Study of GRACE and TIMI Risk Scores' Application in the Risk Stratification in Patients with Acute Coronary Syndrome in Qinghai

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Abstract: Objective: To compare the risk stratification ability and prognostic evaluation values of GRACE and TIMI risk scores in patients with Acute Coronary Syndrome (ACS) in Qinghai. Methods: The clinical data of 385 patients with ACS treated at our hospital from January 2021 to October 2022 were analyzed to calculate the Grace and TIMI risk scores of each patient. The main adverse cardiovascular events (MACE) within 30 days of onset and 1 year after discharge were followed up. The receiver operating characteristic (ROC) curves of the two scoring systems were plotted, and the area under the curve (AUC) was compared. Results: There was no statistically significant difference between the risk stratification in patients with ACS according to GRACE and TIMI scores ($\chi2$=0.316, P=0.854). The scores of both grading systems showed a tendency to increase with increasing risk stratification (P<0.001). In addition, the higher the GRACE and TIMI risk scores, the higher the incidence rate of MACE in patients within 30 days of the onset and 1 year after discharge (P<0.01). Taking 143 points of the GRACE risk score as the cut-off value, the sensitivity and specificity of predicting MACE within 1 year after discharge were 89.93% and 90.83%, respectively. The AUC value under the ROC curve was 0.775. However, if 3.8 points of TIMI risk score was taken as the cut-off value, the sensitivity and specificity of predicting MACE within 1 year after discharge were changed to 81.15% and 89.27%, respectively, while the AUC value was 0.743. The difference between the AUC values calculated using the two risk scores was statistically significant. (Z=5.436, P<0.01). Conclusion: GRACE and TIMI risk scores can be used for risk stratification of patients with ACS in Qinghai. The GRACE risk score had a higher predictive value for recent adverse cardiovascular events in patients with ACS.

Keywords: Global Registry of Acute Coronary Events (GRACE) Risk Score; The Thrombolysis in Myocardial Infarction (TIMI) Risk Score; Acute Coronary Syndrome (ACS); Risk Stratification; Prognosis; Adverse Cardiovascular Events

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1 Introduction

Acute coronary syndrome (ACS) involves the formation of coronary artery thrombosis arising from the rupture or erosion of unstable atherosclerotic plaques in the coronary artery, leading to partial or complete blockage of the coronary lumen. It is a group of acute myocardial ischemia syndromes whose main clinical manifesta-

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tion is chest pain [1, 2] Owing to its sudden onset, rapid disease progression, and life-threatening conditions, ACS has become the leading cause of medical emergency and hospitalization [3]. Because ACS has a higher risk of developing malignant cardiovascular events such as cardiac death, angina, and myocardial infarction, it is of important clinical significance to execute effective and rapid risk stratification in patients with ACS in the early stage so as to take timely and reasonable treatments. It is also conducive to reducing the incidence of adverse cardiovascular events and improving patient prognosis [4]. At present, there are numerous scoring systems for risk stratification in ACS patients, such as the Global Registry of Acute Coronary Events (GRACE) [5] and thrombolysis in myocardial infarction (TIMI) risk scores [6], with good judgement for the prognosis of patients. Qinghai Province is located in the northeast of the Qinghai-Tibet Plateau with a high altitude of 2260-5000 m. On account of alpine hypoxia, relatively backward economic level, and poor medical and health environment, the incidence of ACS in Qinghai remains extremely high, resulting in steadily increasing adverse cardiovascular events. Our aim was to predict and evaluate the risk stratification and prognosis of ACS patients by analyzing the GRACE and TIMI risk scores of ACS patients in the Qinghai plateau area, which can provide a scientific basis for reducing mortality and improving the quality of life of ACS patients in plateau areas.

2 Objects and Methods

2.1 Objects of Study

Patients who visited our hospital for emergency treatment in the Department of Cardiology with ACS from January 2021 to October 2022 were chosen for analysis, with a total of 385 cases. The surveyed patients included 216 males and 169 females, aged from 48 to 73 years (mean: 63.57±6.42) years. They were of many different nationalities, including 178 Han, 104 Hui, 44 Zang, 32 Salar, 15 Mongolian, and 12 Tu. Among these, 146 patients had unstable angina pectoris (37.92%), 73 had ST-segment elevation myocardial infarction (18.96%), and 166 had non-ST-segment elevation myocardial infarction (43.12%).

2.2 Inclusion and Exclusion Criteria

Inclusion criteria: I) All subjects were in accordance with the diagnosis criteria of ACS in “Internal Medicine” (seventh edition) [7], whose chest pain lasted for more than 10 min and accompanied by inversion of T wave and ST-segment depression in electrocardiogram; II) The level of myocardial injury markers as creatine kinase isoenzyme and troponin I increased; III) Their clinical data were complete; IV) The patients had been living in Qinghai area for more than 10 years; V) All patients involved in this study gave their informed consent.

Exclusion criteria: Patients meeting the following conditions were excluded from the study: I) Patients with an incidence of more than 1 month and had past the acute phase of myocardial infarction; II) patients with chest pain induced by pulmonary embolism and aortic dissection; III) patients who also suffered from liver and kidney function failure, acute cerebrovascular accident, severe infection, thrombotic lesion, and malignant tumor at the same time; and IV) patients lacking complete clinical data.

2.3 Methods

2.3.1 Clinical Data Collection

Medical records were examined and used to complete a self-designed questionnaire. The clinical data of the study subjects included admission number, sex, age, physical signs, past medical history, previous coronary events, the results of blood biomedical tests, coronary angiography, electrocardiogram, and so on. Next, risk scoring was performed based on the clinical data of the subjects.

2.3.2 GRACE Risk Score [8]

Based on age, heart rate, serum creatinine, systolic blood pressure, Killip score, elevated myocardial injury markers, and whether there was a known cardiac event and ST-segment deviation when patients were admitted to the hospital, the patients were graded. The sum of each variable is the GRACE score, with a total score of 372 points. The standard of evaluation is shown in Table 1, where a score < 113 points represents low-risk patients, a score between 113 and 159 points represents intermediate-risk patients, and a score >160 points represents high-risk patients.

Table 1 The standard of evaluation for GRACE risk score

Age (years)	score	Heart rate (times/min)	score	Creatinine (mg/L)	score	Systolic blood pressure (kPa)	score	Killip grading	score	Known cardiac event	score
<30	0	<50	0	0-3.9	1	<10.7	58	I	0	elevated myocardial injury markes	14
30-39	8	50-69	3	4.0-7.9	4	10.7-13.2	53	II	20		
40-49	25	70-89	9	8.0-11.9	7	13.3-15.9	43	III	39	ST-segment deviation	28
50-59	41	90-109	15	12.0-15.9	10	16.0-18.5	34	IV	59		
60-69	58	110-149	24	16.0-19.9	13	18.6-21.2	24			cardiac arrest before admission	39
70-79	75	150-199	38	20-39.9	21	21.3-26.5	10				
80-89	91	≥200	46	≥40	28	≥26.6	1				
≥90	100										

2.3.3 TIMI Risk Score [9]

The evaluation variables included age ≥ 65 years, elevated myocardial injury markers, treatment with aspirin in the last 7 days, more than three high-risk factors of coronary heart disease, ST-segment deviation on electrocardiogram, degree of coronary artery stenosis ≥ 50% in known coronary angiogram, and attack of angina ≥ 2 times within 24 h. All the variables count for 1 point, with a maximum TIMI score of 7 points; in this scoring system, a score of 1-2 points represented low-risk patients, while a score of 3-4 points for intermediate-risk patients, and a score of 5-7 points for high-risk patients.

2.3.4 Follow-up Visit

The occurrence of major adverse cardiovascular events (MACE) within 30 days of onset and 1 year after discharge was followed up by telephone or outpatient services. The following conditions were considered: MACE, cardiac death, cardiogenic shock, unstable angina pectoris, acute left heart failure, non-fatal myocardial infarction, ventricular tachycardia and ventricular fibrillation, other severe high-risk arrhythmias, coronary revascularization, and so on. The prediction accuracy of MACE was compared between patients using the GRACE and TIMI risk scores. A one-year follow-up was completed in 371 cases, while there were 14 cases lost to follow-up, with a missed follow-up rate of 3.64%. Among these, 6 patients died from gastrointestinal bleeding, traffic accidents, or other non-cardiac deaths. The other 8 patients were lost to follow –up due to phone shutdown or no answer. There was no statistically significant difference in the gender, age, and state of the illness between the 371 cases included in the final study and the 14 cases lost to follow-up.

2.4 Statistical Analysis

The data were analyzed using SPSS22.0 statistical software. The measurement data are expressed as the mean ± standard deviation ($\bar{x}$ ±s). Group t-test was adopted for the comparison between two groups, while one-way analysis of variance was chosen for the comparison among the three groups of data. The count data were presented as percentages (%), and comparisons between groups were performed using the Pearson χ^2 test. Spearman correlation analysis was used for correlation analysis. Moreover, ROC curves were used to analyze the prediction effectiveness. The test level α value was 0.05, and the difference was statistically significant with a P-value < 0.05.

3 Results

3.1 Comparison Between the Risk Stratification by Two Different Risk Scores

There was no statistically significant difference between the constituent ratios of risk stratification according to GRACE and TIMI risk scores (χ^2=0.316, P=0.854). With increasing risk stratification, the scores of the two scoring system showed an upward trend. The difference between the GRACE scores of the different risk stratifications was statistically significant (F=68.527, P<0.001). There was a statistically significant difference between the TIMI scores of different risk stratifications (F=16.902, P<0.001) (Table 2).

Table 2 The comparison between the risk stratification results in patients with ACS by GRACE and TIMI risk scores

Risk stratification	Case number (n(%))		Score ($\bar{\chi}$ ±s)	
	GRACE score	TIMI score	GRACE score	TIMI score
Low risk	257 (66.75%)	264 (68.57%)	84.73±23.67	1.45±0.28
Intermediate risk	89 (23.12%)	83 (21.56%)	132.84±28.43	3.37±0.34
High risk	39 (10.13%)	38 (9.87%)	194.82±33.06	5.88±0.36
χ^2(F)	0.316		68.527	16.902
P	0.854		<0.001	<0.001

3.2 Correlation Analysis of GRACE and TIMI Risk Scores

The results of the Spearman correlation analysis indicated a strong positive correlation between GRACE and TIMI risk scores. The correlation coefficient (r) values were 0.714 for the low-risk group (P<0.05), 0.742 for the intermediate-risk group (P<0.05), and 0.833 for the high-risk group (P<0.05).

3.3 Occurrence of MACE During the Follow-up Period Predicted by Two Scoring System

Among the 371 ACS patients who were followed up, the occurrence rate of MACE increased with increasing GRACE and TIMI risk scores. The occurrence of MACE in patients with different risk stratifications obtained by GRACE risk scores was compared. The results indicated that there was statistical significance in the occurrence of MACE at 30 days and 1 year between the different risk groups (χ^2 = 39.342, 52.786 respectively, P<0.01). Similarly, the difference in the MACE occurrence at 30 days and 1 year between different risk groups determined by TIMI risk score was statistically significant (χ^2 were 33.965, 50.153 respectively, P<0.01) (Table 3).

3.4 ROC Curves of GRACE and TIMI Risk Scores

The prediction sensitivity and specificity of MACE occurrence within 1 year were 83.93% and 90.83%, respectively, when 143 points of the GRACE risk score were taken as the cut-off values. The corresponding AUC value was 0.775. While 3.8 points of TIMI risk score was taken as the cut-off value, the prediction sensitivity and specificity of MACE occurrence within 1 year changed to 81.15% and 89.27%, respectively, with a corresponding AUC value of 0.743 (Figure 1). The difference in the AUC between the two scoring systems was statistically significant (P<0.01) (Table 4). The results suggested that the predictive value of the GRACE risk score was better than that of TIMI.

Table 3 Occurrence of MACE during the follow-up period predicted by GRACE and TIMI risk scores

Risk stratification	GRACE score			TIMI score		
	Case number	MACE occurrence within 30 days (n(%))	MACE occurrence within 1 year (n(%))	Case number	MACE occurrence within 30 days (n(%))	MACE occurrence within 1 year (n(%))
Low risk	249	10 (4.02)	20 (8.03)	255	12 (4.71)	21 (8.24)
Intermediate risk	85	12 (14.12)	24 (28.24)	80	14 (17.50)	23 (28.75)
High risk	37	13 (35.14)	19 (51.35)	36	12 (33.33)	18 (50.00)
χ^2		39.342	52.786		33.965	50.153
P		<0.01	<0.01		<0.01	<0.01

Table 4 Comparison of ROC curves between GRACE and TIMI risk scores

Risk stratification	AUC	SE	95%CI	Z	P
GRACE	0.775	0.038	0.641-0.928	5.436	<0.01
TIMI	0.743	0.042	0.622-0.905		

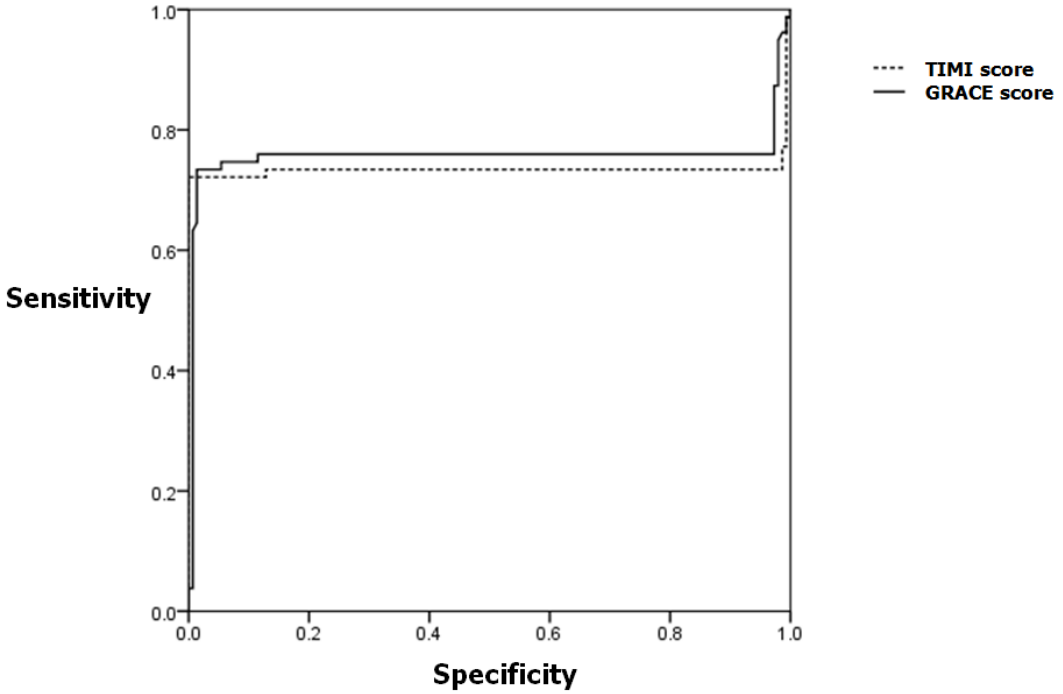

Figure 1 ROC curves of GRACE and TIMI risk scores

4 Discussion

With the improvement of social economic level, the changes in dietary habits and lifestyle, and the morbidity and fatality rate of cardiovascular diseases such as ACS in our country are gradually rising. The risk of adverse cardiovascular events also varies, since there are individual differences in coronary artery lesions and systemic conditions of different crowds. ACS comprises a group of syndromes with differential clinical features and risk stratification. The evaluation of patients' risk stratification at an early stage and the corresponding treatment has vital significance in preventing adverse cardiovascular events and improving prognosis. The evaluation is based on clinical symptoms and signs, blood biochemical examination, and electrocardiography manifestations when the patient is admitted to the hospital [10]. Many factors contribute to high ACS morbidity in the Qinghai area. They are located in the plateau, with many ethnic minority residents, special dietary structures and living habits, poor health care consciousness, relatively backward local medical environment, and level. Therefore, the evaluation of risk stratification of ACS occurrence in the Qinghai area and prediction of the occurrence of adverse cardiovascular events within a certain period are meaningful in early coronary artery revascularization, salvage of the cardiac muscle cells, and thus, the improvement of survival rate [11].

In recent decades, a myraid of different coronary heart disease risk-scoring systems has been developed. Among these, the GRACE and TIMI risk scores are two scoring systems with wide representativeness [12]. The two scoring systems collected clinical data from large-scale clinical trials and long-term follow-up studies and screened out individual predictive indices and their corresponding scores by means of multi-factor logistic regression analysis. Afterwards, different risk stratification was made according to the total scores, and a prognostic evaluation was made based on it as well. Thus, personalized treatments can be formulated using guidance. Stracke et al. distinguished low-risk and high-risk patients with chest pain using the GRACE risk score. Moreover, there was a significant correlation between the scores and hospital mortality [13]. Koonsiripaiboon et. al also showed that the GRACE risk score had a significant predictive value in hospital mortality of patients [14]. Damman et. indicated that the TIMI risk score could accurately predict the risk of short-term adverse endpoint events. The occurrence rate gradually increases with increasing risk scores [15]. Our study aimed to stratify the risk of ACS in the Qinghai area using GRACE and TIMI risk scores. The results showed that both GRACE and TIMI risk scores could be applied in

the risk stratification of patients with ACS, where the corresponding risk scores increased with higher risk levels. There was no statistically significant difference in the risk stratification of patients with ACS according to the GRACE and TIMI risk scores. Correlation analysis indicated that the GRACE score had a strong positive correlation with the TIMI score. These results suggest that the two risk scores could achieve the same effect on the risk stratification of patients with ACS.

Our study showed that the occurrence rate of MACE within 30 days or 1 year increased correspondingly with higher GRACE and TIMI scores in patients with ACS. The difference in MACE occurrence within 30 days or 1 year of patients with different risk levels was statistically significant, which is in good agreement with the research conducted by Wu et al. [16]. By comparing the predictive value in predicting MACE occurrence in patients with ACS within 1 year, we found that both GRACE and TIMI risk scores had satisfactory results in their sensitivity and specificity in MACE prediction, consistent with research at home and abroad [17-19]. The predictive value of the GRACE score was higher when it was applied in the prediction of MACE occurrence within 1 year in patients with ACS, based on the comparison of ROC curves ($P<0.01$). Aragam et. al [20] also indicated that the accuracy of the GRACE score in predicting the adverse end of patients with non-ST-segment elevation myocardial infarction or unstable angina pectoris was better than that of the TIMI score, and it was speculated that the contributor might be the different risk factors used in the two scoring systems. In addition to the same factors as advanced age, myocardial injury markers and ST-segment deviation, heamodynamics index as heart rate, blood pressure, cardiac function, and renal function index were also included in the GRACE risk score. All of these are individual risk factors affecting the prognosis of patients [9].

5 Conclusion

In conclusion, both GRACE and TIMI risk scores are suitable for risk stratification of patients with ACS in the Qinghai area. The GRACE risk score is more complexwith a higher value in predicting recent adverse cardiovascular events in patients with ACS, which is appropriate for the prognosis of patients. However, it should be clear that the risk score is a tool that assists in clinical judgement. Clinicians should make personalized risk assessments of patients based on risk scores and optimize the therapeutic regimen to improve prognosis. In the meantime, our study only evaluated the predictive ability of the two risk scoring systems in recent prognosis. In the future, an increased number of ACS patients should be investigated, and long-term prognosis should be followed up in order to compare the predictive value in long-term prognosis of ACS patients between GRACE and TIMI risk scores.

Ethical Compliance

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Data Access Statement

Research data supporting this publication are available from the Qinghai Provincial People's Hospital and Qinghai Red Cross Hospital.

Conflict of Interest Declaration

The authors declare that they have NO affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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