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ORIGINAL RESEARCH

Combination of the Barthel Index at Discharge with GRACE Leads to Improved One-Year Mortality Prediction in Older Patients with Acute Myocardial Infarction

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Purpose: Many older patients with acute myocardial infarction (AMI) have impaired ability for activities of daily living (ADL). Impaired ADL leads to poor prognosis in elderly patients. The Global Registry of Acute Coronary Events (GRACE) score is widely used for risk stratification in AMI patients but does not consider physical performance, which is an important prognosis predictor for older adults. This study assessed whether the Barthel Index (BI) score combine the GRACE score would achieve improved one-year mortality prediction in older AMI patients.

Patients and Methods: This single-center retrospective study included 688 AMI patients aged ≥65 years who were divided into an impaired ADL group (BI ≤60, n = 102) and a normal ADL group (BI >60, n = 586) based on BI scores at discharge. The participants were followed up for one year. Cox survival models were constructed for BI score, GRACE score, and BI score combined GRACE score for one-year mortality prediction.

Results: Patients had a mean age of 76.29 ± 7.42 years, and 399 were men (58%). A lower BI score was associated with more years of hypertension and diabetes, less revascularization, longer hospital stays, and higher one-year mortality after discharge. Multivariable Cox regression analysis identified BI as a significant risk factor for one-year mortality in older AMI patients (HR 0.977, 95% CI, 0.963–0.992, P = 0.002). BI (0.774, 95% CI: 0.731–0.818) and GRACE (0.758, 95% CI: 0.704–0.812) scores had similar predictive power, but their combination outperformed either score alone (0.810, 95% CI: 0.770–0.851).

Conclusion: BI at discharge is a significant risk factor for one-year mortality in older AMI patients, which can be better predicted by the combination of BI and GRACE scores.

Keywords: older adults, acute myocardial infarction, Barthel Index, GRACE, prognosis

Introduction

Acute myocardial infarction (AMI), broadly classified as ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI), remains a leading cause of death worldwide, despite considerable progress in reducing morbidity and mortality associated with AMI in the United States and European countries.[1] However, the incidence of AMI is still trending upwards in many developing countries, including China.[2,3] Prognosis for patients with STEMI has seen steady improvement largely as a result of revascularization techniques such as percutaneous coronary intervention (PCI).[4] Patients with NSTEMI also benefit from timely PCI and medications in the short-term, but long-term outcomes have not improved as much as in those with STEMI, likely because of complex clinical conditions involving older age and comorbidities.[5]

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As population aging continues, increasing numbers of patients will be diagnosed with NSTEMI. In addition, AMI in older adults is usually accompanied by other conditions, such as hypertension, obesity, diabetes, and frailty, which are themselves risk factors for cardiovascular disease, which may complicate the management of AMI and contribute to increased adverse events, rehospitalization, and mortality.[6,7] Therefore, there is a pressing need to identify patients at high risk of poor prognosis so that appropriate treatment options can be implemented. Physical functional performance has been recognized as a prognostic factor for long-term mortality in acute coronary syndrome (ACS) and heart failure.[8,9] The Barthel Index (BI) measures essential daily activities, shows excellent reliability and validity, and is especially recommended for the assessment of older patients during rehabilitation.[10,11] A recent study with a median follow-up of over 10 months demonstrated that the BI score at hospital admission could be helpful in risk stratification of ACS patients and treatment planning.[12] Another study involving very elderly ACS patients treated with PCI showed that the BI score at discharge was a valuable predictor for one-year mortality.[13]

The Global Registry of Acute Coronary Events (GRACE) score was originally developed to predict the risk of death at six months in ACS patients and has also shown good value in predicting one-year and three-year mortality of different ACS types.[14] However, the GRACE lacks parameters to address impaired physical capability, a common characteristic in older adults. In this study, we hypothesized that the ability to conduct activities of daily living (ADL) has an impact on the prognosis of AMI patients and assessed whether the combination of the BI score and GRACE score at hospital discharge would achieve improved accuracy in predicting one-year mortality in older AMI patients.

Materials and Methods

Study Population

This retrospective study collected data from 688 older AMI patients treated at the Department of Cardiology, Beijing Friendship Hospital, Capital Medical University between 2017 and 2019. The criteria of the Fourth Universal Definition of Myocardial Infarction for type 1 myocardial infarction were used for the diagnosis of STEMI and NSTEMI.[15] Patients ≥65 years diagnosed with STEMI or NSTEMI were included. Those with cancer, incomplete medical records, or lost to follow-up were excluded. All patients were followed up for at least one year. The research protocol was approved by the Ethics Committee of Beijing Friendship Hospital, and informed consent was obtained from participating patients.

BI Score and Group Assignment

We used the original 10-item BI to evaluate a patient's ability to perform ADL. The form contained 10 categories, feeding (0, 5), bathing (0, 5), grooming (0, 5), dressing (0, 5, 10), bladder (0, 5, 10), bowels (0, 5, 10), toilet use (0, 5, 10), transfers (0, 5, 10, 15), mobility (0, 5, 10, 15), and stairs (0, 5, 10). The total score ranges from 0 (completely dependent) to 100 (completely independent). The evaluation was administered by trained nurses less than 48 hours before the patient's hospital discharge. The BI score is grouped into two standard diagnostic categories according to the standard BI grouping method:[16] impaired ADL group (BI ≤60, n = 102) and a normal ADL group (BI >60, n = 586).

Assessment of GRACE Score

The GRACE score was calculated after hospital admission. The variables included age, systolic blood pressure, heart rate, serum creatinine, Killip class at admission, cardiac arrest at admission, ST segment deviation, and abnormal cardiac enzymes.

Clinical and Laboratory Data

Data extracted from patient records included medical history, laboratory test results, physical examinations, coronary angiography, and medications. Participants' profiles were composed of age, sex, smoking status, length of hospitalization, type of myocardial infarction, history of coronary artery disease and years, past myocardial infarction, past cardiac procedures, hypertension, diabetes, heart failure, hyperlipidemia, and family history of coronary artery disease. Standard clinical laboratory tests were conducted to measure total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

The Killip classification was used for patient risk stratification at admission, with the following criteria:[17] Class 1: no evidence of heart failure; Class 2: rales up to one-third of the lung field signs or existence of a third heart sound and systolic blood pressure >90 mmHg; Class 3: frank pulmonary edema and systolic blood pressure >90 mmHg; Class 4: cardiogenic shock with rales and systolic blood pressure <90 mmHg.

Revascularization usually refers to PCI or coronary artery bypass grafting (CABG). Since no patient was treated with CABG in this study, PCI was the only revascularization therapy received by participants.

Follow-Up and Endpoint

After hospitalization, patients were followed up for at least one year through telephone interviews or in-person visits to monitor one-year mortality. In this study, mortality was defined as all-cause mortality.

Statistics Analysis

All statistical analyses were performed using SPSS 26.0 (SPSS Inc., Chicago, IL, USA) and R version 4.1.2. The Kolmogorov–Smirnov test was used to confirm normal distribution, and continuous data are expressed as mean ± standard deviation (SD) and analyzed with the *t*-test. Discrete or qualitative data are presented as numbers or percentages and analyzed with the Pearson's χ^2 test or Fisher's exact test. All variables except TC (8.6%), TG (8.6%), HDL-C (8.6%), LDL-C (8.6%) had no missingness. After verifying that the data is normally distributed, we filled in the missing values by means of mean value filling.

The log rank test was used to determine whether there was a difference in one-year survival between the two groups. To examine the association of the BI score with all-cause mortality, Kaplan–Meier curves were generated for the subgroups and compared. Cox regression analysis was conducted to obtain hazard ratios and 95% confidence intervals (CIs). Only variables showing statistical significance in univariate Cox regression analysis were tested in multivariable survival analysis using Cox regression models.

To assess the predictive power of the BI score alone, GRACE score alone, and the GRACE score plus the BI score for survival within one year, the area under the receiver operating characteristic curve (AUC) was constructed for each group, and Delong's test was used to compare the AUCs. The performance of the variables was validated using a bootstrap resembling process, and a nomogram based on Cox regression models was established. All tests were two-tailed, and statistical significance was set at 0.05.

Results

Baseline Characteristics

There was a total of 688 AMI patients in this study, including 399 men (58%) and 289 women (42%), with an average age of 76.29 ± 7.42 years. Compared with the normal ADL group, patients in the impaired ADL group had a longer history of hypertension (13.98 ± 14.54 years vs 12.76 ± 12.87 years, $P = 0.038$), a longer history of diabetes (7.20 ± 11.25 years vs 4.90 ± 8.19 years, $P < 0.001$), more cases with past heart failure (9.8% vs 1.2%, $P < 0.001$), and longer hospitalization (10.88 ± 10.36 days vs 9.64 ± 9.23 days, $P = 0.001$). The impaired ADL group also had more patients in Killip class IV than the normal ADL group (33.3% vs 1.4%, $P < 0.001$). In addition, the impaired ADL group showed higher GRACE scores ($P = 0.004$) and had fewer patients receiving revascularization therapy ($P < 0.001$) during hospitalization than the normal ADL group (Table 1).

Patient Outcomes

Of the 688 patients, 41 died during hospitalization (38 from the impaired ADL group and 3 from the normal ADL group), and 647 were followed up after discharge. Within one year of follow-up, there were 45 deaths, 13 from the impaired ADL group with a 20.3% (13/64) mortality, and 32 from the normal ADL group with a 5.5% (32/583) mortality. Figure 1A shows that the Kaplan–Meier survival curves and the difference in mortality between the two groups were statistically significant ($P < 0.001$).

Table 1 Baseline Patient Characteristics

	Number of All Patients	BI ≤60	BI >60	*P* value
	n = 688	n = 102	n = 586	
Men (%)	399 (58)	51 (50)	348 (59.4)	0.076
Women (%)	289 (42)	51 (50)	238 (40.6)	
Age	76.29±7.42	80.45±7.45	75.57±7.18	0.097
Years of CAD	3.24±6.71	3.65±7.76	3.17±6.52	0.101
Past AMI (%)	99 (14.4)	18 (17.6)	81 (13.8)	0.310
Past CABG (%)	19 (2.8)	4 (3.9)	15 (2.6)	0.439
Hypertension (%)	506 (73.5)	71 (69.6)	435 (74.2)	0.328
Years of Hypertension	12.94±13.13	13.98±14.54	12.76±12.87	0.038
Diabetes (%)	269 (39.1)	45 (44.1)	224 (38.2)	0.260
Years of diabetes	5.24±8.74	7.20±11.25	4.90±8.19	<0.001
Heart failure (%)	17 (2.5)	10 (9.8)	7 (1.2)	<0.001
Smoking (%)	167 (24.3)	12 (11.8)	155 (26.5)	0.005
Drinking (%)	172 (25.1)	16 (15.8)	156 (26.7)	0.073
Family history of CAD (%)	134 (19.5)	11 (10.8)	123 (21.0)	0.016
Length of hospitalization (days)	9.83±9.41	10.88±10.36	9.64±9.23	0.001
Type of AMI (%)				0.846
-STEMI	269 (39.1)	39 (38.2)	230 (39.2)	
-NSTEMI	419 (60.9)	63 (61.8)	356 (60.8)	
Killip class (%)				<0.001
1	394 (57.3)	25 (24.5)	369 (63.0)	
2	214 (31.1)	35 (34.3)	179 (30.5)	
3	38 (5.5)	8 (7.8)	30 (5.1)	
4	42 (6.1)	34 (33.3)	8 (1.4)	
TC	4.17±1.95	3.78±1.04	4.22±1.09	0.765
TG	1.39±0.92	1.22±0.53	1.42±0.97	0.025
HDL-C	1.07±0.26	1.05±0.26	1.08±0.26	0.822
LDL-C	2.34±0.78	2.07±0.77	2.38±0.78	0.901
GRACE score	159.02±31.06	191.58±32.85	153.35±27.01	0.004
Charlson Comorbidity Index	5.99±1.99	6.21±2.10	5.95±1.97	0.234
Revascularization (%)	430 (66.2)	26 (40.6)	404 (68.9)	<0.001

Abbreviations: CAD, coronary artery disease; AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; STEMI, ST elevated myocardial infarction; NSTEMI, non-ST elevated myocardial infarction; TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; GRACE, Global Registry of Acute Coronary Events; revascularization, treated with PCI during hospitalization.

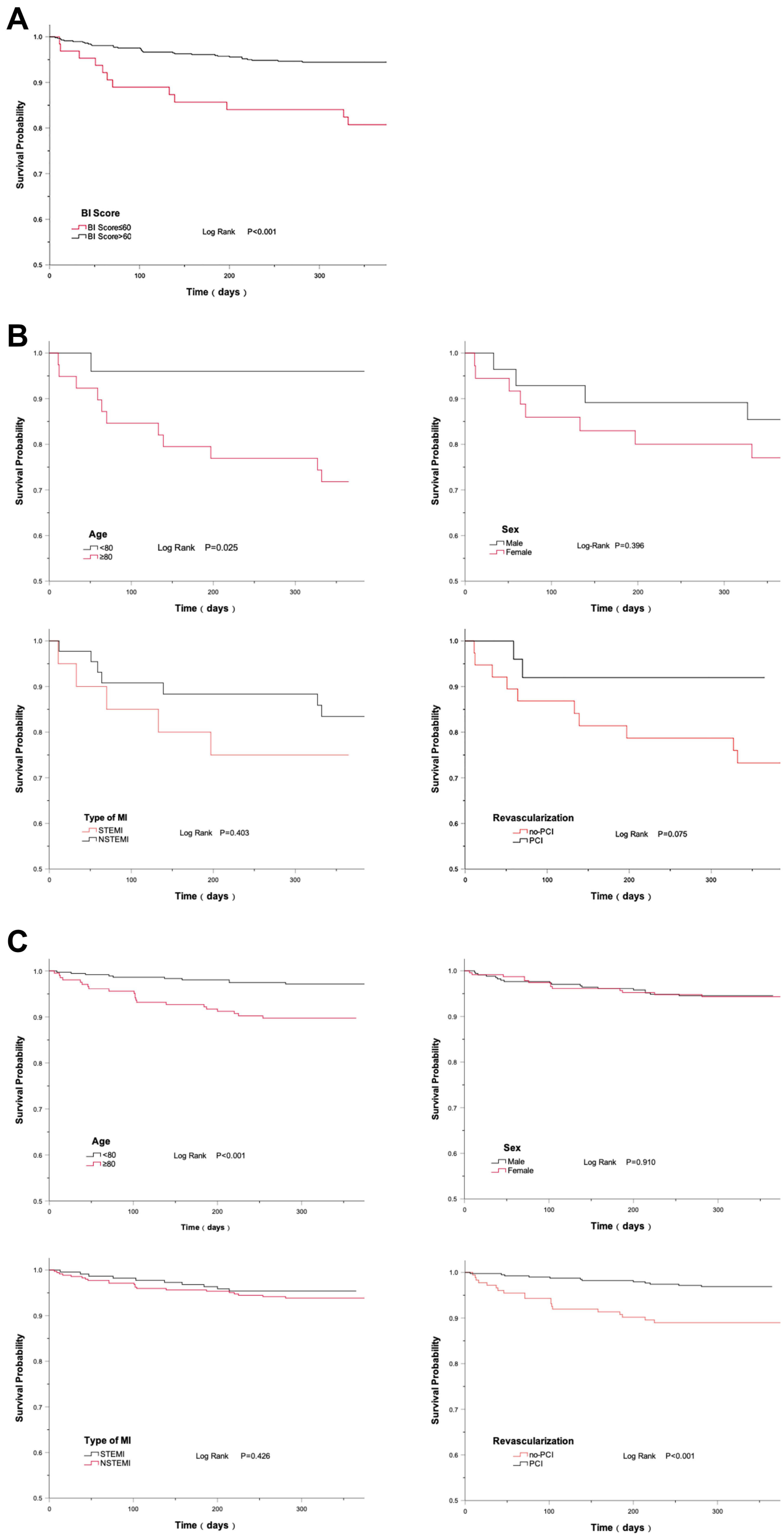

Figure 1 Kaplan-Meier survival curves for different BI score groups (**A**), impaired ADL sub-groups of BI Score≤60 (**B**), normal ADL sub-groups of BI Score>60 (**C**).

Influencing Factors and Subgroup Analysis

To identify potential clinical factors influencing the one-year mortality of older AMI patients, univariate and multivariable Cox regression analyses were conducted (Table 2). In univariate analysis, BI score, GRACE score, and revascularization therapy were correlated with adverse outcomes. After adjustment for sex, comorbidities, and type of AMI, multivariable Cox regression analysis revealed that BI score, GRACE score, and revascularization therapy remained significant influencing factors for one-year mortality in older AMI patients. Specifically, a lower BI score or a higher GRACE score was associated with a higher risk of death (for BI score, hazard ratio (HR) = 0.977, 95% CI: 0.963–0.992, P = 0.002; for GRACE score, HR = 1.024, 95% CI: 1.013–1.036, P < 0.001), whereas revascularization therapy had a protective effect (HR = 0.406, 95% CI: 0.209–0.788, P = 0.008).

When stratified by advanced age (≥80), sex, type of AMI, and revascularization therapy, further analysis found that survival dropped sharply with advanced age in the impaired ADL group (Figure 1B) and that advanced age and revascularization therapy exerted greater influence than sex and type of AMI on one-year survival in the normal ADL group (Figure 1C).

Predictive Models

Following the establishment of Cox regression models for survival analysis, ROCs were obtained for BI score, GRACE score, and BI score plus GRACE score, and AUCs were compared using the Delong's test. As can be seen in Figure 2, BI score and GRACE score had an AUC value of 0.774 (95% CI: 0.731–0.818) and 0.758 (95% CI: 0.704–0.812), respectively, indicating solid predictive power. There was no statistical difference between the two by using Delong's test for AUC comparison (P = 0.625). When the two scores were used together, the AUC reached 0.810 (95% CI: 0.770–0.851), further improving the predictive ability. It had significant difference compared with GRACE score (P = 0.003). After validation, it was clear that the predicted survival probability of the model and the observed survival probability were very close (Figure 3). The nomogram incorporating variables for one-year survival prediction is shown in Figure 4.

Discussion

One major objective of this study was to explore the association of the physical function, as measured by the BI at hospital discharge with one-year all-cause mortality and its predictive value in AMI patients over 65 years of age. Our results showed a 20.3% one-year mortality in patients with impaired ADL (BI ≤60) at the time of hospital discharge, which was much higher compared to patients with normal ADL. We also found that the BI score was a risk factor and had similar predictive power to the GRACE score for one-year mortality in these patients. More significantly, the combination of the BI score and GRACE score outperformed either score alone. To our knowledge, there has been no previous research using such a combination to predict mortality in older AMI patients. Our study provides a basis for leveraging currently available assessment tools to deliver more prognostic accuracy for older AMI patients.

Table 2 Risk Factors from Univariate and Multivariable Cox Analysis

	Univariate		**Multivariable**	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***
Sex	1.360 (0.753–2.456)	0.308		
Hypertension	2.154 (0.909–5.105)	0.081		
Diabetes	0.928 (0.500–1.723)	0.813		
Past AMI	1.391 (0.645–2.999)	0.400		
AMI type	1.166 (0.623–2.183)	0.631		
Charlson Comorbidity Index	1.130 (0.997–1.280)	0.055		
BI score	0.963 (0.950–0.975)	<0.001	0.977 (0.963–0.992)	0.002
GRACE score	1.033 (1.022–1.043)	<0.001	1.024 (1.013–1.036)	<0.001
Revascularization	0.230 (0.122–0.436)	<0.001	0.406 (0.209–0.788)	0.008

Abbreviations: AMI, acute myocardial infarction; BI, Barthel Index; GRACE, Global Registry of Acute Coronary Events.

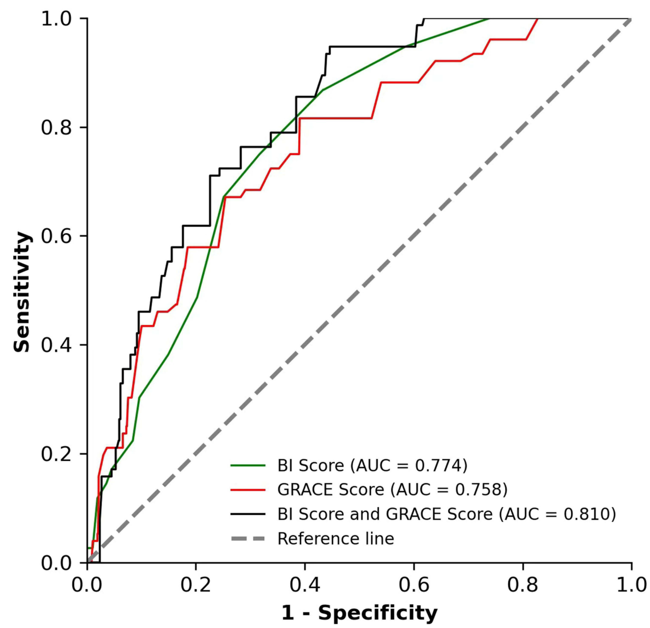

Figure 2 ROC curves of BI score, GRACE score, and BI score plus GRACE score for one-year survival.

Population aging will result in increased proportions of older people living with comorbidity, frailty, and disability. Consequently, there is a pressing need for a shift from the single disease management model to a more comprehensive approach that integrates risk factors commonly encountered in older patients but not yet routinely considered in clinical

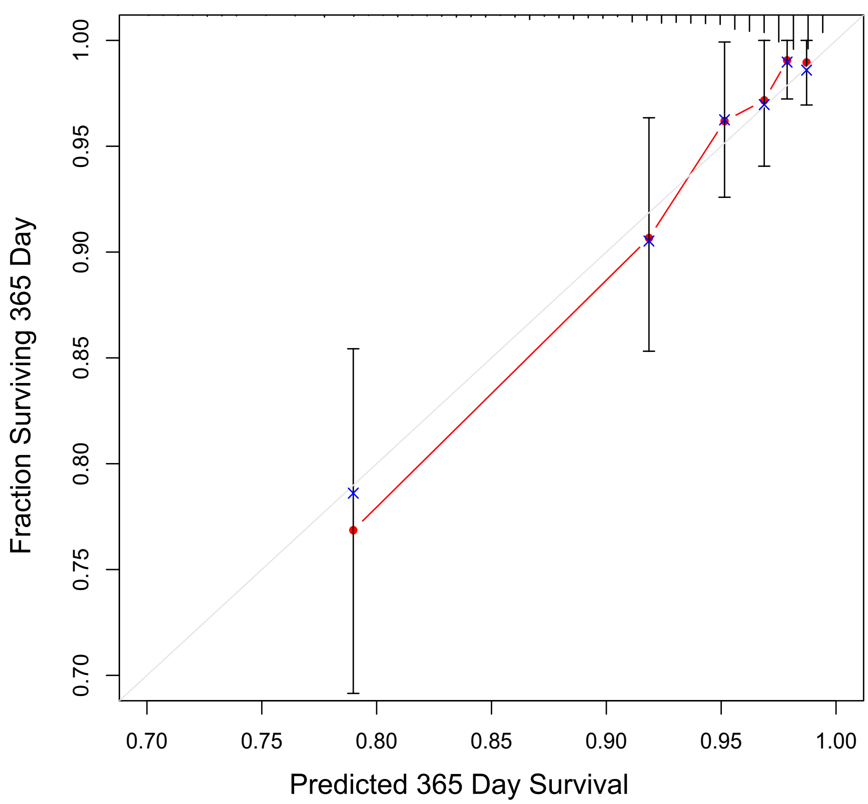

Figure 3 Calibration plots of overall survival probabilities at one year. The x-axis represents the overall survival rate predicted by the nomogram, and the y-axis represents the actual overall survival rate observed. The grey line of dashes along the diagonal passing through the origin represents a perfect calibration model, where the prediction probabilities are consistent with the observation probabilities. The red line represents the calibration curve, which connected by the red dots that indicate observed 1-year mortality rate. The blue crosses mean bias-corrected estimates and the black vertical bars indicate 95% CIs.

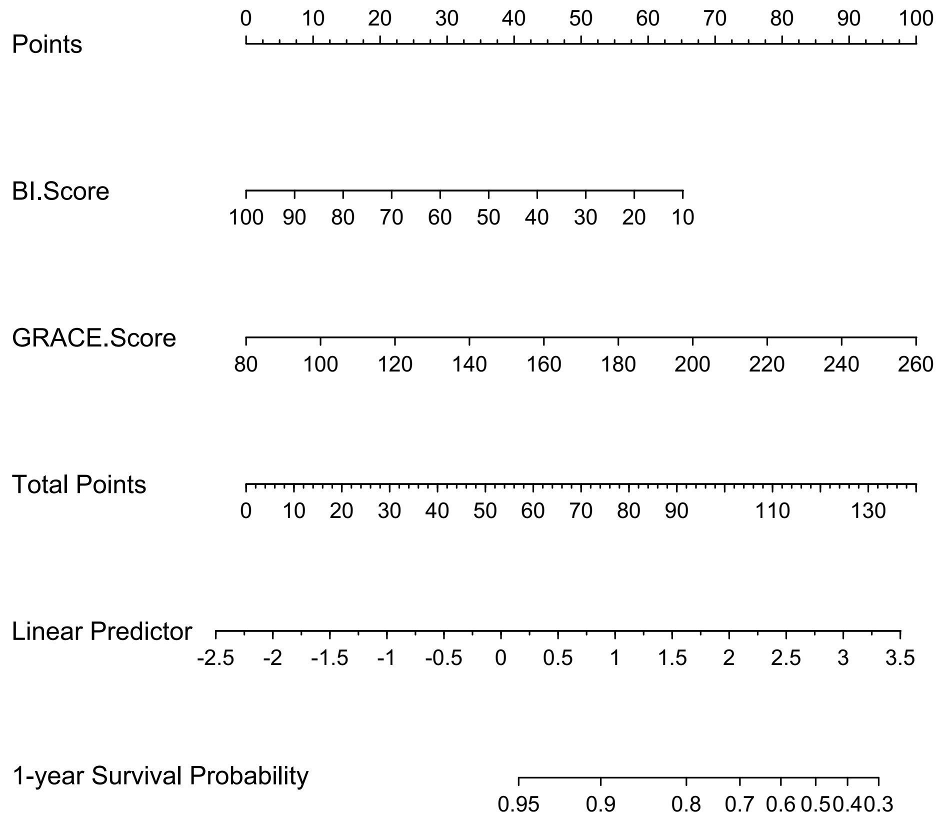

Figure 4 Nomogram of one-year survival probabilities after hospital discharge. The presence or absence of each score indicates a certain number of points. The points for each score are summed together to generate a total-points score for one-year survival probabilities.

practice. A variety of tools have been developed for the assessment of comorbidity, frailty, and disability, although there is a considerable overlap between these pathological states.[18] There is evidence that the Charlson Comorbidity Index can be an indicator for in-hospital and one-year outcomes of ACS, but the exact impact of the individual conditions in the index on the survival of AMI patients is not clear.[19,20] Frailty is consistently found to be related to poor outcomes of numerous cardiovascular conditions and procedures.[21,22] Among methods for its assessment, the frailty phenotype collects data that may not be readily available, the frailty index requires a multidisciplinary team, and the clinical frailty scale (CFS) contains many impression-based components.[23–25] BI is widely used to evaluate physical functional ability, is easy to implement, and, with adequate training, has demonstrated very high reliability.[10,11]

Thus far, only a limited number of studies have adopted BI as a prognostic measure for ACS patients. In a multicenter study involving 2908 ACS patients with a median follow-up of 10.6 months, the BI score at hospital admission was a significant risk factor for both all-cause mortality and cardiac mortality.[12] It needs to be pointed out, however, that the above study included young adults, although the average age of the total population was 65.9 years. Another study focused on very elderly ACS patients (≥85 years) who had undergone PCI and assessed the potential of BI at admission and BI at discharge to predict one-year mortality. This study reported that the BI score at discharge, not at admission, was a risk factor.[13] Our study had a different age profile and was intended to be representative of the older adult population. Given that disease development and treatment during hospitalization might significantly influence a patient's physical capabilities, we decided to use BI at hospital discharge for mortality prediction. Together with the other two studies, we have demonstrated that BI is a valuable indicator for one-year mortality.

There was no significant difference in age between the two groups in our study, but patients with lower BI scores were more likely to have more years of hypertension, diabetes, and heart failure, longer hospital stays, and higher Killip classes than patients with higher BI scores, suggesting that impaired ability of ADL is closely associated with comorbidities in older patients. A decline in physical capabilities increases the risk of bed confinement, which in turn may lead to disuse syndrome, bedsores, and infections.[26,27] The relationship between physical functional status and mortality has been extensively investigated in numerous settings and health conditions. Low BI scores are correlated with increased mortality in community-dwelling residents and patients at hospital admission or discharge.[28–30] For patients with specific diseases, such as hip fractures, dementia, pneumonia, heart failure and nonvalvular atrial fibrillation, a low BI score usually indicates poor outcomes.[31–35] These findings constitute compelling evidence that another dimension, physical performance, should be taken into consideration in the management of diseases. Older adults make up a significant portion of ACS patients, but it has been recognized that age alone may not be sufficient for risk stratification. Since physical functional status has a major impact on outcomes, frailty assessment and comprehensive geriatric assessment have been advocated for older ACS patients.[36,37] However, a lack of relevant trial data has impeded the development of effective treatment strategies for ACS patients with comorbidities.

GRACE is the standard risk stratification tool in the clinical management of ACS. One of its parameters is age, but physical functional status is not included. Gait speed is a component of physical performance in the assessment of sarcopenia and in Fried's frailty phenotype.[23] One study found that slow gait speed was strongly associated with future cardiovascular events in STEMI patients successfully treated with PCI.[38] Other researchers conducted frailty assessment alongside the GRACE score for risk prediction in AMI. Using CFS as the measure of frailty, they discovered that the GRACE score overestimated 12-month mortality risk in older AMI patient and frailty assessment was able to improve risk prediction by identifying physically fit patients.[39] In our study, BI was added for risk prediction because we felt the physical performance aspect needed to be addressed. Similarly, its combination with the GRACE score achieved better prediction. As stated above, BI is known for its reliability. However, it would be interesting to see whether CFS or BI can generate more robust prediction.

Notably, revascularization therapy during hospitalization was found to be a protective factor in our multivariable Cox regression analysis. Further examination of sub-group data showed that only patients with normal ADL clearly benefited from the treatment. Although revascularization seemed to be helpful for mortality reduction, this variable did not reach statistical significance in patients with impaired ADL. This was consistent with other reports,[40,41] indicating that the decision to treat with revascularization should take into consideration a patient's physical functional status.

This study had several limitations. First, as a retrospective study with a moderate sample size in one-single center, especially a relatively small number of patients in the impaired ADL group, the results might have been affected by certain biases and unidentified confounding factors, even after adjustment for some variables. Second, cognitive impairment is common in older adults and may influence ADL and disease outcomes, but this factor was not assessed in this study. Third, as the small sample size, we were unable to collect enough data for external validation. Additionally, all-cause mortality was the only outcome endpoint and other cardiovascular events should be included in further analyses.

Conclusion

GRACE lacks a physical performance component for risk stratification in older AMI patients. The combination of BI and GRACE improves the predictive sensitivity and thus achieves better one-year mortality prediction.

Ethics Approval and Informed Consent

The study was conducted in agreement with the Declaration of Helsinki and was approved by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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