TIMI risk score underestimates prognosis in unstable angina/non-ST segment elevation myocardial infarction

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TIMI risk score underestimates prognosis in unstable angina/non-ST segment elevation myocardial infarction

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Abstract

Objectives: To determine the value of the TIMI risk score in the individual risk stratification of patients with unstable angina/non-ST segment elevation myocardial infarction (UA/NSTEMI). Background: TIMI risk score is a validated tool to identify groups of patients at high risk for major cardiac events. Its prognostic value in individual patients with current diagnostic tools and therapy is unknown. Methods: TIMI risk score was assessed in patients with UA/NSTEMI admitted to six Belgian hospitals and related to clinical outcome at 30 days. Results: Of the 500 patients enrolled, 49.4% were placed in the low TIMI risk group (score = 0–3) and 50.6% in the high-risk group (score = 4–7). Multivariate analysis identified raised cardiac markers and invasive strategy, but not high TIMI risk score as independent predictors of death and new myocardial infarction (MI). Moreover, the incidence of death and MI in the low TIMI risk group with positive cardiac markers was not lower than in the high TIMI risk group with positive markers: 15.1% versus 17.8% (P = 0.7). Conclusions: TIMI risk score is of limited value for individual risk stratification. The presence of positive cardiac markers (troponin) appears to be a more powerful prognostic marker.

Key Words: Myocardial infarction, mortality, biomarkers, TIMI risk score

Introduction

In patients with unstable angina/non-ST segment elevation myocardial infarction (UA/NSTEMI), the thrombolysis in myocardial infarction (TIMI) risk score is a simple tool that uses baseline variables to identify groups of patients at high risk for recurrent ischemia and major cardiac events such as death and myocardial infarction (1). These baseline variables include clinical, electrocardiographic and laboratory parameters. Using historical data from populations of large international trials during 1994–1998, the score was developed in 2000 by Antman and co-workers. The TIMI risk score was also validated as a tool to compare the risk of populations enrolled in clinical studies (2). Since the inception of the TIMI risk score, new diagnostic tools and treatment strategies are routinely used in UA/NSTEMI patients. At present, the predictive value of the TIMI risk score for prognosis in the individual patient when these contemporary therapy strategies and diagnostic tools are used is not known.

In this study, the TIMI risk score was assessed in 500 patients with UA/NSTEMI presenting at the emergency department. The assessment was then related to the patient’s clinical outcome in order to identify any benefit in using this tool to evaluate patient prognosis and risk stratification after conventional treatments.

Methods

Patient population

Between May 2004 and May 2005, 500 patients presenting with UA/NSTEMI and admitted to the emergency department of six hospitals with catheter laboratory facilities in Belgium were enrolled in this study. The 500 patients were enrolled using the following admission criteria for UA/NSTEMI: new and severe anginal pain, prolonged anginal pain or repetitive episodes of angina at rest or during minimal exercise in the previous 12 h. Patients were
excluded if they had persistent electrocardiographic ST-segment elevation \( \geq 1 \text{ mm} \), or a Q-wave myocardial infarction.

**Baseline clinical data**

The baseline clinical data included TIMI risk score and treatment. The different parts of the TIMI risk score for UA/NSTEMI are outlined in the literature and Table I (1). Risk factors for coronary artery disease included family history, active smoking, hypertension, hypercholesterolemia and diabetes mellitus. Documented coronary artery disease was described as a prior coronary stenosis of \( \geq 50\% \) or prior myocardial infarction, coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). Severe anginal symptoms were outlined as \( \geq 2 \) anginal events in the last 24 h. Elevated serum cardiac markers included cardiac-specific troponin level in all hospitals and creatine kinase MB (CK-MB) in some. Using seven variables, TIMI risk score was calculated and applied to stratify the study population into low (score: 0–3) and high risk (score: 4–7) groups. Data were also collected on drug therapy during the first 24 h, including medication at home.

The intended treatment, either conservative therapy (initial drugs) or an invasive strategy (coronary angiography within 48 h of admission) was then assessed. Indications for subsequent coronary angiography were registered and the use of glycoprotein IIb/IIIa inhibitors (GP IIb/IIIa inhibitors) before and during PCI was measured. The different parts of the TIMI risk score underestimates UA/NSTEMI prognosis

**Statistical methods**

Continuous variables are expressed as the mean along with standard deviation (\( \pm \) SD). The Chi-square test was used to compare discrete variables. Logistic regression analysis was performed to study the independent predictors of clinical outcome. A P-value of \( <0.05 \) was considered to indicate significance.

**Results**

Five hundred patients (73\% male) with a mean (SD) age of 64 years (\( \pm 12 \)) were enrolled in the registry. The values for the TIMI score were normally distributed and 49.4\% of patients fell into low risk (TIMI score 0–3) and 50.6\% into the high-risk score group (TIMI score 4–7). The variables of the TIMI score for the low and high-risk patients are presented in Table I. Note that 25\% of patients in the low-risk group had elevated cardiac serum markers.

In the low risk TIMI group, 52\% of patients received a routine coronary angiogram and in the high-risk group, 73\% of patients received this invasive strategy. At the end of the study, 384 (76.8\%) patients received coronary angiography: 67\% in the low risk and 87\% in the high TIMI risk group. Mechanical revascularization was performed in 55.2\% of patients: 46.4\% by PCI and 11.2\% by CABG. Anti-thrombotic therapy during the first 24 h included GPIIb/IIIa inhibitors for 42\% of patients at admission and an additional 6\% during PCI.

At 30 days, 16 patients (3.5\%) had died, 25 patients (5.3\%) suffered a new acute myocardial infarction and 37 patients (7.9\%) had recurrent ischemia. The adverse cardiac event rate at 30 days was 11\% in the low risk group and 21\% in the high-risk group (\( P<0.0024 \)). Comparable reports can be found in the literature (3). Multivariate analysis evaluating the different predictors of all cardiac adverse events identified invasive strategy (RR 0.21, CI: 0.11–0.39, \( P=0.0001 \)), and higher TIMI risk score (RR 2.22, CI: 1.14–4.42, \( P=0.02 \)) as independent predictors (see Table II).

When the analysis was restricted to the MACE, death and recurrent myocardial infarction, this rate was 4\% in the low TIMI risk group versus 12\% in the high risk group (\( P=0.0015 \)). Multivariate analysis evaluating the different predictors of death

<table>
<thead>
<tr>
<th>TIMI risk score</th>
<th>Low TIMI risk ( n=247 )</th>
<th>High TIMI risk ( n=253 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ( \geq 65 \text{ years} )</td>
<td>35% (87)</td>
<td>71% (179)</td>
</tr>
<tr>
<td>( \geq 3 \text{ Risk factors for coronary artery disease} )</td>
<td>25% (62)</td>
<td>53% (135)</td>
</tr>
<tr>
<td>Documented coronary artery disease</td>
<td>17% (42)</td>
<td>41% (104)</td>
</tr>
<tr>
<td>Aspirin use last 7 days</td>
<td>34% (83)</td>
<td>70% (176)</td>
</tr>
<tr>
<td>Severe angina</td>
<td>64% (159)</td>
<td>92% (234)</td>
</tr>
<tr>
<td>ECG: ST-segment changes</td>
<td>22% (54)</td>
<td>64% (162)</td>
</tr>
<tr>
<td>Raised cardiac markers</td>
<td>25% (62)</td>
<td>70% (178)</td>
</tr>
</tbody>
</table>
and recurrent myocardial infarction identified invasive strategy (RR 0.25, CI: 0.12–0.55, \(P = 0.0006\)) and raised cardiac markers (RR 8.2, CI: 2.45–27.78, \(P = 0.0007\)) as independent predictors. High TIMI risk score (RR 1.8, CI: 0.65–4.83, \(P = 0.26\)) was no longer found to be related to adverse outcome (Table III). Additional analysis revealed that the adverse event rate for death and myocardial infarction in the low TIMI risk group with positive cardiac markers on admission was not lower than in the high TIMI risk group with positive markers: 15.1% versus 17.8% (\(P = 0.7\)), respectively (see Figure 1).

**Discussion**

The TIMI risk score in UA/NSTEMI was developed in 2000 by Antman and co-workers using the data of the TIMI 11B trial (August 1996–March 1998) and the efficacy and safety of subcutaneous enoxaparin in unstable angina and non q-wave MI trial (ESSENCE; October 1994–May 1996)(1). In these historical trials there were, to the best of our knowledge, low use of troponin as a cardiac marker, no use of GP IIb/IIIa inhibitors and a very low rate of PCI: 11–12% for TIMI 11B and 14–18% for ESSENCE trial (4,5). The score was validated in two large trials: platelet receptor inhibition for ischemic syndrome management in patients limited to very unstable signs and symptoms (PRISM-PLUS; November 1994–September 1996) and the tactics TIMI-18 UA/NSTEMI (December 1997–December 1999) trial (3,6). These trials had, by design, high use of GP IIb/IIIa inhibitors, but PCI rate was variable: 41% in Tactics and 30% in Prism-plus (7). Creatine kinase was the only diagnostic marker used for inclusion in prism-plus (8).

Since then, new diagnostic tools and new treatment strategies are used routinely in the treatment of UA/NSTEMI. Therefore, prognosis and hence the prognostic value of the TIMI risk score remained to be determined under these new conditions. In this study, we showed that the prognostic value of the TIMI risk score is not as strong as it once was. The value of cardiac markers, especially troponin, is underrated in the risk score. In addition, a more invasive approach of acute coronary syndromes is an important determinant in the changed prognostic value of the TIMI risk score.

As shown in the Tactics trial, an early invasive strategy in patients with acute coronary syndromes significantly improves prognosis. Even compared to Tactics, a revascularization rate by PCI in 46.2%
(versus 41%) of patients is high. Since revascularization is not implemented in the risk score, this influences the prognostic power of the TIMI risk score.

The prognostic value of the TIMI risk score was also challenged in recent publications. For prediction of death or myocardial infarction at 30 days, the TIMI risk score presented the lowest discriminatory accuracy compared to the GRACE (global registry of acute coronary events) and PURSUIT risk scores (platelet GP IIb/IIIa in unstable angina: receptor suppression using integrilin) (15). Furthermore, Rahimi and co-workers concluded that the TIMI risk score in NSTE MI was a predictor for in-hospital mortality but could not discriminate between patients with early malignant ventricular arrhythmias and those without. Patients with NSTEMI treated aggressively with early revascularization were at low risk for life-threatening arrhythmias (16).

In clinical practice, the presence of positive cardiac markers carries a poor prognosis and is an argument for more invasive evaluation. In the absence of elevated cardiac markers, we believe that the TIMI risk score is still useful to identify patients at increased risk for future thrombotic events.

**Conclusion**

Although the TIMI risk score is a validated tool to estimate risk of adverse cardiac events in populations with UA/NSTEMI, its value is limited for individual risk stratification when current diagnostic tools and therapy are used. The presence or absence of positive cardiac markers (troponin and/or creatine kinase) is a more important predictor for clinical outcome.

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**References**


