) of them belong to group 2 (intermediate risk group), and 37 (15.1%) of them belong to group 3 (high risk group). There were 177 (72%) male and 69 (28%) female. Among the group 1, group 2, and group 3; the percentage was 76.1%, 71.1%, and 67.6% for males, and 23.9%, 28.9%, and

ORIGINAL RESEARCH
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Doi: https://doi:10.26505/DJM.22026330109

32,4% for females, respectively, without statistical significance (P-value 0.08) of sex distribution between the three groups Table (3). The age range was between 40-70 years and mean age of the sample was 62.5±2.3 years. with mean age is highest in group 3 (66.5 ±1.6 year), and the mean age of group 2 and group 1 are 63.1 ±3.1 and 58.6 ±4 year, respectively Table (2), with significant difference among the three groups (P-value <0.001). 97.2% of patients in group 3 were older than 65 years as compared with 42.9% and 1.4% of patients in group 2 and 1, respectively, with statistical significance (P-value <0.001) among three groups (Table 2). Serum Troponin I was positive in 117 patients, with higher percentage (81%) of patients in group 3 had positive Troponin I compared with 51% and 22% of patients in groups 2 and 1, respectively, P value <0.001 Table (2).

Table (2): Characteristics baseline of patients based on TIMI score status

TIMI Risk score					Total	P-value
		Group 1 n=67	Group 2 n=142	Group 3 n=37		
Mean age	Mean age within TIMI group ± SD	58.6 ± 4.0	63.1 ± 3.1	66.5 ±1.6		< 0.001
age ≥ 65year	Count	1	61	36	98	< 0.001
	% within TIMI group	1.4%	42.9	97.2		
	% within the Variable	1.0%	62.2%	36.7%	100%	
	% of Total	0.4%	24.4%	14.6%	39.4%	
≥ 3 risk factors	Count	2	71	36	109	< 0.001
	% within TIMI group	2.9%	50%	97.2		
	% within the Variable	1.8%	65.1%	33.0%	100%	
	% of Total	0.8%	28.8%	14.6%	44.2%	
≥2episode of chest pain in last 24hr	Count	61	130	34	225	0.1
	% within TIMI group	91%	91%	91.8%		
	% within the Variable	27.1%	57.8%	15.1%	100%	
	% of Total	24.4%	52.8%	13.8%	91.2	
known CAD (>50% stenosis)	Count	5	28	16	49	< 0.001
	% within TIMI group	8%	19%	43%		
	% within the Variable	10.2%	57.1%	32.7%	100%	
	% of Total	2%	11.3%	6.5%	19.8%	
positive serum Troponin I	Count	14	73	30	117	< 0.001
	% within TIMI group	22%	51%	81%		
	% within the Variable	12.0%	62.4%	25.6%	100%	
	% of Total	5.6%	29.6%	12.1%	47.3%	
ST-segment deviation	Count	21	72	34	127	< 0.001
	% within TIMI group	31.3%	50.7%	92%		
	% within the Variable	16.6%	56.7%	26.7%	100%	
	% of Total	8.5%	29.2%	13.8%	51.5%	
Aspirin use in last 7 days	Count	17	48	13	78	0.2
	% within TIMI group	25.3%	33%	35%		
	% within the Variable	21.8%	61.5%	16.7%	100%	
	% of Total	6.9%	19.5%	5.2%	31.6%	

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The most prevalent variable among three groups was chest pain Table (2), with 225 (91.2%) of patients had two or more episodes of typical chest pain or chest pain equivalent during last 24 hours before admission to the hospital, there was no significant difference statistically in the percentage of chest pain between the three groups (P-value 0.1).

Of total, 127 (54.3%) patients had ST-Segment deviation on ECG, 92% of patients in group 3 had ST-Segment deviation on ECG compared with 50.7% of patients in group 2 and only 31.3% of patients in group 1 (P-value=<0.001). The pattern of ST-Segment deviation either >0.5mm ST-Segment depression or >3mm T-Wave inversion also shows statistically significant difference among three groups (P-value <0.001), as shown in Table (4). The percentage of the patients take aspirin in at least one week before admission is slightly higher in group 3 (35%) and group 2 (33%) than in group 1 (25.3%) without statistical significance (P-value=0.2). As shown in Table (2). Of total, 49 patients had documented previous coronary angiography reports, Table (2) shown at least one coronary artery stenosis of ≥ 50% (except for left main coronary artery). With significantly higher percentage in group 3 (43%) than in group 2 (19%) and group 1 (8%), P value < 0.001.

Table (3): Distribution of patients gender among TIMI groups

			Timi Risk Score				
			Group 1	Group 2	Group 3	Total	P-value
GENDER	MEN	Count	51	101	25	177	0.08
		% within GENDER	28.8%	57.1%	14.1%	100.0%	
		% within TIMI GROUP	76.1%	71.1%	67.6%	72.0%	
	WOMEN	Count	16	41	12	69	0.08
		% within GENDER	23.2%	59.4%	17.4%	100.0%	
		% within TIMI GROUP	23.9%	28.9%	32.4%	28.0%	
Total		Count	67	142	37	246	
		% within GENDER	27.2%	57.7%	15.0%	100.0%	
		% within TIMI GROUP	100.0%	100.0%	100.0%	100.0%	

The collection of three or more risk factors for CAD as a single variable were present in 109 (44.2%) patients Table (2), with incidence rate was highest in group 3 (97.2%) than in group 2 (50%) and lowest rate was in group 1 (2.9%) with statistically significant difference between three group (P-value= <0.001). Among the TIMI risk score defined five risk factors for coronary artery diseases; the history of hypertension was the most prevalent risk factor (70.3%) followed by hyperlipidemia (47.4%), current smoker (45.8%), diabetes mellitus (40.6%), and family history of premature coronary artery diseases (21.9%). Each one of these risk factors presented more commonly in group 3 and group 2 than group 1, as shown in Table (5).

Table (6) shows the coronary angiography results, 58 (23.6%) patients with normal or non-significant CAD, 67 (27.2%) patients had significant one-vessel CAD, 51 (20.7%) patients had significant two-vessels CAD, 50 (20.3%) patients had significant three-vessels CAD, and 20(8.1%) patients had left main CAD with or without other vessels CAD.

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Table (4): Ass Pattern of ST-Segment deviation among TIMI groups

ST-Segment deviation		Timi Risk Score			Total
		Group 1 n=67	Group 2 n=142	Group 3 n=37	
>0.5 ST-Segment depression	Count	5	38	29	72
	% within ST-Segment deviation	6.9%	52.8%	40.3%	100.0%
	% within TIMI RISK SCORE	7.4%	26.7%	78.3%	
>3mm T-Wave inversion	Count	16	34	5	55
	% within ST-Segment deviation	29.1%	61.8%	9.1%	100.0%
	% within TIMI RISK SCORE	23.8%	23.9%	13.5%	
Total	Count	21	72	34	127
	% within ST-Segment deviation	16.5%	56.7%	26.8%	100.0%
	% within TIMI RISK SCORE	100.0%	100.0%	100.0%	100.0%

Table (5): Distribution of risk factors of CAD among TIMI groups

RISK FACTORS FOR CAD		TIMI risk score			Total	P-value
		Group 1	Group 2	Group 3		
Family history of premature CAD	Count	13	31	10	54	0.01
	% within TIMI group	19.4%	21.8%	27%		
Hypertension	Count	31	109	33	173	<0.001
	% within TIMI group	46.2%	76.7%	89%		
Diabetes Mellitus	Count	16	59	25	100	<0.001
	% within TIMI group	23.8%	41.5%	67.5%		
Hyperlipidemia	Count	21	69	27	117	<0.001
	% within TIMI group	31.3%	48.6%	73%		
Current smoker	Count	25	71	17	113	0.03
	% within TIMI group	37.3%	50%	45%		

Normal or non-significant CAD occurs more commonly and statistically significant (P-value <0.01) in patients with group 1 (52.2%) than in patients with group 2 (15.5%) and group 3 (2.7%). On the other hand, one-vessel CAD occurs more commonly and statistically significant (P-value <0.001) in group 2 (31.7%) than in patients in group 1 (26.9%) and group 3 (10.8%). Significant two-vessels CAD occurs in higher percentage in group 2 (27.5%) and in lower percentage in group 3 (13.5%) and group 1 (10.4%). 54.1% of patients in group 3 had significant three-vessels CAD disease, while 17.6% of patients in group 2 and only 7.5% of patients in group 1 had these lesions on coronary angiography. Left main CAD with or without involvement of other major coronaries occurs more commonly in group 3 (18.9%) than in group 2 (7.7%) and in group 1 (3%), as shown in Table (6).

In multiple logistic regression analysis, shown by the C statistic (area under the ROC curve), the predictive power of TIMI score to distinguish who will have a coronary lesion was determined as follow: TIMI score area under the ROC curve = 0.747, confidence interval [CI] 95% from 0.675 to 0.820, p < 0.001 Figure (1).

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Table (6): Coronary angiographic result among TIMI groups

Coronary Angiogram results		TIMI Risk score			Total	P-value
		Group 1	Group 2	Group 3		
Normal or non-significant CAD	Count	*35*	*22*	*1*	*58*	<0.01
	% within Coronary Angiogram results	60.3%	37.9%	1.7%		
	% within TIMI Risk score	52.2%	15.5%	2.7%		
Significant one-vessel CAD	Count	*18*	*45*	*4*	*67*	0.03
	% within Coronary Angiogram results	26.9%	67.2%	6.0%		
	% within TIMI Risk score	26.9%	31.7%	10.8%		
Significant two-vessels CAD	Count	*7*	*39*	*5*	*51*	<0.01
	% within Coronary Angiogram results	13.7%	76.5%	9.8%		
	% within TIMI Risk score	10.4%	27.5%	13.5%		
Significant three-vessels CAD	Count	*5*	*25*	*20*	*50*	<0.01
	% within Coronary Angiogram results	10.0%	50.0%	40.0%		
	% within TIMI Risk score	7.5%	17.6%	54.1%		
Significant Left Main CAD with or without other vessels CAD	Count	*2*	*11*	*7*	*20*	<0.01
	% within Coronary Angiogram results	10.0%	55.0%	35.0%		
	% within TIMI Risk score	3.0%	7.7%	18.9%		

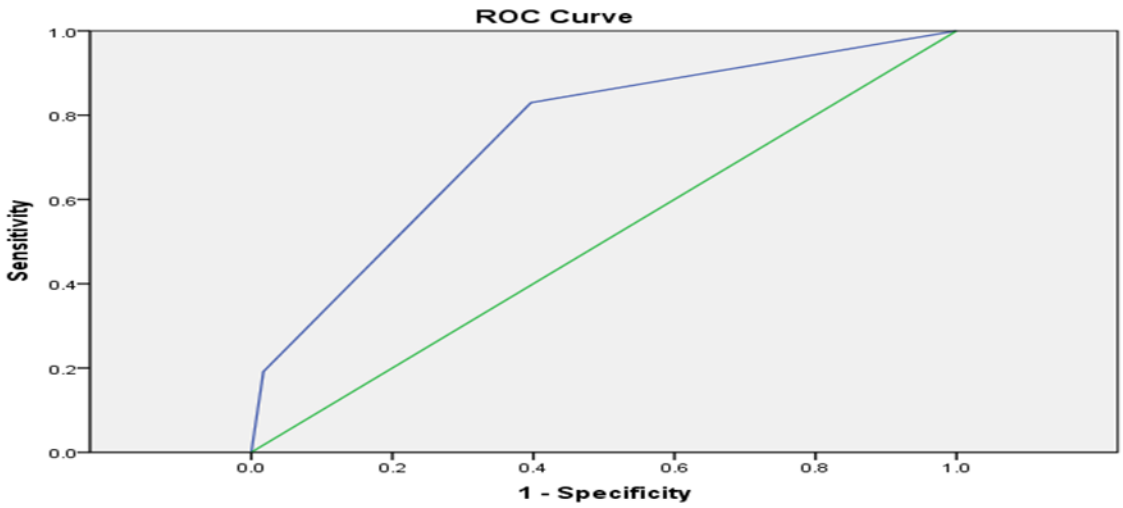

Figure (1): Area under RCO curve of TIMI risk score

Discussion

In our study the ECG showed significant ST- T changes in 51.5% of the patients, out of the 37 patients in group 3, 91.8% of patients with ST segment change had significant CAD. The ECG changes in this study well correlated with a study done by Colton R. *et al* conducted on 100 patients with unstable angina who underwent coronary angiogram demonstrated that 54% of the patients had ST segment deviation [28]. Another study by Weber T, Maurer E *et al* conducted on 30 patients who stratified on the basis of severity of ECG changes and thereafter underwent coronary angiogram which revealed that patients with significant

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ECG changes showed significant coronary artery lesions as compared with normal ECG [29].

In this study, we categorized the patients into three groups according to the TIMI scores and examined the relationship of this risk score with the CAD extension. 54.1% of patients in group 3 had significant three-vessels CAD disease when compared with 17.6% of patients in group 2 and only 7.5% of patients in group 1 had these lesions on coronary angiography (P-value <0.01) . On the other hand, one-vessel CAD occurs more commonly and statistically significant (P-value <0.001) in group 2 (31.7%) than in patients in group 1 (26.9%) and group 3 (10.8%) and according to these results; higher TIMI score patients were more probably to have significant left main CAD or significant multi-vessel CAD as compared with those with intermediate or low TIMI score.

These findings well correlated with the results of Mega *et al*, who analyzed the relationship between TIMI score as a risk stratification model and coronary anatomy in a study conducted on 1,491 patients diagnosed with NSTE-ACS, patients with TIMI scores of 5 - 7, were more probably to have a severe CAD (81% vs 58%, p < 0.001) and multivessel disease (80% vs 43%, p <0.001), in comparison to those with those who TIMI score of 0 to 2, as well as the possibility of significant left main disease (p <0.001) also progressively increased with elevated TIMI risk scores (p <0.001). On the other hand, past history of CAD, elderly, and ST-segment deviation were the TIMI score variables that exhibit significant relationship with the CAD severity. Moreover, elevated serum troponin, deviation of ST-segment and prior aspirin use were associated significantly with coronary thrombus and/or decline of the blood supply in that culprit coronary artery [30].

Zheng and colleagues found that significant relationship of TIMI score with clinical type of CAD (p< 0.001) in their study [31].

Likewise, in a retrospective study of 688 patients serial medical reports admitted with NSTE-ACS who underwent coronary angiography, Garcia and coworkers evaluated the association between TIMI risk score and CAD severity and showed that three vessel CAD or left main CAD was found more frequently in patients with TIMI risk score of 3-5 than in patients with TIMI score of 0-2 (OR 3.96, 95% CI 2.00 - 5.10; p < 0.001), and in patients with TIMI risk score of 5 - 7 (OR 6.34, 95% CI 3.88 - 10.36; p < 0.001), and the they concluded that for any increase in the TIMI risk score, there is an increase percentage of the adverse events and probability that the patients will have multi-vessels or left main coronary artery disease [32].Differs from our study, this study information were confined by the retrospective evaluation of only the TIMI score.

In a recent retrospective study, Ben Salem *et al* studied the CAD extension and severity in 239 patients with NSTE-ACS. It was noticed that patients who had low risk score (TIMI score of 0-2) had no coronary lesion on coronary angiography or non-significant coronary artery lesion, in comparison with high score of 5-7 (36.3% versus 13%, p < 0.001), alternatively; lesions affecting three vessels or left main coronary artery were

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published: 23 June 2022
Doi: https://doi:10.26505/DJM.22026330109

present frequently in patients with high risk [33].

In our study, from the C statistic calculation (area under the ROC curve) it can be shown that the TIMI score display the fair predictive ability to distinguish those probably to have a significant coronary lesion from those who have not significant coronary lesion (area under the ROC curve = 0.747, confidence interval [CI] 95% from 0.675 to 0.820, p < 0.001). Mahmood *et al* showed in a cohort study conducted on 406 patients with NSTE-ACS, that a TIMI score more than 4 and GRACE score more than 133 were significantly correlated with multi- vessel CAD and left main CAD, while TIMI risk score equal or less than 4 and GRACE score equal or less than 133 were correlated with normal coronary arteries or non-significant coronary lesion (p<0.01). They applied C-statistics to predict the accuracy of above two scores for assessing angiographic disease, the results was between 0.56- 0.65 for the TIMI risk score and ranging between 0.57- 0.72 for the GRACE risk score for different lesions, clarify that the GRACE risk score had better discriminating accuracy [34].

Limitations

Our study did have some limitations: First; because there was a predominance of male patients in our study, the results may be inapplicable to a group with a female predominance. Second; The absence of quantitative coronary angiography methods of both Intravascular Ultrasound imaging (IVUS) and Fractional Flow Reserve (FFR) application (IVUS to assess the intermediate lesion severity and FFR to assess physiological information about the lesion severity). Like most of the studies; application of coronary angiography in lesion assessment has its own limitations. Though coronary angiography is regarded as the standard golden study for the estimation of coronary artery lesions. The plaque volume & characteristics cannot be assessed by coronary angiography. In case of eccentric lesions; Multiple views has to be assessed before lesion assessment. In this study, the assessment of coronary lesion is subjective and qualitative.

Conclusions

Our study supports that the TIMI risk score has significant role for assessment of extension and severity of the CAD in NSTE-ACS patients. Among patients referred for coronary angiography who are presenting with NSTE-ACS (UA / NSTEMI), stratify the risk according to the TIMI risk score well correlates with the results of coronary angiographic extent and severity of CAD. Patients with elevated TIMI risk score were more probably to have severe three or more vessels or left main CAD in contrast to those with lower scores. A routine interventional protocol in elevated TIMI risk score patients could be advised as the preferred protocol. The TIMI score can be simply calculated at the bedside with easy-to-get its seven variables depending on clinical, laboratory, and electrocardiographic parameters.

Recommendations

Because of its simplicity in calculation and easiness to obtain its variable, advise to consider TIMI risk score as the most important score in stratify the risk of patients presented with NSTE-ACS to identify patients with high risk who will beneficial from early coronary intervention, by timely referral (in remote area without cath lab

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published: 23 June 2022
Doi: https://doi:10.26505/DJM.22026330109

facilities) or by aggressive use of anti-ischemic medications.

Source of funding: This research was funded by ourselves and there is no other funding cover this study or manuscript preparation and publication.

Ethical clearance: Data collection, research conduction and statistical analysis done by Dr.Mustafa S. Hussein and Dr.Sabah H. Ibrahim.

Conflict of interest: Nill

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Diyala Journal of Medicine

ORIGINAL RESEARCH
published: 23 June 2022
Doi: https://doi:10.26505/DJM.22026330109

دور حسبة تيمي "TIMI" التخمينية بالترابط مع فحص تصوير الاوعية التاجية لتحديد خطورة و امتداد مرض الشريان التاجي الحاد لمرضى تم تعريف اصابتهم بمتلازمة الشريان التاجي الحاد غير المرتبط بمقطع"ST"

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الملخص

خلفية الدراسة: ان تدرج الخطورة الصحيح للمرضى المشخصين سريرا كحالات متلازمة الشريان التاجي الحادة غير المرتبط بمقطع "ST"هو مهم لتقييم توقعات سيرة المرض بالاضافة الى التنبؤ باحتمالية حصول احداث غير مرغوبة للمرضى الذين لديهم خطورة عالية .ومن مؤشرات الخطورة تلك، حسبة انحلال الخثرة في احتشاء العضلة القلبية "TIMI" ذو تعزيز جيد لتخمين توقعات سيرة المرض للمرضى الذين يعانون من متلازمة الشريان التاجي الحاد غير المرتبط بمقطع "ST"؛ ومع ذلك، دوره في التنبؤ بخطورة داء الشريان التاجي مازالت دراستها قليلة.

اهداف الدراسة: لتقييم دور حسبة تيمي "TIMI" لتقدير خطورة وامتداد مرض الشريان التاجي بربط نتيجة حسبة "TIMI" مع نتيجة تصوير الاوعية التاجية لمرضى متلازمة الشريان التاجي الحاد غير المرتبط بمقطع "ST".

المرضى والطرائق: هذه الدراسة هي دراسة مقطعية اجريت على ٢٦٤ مريضا على التوالي كانوا قد تم تعريف اصابتهم بمتلازمة الشريان التاجي الحادة غير المرتبط بمقطع "ST" في مركز ابن البيطار لجراحة القلب ، بغداد للفترة من الاول من تشرين الاول ٢٠١٧ الى الاول من تشرين الاول ٢٠١٨. تم اعادة ترتيب المرضى الى ثلاث مجموعات استنادا الى المتغيرات السبعة لحسبة "TIMI" ،وتم تقييم مدى تاثر الشرايين التاجية بواسطة فحص تصوير الاوعية التاجية. واعتبرت على انها اصابة مؤثرة للشريان التاجي بتعريف نسبة التضيق اكثر من او يساوي% ٧٠ في اي واحد من الشرايين الكبيرة الثلاثة او اكثر من او يساوي% ٥٠ بالنسبة للشريان الرئيسي الايسر.

النتائج: معدل العمر في العينة كان ٢,٣±٦٢,٥ سنة، كان هناك٦٧ (٢٧,٢%) من المرضى ينتمون للمجموعة الاولى (مجموعة المنخفضة الخطورة)، ١٤٢ (٥٧,٧%) مريضا ينتمون للمجموعة الثانية (مجموعة المتوسطة الخطورة) و ٣٧ (١٥,١%) منهم ينتمون للمجموعة الثالثة (مجموعة العالية الخطورة). ٥٤,١% من المرضى في المجموعة الثالثة لديهم اضرار مؤثرة في ثلاثة شرايين تاجية بالمقارنة مع ١٧,٦% من المرضى في المجموعة الثانية وفقط ٧,٥% من المرضى في المجموعة الاولى لديهم تلك الاضرار عندما تم فحص تصوير الاوعية التاجية ((p-value <0.01. من جانب اخر، كان الضرر المؤثر في شريان تاجي واحد فقط اكثر شيوعا ومؤثر احصائيا ((p-value <0.01 في المجموعة الثانية ٣١,٧% بالمقارنة مع المجموعة الاولى ٢٦,٩% والمجموعة الثالثة ١٠,٨%.

الاستنتاجات: المرضى الذين لديهم حسبة "TIMI"عالي الخطورة كانو اكثر احتمالا لوجود اضرار مؤثرة في عدة شرايين تاجية بالمقارنة مع المرضى الذين لديهم حسبة "TIMI"متوسط او منخفض الخطورة وهذا يساعد على معرفة مدى تدرج الخطر واحتمالية اجراء التداخل المبكر.

الكلمات المفتاحية: تصوير الأوعية التاجية ، متلازمة الشريان التاجي الحادة غير المرتفعة ، التقسيم الطبقي لخطر متلازمة الشريان التاجي الحادة ، حسبة TIMI

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تاريخ استلام البحث: ٩ كانون الثاني ٢٠٢٢

تاريخ قبول البحث: ١٠ نيسان ٢٠٢٢

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