Clinical Research

Accuracy of Dedicated Risk Scores in Patients Undergoing Primary Percutaneous Coronary Intervention in Daily Clinical Practice

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See page 130 for disclosure information.

ABSTRACT

Background: Comparisons between dedicated risk scores in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) in real-world clinical practice are scarce. The aim of this study was to assess the diagnostic performance of the Global Registry of Acute Coronary Events (GRACE), Primary Angioplasty in Myocardial Infarction (PAMI), Thrombolysis in Myocardial Infarction (TIMI), and Zwolle scores in STEMI patients undergoing pPCI in contemporary clinical practice.

Methods: This was a prospective cohort study of consecutive patients with STEMI undergoing pPCI between December 2009 and November 2010 in a high-volume tertiary referral centre. The outcomes assessed were major cardiovascular events (MACEs) and death within 30 days. The diagnostic accuracy of the scores was assessed using receiver operating characteristic curves, and scores were compared using the DeLong method.

Results: During the study period, 501 patients were included. Within 30 days, 62 patients (12.4%) presented a MACE and 39 individuals (7.8%) died. All scores were statistically associated with death and MACE within 30 days (P < 0.01). The c-statistic and 95% confidence intervals for 30-day mortality were: GRACE, 0.84 (0.78-0.90); TIMI, 0.81 (0.74-0.87); Zwolle, 0.80 (0.73-0.87); and PAMI, 0.75 (0.68-0.82) (P < 0.01). There was no statistically significant difference regarding the accuracy of the TIMI, GRACE, and Zwolle scores for 30-day mortality, but the GRACE score was superior to the PAMI score (P < 0.01).

In recent years, significant advances have been made in the treatment of ST-segment elevation acute myocardial infarction (STEMI). In current daily clinical practice there are patients with very low predicted mortality. These patients could benefit from early discharge from the intensive care unit and from the hospital, resulting in better clinical care and optimization of health resources. In contrast, morbidity and mortality after STEMI are still high in other subgroups. With the aim of identifying these patients, dedicated risk scores have been developed, which might allow individualized management and treatment of patients with STEMI. A comparison among these scores is available in Supplemental Table S1.

Despite their frequent use, some scores present the limitations of having been developed more than a decade ago. The inclusion of patients of randomized clinical trials

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Conclusions: The TIMI, GRACE, and Zwolle scores performed equally well as predictors of mortality in patients who underwent pPCI in current practice. These results suggest that these scores are suitable options for risk assessment in a real-world setting.

Methods

Patients
This was a prospective cohort study that consecutively included patients with STEMI who underwent pPCI at the Instituto de Cardiología do Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil, from December 2009 to November 2010. Our facility is a tertiary referral centre that performs approximately 3000 percutaneous coronary interventions per year. pPCI is the routine STEMI treatment at our institution, and the catheterization laboratory is open 24 hours per day, 7 days per week. The project was approved by the local Research Ethics Committee, and all patients received information regarding the study and provided written informed consent. The authors are responsible for the design and conduct of the study, analysis, writing and editing, and final content of the manuscript. No extramural funding was used to support this work.

The inclusion criterion was STEMI submitted to pPCI as the initial reperfusion strategy, determined by the assisting physician. STEMI was defined as typical chest pain at rest associated with ST-segment elevation of at least 1 mm in two contiguous leads in the frontal plane or 2 mm in the horizontal plane, or typical pain at rest in patients with a new, or presumably new, left bundle-branch block. The exclusion criteria were delta T greater than 12 hours, use of lytic therapy as the primary reperfusion therapy for the index event, age younger than 18 years, or refusal to participate. Delta T was defined as the time from the onset of chest pain to hospital arrival.

pPCI procedures
The medications used in the patient’s initial care and the indications for pPCI were at the discretion of the medical team. Patients received a bolus dose of acetylsalicylic acid (300 mg) and clopidogrel (300-600 mg). After conventional coronary angiography, unfractionated heparin was administered at a dose of 60 U/kg to 100 U/kg and pPCI was performed as previously described. Aspects related to the procedure, such as access site, administration of glycoprotein IIb/IIIa inhibitors and adjunctive aspiration thrombectomy, were left to the operators’ discretion. An intra-aortic balloon was used only in patients with cardiogenic shock.

Data collection
Patients were interviewed by 1 of the investigators (A.P.A., R.B.D.) on hospital admission, and clinical, angiographic, and laboratory data were collected using a standard questionnaire. Blood samples for laboratory tests were collected from all patients at admission. Angiography was performed in at least 2 different views by experienced operators using a previously validated digital electronic system (Siemens Axiom Artis, Munich, Germany). Intracoronary nitroglycerin was routinely administered at a dose of 200 μg before measurements. Coronary flow before and after the procedures was assessed and described according to the TIMI criteria.

Outcomes and follow-up
All patients were visited daily during the in-hospital period by 1 of the investigators (A.P.A., R.B.D.) to assess in-hospital events. The occurrence of events 1 month after the index event was evaluated in a telephone call and by review of medical records. All-cause mortality and major cardiovascular events (MACEs) were assessed and registered by 1 of the study investigators. MACEs were defined as a combination of all-cause mortality, new acute myocardial infarction (MI), or stroke. New MI was defined by recurrent chest pain with new elevation of serum biomarkers, after the initial decline of the natural curve, with ST-segment elevation or new Q waves, according to the universal definition of MI. Stroke was defined as a new, sudden-onset focal neurological deficit, of presumably cerebrovascular cause, irreversible (or resulting in death) within 24 hours, and not caused by another readily identifiable cause. Stroke was classified as ischemic or hemorrhagic.
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occurred in 62 patients (12.4%), new MI in 32 cases (6.4%),

Figure 1. Study flow chart. pPCI, primary percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

Statistical analysis
Data were collected in a Microsoft Access database and statistical analysis was performed using SPSS for Windows 17.0. Results are expressed as mean ± SD, median (interquartile range), or absolute and relative frequencies as appropriate. Sample size calculation was performed considering the smallest area under the receiver operating characteristic (ROC) curve between the original scores (0.78) and a 30-day mortality rate of 8%. The minimum sample size for 80% statistical power and a significance level of 0.05 was estimated at 400 patients.

The individual risk scores were calculated as previously published (Supplemental Table S2).14-17 The accuracy of the GRACE, PAMI, TIMI, and Zwolle scores for predicting MACE and 30-day mortality was assessed according to the area below the ROC curve.23 Comparison between the ROC curves was performed with the nonparametric DeLong test, using MedCalc software for Windows, version 12.1.4.0 (MedCalc Software, Mariakerke, Belgium).24 Statistical significance was defined as a 2-tailed P value < 0.05.

Results
Patients
During the study period, 501 patients with STEMI who underwent pPCI were included, according to the flow chart in Figure 1. In the study period, no patient received lytic therapy as the primary reperfusion therapy at our hospital. The baseline sample profile is shown in Table 1. Total ischemic time was 5.2 ± 2.9 hours, with a delta T of 3.6 ± 2.8 hours. The median door-to-balloon time was 76 (56-105) minutes, and 71% of the patients were treated within 90 minutes of hospital arrival.

Outcomes and risk scores
All patients were available for 30-day follow-up. MACEs occurred in 62 patients (12.4%), new MI in 32 cases (6.4%), and the 30-day mortality rate was 7.8% (n = 39). All risk scores were significantly associated with MACE, and the diagnostic accuracy assessment for combined events is presented in Figure 2. The Zwolle, GRACE, and TIMI scores presented higher accuracy than the PAMI score for MACE (P < 0.05 for all comparisons). There were no significant differences between scores on any other comparisons.

All scores were also statistically associated with 30-day mortality (Fig. 3). The GRACE, TIMI, and Zwolle scores presented similar diagnostic accuracy for death within 30 days, and the diagnostic accuracy of the GRACE score was higher than that of the PAMI score (Table 2). There was no statistically significant difference in any other comparisons.

We also addressed the influence of age on the accuracy of the risk scores. The study population was stratified according to the cut point of 65 years, and 162 patients were identified (32% of the total). In patients aged 65 years or younger, all risk scores presented statistical significance (P < 0.001) to the 30-day mortality outcome, but c-statistics were lower than in the total cohort. In patients older than 65 years, the GRACE and TIMI risk scores maintained statistical significance (P < 0.01), and the Zwolle and PAMI risk scores did not. In this

Table 1. Characteristics of the study sample (n = 501)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60.5 ± 11.8</td>
</tr>
<tr>
<td>CAD risk factors</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>342 (68)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>335 (67)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>185 (37)</td>
</tr>
<tr>
<td>Smoking</td>
<td>212 (42)</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>158 (32)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>94 (19)</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>119 (24)</td>
</tr>
<tr>
<td>PCI</td>
<td>37 (7)</td>
</tr>
<tr>
<td>CABG</td>
<td>17 (3)</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>212 (42)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>135 ± 31</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>82 ± 19</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>79 ± 20</td>
</tr>
<tr>
<td>Killip class III/IV</td>
<td>27 (5)</td>
</tr>
<tr>
<td>Ischemic time, h</td>
<td>5.2 ± 2.9</td>
</tr>
<tr>
<td>Delta T, h</td>
<td>3.6 ± 2.8</td>
</tr>
<tr>
<td>Angiographic and procedural variables</td>
<td></td>
</tr>
<tr>
<td>Door-to-balloon time, min</td>
<td>76 (56-105)</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>96 (19)</td>
</tr>
<tr>
<td>LAD involvement</td>
<td>214 (43)</td>
</tr>
<tr>
<td>Direct-stent placement</td>
<td>165 (33)</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa</td>
<td>147 (30)</td>
</tr>
<tr>
<td>Aspiration thrombectomy</td>
<td>154 (31)</td>
</tr>
<tr>
<td>Reference vessel diameter, mm</td>
<td>3.2 ± 0.49</td>
</tr>
<tr>
<td>Lesion length, mm</td>
<td>17.3 ± 8.5</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD or n (%); door-to-balloon time is expressed as median (interquartile range).

CABG, coronary artery bypass graft; CAD, coronary artery disease; LAD, left anterior descending artery; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.
subgroup, c-statistics were lower than in those aged 65 years or younger for all scores.

Risk of death according to score stratification

Aiming to explore the ability of the scores to identify very low- and high-risk patients, we assessed 30-day death rates according to quartiles of risk in each score (Fig. 4). All scores showed a statistically significant linear relationship with this outcome ($P < 0.001$). Of note, this stratification identified a subgroup of patients with a 30-day mortality of 1% or less in patients within the first quartile of risk in all the scores. Those in the highest quartile of risk showed mortality rates of 17%-25%.

Discussion

In this study, we demonstrated that dedicated risk scores for STEMI present adequate accuracy for prediction of 30-day mortality in patients undergoing pPCI in a contemporary, real-world clinical setting. Our report can be considered representative of current pPCI practice in tertiary centres, demonstrated by the in-hospital mortality rate, door-to-balloon time, and percent of patients treated within 90 minutes of hospital arrival. The GRACE, TIMI, and Zwolle scores presented similar c-statistics for the mortality and MACE outcomes, but the PAMI score performed comparatively poorly. The European Society of Cardiology Guidelines for the Management of Acute Myocardial Infarction in Patients Presenting with ST-segment Elevation suggest the use of schemes such as the PAMI-II criteria or the Zwolle risk score to identify low-risk patients with the goal of early discharge.\textsuperscript{25} In contrast, specific recommendations regarding the use of risk scores in STEMI patients were not addressed in the latest American College of Cardiology/American Heart Association Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction.\textsuperscript{26} The present study shows that the Zwolle, TIMI, and GRACE scores can be used to identify high-risk patients with STEMI undergoing pPCI. Besides, our results also support the notion that the risk scores should be used to identify very low risk patients. The subgroup within the lower quartile of risk presented a mortality rate of 1% or less in any of the scores.

In the context of STEMI, the most appropriate risk score should adequately stratify patients to support therapeutic decisions and the length of hospital stay, including stay in intensive care units. This approach is associated with lower costs, and has already proved to be safe and effective.\textsuperscript{6-8} The use of validated scoring systems allows the physician to obtain a numerical prediction for an outcome, which is a valuable tool in the clinical decision-making process. Most variables included in these models are known to clinicians to be associated with poorer outcomes, but the integration in a risk score provides a more reliable perspective; incorporating the use of risk scores will also make clinicians more familiar with

Figure 2. ROC curves: Major adverse cardiovascular events at 30 days. GRACE, Global Registry of Acute Coronary Events; PAMI, Primary Angioplasty in Myocardial Infarction; ROC, receiver-operator characteristic; TIMI, Thrombolysis in Myocardial Infarction.
those variables. The use of novel internet portable devices might also facilitate the use of risk scores at the bedside. Another important use of risk scores is as a research tool, to adjust for different baseline patient characteristics in quality of care assessment initiatives comparing outcomes among institutions or operators.

In previous studies, the assessment of the accuracy of dedicated risk scores for STEMI in the daily practice has provided mixed results. A recent meta-analysis showed a pooled c-statistic of 0.77 for the TIMI score and 0.82 for the GRACE score for short-term outcomes. Kozieradzka et al. found that the TIMI, GRACE, and Zwolle scores had similar results for a 30-day mortality outcome. This study included patients treated in the 2000-2002 period, and is limited by the lack of a statistical comparison among the ROC curves. Aragam and colleagues found similar accuracy of the TIMI and GRACE scores for in-hospital mortality (0.84 vs 0.83) and mortality at 6-month follow-up (0.72 vs 0.71), but these patients were also treated more than a decade ago. Other studies were limited by exclusion of higher-risk patients, low number of scores analyzed, and retrospective design.

The Zwolle score is the only model using angiographic variables, taking into account the outcome of pPCI and the presence of multivessel disease (Supplemental Table S1). Risk scores are generally used by cardiologists, and the need to evaluate angiographic data might explain why this score has not become as popular as others, despite similar diagnostic accuracy. In our study, the c-statistic of the TIMI score was not statistically different from the GRACE score. Considering that the TIMI score is simpler and easier to apply, this finding might favour its use in daily clinical practice. The worst performer among the scores was the PAMI score, and the restrictive selection criteria used to develop this model might explain this lower accuracy.

Another practical challenge in risk stratification refers to the elderly patients, and all the risk scores performed worse in

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>C-Statistic</th>
<th>P</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI</td>
<td>0.806</td>
<td>&lt;0.01</td>
<td>0.740 – 0.872</td>
</tr>
<tr>
<td>GRACE</td>
<td>0.839</td>
<td>&lt;0.01</td>
<td>0.776 – 0.902</td>
</tr>
<tr>
<td>Zwolle</td>
<td>0.799</td>
<td>&lt;0.01</td>
<td>0.726 – 0.871</td>
</tr>
<tr>
<td>PAMI</td>
<td>0.752</td>
<td>&lt;0.01</td>
<td>0.680 – 0.824</td>
</tr>
</tbody>
</table>

Table 2. Comparison of ROC curves between scores for prediction of death at 30 days

<table>
<thead>
<tr>
<th></th>
<th>TIMI vs PAMI</th>
<th>TIMI vs GRACE</th>
<th>TIMI vs Zwolle</th>
<th>PAMI vs GRACE</th>
<th>PAMI vs Zwolle</th>
<th>GRACE vs Zwolle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference between areas</td>
<td>0.05</td>
<td>0.03</td>
<td>0.01</td>
<td>0.09</td>
<td>0.05</td>
<td>0.04</td>
</tr>
<tr>
<td>Standard error</td>
<td>0.03</td>
<td>0.03</td>
<td>0.04</td>
<td>0.03</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.00 to 0.11</td>
<td>-0.03 to 0.09</td>
<td>-0.06 to 0.08</td>
<td>0.02 to 0.15</td>
<td>-0.04 to 0.13</td>
<td>-0.04 to 0.12</td>
</tr>
<tr>
<td>z statistic</td>
<td>1.84</td>
<td>1.07</td>
<td>0.20</td>
<td>2.59</td>
<td>1.11</td>
<td>0.94</td>
</tr>
<tr>
<td>P</td>
<td>0.07</td>
<td>0.28</td>
<td>0.84</td>
<td>&lt; 0.01</td>
<td>0.27</td>
<td>0.34</td>
</tr>
</tbody>
</table>

CI, confidence interval; GRACE, Global Registry of Acute Coronary Events; PAMI, Primary Angioplasty in Myocardial Infarction; ROC, receiver-operator characteristic; TIMI, Thrombolysis in Myocardial Infarction.
patients older than 65 years. It is important to note that age is
the only variable contemplated in all of the scores, but
computed differently in each of them (Supplemental
Table S2). We believe that an accurate assessment of the
influence of age in the performance of these risk scores will
have to be addressed by further studies with larger numbers of
patients.

Strengths and limitations
Some strengths and limitations of this study are worthy of
note. No data were available from longer-term follow-up,
which could have influenced the accuracy of the scores.
However, 30-day mortality is a clinically relevant end point
that has been used in several previous studies. Despite a priori
sample size calculation, the present study included a relatively
small number of patients. Our institution is a high-volume
centre (approximately 500 pPCIs per year), and we chose to
focus this analysis within a 1-year time frame to keep results
representative of contemporary pPCI practice. Because of
insufficient statistical power, we were not able to consistently
assess the diagnostic accuracy of the risk scores in the elderly
(older than 65 years) and very elderly (older than 75 years).
When comparing the results of original score development
studies with those of the present study, the different risk
profile of the patient populations must be taken into account.
Finally, our study excluded patients who underwent pPCI
with a delta T symptom time greater than 12 hours, who
would benefit less from a primary reperfusion strategy.

Conclusions
The TIMI, GRACE, and Zwolle scores performed similarly as predictors of 30-day mortality, suggesting that these
scores can be used to assess prognosis in this setting. The
PAMI risk score presented significantly worse diagnostic
accuracy than the other 3 scores, and we suggest that this score
should not be used in contemporary practice. Patients within
the lower quartile of risk had an estimated 30-day mortality of
1% or less estimated according to all the scores, suggesting
that a very low risk subgroup can be identified. The GRACE,
PAMI, TIMI, and Zwolle scores were not adequately accurate
as predictors of MACE within 30 days. Our results reinforce
the importance of periodic evaluations of the diagnostic
accuracy of risk scores in daily clinical practice.

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Disclosures
The authors have no conflicts of interest to disclose.

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trends (1975 to 2005) in the magnitude of, management of, and hospital
death rates associated with cardiogenic shock in patients with acute

![Figure 4. Risk of death at 30 days (%) according to quartiles of risk. GRACE, Global Registry of Acute Coronary Events; PAMI, Primary Angioplasty in Myocardial Infarction; TIMI, Thrombolysis in Myocardial Infarction.](image-url)


Supplementary Material
To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at [www.onlinecjc.ca](http://www.onlinecjc.ca) and at [http://dx.doi.org/10.1016/j.cjca.2013.07.673](http://dx.doi.org/10.1016/j.cjca.2013.07.673).