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New insights in management and prognosis in acute myocardial infarction

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Survival of patients after ST-elevation myocardial infarction: external validation of a predictive biomarker model

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To the Editor:

Early risk stratification has the potential to play an important role in ST-elevation myocardial infarction (STEMI) patients who are to be treated with primary percutaneous coronary intervention (PCI). Several risk scores have been developed for STEMI patients; however, most risk scores require many variables, making them more difficult to use in clinical practice. The long-term prognostic value of biomarker measurements for glucose, N-terminal pro–brain type natriuretic peptide (NT-proBNP), and estimated glomerular filtration rate (eGFR) taken early after admission has recently been demonstrated for STEMI patients.[1] Damman and coworkers have shown that a multimarker model including these biomarkers improved the prediction of mortality over that provided by established risk factors derived from the Thrombolysis In Myocardial Infarction (TIMI) score, which include age, body mass index, diabetes, hypertension, systolic blood pressure, heart rate, anterior myocardial infarction, and time to treatment.[1,2] Moreover, a simplified risk score developed with the 3 biomarkers identified low-, intermediate- and high-risk subgroups with respect to mortality. The best way to evaluate such a model is to perform an external validation study of the predictors in a new and independent STEMI cohort.[3]

To assess the general validity of this multimarker model and the simplified risk score, we evaluated both in an external STEMI cohort treated with primary PCI in a large single center in Groningen, the Netherlands. We analyzed the data of all 1645 consecutive STEMI patients treated with primary PCI from 2006 to 2010. A STEMI cohort of 1321 patients was defined according to the criteria of the original cohort.[1] The baseline characteristics of the validation cohort and the original cohort were generally comparable. Blood samples for the biomarker measurements were routinely obtained at admission before the primary PCI. The diagnostic methods used were all identical to the systems used for the original cohort.[1] The primary end point of the study was all-cause mortality. These data were collected from the municipal civil registry, which has complete information regarding the vital status of all residents registered in the Netherlands. Statistical analysis was performed with IBM SPSS Statistics (version 18.0) and R software.

In the multimarker study, the discriminative value was estimated for the multimarker model with only established risk factors and for the multimarker model with the glucose, NT-proBNP, and eGFR biomarkers in addition to established risk factors. Discriminative value was measured with the Harrell C index, the categoryless net reclassification improvement (NRI), and integrated discrimination improvement (IDI). These indices were calculated for patients with a complete follow-up at 2 years. These analyses have previously been described in detail.[1] In the validation cohort, the ability to predict mortality was high for the model with only established risk factors (Harrell C index, 0.855). The discriminative power increased for the model with all 3 biomarkers added [Harrell C index, 0.872; NRI, 0.25 (p<

0.05); IDI, 0.04 (p < 0.01)].

For the simplified risk score, points were assigned on the basis of the hazard ratio coefficients of the original cohort: 2 points for a glucose value of 144–162 mg/dL (8–9 mmol/L), an NT-proBNP value of 150–599 ng/L, or an eGFR value of 60–89 mL/min; 3 points for a glucose value ≥180 mg/dL (≥10 mmol/L) or an NT-proBNP value ≥600 ng/L; and 4 points for an eGFR value <60 mL/min. The total point score classifies patients into low-risk (≤4 points), intermediate-risk (5 or 6 points), and high-risk (>6 points) subgroups. All-cause mortality for the risk subgroups was estimated with the Kaplan–Meier method, and the groups were compared with the log-rank test. In the validation study, 103 patients died at a median follow-up of 2.1 years. Using the simplified risk score, we classified 830 patients (63%) within the low-risk subgroup, 248 patients (19%) within the intermediate-risk subgroup, and 243 patients (18%) within the high-risk subgroup. The mortality rate

Fig. 1 | Prediction of mortality in the validation cohort by use of the simplified risk score
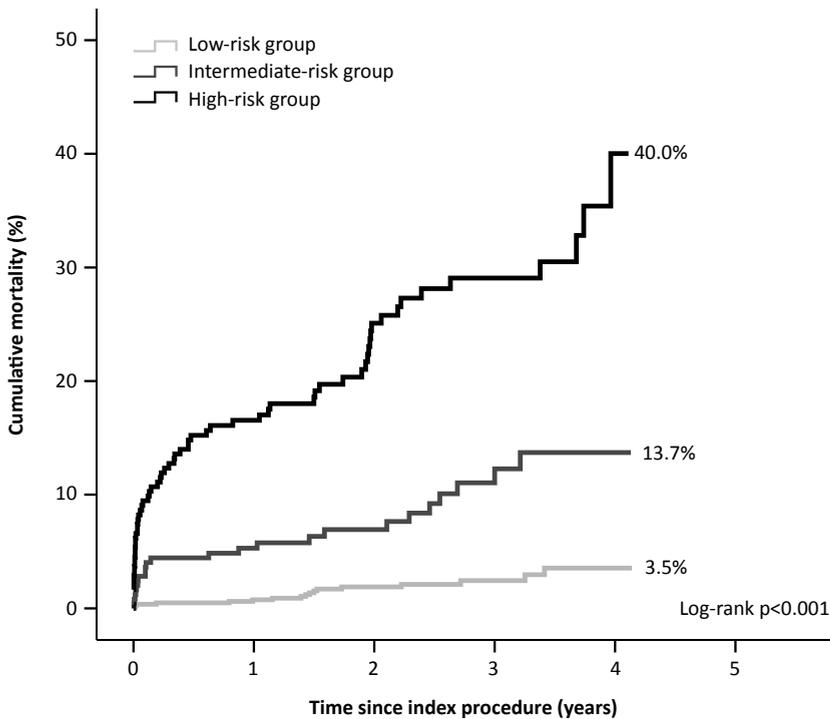
No. at risk					
Low	830	767	469	238	34
Int	248	203	135	58	11
High	243	175	108	63	8

increased significantly from the low-risk to the high-risk subgroups (3.5% to 13.7% to 40.0%; log-rank p< 0.001) (Figure 1).

In conclusion, this study conducted an external validation of a multimarker model and risk score based on admission glucose, NT-proBNP, and eGFR measures for predicting mortality in STEMI patients treated with primary PCI. Our data supported the additional value of commonly available biomarkers at admission on top of established risk factors in predicting mortality. Moreover, a simplified risk score including these biomarkers accurately identified low-, intermediate-, and high-risk patients in the validation cohort and identified the majority of STEMI patients as having a low risk of mortality. This risk stratification is clinically applicable with biomarkers that are available early and has the ability to predict high and low risk for adverse events per patient at the time of primary PCI. This discrimination of subgroups may help the triage process of identifying patients who could benefit from additional treatment and those who can be safely discharged at an earlier stage, and it therefore may optimize outcomes and reduce costs.

References

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