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RESEARCH LETTER

GRACE 2.0 Score for Risk Prediction in Myocardial Infarction With Nonobstructive Coronary Arteries

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Myocardial infarction with nonobstructive coronary arteries (MINOCA) is a condition that is gaining increasing interest.[1,2] Around 5% to 10% of all patients with myocardial infarction (MI) have MINOCA,[1] and women are relatively overrepresented. The cause of MINOCA is heterogeneous, with coronary plaque disruption, spasm, thromboembolism, dissection, microvascular dysfunction, or myocardial injury attributable to supply/demand mismatch as causative or contributing factors. Patients with MINOCA have a guarded prognosis.[1] This emphasizes the need of accurate risk prediction to customize management.

Risk modeling in MI can be facilitated by the use of scoring tools. One of the best-validated instruments is the GRACE (Global Registry of Acute Coronary Events) score, which is built on 8 clinical variables and has recently received a class IIa recommendation in European guidelines.[2] Compared with previous versions, the GRACE 2.0 score uses values derived from β coefficients of regression models using nonlinear functions. These values are added to provide a sum estimate of the probability of adverse outcome without conversion to a point system.[3] However, the score was derived without taking coronary status into consideration, and evidence is lacking on its performance in patients with MINOCA. In the present analysis, we aimed to investigate the prognostic value of the GRACE 2.0 score in a large population of patients with MINOCA, including subanalyses in cohorts defined by sex and MI type.

This analysis is part of the TOTAL-AMI (Tailoring of Treatment in All Comers With Acute Myocardial Infarction) project.[4] Briefly, the TOTAL-AMI project aims to closer characterize different MI types using data from the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) registry and mandatory registries, held by the Swedish National Board of Health and Welfare. Written informed consent for registration in SWEDEHEART registry is not required according to Swedish law. The study had been approved by the Regional Ethical Review Board in Stockholm (2012/60-31/2). The data that support the findings of this study are available from Uppsala Clinical Research Center on reasonable request, and under the provision that the data are accessed onsite and do not leave Uppsala University.

Patients with MINOCA included in the present analysis had been admitted to Swedish coronary care units from January 2005, and were followed up on 1-year all-cause mortality until May 2018 and on the composite of 1-year all-cause mortality or recurrent MI until December 2017. MINOCA was retrospectively defined as MI with normal or near-normal coronary arteries (<50% stenosis), according to invasive coronary angiography, no history of MI or coronary intervention, and

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no coronary intervention during the index hospitalization. For comparative purposes, a cohort of patients with MI with significant (≥50%) coronary stenoses (MI–coronary artery disease) admitted during the same period was also considered. Calculation of the c-statistics and Kaplan-Meier analyses were applied to assess the prognostic value of the GRACE 2.0 score.

Of a total of 10 059 unique patients with MINOCA, 8741 had complete data for the calculation for the GRACE 2.0 score and were included in this analysis. A total of 5504 (63.0%) patients were women, and the median age was 67 years. Further information on clinical characteristics and the components of the GRACE 2.0 score is presented in the Table. One-year rates of mortality and death/MI were 3.7% and 5.4%, respectively. The estimated probabilities for both outcomes, according to the GRACE 2.0 score, were 3.8% (interquartile range, 2.2%–7.0%) and 7.6% (interquartile range, 5.3%–11.9%), respectively. One-year mortality rates in previously defined categories of low (<3%), intermediate (3%–8%), and high (>8%) mortality probabilities[5] were 1.2% (n=42/3449), 3.1% (n=107/3456), and 9.4% (n=172/1836), respectively, with constantly diverging cumulative incidence curves in Kaplan-Meier analyses (log-rank=236.8; *P*<0.001). The c-statistics of the GRACE 2.0 score were 0.750 (95% CI, 0.723–0.778) for

Table 1. Clinical Characteristics and GRACE 2.0 Score Results

Variable	1-y Death		1-y Death/MI	
	No (n=8420)	Yes (n=321)	No (n=7980)	Yes (n=456)
Clinical characteristics				
Female sex	5310 (63.1)	194 (60.4)	5401 (63.2)	274 (60.1)
Current smoking	1506 (17.9)	65 (20.2)	1429 (17.9)	97 (21.3)
Diabetes	962 (11.4)	62 (19.3)	902 (11.3)	91 (20.0)
Hyperlipidemia	1551 (18.4)	61 (19.0)	1464 (18.3)	93 (20.4)
Congestive heart failure	206 (2.4)	39 (12.1)	197 (2.5)	42 (9.2)
Previous stroke	380 (4.6)	30 (9.5)	357 (4.5)	42 (9.4)
COPD	695 (8.3)	69 (21.5)	645 (8.1)	87 (19.1)
Peripheral artery disease	149 (1.8)	14 (4.4)	138 (1.7)	19 (4.2)
Previous/present cancer	149 (1.8)	37 (11.5)	139 (1.7)	39 (8.6)
Atrial fibrillation at admission	735 (8.7)	76 (23.7)	693 (8.7)	90 (19.7)
GRACE 2.0 score components				
Age, y	67 (58–74)	74 (66–81)	67 (58–74)	73 (64–79)
Heart rate, bpm	79 (67–95)	88 (75–110)	79 (67–95)	88 (75–109)
Systolic blood pressure, mm Hg	150 (131–170)	140 (120–160)	150 (131–170)	140 (120–163)
Creatinine, mg/dL	0.84 (0.70–0.99)	0.89 (0.70–1.22)	0.84 (0.70–0.98)	0.88 (0.71–1.13)
Killip class				
I	7775 (92.3)	252 (78.5)	7363 (92.3)	378 (82.9)
II	451 (5.4)	43 (13.4)	428 (5.4)	50 (11.0)
III	85 (1.0)	8 (2.5)	83 (1.0)	9 (2.0)
IV	109 (1.3)	18 (5.6)	106 (1.3)	19 (4.2)
Cardiac arrest	37 (0.4)	12 (3.7)	34 (0.4)	11 (2.4)
cTn >99th percentile	8344 (99.1)	318 (99.1)	7906 (99.1)	453 (99.3)
Ischemic ECG changes	2581 (30.7)	152 (47.4)	2458 (30.8)	190 (41.7)
GRACE 2.0 score results				
Estimated probability, %	3.8 (2.2–7.0)		7.6 (5.3–11.9)	
C-statistics (95% CI)				
Overall	0.750 (0.723–0.778)		0.685 (0.659–0.711)	
Men	0.765 (0.725–0.806)		0.699 (0.660–0.739)	
Women	0.744 (0.708–0.780)		0.678 (0.643–0.712)	
STEMI	0.773 (0.718–0.828)		0.738 (0.684–0.792)	
NSTEMI	0.736 (0.704–0.767)		0.667 (0.637–0.692)	

Categoric variables are presented as numbers (percentages), and continuous variables are presented as medians (interquartile ranges), unless stated otherwise. bpm indicates beats per minute; COPD, chronic obstructive pulmonary disease; cTn, cardiac troponin; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction; NSTEMI, non–ST-segment–elevation MI; and STEMI, ST-segment–elevation MI.

1-year mortality and 0.685 (95% CI, 0.659–0.711) for 1-year death/MI. In subgroups defined by sex and MI type, numerically higher c-statistics were noted in men and patients with ST-segment–elevation MI (n=1402 [16.0%]). The GRACE 2.0 score was, however, not optimally calibrated (Hosmer-Lemeshow $P<0.001$ for both outcomes). The overall c-statistics were lower compared with estimates obtained from 115 221 patients with MI–coronary artery disease (1-year mortality: 0.810 [95% CI, 0.806–0.815]; 1-year death/MI: 0.748 [95% CI, 0.743–0.753]; $P<0.001$ for both comparisons).

The prognostic accuracy of the GRACE 2.0 score in patients with MINOCA was, thus, fairly high for 1-year mortality, but only moderate for 1-year death/MI and lower compared with patients with MI–coronary artery disease. These findings are not surprising given the multitude of causative or contributing factors in MINOCA[1] together with potential variations in their impact on outcome. Moreover, cardiovascular risk factors and comorbidities were less common in our patients with MINOCA compared with the GRACE 2.0 score derivation cohort,[3] and this score does not consider risk indicators being specifically important in MINOCA (eg, male sex, congestive heart failure, or chronic obstructive pulmonary disease).[4]

Our analysis is potentially limited by its retrospective approach using registry data, unavailability of results from other investigations than invasive coronary angiography, and the lack of formal adjudication of index and outcome events. Nonetheless, the findings presented herein suggest that risk prediction using the GRACE 2.0 score may not be optimal in MINOCA, and that prognostication and subsequent management to a greater degree need to be individualized than in patients with MI–coronary artery disease.

ARTICLE INFORMATION

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Disclosures

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