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Original article

In-hospital mortality analysis of Japanese patients with acute coronary syndrome using the Tokyo CCU Network database: Applicability of the GRACE risk score

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ABSTRACT

Background: The GRACE risk score was developed to predict in-hospital mortality for acute coronary syndrome (ACS) using multinational registries, but did not include Japanese data. Therefore, GRACE risk scores are not extensively used in Japan. The present study aimed to evaluate the relationship between the GRACE risk score and in-hospital mortality among Japanese patients with ACS using the Tokyo CCU (cardiovascular care unit) Network Database.

Methods and results: A total of 9460 patients with ACS hospitalized at 67 Tokyo CCUs between January 2011 and December 2013 were retrospectively reviewed and GRACE risk scores were calculated. Patients in the Tokyo CCU Network database had more severe conditions compared to those of the original GRACE study. There was a strong correlation between the GRACE risk score and in-hospital mortality for patients with ST-segment elevation myocardial infarction (STEMI) or non ST-segment elevation myocardial infarction (NSTEMI) ($r = 0.99$, $p < 0.001$); however, the correlation was not significant for patients with unstable angina ($r = 0.35$, $p = 0.126$). For STEMI + NSTEMI patients, the discrimination ability of the GRACE risk score was excellent, with a c statistic of 0.87 (95% confidence interval, 0.86–0.89).

Conclusions: The GRACE risk score is a good predictor of in-hospital mortality for Japanese patients with STEMI or NSTEMI, and can help clinicians stratify patients by risk for optimal patient triage and early treatment management.

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Introduction

Acute coronary syndrome (ACS) represents a major cause of morbidity and mortality throughout the world [1,2]. ACS comprises a wide spectrum of conditions including ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA). The presence of ACS guides triage and key management decisions. Prognostic scoring systems, including the GRACE risk score [3], TIMI risk score

[4], and PURSUIT risk score [5], have been reported to be useful in predicting not only long-term mortality, but also in-hospital mortality among patients with ACS [5–7]. Among these scoring systems, the GRACE risk score has the highest validity [8,9]. It was designed to reflect an unbiased population of patients with ACS from 94 hospitals in 14 countries (Australia, Austria, Argentina, Belgium, Brazil, Canada, France, Germany, Italy, New Zealand, Poland, United Kingdom, USA, and Spain). All cases were assigned to one of the following categories: STEMI, NSTEMI, or UA. All eight factors used to calculate the GRACE risk score can be obtained at the initial examination. These predictive factors include age, heart rate, systolic blood pressure, initial serum creatinine level, Killip class [10], cardiac arrest at hospital admission, elevated cardiac markers, and ST-segment deviation, which are weighted to

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calculate the risk of in-hospital mortality [3]. In the guidelines of the European Society of Cardiology (ESC), GRACE risk scores >140 are defined as a high risk of in-hospital mortality for patients with ACS [11].

In Japan, the GRACE risk scoring system is not widely used. Japanese facilities did not participate in the GRACE study; thus, the guidelines for the management of patients with STEMI issued by the Japanese Circulation Society in 2013 stated that it is necessary to pay attention to its use in Japan [12]. Moreover, the guidelines for the management of ACS without persistent ST-segment elevation issued by the Japanese Circulation Society in 2012 identified limitations in the use of the GRACE risk score in Japan owing to a higher prevalence of vasospastic angina in the Japanese [13]. Therefore, the aim of the present study was to examine the relationship between the GRACE risk score and the in-hospital mortality among Japanese patients with ACS using data from the Tokyo CCU (cardiovascular care unit) Network Database.

Methods

Patients

A retrospective review of data from the Tokyo CCU Network database was conducted. This network was established in 1978 by the Metropolitan Tokyo CCU Communication Society with help from the ambulance units and control room of the Tokyo Fire Department [14–16].

In 2012, the Tokyo CCU Network included 67 hospitals. Hospitals belonging to the Tokyo CCU Network routinely record and submit the details of all patients treated in their CCUs using dedicated survey forms. In the GRACE study, the enrolled patients who were similar to those in the MONICA Project [17] had to be at least 18 years of age, be admitted to participating hospitals with symptoms consistent with acute coronary ischemia, and have at least 1 of the following items: electrocardiographic changes consistent with ACS, serial increases in serum markers of cardiac necrosis, and/or documentation of coronary artery disease [3,18]. The present study used the same inclusion criteria, with the exception that patients had to be admitted to participating

CCUs of the Tokyo CCU Network. In the present study, 13,325 patients with ACS, treated at participating institutions of the Tokyo CCU Network between January 2011 and December 2013, met inclusion criteria. Among them, 3865 patients who lost their medical history and the 8 factors needed for calculating the GRACE risk score were excluded, and 9460 patients were analyzed in this study.

Clinical definitions and end points

“STEMI” was defined as ACS with persistent ST-segment elevation in the electrocardiogram, “NSTEMI” was defined as ACS without persistent ST-segment elevation in the electrocardiogram, and “UA” was defined as myocardial ischemia at rest or minimal exertion in the absence of cardiac necrosis. Death was defined as all-cause mortality during hospitalization. Vital signs, Killip class, and biochemical and electrocardiographic findings were collected at the time of hospital admission. Electrocardiograms were interpreted locally in terms of ST-segment depressions of at least 1 mm in the anterior, inferior, or lateral lead groups, and Q waves measuring either one-third the height of the R waves or lasting longer than 0.04 s. Initial cardiac markers were defined as positive when troponin T/I or other cardiac enzymes were elevated according to the GRACE scoring system.

Calculation of the GRACE risk score

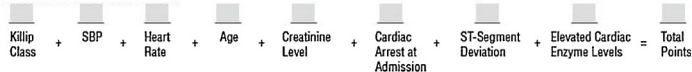
The GRACE prediction score card and nomogram were used to calculate the prognostic score and estimate the risk of mortality for individual patients (Fig. 1). The calculation of the GRACE risk score was performed in 3 steps. Step 1 involved identifying the score for each individual predictive factor (age, heart rate, systolic blood pressure, initial serum creatinine level, Killip class, cardiac arrest at hospital admission, elevated cardiac markers, and ST-segment deviation). Step 2 involved summing the individual factor scores to obtain a total score. Step 3 involved determining the risk of in-hospital mortality using a nomogram. The GRACE risk score can also be calculated online (www.outcomes.org/grace). In addition, smartphone applications are available as free downloads; thus, the GRACE risk score can be easy to use in emergency medical situations.

1. Find Points for Each Predictive Factor:

Killip Class	Points	SBP, mm Hg	Points	Heart Rate, Beats/min	Points	Age, y	Points	Creatinine Level, mg/dL	Points
I	0	≤80	58	≤50	0	≤30	0	0-0.99	1
II	20	80-99	53	50-59	3	30-39	8	0.40-0.79	4
III	39	100-119	43	70-99	9	40-49	25	0.80-1.19	7
IV	59	120-139	34	90-109	15	50-59	41	1.20-1.59	10
		140-159	24	110-149	24	60-69	58	1.60-1.99	13
		160-199	10	150-199	38	70-79	75	2.00-3.99	21
		≥200	0	≥200	46	80-89	91	>4.0	28
						≥90	100		

Other Risk Factors	Points
Cardiac Arrest at Admission	39
ST-Segment Deviation	28
Elevated Cardiac Enzyme Levels	14

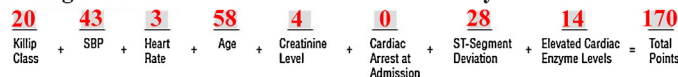
2. Sum Points for All Predictive Factors:



3. Look Up Risk Corresponding to Total Points:

Total Points	≤60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	≥250
Probability of In-Hospital Death, %	≤0.2	0.3	0.4	0.6	0.8	1.1	1.6	2.1	2.9	3.9	5.4	7.3	9.8	13	18	23	29	36	44	≥52

For example, a patient has Killip class II, SBP of 100 mmHg, heart rate of 60 beats/min, is 65 years of age, has serum creatinine level of 0.70 mg/dL, did not have a cardiac arrest on admission, but have ST-segment deviation and elevated cardiac enzyme.



This patient would have about a 7.3% risk of having an in-hospital death.

Fig. 1. GRACE risk nomogram. The GRACE risk score is calculated in 3 steps. In step 1, the points for each predictive factor are determined. In step 2, the individual factors points are summed. In step 3, the risk corresponding to the total points is identified [3]. SBP, systolic blood pressure.

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