The Prognostic Implications of TIMI Risk Scores in Jordanian Patients with Acute Coronary Syndrome. Results from the Glucometabolic Abnormalities in Acute Coronary Syndrome in Jordan (GLORY) Study

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Abstract

Background and Aims: Western studies have shown that TIMI (Thrombolysis In Myocardial Infarction) risk scores predict adverse events in patients with non ST-elevation acute coronary syndrome (NSTEACS) and ST-elevation myocardial infarction (STEMI). Whether this also applies to Jordanian patients is largely unknown.

Materials and Methods: We prospectively followed up 656 patients with ACS for total mortality, combined events of death, nonfatal MI or urgent coronary revascularization up to one year after admission.

Results: Of the whole group, 472 patients (72%) had NSTEACS, and 184 patients (28%) had STEMI. Among NSTEACS patients, 31.0% had a low risk score (total points 0 - 2 of 7), 43.5% had an intermediate risk score (total points 3 - 4), and 25.5% had a high risk score (total points 5 - 7). In-hospital mortality was not different in the respective risk score groups (1.4%, 0.5%, and 3.4%, p = 0.123). At 1 year, mortality was significantly higher in the high risk score group (12.8%) compared with the intermediate (4%) and low (1.4%) risk groups (p = 0.001). Among STEMI patients, 58.6% had a low risk score (total points 0 - 3 of 13 - 14), 31.0% had a low intermediate risk score (total points 4 - 6), 8.0% had a high intermediate score (total points 7 - 9), and 2.4% had a high risk score (total points $\geq$ 10). In-hospital mortality rate was significantly higher in the two intermediate risk score groups (7.4%, 14.3%, respectively) and the high risk score group (50%) compared with the low risk score group (1.0%, p = 0.001). The high risk and the two intermediate risk groups also had higher one-year mortality (75%, 28.6% and 16.7%, respectively) than the low risk group (3.9%, p = 0.001). Similarly, composite events occurred at a significantly higher rate in patients with high risk scores than intermediate or low risk scores among NSTEACS and STEMI patients.

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Conclusions: In Jordanian ACS patients, high TIMI risk scores were associated with a high risk of cardiovascular events. Such patients are candidates for early aggressive therapeutic strategies.

Keywords: Acute coronary syndrome, TIMI risk score, Jordanian patients.

(J Med J 2012; Vol. 46 (3):237- 245)

Received	***Accepted***
October 30, 2011	*February 14, 2012*

Introduction

Cardiovascular disease (CVD) is the leading cause of death in the Middle East and Jordan.[1-3] A high prevalence of smoking, diabetes, hypertension, obesity and dyslipidemia contribute to the rising incidence of CVD even among young individuals in this area.[4-6] Predictors of adverse cardiovascular events among patients sustaining acute coronary syndrome (ACS) are important tools that are used to identify high risk patients who might benefit from aggressive therapeutic strategies during index admission, thus reducing short and long term mortality and morbidity.[7,8] Such predictors include old age, female gender, diabetes mellitus, high-sensitivity C-reactive protein, and low left ventricular ejection fraction (LVEF).[9,10] Moreover, a number of risk assessment scores, based on the sum of several clinical, electrocardiographic, and laboratory variables, are widely used in clinical practice.[11] One of these scores is the Thrombolysis In Myocardial Infarction (TIMI) risk score system that has not been studied in Jordanian patients with ACS, including non ST-segment elevation ACS (NSTEACS) and ST-segment elevation MI (STEMI). The GLORY (glucometabolic abnormalities in acute coronary syndrome in Jordan) study is a prospective evaluation of patients with ACS who were followed up for 1 year after the index admission. The objective of the study was to evaluate the incidence of cardiovascular events among all patients during the follow up period in relation to the TIMI risk scores at admission.

Materials and Methods

Between December 2007 and December 2008, 656 consecutive patients admitted to the coronary care units were enrolled in the study. On admission, clinical, electrocardiographic, and laboratory findings were recorded. Medical treatment, coronary diagnostic and revascularization procedures and adverse cardiovascular events were documented. All patients had chest pain suggestive of myocardial ischemia. ACS was classified as 1) acute STEMI, defined by an ST-segment elevation of $\geq$2 mm in at least 2 contiguous leads on the 12-lead electrocardiogram and elevated cardiac troponin or CPK-MB >2 upper limit of normal, 2) non ST-elevation MI (NSTEMI) defined by the ST-segment depression and/or inverted T wave and elevated cardiac troponin or CPK-MB >2 upper limit of normal, or 3) unstable angina (UA) defined by the ST-segment depression and/or inverted T wave and normal cardiac troponin on admission and 8-12 hours later. LVEF was assessed either by 2D-echocardiography or contrast left ventriculography.

Patients were treated either conservatively or by invasive diagnostic and coronary revascularization strategy according to the decision of the treating cardiologists.

The TIMI risk score in each of the 459 patients with NSTEACS was determined by the sum of the presence of 7 variables at admission; 1 point was given for each of the following variables: age $\geq$ 65 years; $\geq$ 3 coronary artery disease (CAD) risk factors; past history of CAD ($\geq$50% stenosis); ST segment deviation; use of aspirin in the prior 7 days; $\geq$ 2 episodes of angina in the past 24 hours; and elevated serum cardiac biomarkers.[12] Scores were classified as low (0 - 2 points), intermediate (3 - 4 points), or high ($\geq$ 5 points).

The TIMI risk score in each of the 157 patients with STEMI was computed by the sum of points (total of 13 - 14) of the following variables: age ≥ 75 years (3 points) or 56 - 74 years (2 points); presence of diabetes mellitus, hypertension or angina (1 point); systolic blood pressure <100 mm Hg (3 points); heart rate >100 beats per minute (2 points); Killip class II - IV (2 points); weight < 67 kg (1 point); anterior ST elevation or left bundle branch block (1 point); and time to reperfusion therapy > 4 hours (1 point).[13] Scores were classified as low (0- 3 points), low intermediate (4 - 6 points), high intermediate (7 - 9 points), or high (≥ 10 points).

After discharge from the hospital, patients were evaluated at 1, 6 and 12 months for the occurrence of death, nonfatal MI, or urgent percutaneous coronary intervention (PCI).

Statistical Analysis

Data were entered into a computer using the Statistical Package for Social Sciences software, SPSS version 15 (SPSS Inc., Chicago, IL, USA). Participants' characteristics were described using means, standard deviations, and percentages wherever appropriate. The differences between percentages were analyzed using the χ^2 test. A p-value of less than 0.05 was considered statistically significant.

Results

Patients' Characteristics

The baseline characteristics and admission variables of the 656 patients are shown in Table (1). The mean age of men, who comprised 71% of the whole study group, was 7 years younger than that of women. About half of the patients had MI (STEMI and NSTEMI) and the other half had UA. Aspirin was used in 95%, clopidogrel in 55%, statins in 90%, angiotensin converting enzyme inhibitors or angiotensin I receptor blockers in 45%, and heparin (unfractionated or low molecular weight) in 89%. Glycoprotein IIb/IIIa inhibitor was used in 32% of patients (54% of patients with STEMI, 44% of NSTEMI, and 16% of UA).

Table (1): Clinical characteristics and admission variables of 656 consecutive patients with acute coronary syndrome.

Clinical feature	*N (%)*
Men: Women	***465 (71%): 191 (29%)***
Mean Age (Year)	
All	*60 ± 11*
Men	*57.8 ± 11*
Women	*65.4 ± 9*
Current cigarette smoking	*282 (43%)*
Dyslipidemia	*406 (62%)*
Hypertension	*400 (61%)*
Diabetes mellitus	*302 (46%)*
Baseline electrocardiogram:	
ST elevation	*164 (33%)*
ST depression	*114 (23%)*
T wave inversion	*110 (22%)*
Q wave	*32 (6.4%)*
Diagnosis (acute coronary syndrome):	
ST elevation myocardial infarction	*184 (28.0%)*
Non-ST elevation myocardial infarction	*176 (26.8%)*
Unstable angina	*296 (45.2%)*
Past history:	
Previous coronary intervention	*57 (11.4%)*
Myocardial infarction	*42 (8.4%)*
Coronary bypass surgery	*24 (4.8%)*
Stroke	*8 (1.6%)*
Peripheral arterial disease	*2 (0.4%)*

During index admission, coronary angiographs were performed in 79% of all patients (87% of STEMI patients, 79% of NSTEMI patients, and 72% of UA patients). PCIs were performed in 47% of patients (63% in STEMI patients, 48% in NSTEMI patients, and 37% in UA patients), and 1% of the whole group underwent coronary artery bypass surgery.

Table (2) shows the TIMI risk scores in patients with NSTEACS and STEMI at admission. Only a minority of STEMI (2.4%) and about ¼ of NSTEACS patients (25.5%) had high risk scores. About 6/10 and 3/10 of patients with STEMI and NSTEACS, respectively, had low risk scores.

Table (2): TIMI risk scores at admission among patients with acute coronary syndrome.

ACS	***N (%)***
NSTEACS	
Low score	*142 (31.0%)*
Intermediate score	*200 (43.5%)*
High score	*117 (25.5%)*
All patients	*459 (100%)*
STEMI	
Low score	*102 (58.6%)*
Low intermediate score	*54 (31.0%)*
High intermediate score	***14 (8.0%)***
High score	*4 (2.4%)*
All patients	***157 (100%)***

NSTEACS= non ST-segment elevation acute coronary syndrome; STEMI= ST-segment elevation myocardial infarction.

Cardiovascular Events Among NSTEACS Patients

During hospitalization, mortality was 1.5% among all of these patients. Patients with high TIMI risk scores had higher, but not statistically significantly, mortality (3.4%) than those with intermediate (0.5%) and low (1.4%) risk scores (Table 3). Mortality at one month was 2.2% among all patients and was significantly higher among the high risk score group (5.1%) compared with the intermediate (1.0%) and low (1.4%) risk score groups (p = 0.039). Mortality at 6 months was 4.8% in the whole group, and was significantly higher (11.1%) in the high risk score group than the intermediate (3.5%) and low (1.4%) risk score groups (p = 0.001). One-year mortality was 5.4% and was also significantly higher (12.8%) among the high risk score group than the intermediate (4.0%) and low (1.4%) risk score groups (p = 0.001).

The rate of composite events (death, nonfatal MI, or urgent PCI) at one month was 4.6%, and this was higher among the high risk score group (9.4%) than the intermediate (3.5%) and low (2.1%) risk score groups (p = 0.013).

At 6 months, composite events occurred in 14.8% of all patients, with a higher incidence among the high risk score group (23.9%) than the intermediate (13.0%) and low (9.9%) risk score groups (p = 0.004). At 1 year, composite events occurred in 20.3% of all patients, with a higher rate among patients with high risk scores (32.5%) than those with the intermediate (18.5%) and low (12.7%) risk scores (p = 0.001).

Cardiovascular Events Among STEMI Patients

During hospitalization, mortality rate was 5.2%. Patients with a high TIMI risk score had significantly higher mortality (50%) than those in the two intermediate (14.3% and 7.4%) and low (1.0%) risk score groups (p = 0.001, Table 4). The mortality rate at one month was 8.6% among all patients and was also higher in the high risk score group (50%) than the two intermediate (21.4% and 13.0%) and low (2.9%) risk score groups (p=0.001). At 6 months, the mortality rate was 10.9% in the whole group and was higher (75%) in the high risk score group than the two intermediate (21.4% and 16.7%) and low (3.9%) risk score groups (p = 0.001). One-year mortality was 11.5% and was higher (75%) among the high risk score group than the two intermediate (28.6% and 16.7%) and low (3.9%) risk score groups (p = 0.001).

Composite events occurred in 13.2% at one month, at a higher rate among the high risk score group (75%) compared with the two intermediate (28.6% and 20.4%) and low (4.9%) risk score groups. At 6 months, composite endpoints occurred in 19.0% of all patients, at a higher rate in patients with high scores (75.0%) and the two intermediate (42.9% and 27.8%) than low (8.8%) risk scores (p = 0.001). At 1 year, composite events occurred in 24.1% of all patients, at a higher rate among the high risk (75.0%) and the two intermediate risk (42.9% and 33.3%) score patients than low risk score patients (14.7%), (p= 0.001).

Table (3): Coronary events by TIMI risk scores in patients with NSTEACS.

Time and events	***Low score***	***Intermediate score***	***High score***	***P Value***
Admission				
Mortality	*1.4%*	*0.5%*	*3.4%*	*0.123*
*Composite**	-	-	-	-
1 month				
Mortality	*1.4%*	*1.0%*	*5.1%*	*0.039*
*Composite**	*2.1%*	*3.5%*	*9.4%*	*0.013*
6 months				
Mortality	*1.4%*	*3.5%*	*11.1%*	*0.001*
*Composite**	*9.9%*	*13.0%*	*23.9%*	*0.004*
1 year				
Mortality	*1.4%*	*4.0%*	*12.8%*	*0.001*
*Composite**	*12.7%*	*18.5%*	*32.5%*	*0.001*

Composite end-points (deaths, nonfatal myocardial infarction, and urgent coronary revascularization)

Table (4): Coronary events by TIMI risk scores in patients with STEMI.

Time and events	***Low score***	***Low Intermediate score***	***High Intermediate score***	***High score***	***P Value***
Admission					
Mortality	*1.0%*	*7.4%*	*14.3%*	*50.0%*	*0.001*
*Composite**	-	-	-		-
1 month					
Mortality	*2.9%*	*13.0%*	*21.4%*	*50.0%*	*0.007*
*Composite**	*4.9%*	*20.4%*	*28.6%*	*75.0%*	*0.001*
6 months					
Mortality	*3.9%*	*16.7%*	*21.4%*	*75.0%*	*0.001*
*Composite**	*8.8%*	*27.8%*	*42.9%*	*75.0%*	*0.001*
1 year					
Mortality	*3.9%*	*16.7%*	*28.6%*	*75.0%*	*0.001*
*Composite**	*14.7%*	*33.3%*	*42.9%*	*75.0%*	*0.001*

Composite end-points (deaths, nonfatal myocardial infarction, or urgent coronary revascularization).

Discussion

Several risk assessment systems have been developed to assist in estimating the risk of occurrence of adverse cardiovascular events in patients who present with ACS, thereby providing a basis for an early invasive therapeutic decision making.[13,14] These systems include the TIMI risk score, PURSUIT (Platelet Glycoprotein IIb-IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy) trial risk model, and GRACE (Global Registry of Acute Coronary Events) study risk model.[12,15,16]

The TIMI and PURSUIT risk scores were derived from clinical trial databases, whereas the GRACE risk score was derived from a large international regsitry.[17] The major advantage of the TIMI risk score is that it is a single integer sum that can be calculated at bedside based on the combination of clinical, electrocardiographic, and laboratory variables on presentation, whereas the other two risk scores use weighted averages of multiple risk factors and might require a calculator. The TIMI risk score, however, does not include heart failure as a variable in the calculation.[12]

The important value of the TIMI risk score is its benefit in selecting patients with a high likelihood of sustaining adverse cardiac events, and thus can benefit patients by an early invasive strategy.[18] To our knowledge, this is the first prospective Middle Eastern study that demonstrates a correlation between the TIMI risk scores and adverse cardiovascular events in Jordanian

patients with NSTEACS or STEMI from the time of admission up to one year later. A study from the Arab Gulf countries (Gulf RACE) observed the correlation of the GRACE risk model with the occurrence of in-hospital events in ACS patients, but no long term follow up was available.[19]

Compared with western studies, a higher proportion of our patients had low risk scores, and a lower proportion had high risk scores. In a NSTEACS study,[12] 16% and 31% of the enrolled patients had low and high risk scores, respectively, compared with 32% and 23%, respectively in our study. Among the STEMI group in our study; only 10% had scores ≥7. The prevalence of low risk scores among our patients could be related to the relatively younger age of these patients, who were less likely to have coexisting multiple risk factors or past history of CAD. This, along with the high prevalence of unstable angina (absence of elevated cardiac enzymes) in about half of the patients, will subtract more points from the score sum. Furthermore, being < 56 years of age with an STEMI, stable blood pressure and heart rate, and absence of heart failure on admission subtracts 9-10 points from the total score in these patients.

The mortality rates in our study were lower than or equal to those observed in western studies. NSTEACS patients with low risk scores in our study had a 1.4% one month mortality, which is lower than the 4.7% and 8.3% mortality rates among western patients with scores of 0 - 1 and 2, respectively.[12] Patients in our study with high risk scores (5 - 7) had lower mortality (3.4%) compared with the 26% and 41% mortality rates among those with scores of 5 and 6 -7, respectively.[12] Moreover, the six-month mortality in our patients (4.8%) was not different from that among unstable angina and NSTEMI patients (3.6% and 6.2%, respectively) in another study.[20] Mortality at 1 year among NSTEACS in our study (5.4%) was less than that of ACS patients in either arms of the PLATO (Platelet Inhibition and Clinical Outcomes) trial (10.2% and 12.3%.[21]

Similarly, the one month mortality among STEMI patients with low TIMI risk scores, who comprised about 60% of this group, was very low (2.9%), and among all STEMI patients was 8.6%, which is not different from the mortality rates demonstrated in patients treated by primary PCI (7%) or thrombolysis (9%) reported in a meta-analysis of 23 trials.[22] One year mortality in our patients (11.5%) was not different from that of a large STEMI western population (11.2%).[23]

The use of standard medications (antiplatelets, beta blockers, renin angiotensin system blockers, and statins) and the utilization of coronary revascularization procedures were also comparable with western data. We believe, based on results of our study, that the presence of high TIMI risk scores at admission among patients with ACS in Jordan should be one of the key factors that determine the early utilization of an aggressive diagnosing and therapeutic strategy in such patients.

Conclusions

In this Jordanian population with ACS, we demonstrated that the presence of a high TIMI risk score at admission predicts higher rates of adverse cardiovascular events in hospital up to 1 year of follow up. We recommend that cardiologists adopt this risk score system to guide early aggressive strategies for such patients.

Acknowledgments

We would like to thank Hikma Pharmaceuticals for supporting the study and the physicians of the coronary care units in the participating hospitals for recruiting patients in the participating hospitals.

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الآثار المترتبة لاستخدام معامل (TIMI) لقياس درجة خطر التعرض للمضاعفات لدى مرضى متناذرة الاصابات التاجية الحادة لدى المرضى الأردنيين الذين يعانون من متلازمة الشريان التاجي الحادة

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الملخص

الأهداف والوسائل: أثبتت الدراسات الغربية فعالية استخدام معامل (TIMI) لقياس درجة خطر التعرض للمضاعفات لدى مرضى متناذرة الاصابات التاجية الحادة. لكن هذا الموضوع لم تتم دراسته سابقا في الأردن أو الشرق الأوسط. لقد قمنا بمتابعة 656 مريضا أدخلوا المستشفى اثر اصابتهم بمتناذرة الاصابات التاجية الحادة حيث تمت متابعتهم لمدة سنة واحدة بعد الادخال وذلك لدراسة مدى تعرضهم لمضاعفات الوفاة، ومجموع مضاعفات الوفاة والاحتشاء الحاد غير القاتل والتداخل الشرياني التاجي الطارئ.

النتائج: من ضمن مجموعة الدراسة الكلية، تم ادخال 472 (72%) مريضا مصابا بمتناذرة الاصابات التاجية الحادة غير المصاحبة بارتفاع (ST segment)، و184 (28%) مصابين باحتشاء عضلة القلب المصاحب بارتفاع (ST segment). بالنسبة للمجموعة الأولى، فقد كان معامل (TIMI) منخفضا (مجموع نقاط المعامل 0-2 نقطة) لدى 31%، و متوسطا (مجموع نقاط المعامل 3-4 نقاط) لدى 43.5%، ومرتفعا (مجموع نقاط المعامل 5-7 نقاط) لدى 25.5%. لم تختلف نسبة الوفاة خلال فترة العلاج داخل المستشفى في هذه الفئات الثلاث (1.4%، 0.5% و 3.4% [p=0.123]). لكن نسبة الوفاة بعد مرور سنة كانت أعلى في فئة معامل (TIMI) المرتفع (12.8%) مقارنة مع نسبتي الوفاة في فئة المعامل المتوسط (4 %) والمنخفض (1.4%)، p=0.001 . أما مجموعة المصابين باحتشاء عضلة القلب المصاحب بارتفاع (ST segment)، فقد كان معامل (TIMI) منخفضا (مجموع نقاط المعامل 0-3 نقطة) لدى 58.6 %، و متوسطا منخفضا (مجموع نقاط المعامل 4-6 نقاط) لدى 31 %، و متوسطا عاليا (مجموع نقاط المعامل 7-9 نقاط) لدى 8% ، ومرتفعا (مجموع نقاط المعامل 10 نقاط أو أكثر) لدى 2.4 %. كانت نسب الوفاة خلال فترة العلاج داخل المستشفى في فئتي معامل (TIMI) المتوسطتين (7.4 %، 14.3 %) والفئة المرتفعة (50%) أعلى منها في فئة المعامل المنخفض (1.0%)، p=0.001. كما كانت نسب الوفاة بعد مضي سنة واحدة في مرضى فئة المعامل المرتفع (75%) وفئتي المعامل المتوسطتين (28.6%،16.7%) أعلى منها في فئة المعامل المنخفض (3.9%)، p=0.001.

الخلاصة: أثبتت هذ الدراسة فعالية معامل (TIMI) في قياس خطر التعرض للمضاعفات لدى مرضى متناذرة الاصابات التاجية الحادة في الأردن، حيث كانت نسب الوفاة مرتفعة بين المرضى الذين كان معامل (TIMI) مرتفعا لديهم. ويوصى بإخضاع مثل هؤلاء المرضى لعلاج تداخلي مبكر حال دخولهم المستشفى.

الكلمات الدالة: متلازمة الشريان التاجي، معامل TIMI، المرضى الأردنيين.