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Risk Estimation in Type 2 Myocardial Infarction and Myocardial Injury: The TARRACO Risk Score

Clinical Research Study

Running Title: The TARRACO Risk Score

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All authors had full access to all the data in the study, had a role in writing the manuscript, and had final responsibility for the decision to submit for publication.

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Highlights

- The TARRACO risk score incorporates cardiac troponin and clinical predictors of adverse cardiovascular events: age, hypertension, absent of chest pain, dyspnea, and anemia.
- This risk score showed good discriminative accuracy for patients with type 2 myocardial infarction and patients with myocardial injury (AUC 0.75 and 0.74, respectively.
- Prognosis in type 2 myocardial infarction could efficiently be estimated early, prior to hospital discharge.

ABSTRACT

OBJECTIVE: Despite adverse prognoses of type 2 myocardial infarction and myocardial injury, an effective, practical risk stratification method remains an unmet clinical need. We sought to develop an efficient clinical bedside tool for estimating the risk of major adverse cardiovascular events at 180 days for this patient population.

METHODS: The derivation cohort included patients with type 2 myocardial infarction or myocardial injury admitted to a tertiary hospital between 2012 and 2013 (n=611). The primary outcome was a major adverse cardiovascular event (death, re-admission for heart failure or myocardial infarction). The score included clinical variables significantly associated with the outcome. External validation was conducted using the UTROPIA cohort (n=401).

RESULTS: The TARRACO score included cardiac troponin (cTn) concentrations and five independent clinical predictors of adverse cardiovascular events: age, hypertension, absence of chest pain, dyspnea, and anemia. The score exhibited good discriminative accuracy (AUC=0.74; 95%CI, 0.70–0.79). Patients were classified into low-risk (score 0–6) and high-risk (score ≥7) categories. Major adverse cardiovascular events rates were five-times more likely in high-risk patients compared with those at low risk (78.9 vs. 15.4 events/100 patient-years, respectively; log rank *P*<0.001). The external validation showed equivalent prognostic capacity (AUC=0.71, 0.65–0.78).

CONCLUSION: A novel risk score based on bedside clinical variables and cTn concentrations allows risk stratification for death and cardiac-related rehospitalizations in patients with type 2 myocardial infarctions and myocardial injury. This score identifies patients at the highest risk of adverse events, a subset of patients who might benefit from close observation and/or medical intensification.

Key words: Troponin elevation; non-acute coronary syndrome; risk stratification.

INTRODUCTION

Cardiac troponin (cTn) is the recommended and preferred biomarker for diagnosing acute myocardial infarction.[1,2] The use of high-sensitivity (hs) cTn assays and broad testing across various clinical scenarios has led to a progressive increase in the number of patients displaying increased cTn concentrations >99th percentile in the settings of acute and chronic pathologies other than type 1 myocardial infarction. Several studies suggest that most increased levels of cTn in contemporary practice are due to either type 2 myocardial infarction or myocardial injury.[3-6] Compared to patients without myocardial necrosis, patients with type 2 myocardial infarction or myocardial injury are at high risk for both short- and long-term adverse outcomes.[7-9] No guidelines exist for addressing the management of these conditions, despite their association with a poor prognosis.

Clinical risk scores have been implemented in cardiovascular medicine as ancillary tools to provide a quantifiable and objective assessment of the risk of developing adverse events during follow-up. Most clinical practice guidelines recommend risk stratification for patients with acute coronary syndrome.[10, 11] Nonetheless, we lack an effective, practical risk stratification model for patients with type 2 myocardial infarction or myocardial injury. Accurate risk assessment in this population could facilitate the triaging and management of these patients, and aid in the identification of patients at high risk. Such a strategy could be valuable in selecting patients for future research and clinical trials, as well as identification of those at the greatest risk for adverse events, whose outcomes could potentially be improved through better monitoring and/or medical intensification.

In this study, we aimed to develop a scoring system based on clinical variables that were easily obtained in routine clinical care and that were associated with the incidence of major adverse cardiovascular events at 180 days to facilitate risk stratification of patients with type 2 myocardial infarction or myocardial injury.

PATIENTS AND METHODS

Patient cohorts

TARRACO derivation cohort (Troponin Assessment for Risk stRatification of patients without Acute COronary athero-thrombosis): a retrospective single-center observational cohort study including data from patients admitted consecutively to the emergency department (ED) of the Joan XXIII University Hospital (Tarragona, Cataluña, Spain) between 2012 and 2013 who underwent cTnI measurement based on clinical indication. The design and primary results have been reported previously.[7] All contemporary cTnI measurements were carried out using the same immunoassay technique (ADVIA Centaur cTnI-Ultra, Siemens). The analytical performance of this assay was validated previously.[12] The 99th percentile was 0.04 µg/L. We reviewed the electronic clinical records of all patients to obtain data on medical history, presenting symptoms, physical examination at the initial evaluation in the ED and electrocardiographic findings. Patients were excluded based on the following criteria: a maximum cTnI level ≤99th percentile, occurrence of a type 1 myocardial infarction, age below 18 years, recovering from cardiac arrest, and in-hospital mortality. Patients were classified according to the Third Universal Definition of Myocardial Infarction.[1] Type 2 myocardial infarction was diagnosed in a clinical setting unrelated to acute coronary athero-thrombosis leading to an imbalance in myocardial oxygen supply and demand using the specific criteria proposed by Saaby et al.[5] Myocardial injury was defined as any cTnI increase to >99th percentile that was not classified as myocardial infarction.

UTROPIA validation cohort (Use of TROPonin In Acute coronary syndromes, NCT02060760): a prospective single-center observational cohort study of consecutive, unselected patients presenting to the ED in whom preset serial cTnI measurements were ordered upon clinical indication at Hennepin County Medical Center (Minneapolis, Minnesota,

USA). The design and primary results have been reported previously.[3,13] For inclusion, patients needed a baseline cTnI measurement at presentation, at least one additional cTnI measured within 24 h of presentation before discharge. All patients had cTnI measured with both the contemporary cTnI (clinically used) and hs-cTnI (investigational) assays on the Abbott ARCHITECT $i1000_{SR}$ or $i2000_{SR}$ analyzers (Abbott, Abbott Park, Ill). For the present study, analyses are based on the contemporary cTnI assay results (99^{th} percentile, 0.030 µg/L). All cases with at least one cTnI value >99^{th} percentile were adjudicated according to the Third Universal Definition of Myocardial Infarction by 2 clinicians following a review of all available medical records. Cases with an adjudication discrepancy were reviewed and adjudicated by a third senior clinician. Type 2 myocardial infarction was defined as myocardial infarction secondary to an ischemic imbalance between myocardial oxygen supply and/or demand not due to atherothrombosis, and was adjudicated following the use of broad criteria,[13,14] an approach in which adjudicators evaluate all contributing supply/demand variables and give a diagnosis of type 2 myocardial infarction. For type 2 myocardial infarction to be adjudicated, cases were required to have definite evidence or documentation of a supply/demand imbalance. The term myocardial injury applied to any cTnI increase >99^{th} percentile that was not adjudicated as myocardial infarction.

Both cohorts were approved by the local Ethics Committees. This study was conducted in accordance with the Declaration of Helsinki.

Clinical outcomes

The primary outcome was a composite of post-discharge major adverse cardiovascular events at 180 days that included: all-cause death and re-admission for congestive heart failure or acute myocardial infarction. Patients were followed up for 180-days and events were recorded at the time of the last patient contact or at the time of a major adverse cardiovascular event. Follow-

up events were obtained by searching the patients' electronic clinical records and death registers.

Statistical analysis

Data are presented as the median and interquartile range for continuous variables, and as the number and percentage for categorical variables. We transformed several continuous variables into categorical variables according to clinically meaningful cutoff values. Age was categorized into 3 groups (<70, 70–79, ≥80 years), systolic blood pressure into 3 groups (<90, 90–159, ≥160 mmHg), heart rate into 20-beat/min groups, and glomerular filtration rate into 3 groups (>60, 30–59, <30 mL/min/1.73 m^2). Similarly, a cut-off point of the upper reference limit (URL) x5 was chosen for cTnI, based on current evidence indicating that there is a differential relationship between the magnitude of maximum cTnI concentration and long-term outcomes in several populations.[15, 16] Anemia was defined, according to World Health Organization criteria, as a hemoglobin level <130 g/L in men and <120 g/L in women.

Univariate analyses were performed that included all variables potentially associated with the outcome. Variables that were significantly associated with the outcome and had *P*-values <0.1 were retained for multivariate logistic regression. Multivariable logistic regression was performed with backward elimination to establish the most parsimonious model. Based on the clinical evidence demonstrating that all-cause mortality increases with increasing cTnI concentrations regardless of the cause of increase,[15] cTnI was included in the final model. Results from the regression analyses are presented as odds ratios (ORs) with 95% confidence intervals (CIs).

The TARRACO scoring system was determined by rounding the observed multivariate ORs of the respective variables to whole numbers and assigning them as points to each variable. The discriminative power was assessed, based on the area under the receiver operating

characteristic curve (AUC). The goodness-of-fit was assessed with the Hosmer–Lemeshow test.

According to the TARRACO score, the population was classified into two risk categories: low and high risk. We used the Kaplan–Meier method to estimate time-to-first-event survival associated with each risk category and compared them with a log-rank test. All comparisons of statistical significance were 2-sided and a *P*-value <0.05 was considered significant. STATA V.13.0 (College Station, Texas, USA) was used for derivation analyses. Validation analyses were performed using SAS version 9.4 (Cary, NC, USA).

RESULTS

TARRACO derivation cohort

A total of 611 patients met the inclusion criteria (**Figure 1**). Baseline characteristics of the study subjects are detailed in **Table 1**. In the derivation cohort, the median age was 78 years and 55.5% were men. The main co-morbidities were hypertension, diabetes, and previous myocardial infarction. Dyspnea was a more frequent reason for consultation than chest pain. Patients were diagnosed with either type 2 myocardial infarction (n=164, 26.8%) or myocardial injury (n=447, 73.2%). During follow-up, 90 (14.7%) patients died, 42 (6.9%) experienced hospital readmission due to heart failure, and 6 (1.0%) experienced readmission due to myocardial infarction. When these events were considered mutually exclusive, 122 (20.0%) patients experienced the composite endpoint.

Variable identification and TARRACO score creation

The univariate logistic regression analysis showed that the outcome was associated with age, prior myocardial infarction, heart failure, moderate to severe renal disease, arterial hypertension, absence of chest pain, dyspnea, glomerular filtration rate, and anemia. The multivariate analysis identified five variables that were independently related to clinical

outcome: age, arterial hypertension, absence of chest pain, dyspnea, and anemia (**Table 2**). We used these variables and cTnI to create the score. First, we rounded the observed ORs to integers, then each variable was scored based on whether it was absent (score=0) or present (1–3 points). The total number of points gave the TARRACO score, with a minimum of 0 (no variable present) and a maximum of 13 points (all variables present). Patients were allocated to one of two categories: low risk (0–6 points) and high risk (7–13 points). The high-risk group had a shorter time to the first event than the low-risk group (log-rank $P<0.001$;**Figure 2**). Event rates were five times higher in high-risk patients compared with those at low risk (78.9 vs.15.4 events/100 patient-year, respectively; log rank $P<0.001$). The TARRACO score showed good discriminative accuracy (AUC=0.74, 95%CI, 0.70–0.79), and the predicted risk closely resembled the observed risk (Hosmer–Lemeshow test, 3.43;$P=0.945$;**Figure 3**). The score discriminative accuracy was equivalent for patients with type 2 myocardial infarction and patients with myocardial injury (AUC 0.75 and 0.74, respectively;**Table 3**).

External validation cohort

The 401 patients in the validation cohort had a median age of 60 (52–73) years and 235 (58.6%) were men. This cohort had a similar prevalence of cardiovascular risk factors and prior cardiovascular disease (**Table 1**). The distribution of type 2 myocardial infarction (n=128, 31.9%) and myocardial injury (n=273, 68.1%) was similar to that in the derivation cohort. During follow-up, 34 (8.5%) patients died, 34 (8.5%) experienced hospital readmission due to heart failure, and 6 (1.5%) readmission due to myocardial infarction. The clinical endpoint occurred in 73 (18.2%) patients.

In the validation cohort, the TARRACO score also showed good discrimination ability (AUC=0.71, 95%CI, 0.65–0.78). The predicted risk closely resembled the observed risk (Hosmer–Lemeshow test, $P=0.259$). The TARRACO score also showed equivalent discrimination accuracy in patients with type 2 myocardial infarction and in patients with

myocardial injury (AUC 0.74 and 0.70, respectively;**Table 3**). In this cohort, 56.4% (n=226) and 43.6% (n=175) of patients were classified as low and high risk, respectively. The high-risk group had substantially worse outcomes than the low-risk group during follow-up (**Figure 4**). The probabilities of the outcome for the different score groups were similar in the external validation and the derivation groups (**Figure 5**).

DISCUSSION

We derived and validated the first clinical score for predicting prognosis in a large cohort of consecutive ED patients with type 2 myocardial infarction or myocardial injury. The TARRACO score, consisting of clinical variables associated with death and cardiovascular events at 180 days, identifies patients at high risk of adverse cardiovascular events—a subset of patients in whom the development of targeted evidence-based therapies and/or management strategies may provide the most benefit.

Our study has several strengths. First, the TARRACO score offers a quantifiable and objective method for risk stratification based on variables that are readily available from clinical assessment. Second, rather than relying on individual clinical features or subjective assessments of outcomes, we found that an integrated clinical score was the best predictor of the risk of adverse events among patients with type 2 myocardial infarction or myocardial injury. Third, our results are clinically relevant because they suggest that prognosis could efficiently be estimated early, prior to hospital discharge. Fourth, the model is easy to apply clinically because the variables are easy to ascertain at the patient's bedside. Finally, the score was derived and validated in two well-characterized cohorts of consecutive, unselected European and North American patients admitted to the ED who underwent cTnI measurements on clinical indication using different immunoassays in each cohort, which makes our findings applicable and generalizable across centers.

The use of contemporary and high-sensitivity cTn assays indicates that type 2 myocardial infarction and myocardial injury represent over two-thirds of all cTn increases encountered in unselected patients admitted to the ED.[17-20] These conditions display more diverse clinical presentations, electrocardiographic findings, and biomarker profiles than in patients with type 1 myocardial infarction.[4, 14, 21] These patients have an adverse prognosis during follow-up, similar or worse than that of patients with type 1 myocardial infarction.[4, 7, 22, 23] However, therapies and/or strategies to manage type 2 myocardial infarction and myocardial injury remain undefined. Treatment of the underlying disease and/or triggers leading to type 2 myocardial infarction and myocardial injury are currently the primary therapeutic goal.

Clinical prediction models have been implemented in routine clinical practice to identify patients at both low and high risk of adverse events, and aid in clinical decision-making.[24-26] These instruments are relevant because they can provide a quantifiable and objective understanding of individual risk, but they can also help inform the selection of patients and development of trials aiming to clarify the potential benefit of existing and/or novel treatments, procedures, or management strategies. Given the absence of risk-assessment tools for patients with type 2 myocardial infarction or myocardial injury, their management is variable. It currently relies largely on clinical judgment, the subjective assessment of symptoms at presentation, cardiovascular risk factors, and available findings from information yielded from electrocardiogram and other cardiac imaging studies.

A better knowledge of the individual risk of cardiac rehospitalization—beyond mortality—may influence clinical decisions and improve the selection of patients who may benefit from medical intensification and/or closer observation after hospital discharge. Rehospitalization has been used as an indirect measurement of quality of care, and in some cases potential financial implications for health services.[27]

The variables included in the TARRACO risk score are consistent with prior evidence showing that each variable is associated with the risk of adverse events in patients with cardiovascular disease. The presence of anemia was shown to contribute to an imbalance in the supply and demand of myocardial oxygen.[1] In type 2 myocardial infarction, however, anemia explains only one of the many mechanisms leading to myocardial infarction; further investigation is required to address whether anemia represents a surrogate marker of risk, and whether outcomes can be modified using blood transfusions or other therapies. Prior studies have reported a cross-sectional association between hypertension and the prevalence of elevated cTn[28]: Increased cTn levels among such patients are associated with a higher risk of developing cardiovascular events during long-term follow-up.[29] Consistent with other investigations, we observed that patients with type 2 myocardial infarction and myocardial injury presented more frequently with atypical symptoms, including an absence of chest pain and a high prevalence of dyspnea. These two conditions have previously been associated with a worse prognosis during follow-up.[30, 31] The inclusion of cTn concentrations in the score has also been found to be important based on previous evidence demonstrating a stepwise increase in mortality with increasing levels of this biomarker.[15, 16]

Our study has limitations. First, it was retrospective in design. Second, the type 2 myocardial infarction diagnoses were based on strict, specific criteria in the derivation cohort and broad criteria in the validation cohort; however, these differences have limited impact as irrespective of how the type 2 myocardial infarction diagnosis was established, analyses were based on the entire subset of patients, with cTn increases classified as either type 2 myocardial infarction or myocardial injury. Third, the score was derived and validated using contemporary troponin assays; further validation in large studies using high-sensitivity cTn assays would further improve its applicability. Fourth, the mode of death was not recorded, and thus estimates of the proportion of deaths attributable to cardiovascular disease were lacking. Recent studies,

however, suggest that cardiovascular deaths occur in approximately 24% to 43% of patients with type 2 myocardial infarction and approximately 28% to 41% of patients with myocardial injury.[8, 32]

Conclusions

Among patients with type 2 myocardial infarction and myocardial injury, we have developed a novel risk stratification scoring strategy allowing the precise quantification of risk for death or cardiac rehospitalization at 180 days that should facilitate the identification of high-risk patients in whom closer observation after hospital discharge and/or medical intensification may be helpful. The score may be useful in the design of future studies and aid in the selection of high-risk patients, a group for which the development of novel therapies and/or strategies may provide benefit.

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Conflict of interest

The authors declare no conflict of interests relevant to the content of the manuscript.

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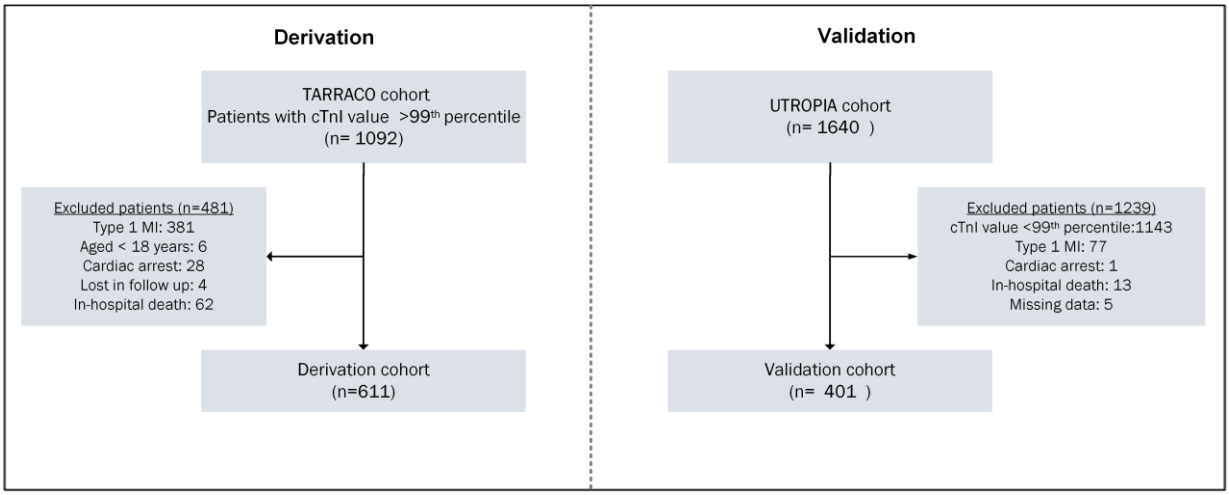

Figure 1 Flow chart of patient selection for the two study cohorts. MI=myocardial infarction.

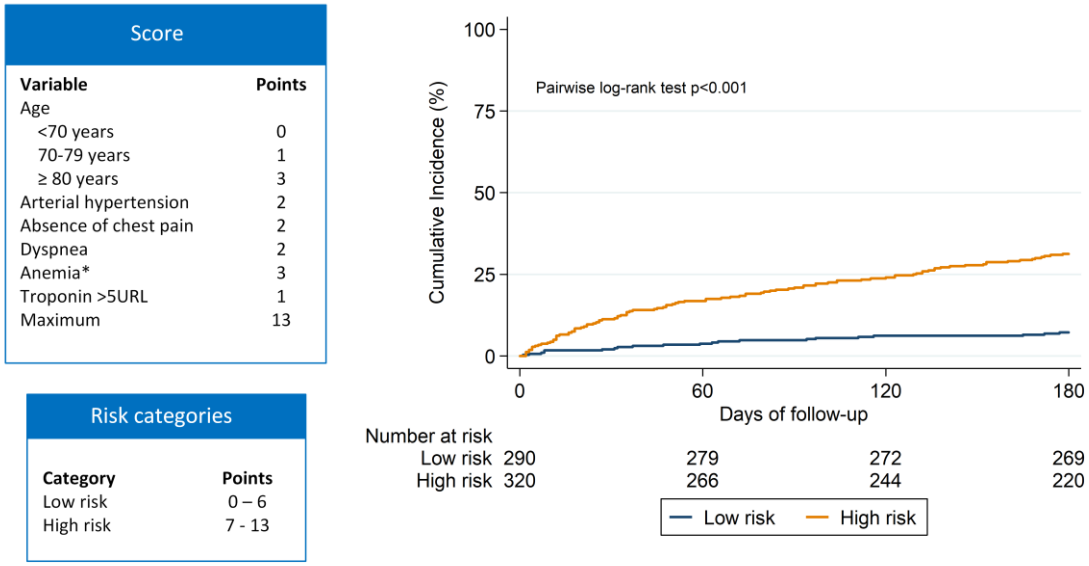

Figure 2 Derivation of the TARRACO score, based on a stepwise multivariable regression analysis, for predicting the risk of major adverse cardiovascular events among patients with type 2 myocardial infarction or myocardial injury. (*Left*, *upper panel*) First, the OR for each variable was rounded to an integer, then these integers were assigned to each variable (1 to 3 points each). The total scores (maximum = 13) were divided into two risk categories, (*left*, *lower panel*) low risk: 0 to 6 points and high risk: 7 to 13 points. (*Right*) Kaplan–Meier analysis of 180-day major adverse cardiovascular events and mortality showed significantly higher rates of major adverse cardiovascular events in the high-risk (gold) group compared to the low-risk (blue) group (derivation cohort). MACE, major adverse cardiovascular events. URL=upper reference limit.

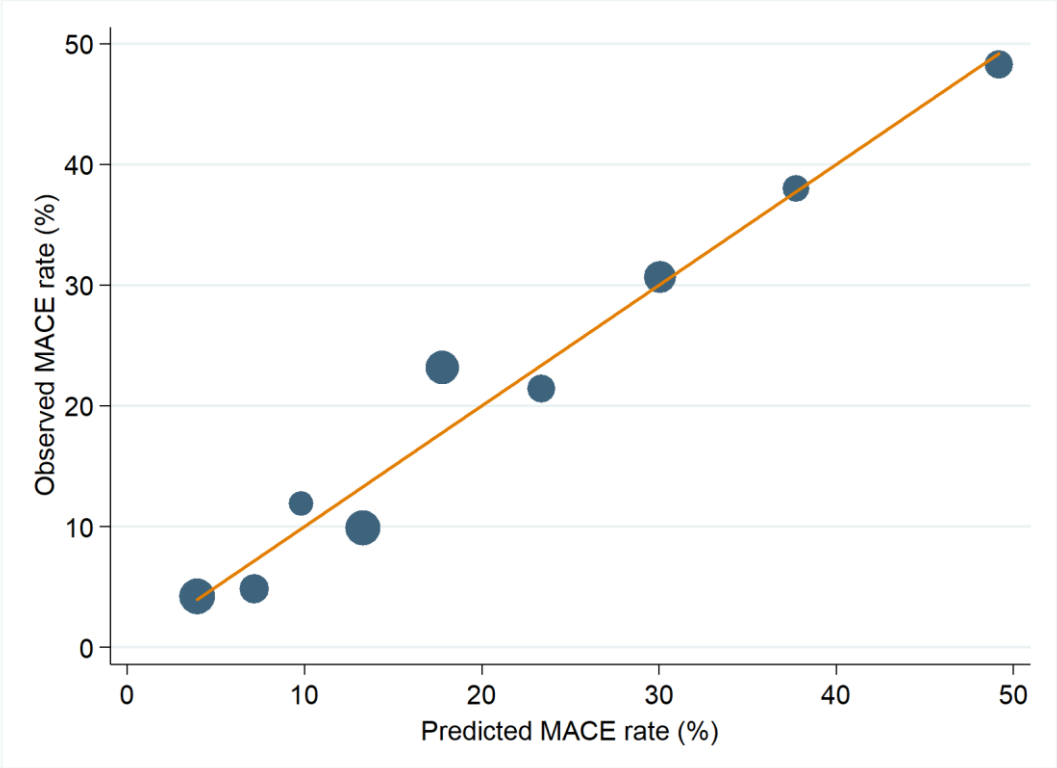

Figure 3 Derivation cohort calibration plot. The derivation cohort was divided into 9 groups of predicted probability of major adverse cardiovascular events. Subsequently, calibration was assessed by plotting the predicted probability of major adverse cardiovascular events against the observed frequency of major adverse cardiovascular events. major adverse cardiovascular events, major adverse cardiovascular events.

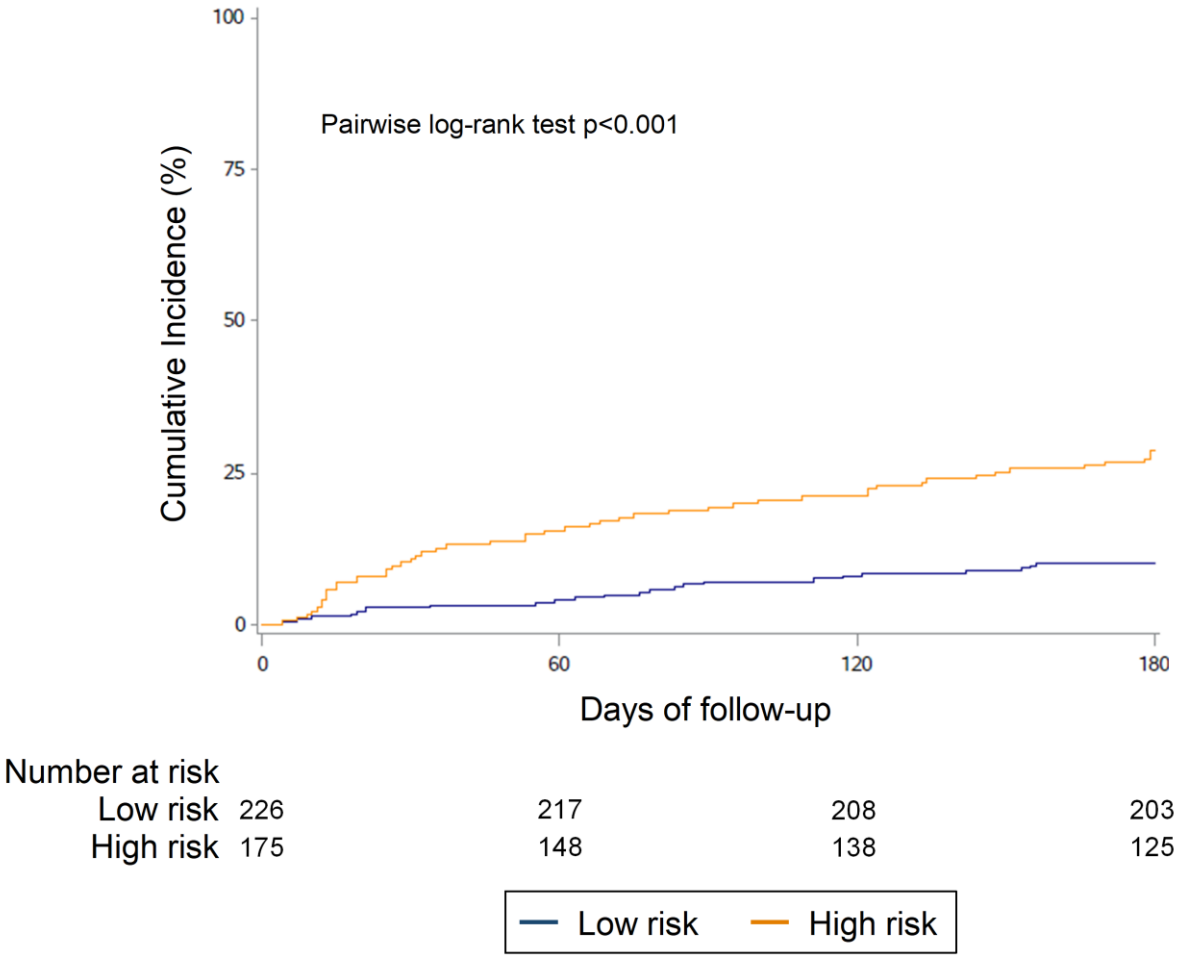

Figure 4 Kaplan–Meier curves depict the incidence of major adverse cardiovascular events, according to risk categories, in the external validation cohort.

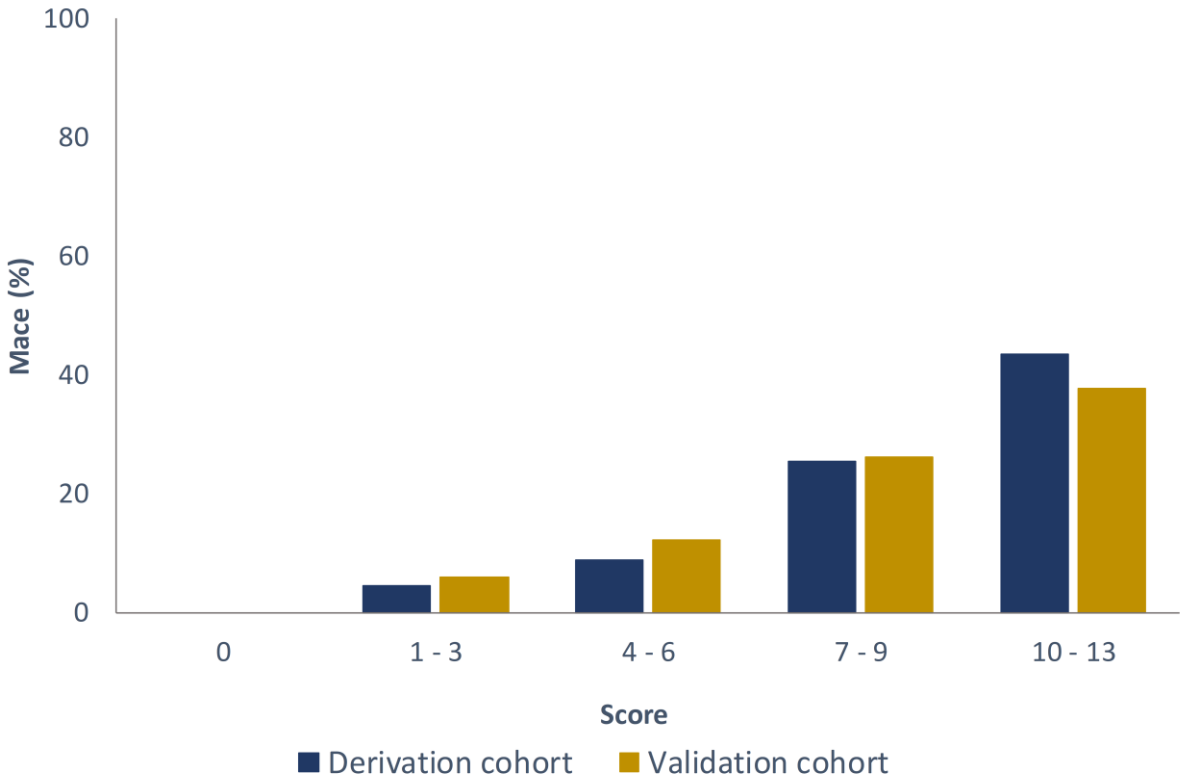

Figure 5 The TARRACO scores increased with increasing major adverse cardiovascular events incidence. The percentages of major adverse cardiovascular events observed in subgroups based on TARRACO scores are shown for the derivation (blue) and validation (gold) cohorts. major adverse cardiovascular events, major adverse cardiovascular events.

Table 1 Baseline characteristics of derivation and validation cohorts

	Derivation cohort (n=611)	**External validation cohort (n=401)**
Demographics		
Age, years	78 (67–84)	60 (52–73)
Male sex	339 (55.5)	235 (58.6)
Clinical history		
Prior myocardial infarction	151 (24.7)	54 (13.7)
Congestive heart failure	108 (17.7)	118 (29.4)
Peripheral arterial disease	74 (12.1)	11 (2.7)
Cerebrovascular disease	89 (14.6)	56 (14.0)
Moderate to severe renal Disease	134 (21.9)	124 (30.9)
Diabetes mellitus	218 (35.7)	145 (36.2)
Arterial hypertension	462 (75.6)	308 (76.8)
Tobacco use	190 (31.1)	131 (32.7)
Clinical symptoms		
Chest pain	171 (28.0)	149 (37.2)
Dyspnea	224 (36.7)	167 (41.7)
Others	279 (45.7)	157 (39.2)
Electrocardiogram		
ST segment elevation	22 (3.8)	96 (23.9)
LBBB or RBBB	139 (24.3)	48 (12.0)
ST segment depression	37 (6.5)	89 (22.2)
Negative T wave	65 (11.3)	133 (33.2)
Atrial fibrillation	192 (33.5)	45 (11.2)
Vital signs on admission		
Heart rate, bpm	90 (71–113)	92 (78–110)
SBP, mmHg	134 (118–155)	144 (125–167)
DBP, mmHg	75 (63–89)	83 (69–100)
Laboratory tests		
Creatinine, mg/dL *	1.16 (0.88–1.60)	1.18 (0.88–2.21)

GFR, mL/min/1.73 m^2 †	57.3 (40.0–79.9)	66 (32–92)
Hemoglobin, g/dL	12.5 (11.1–14.0)	12.8 (10.7–14.4)
TnI peak level, µg/L ‡	0.12 (0.06–0.34)	0.06 (0.04–0.13)
Coronary angiography	42 (6.9)	21 (5.2)
Type 2 myocardial infarction	164 (26.8)	128 (31.9)
Myocardial injury	447 (73.2)	273 (68.1)

Data are presented as the number of patients (%) or the median (IQR), as indicated.

*Data were available for 607 individuals in the derivation cohort and 387 individuals in the validation cohort. †Data were available for 607 individuals in the derivation cohort and 394 individuals in the validation cohort. ‡TnI was measured with the ADVIA Centaur TnI-Ultra, from Siemens, in the derivation cohort, and with the ARCHITECT clinical chemistry analyzer, from Abbott, in the validation cohort.

Abbreviations: LBBB, left bundle branch block; RBBB, right bundle branch block; SBP, systolic blood pressure; DBP, diastolic blood pressure; GFR, glomerular filtration rate; TnI, troponin I.

Table 2 Results of univariate and multivariate logistic regression analyses

	Univariate logistic regression			Multivariate logistic regression		
	OR	**95% CI**	***P***	**OR**	**95% CI**	***P***
Age, years						
<70	--	--	--			
70–79	1.74	0.90–3.36	0.098	1.30	0.62–2.72	0.484
≥80	3.88	2.21–6.82	<0.001	2.74	1.46–5.15	0.002
Female sex	1.21	0.82–1.81	0.340			
Myocardial infarction	1.58	1.02–2.44	0.039			
Heart failure	1.82	1.13–2.93	0.013			
Cerebrovascular disease	1.49	0.88–2.51	0.135			
Peripheral arterial disease	1.23	0.69–2.20	0.491			
Moderate to severe renal disease	1.67	1.07–2.61	0.025			
Arterial hypertension	2.28	1.32–3.96	0.003	2.24	1.12–4.47	0.023
Diabetes mellitus	1.22	0.81–1.83	0.345			
Absence of chest pain	2.28	1.36–3.82	0.002	2.03	1.15–3.58	0.015
Dyspnea	2.58	1.72–3.86	<0.001	1.88	1.19–2.96	0.007
ST segment elevation	0.41	0.09–1.76	0.228			
ST segment depression	0.63	0.24–1.67	0.355			
LBBB or RBBB	1.50	0.95–2.37	0.082			
Atrial fibrillation	1.27	0.82–1.95	0.282			
Heart rate (per 20-bpm increase)	1.04	0.92–1.18	0.548			
SBP <90 mmHg (vs. 110–160 mmHg)	0.74	0.30–1.84	0.521			
SBP ≥160 mmHg (vs. 110–160 mmHg)	0.80	0.45–1.39	0.421			
Creatinine per 1 mg/dL	1.01	0.92–1.10	0.887			

increase						
GFR, mL/min/1.73 m^2						
≥60	--	--	--			
30–59	2.25	1.43–3.54	0.001			
<30	2.33	1.31–4.13	0.004			
Anemia	3.51	2.27–5.42	<0.001	2.80	1.72–4.54	<0.001
Troponin >5 URL	1.27	0.85–1.91	0.248	1.46	0.92–2.32	0.111

Abbreviations: LBBB, left bundle branch block; RBBB, right bundle branch block; bpm, beats per minute; GFR, glomerular filtration rate; SBP, systolic blood pressure; URL, upper reference limit. Multivariate results are presented after backward elimination was completed.

Table 3 Model performance in type 2 myocardial infarction and myocardial injury groups

	Type 2 Myocardial Infarction	Myocardial Injury	All patients
		***c* Statistic (95% CI)**	
Derivation cohort	0.75 (0.67–0.83)	0.74 (0.69–0.80)	0.74 (0.70–0.79)
Validation cohort	0.74 (0.63–0.85)	0.70 (0.62–0.78)	0.71 (0.65–0.78)
		Hosmer–Lemeshow, *P* value	
Derivation cohort	0.347	0.986	0.945
Validation cohort	0.236	0.464	0.259