Diagnostic Accuracy of Global Registry of Acute Coronary Events (GRACE) Risk Score in ST-Elevation Myocardial Infarction for In-Hospital and 360-Day Mortality in Japanese Patients

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**Background:** The purpose of the present study was to confirm the diagnostic accuracy of Global Registry of Acute Coronary Events (GRACE) risk score 1.0 (GRACE 1.0) and updated GRACE 1.0 (GRACE 2.0) for in-hospital and 360-day mortality in ST-elevation myocardial infarction (STEMI) in Japanese patients. GRACE 1.0 and GRACE 2.0 are the established predictive models in acute coronary syndrome, but their application to Japanese patients has not been fully verified.

**Methods and Results:** The present study retrospectively analyzed 412 consecutive STEMI patients who had undergone primary percutaneous coronary intervention from January 2006 to September 2011. All causes of death during hospitalization were examined to confirm the diagnostic accuracy of GRACE 1.0 on receiver operating characteristic (ROC) analysis. Similarly, all causes of death during the 360 days after hospitalization were analyzed to confirm the diagnostic accuracy of GRACE 2.0. The average GRACE 1.0 score was 175.8±50.9. In-hospital and 360-day mortality were 13.1% and 15.5%, respectively. Area under the ROC curve, which describes the diagnostic accuracy of the GRACE 1.0 predicted in-hospital mortality and the GRACE 2.0 predicted 360-day mortality, was as high as 0.95 and 0.92, respectively.

**Conclusions:** Both GRACE 1.0 and GRACE 2.0 had a high diagnostic accuracy for prediction of in-hospital and 360-day mortality in Japanese STEMI patients. (Circ J 2014; 78: 2950–2954)

**Key Words:** GRACE risk score; Mortality; ST-elevation myocardial infarction

#**ST-elevation myocardial infarction (STEMI) had a high mortality rate, but emergency coronary revascularization has dramatically improved this, down to 5–7%.**

The Global Registry of Acute Coronary Events (GRACE) risk score (GRACE 1.0) and updated GRACE 1.0 (GRACE 2.0) have been reported to be useful for prediction of short- and long-term mortality in acute coronary syndrome (ACS). Although these 2 scoring models consist of 8 simple parameters including the vital signs and examination findings on arrival at hospital, prediction ability is superior. These models are useful not only for predicting patient mortality, but also for identifying more critical patients who require intensive treatment.

The GRACE registry collected data from a worldwide population with a central focus on North America, South America, Europe, Australia, and New Zealand, therefore it has not been verified whether these scores can apply to Japanese patients.

The purpose of the present study was to confirm the diagnostic accuracy of GRACE 1.0 and GRACE 2.0 for in-hospital and 360-day mortality for STEMI in Japanese patients.

**Methods**

**Study Design and Subjects**
To study the diagnostic accuracy of GRACE 1.0 and GRACE 2.0 for in-hospital and 360-day mortality in STEMI patients, we retrospectively studied the medical records of STEMI patients who were admitted to Tokai University School of Medicine from January 2006 to September 2011 with acute symptom onset, and who had the diagnosis of STEMI on emer-
in 24h of symptom onset, and electrocardiography (ECG) on arrival showed persistent ST-segment elevation >1 mm in 2 contiguous leads with reciprocal ST depression, new or presumed new left bundle branch block. The final diagnosis was made on emergency coronary angiography.

The estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease (modified for Japanese) equation.

GRACE 1.0 and GRACE 2.0 were calculated from 8 clinical parameters on arrival in hospital: age; heart rate; systolic blood pressure (SBP); serum creatinine; Killip classification; cardiac arrest; ST-segment deviation on ECG; and elevated cardiac enzyme.

These parameters followed the GRACE definitions. Cardiogenic shock was defined as SBP <80 mmHg. Cardiac arrest was defined as rapid ventricular tachycardia with hemodynamic instability, ventricular fibrillation, electrical mechanical dissociation or asystole and requiring cardiopulmonary resuscitation from onset to admission. ST-segment

### Definitions

STEMI was defined as acute when the patient presented with emergency coronary angiography and following primary percutaneous coronary intervention (PCI). Among 436 STEMI patients identified, the present study reviewed records from 412 consecutive STEMI patients whose clinical course could be tracked after 360 days to evaluate mortality.

The exclusion criteria were as follows: patients who did not undergo emergency coronary angiography to confirm the culprit lesion, and those whose mortality could not be tracked during 360 days after STEMI onset were excluded.

All causes of death during hospitalization were taken into consideration to confirm the diagnostic accuracy of GRACE 1.0 on receiver operating characteristic (ROC) analysis. In the same manner, all causes of death during 360 days after PCI were taken into consideration to confirm the diagnostic accuracy of GRACE 2.0.

### Table 1. Baseline Characteristics and Clinical Status on Arrival

<table>
<thead>
<tr>
<th></th>
<th>All (n=412)</th>
<th>Survivors at 360 days (n=348)</th>
<th>Non-survivors in hospital (n=54)</th>
<th>Non-survivors at 360 days (n=64)</th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.9±12.5</td>
<td>64.5±12.0</td>
<td>73.4±12.6</td>
<td>73.5±12.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>79.9</td>
<td>79.9</td>
<td>77.8</td>
<td>79.7</td>
<td>0.9711</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.3±8.4</td>
<td>162.6±8.4</td>
<td>160.6±9.1</td>
<td>161.0±8.6</td>
<td>0.1886</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.2±12.5</td>
<td>63.6±12.3</td>
<td>63.6±14.5</td>
<td>63.6±14.0</td>
<td>0.9614</td>
</tr>
<tr>
<td>Current smoking</td>
<td>65.3</td>
<td>65.2</td>
<td>61.1</td>
<td>65.6</td>
<td>0.9513</td>
</tr>
<tr>
<td>Hypertension</td>
<td>77.9</td>
<td>76.7</td>
<td>87.0</td>
<td>84.4</td>
<td>0.0045</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>68.7</td>
<td>70.7</td>
<td>55.6</td>
<td>57.8</td>
<td>0.0412</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>35.4</td>
<td>33.3</td>
<td>48.1</td>
<td>46.9</td>
<td>0.0374</td>
</tr>
<tr>
<td>Insulin</td>
<td>4.6</td>
<td>3.1</td>
<td>11.1</td>
<td>12.5</td>
<td>0.0011</td>
</tr>
<tr>
<td>Old MI</td>
<td>10.9</td>
<td>8.6</td>
<td>24.1</td>
<td>23.4</td>
<td>0.0005</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>8.3</td>
<td>8.3</td>
<td>7.4</td>
<td>7.8</td>
<td>0.8893</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>0.2</td>
<td>0.3</td>
<td>0</td>
<td>0</td>
<td>0.6677</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>10.7</td>
<td>10.0</td>
<td>13.0</td>
<td>14.1</td>
<td>0.3404</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>2.4</td>
<td>2.6</td>
<td>1.9</td>
<td>1.6</td>
<td>0.6248</td>
</tr>
<tr>
<td>Hemoglobin (mg/dl)</td>
<td>14.1±2.3</td>
<td>14.3±2.1</td>
<td>13.1±2.9</td>
<td>13.0±2.8</td>
<td>0.1409</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>124.2±40.6</td>
<td>127.3±40.2</td>
<td>105.5±40.9</td>
<td>106.7±38.9</td>
<td>0.0002</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>50.0±15.6</td>
<td>51.0±15.7</td>
<td>43.8±14.1</td>
<td>44.6±13.5</td>
<td>0.0034</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>118.6±116.7</td>
<td>121.8±107.9</td>
<td>101.8±168.2</td>
<td>100.9±156.8</td>
<td>0.1946</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.1±1.3</td>
<td>1.10±1.3</td>
<td>1.3±0.9</td>
<td>1.9±0.9</td>
<td>0.1105</td>
</tr>
<tr>
<td>eGFR (ml·min⁻¹·1.73m⁻²)</td>
<td>68.9±27.6</td>
<td>72.1±26.2</td>
<td>53.3±30.6</td>
<td>51.8±29.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BNP (pg/ml)</td>
<td>73 (25.3–234.9)</td>
<td>62.6 (23.6–208.6)</td>
<td>142.1 (48.8–748.5)</td>
<td>178 (53.6–737.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Onset to door (min)†</td>
<td>204.0±224.1</td>
<td>209.5±219.8</td>
<td>163.7±260.0</td>
<td>173.2±246.6</td>
<td>0.2444</td>
</tr>
<tr>
<td>Onset to reperfusion (min)</td>
<td>309.7±232.1</td>
<td>308.0±222.2</td>
<td>297.7±283.3</td>
<td>319.0±280.3</td>
<td>0.7431</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>125.5±41.7</td>
<td>133.3±34.8</td>
<td>74.3±47.3</td>
<td>83.3±50.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>69.8±32.3</td>
<td>75.6±27.0</td>
<td>29.8±36.9</td>
<td>37.8±39.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>21.6</td>
<td>12.6</td>
<td>77.8</td>
<td>70.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart rate (beats/min)‡</td>
<td>74.9±26.0</td>
<td>74.9±22.4</td>
<td>70.2±42.1</td>
<td>74.5±40.5</td>
<td>0.9121</td>
</tr>
<tr>
<td>Killip I/II/III/IV (n)</td>
<td>181/89/49/93</td>
<td>179/84/38/47</td>
<td>0/2/9/43</td>
<td>2/5/11/46</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiac arrest§</td>
<td>7.0</td>
<td>4.0</td>
<td>27.8</td>
<td>23.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peak CK (IU/L)</td>
<td>4,155.3±4,971.9</td>
<td>3,442.8±3,554.9</td>
<td>9,185.8±9,427.2</td>
<td>8,090.5±9,049.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>50.6±13.3</td>
<td>52.8±11.6</td>
<td>34.9±14.3</td>
<td>37.0±14.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>GRACE 1.0 score</td>
<td>175.8±50.9</td>
<td>162.4±40.4</td>
<td>257.0±33.0</td>
<td>248.5±39.4</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data given as mean±SD, %, or median (IQR). †Excluded 5 patients with in-hospital onset. ‡Patients who experienced fatal arrhythmia (pulseless ventricular tachycardia, ventricular fibrillation, electromechanical dissociation) or asystole and requiring cardiopulmonary resuscitation from onset to admission. §360-day survivors vs. non-survivors. BNP, brain natriuretic peptide; CABG, coronary artery bypass graft; CK, creatinine kinase; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure.
were performed using JMP version 9 (SAS Institute, Cary, NC, USA).

Results

Baseline characteristics are listed in Table 1. Mean age was 65.9±12.5 years and 79.9% of the patients were male. In initial evaluation on arrival at hospital, the mean clinical parameters were as follows: SBP, 125.5±41.7 mmHg; heart rate, 74.9±26.0 beats/min; Killip IV, 22.6%; and prevalence of cardiogenic shock, 21.6%. ST-segment deviation was observed in all patients because of STEMI. Seven percent of the patients experienced cardiac arrest from onset to arrival at hospital. Average GRACE 1.0 score was 175.8±50.9 points. Comparing the 360-day survivors (n=348) and non-survivors (n=64), 6 components of GRACE 1.0 were significantly different; heart rate and serum creatinine were not. Notably, the presence of cardiac arrest was a strong predictor of high 360-day mortality rate, which was as high as 23.4%. Among 29 patients who experienced cardiac arrest, more than half of them (15 pa-
patients, 51.7%) did not survive to discharge. There was a significant difference in GRACE 1.0 score between 360-day survivors and those who did not survive 360 days (162.4±40.4 points vs. 248.5±39.4 points, P<0.0001). Table 2 lists clinical outcome for in-hospital and 360-day mortality. In-hospital and 360-day mortality rates were 13.1% and 15.5%, respectively. For 360-day all-cause death, cardiac death accounted for 71.9%, and cause in 15 non-cardiac deaths was as follows: pneumonia, n=7; sepsis or other infection, n=4; subarachnoid hemorrhage, n=1; abdominal aneurysm rupture, n=1; intrathoracic hemorrhage, n=1; and carcinoma, n=1.

Discussion

The present study has demonstrated the diagnostic accuracy of GRACE 1.0 and GRACE 2.0 for in-hospital and 360-day mortality for STEMI in Japanese patients. Both GRACE 1.0 and GRACE 2.0 had a very high ability to predict in-hospital and 360-day death.

Myocardial infarction is one of the leading causes of death, resulting in more than 40,000 deaths per year in Japan, even though primary PCI has improved the mortality associated with STEMI. In order to differentiate the critical patients at high risk of mortality, it is important to improve the predictive mortality rate of such patients with STEMI in emergency care. GRACE 1.0 was established as a useful scoring model to predict the short-term mortality in acute myocardial infarction. This score is so simple to calculate that early evaluation can be done at onset. GRACE 2.0 was an update on GRACE 1.0, issued in 2014 in order to evaluate long-term mortality of these patients. The GRACE registry consists of 10,000 records of ACS patients from 18 cluster sites in 14 countries with a central focus on North America, South America, Europe, Australia, and New Zealand. Asian patients, especially Japanese, were not included, however, therefore it is important to validate whether this scoring system can be used in Japanese patients. To our knowledge, this study is the first to validate the diagnostic ability of these scoring models for Japanese patients.

The clinical value of the GRACE predictive model is not inferior to Thrombolysis in Myocardial Infarction risk score or other predictive models. GRACE 1.0 is a simplified method of producing an initial evaluation in the emergency department, and was reported to have a high diagnostic performance for ACS in predicting short-term mortality, in the range of AUC 0.80–0.91. In a prior study in USA to validate the accuracy of GRACE 1.0 for in-hospital mortality in 698 STEMI patients, GRACE 1.0 had a high accuracy on ROC analysis, with an AUC as high as 0.84. Although minor differences were observed in some studies, validation studies have confirmed the accurate predictive ability of GRACE 1.0 for short-term mortality.

In terms of long-term mortality, some reported an acceptable performance for GRACE 1.0. The original target of GRACE 1.0, however, was in-hospital death, and for that reason the GRACE 2.0 updated version of GRACE 1.0 was reported for long-term mortality in 2014. To our knowledge, the present study is the first to validate the predictive performance of GRACE 2.0 for Japanese patients. GRACE 1.0 is calculated based on the severity of 8 stratified clinical parameters, and the predicted mortality has a linear relationship to the score. In contrast, GRACE 2.0 provides the predicted mortality directly, bypassing scores, because the predicted mortality has a non-linear relationship with score. GRACE 1.0 was updated to GRACE 2.0 in order to evaluate the long-term mortality without changing the scoring parameters. Although the GRACE 2.0 scoring algorithm is complicated compared to GRACE 1.0, the population histogram, which is a feature of the GRACE registry, provides an easy-to-understand visual representation of individual risk stratification.

There are several limitations in this study. First, the present study was a retrospective study. Second, the present study might be underpowered to draw a conclusion on diagnostic ability because of the small sample size, although all-cause death was as high as 15.1%. Third, the subject group was selected with a focus on STEMI. Both GRACE risk scores are the established models for not only STEMI but also unstable angina or non-STEMI, which could produce a different result from STEMI. Fourth, this study had a high mortality because it included a high number of critical patients (cardiopulmonary arrest, 7%; Killip IV, 23%). Therefore, the present subject group might differ slightly from the average Japanese STEMI patients.

Conclusions

GRACE risk score can be applied to Japanese STEMI patients for predicting in-hospital and 360-day mortality with a high diagnostic accuracy.

References


