

Supplementary Material

NSTEMI-CARE: A Calibrated Multilayer Decision-Support Tool for Early Level-of-Care Assignment in Non–ST-Segment Elevation Myocardial Infarction

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This supplementary appendix provides additional methodological details, supporting analyses, and implementation information that complement the main manuscript.

Table S1. Operational definitions of all candidate predictors.

Variable	Definition	Unit / Categories	Time of Assessment	Final Model
Age	Patient age at hospital admission	Years	Admission	✓
Sex	Biological sex	Male / Female	Admission	✓
Body mass index	Body mass index	kg/m ²	Admission	✓
Heart rate	Initial heart rate	beats/min	Admission	✓
Systolic blood pressure	Initial systolic blood pressure	mmHg	Admission	✓
Diastolic blood pressure	Initial diastolic blood pressure	mmHg	Admission	✓
Respiratory rate	Initial respiratory rate	breaths/min	Admission	✓
Hemoglobin	First available hemoglobin concentration	g/dL	Admission	✓
Serum creatinine	First available serum creatinine	mg/dL	Admission	✓
High-sensitivity cardiac troponin	First available hs-cTn value	ng/mL*	Admission	✓
Left ventricular ejection fraction	Quantitative echocardiographic LVEF	%	Initial echocardiogram	✓
Acute heart failure signs	Clinical evidence of acute heart failure at presentation	Yes / No	Admission	✓
Recurrent chest pain	Recurrent ischemic chest pain within the first 24 hours	Yes / No	Initial hospitalization	✓

	hours			
Bradycardia	Clinically significant bradycardia	Yes / No	Admission	✓
Hypertension	Previous diagnosis of hypertension	Yes / No	Medical history	✓
Diabetes mellitus	Previous diagnosis of diabetes mellitus	Yes / No	Medical history	✓
Dyslipidemia	Previous diagnosis of dyslipidemia	Yes / No	Medical history	✓
Previous atrial fibrillation	History of atrial fibrillation	Yes / No	Medical history	✓
Chronic heart failure	Previous diagnosis of heart failure	Yes / No	Medical history	✓
Chronic kidney disease	Previous diagnosis of chronic kidney disease	Yes / No	Medical history	✓
Previous myocardial infarction	History of myocardial infarction	Yes / No	Medical history	✓
Previous PCI	Previous percutaneous coronary intervention	Yes / No	Medical history	✓
Previous CABG	Previous coronary artery bypass graft surgery	Yes / No	Medical history	✓
Smoking status	Current or former smoking	Yes / No	Medical history	✓

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; hs-cTn, high-sensitivity cardiac troponin; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

Table S2. Internal Validation Metrics of the Final Probabilistic Model Using Five-Fold Cross-Validation.

Validation Set	Patients	Events	AUC	Average Precision	Brier Score
Fold 1	197	31	0.847	0.699	0.082
Fold 2	196	31	0.810	0.553	0.102
Fold 3	196	31	0.839	0.710	0.085
Fold 4	196	31	0.824	0.676	0.088
Fold 5	196	31	0.785	0.541	0.105
Overall out-of-fold	981	155	0.821	0.618	0.092

Performance metrics were obtained using five-fold cross-validation with out-of-fold predictions. The overall out-of-fold estimates represent the aggregate performance of the final isotonic-calibrated HistGradientBoosting model across the complete study cohort. AUC, area under the receiver operating characteristic curve.

Table S3. Development of the direct classification layer of the NSTEMI-CARE algorithm.

Panel A. Operating Characteristics of the Selected Probability Thresholds

Threshold	Clinical objective	Sensitivity	Specificity	PPV	NPV	Observed event rate
<8%	Direct ward assignment	0.890	0.433	0.228	0.955	4.5%
≥60%	Direct ICU assignment	0.245	0.995	0.905	0.875	90.5%

Candidate probability thresholds were evaluated according to their operating characteristics. The <8% threshold was selected to identify a subgroup with a low observed event rate and high negative predictive value, whereas the $\geq 60\%$ threshold was selected to identify patients at very high risk suitable for immediate ICU/monitored care assignment.

Panel B. Performance of Predefined Major Clinical Triggers

Major clinical trigger	Patients, n (%)	Primary outcome, n (%)	Median predicted risk	Crude OR (95% CI)	Clinical role
Bradycardia (<45 bpm)	5 (0.5)	2 (40.0)	10.2%	3.59 (0.59–21.64)	Direct ICU trigger
SBP ≤ 90 mmHg	23 (2.3)	14 (60.9)	40.3%	9.01 (3.83–21.22)	Direct ICU trigger
Acute heart failure	81 (8.3)	43 (53.1)	36.7%	7.96 (4.93–12.86)	Direct ICU trigger
Recurrent chest pain (within the first 24 hours)	66 (6.7)	52 (78.8)	60.2%	29.28 (15.68–54.69)	Direct ICU trigger
Any major trigger	150 (15.3)	89 (59.3)	44.0%	16.91 (11.21–25.52)	Immediate ICU assignment

Major clinical triggers were incorporated as predefined safety criteria for direct ICU assignment irrespective of predicted probability. Values are taken from the final derivation cohort.

Table S4. Derivation of the Gray-Zone Secondary Decision Rule

Panel A. Candidate variables retained in the final rule

Variable	Threshold	Patients meeting threshold	Event rate meeting threshold	Event rate not meeting threshold
Predicted risk	<10%	120	3.3%	12.9%
Hemoglobin	≥ 12 g/dL	427	10.3%	12.2%
Serum creatinine	≤ 1.5 mg/dL	426	9.6%	18.0%
Respiratory rate	≤ 22 breaths/min	463	9.9%	30.8%

Panel B. Final performance of the secondary rule

Final assignment	Patients	Primary outcome	Event rate
General ward	109	2	1.8%
ICU / monitored care	367	48	13.1%

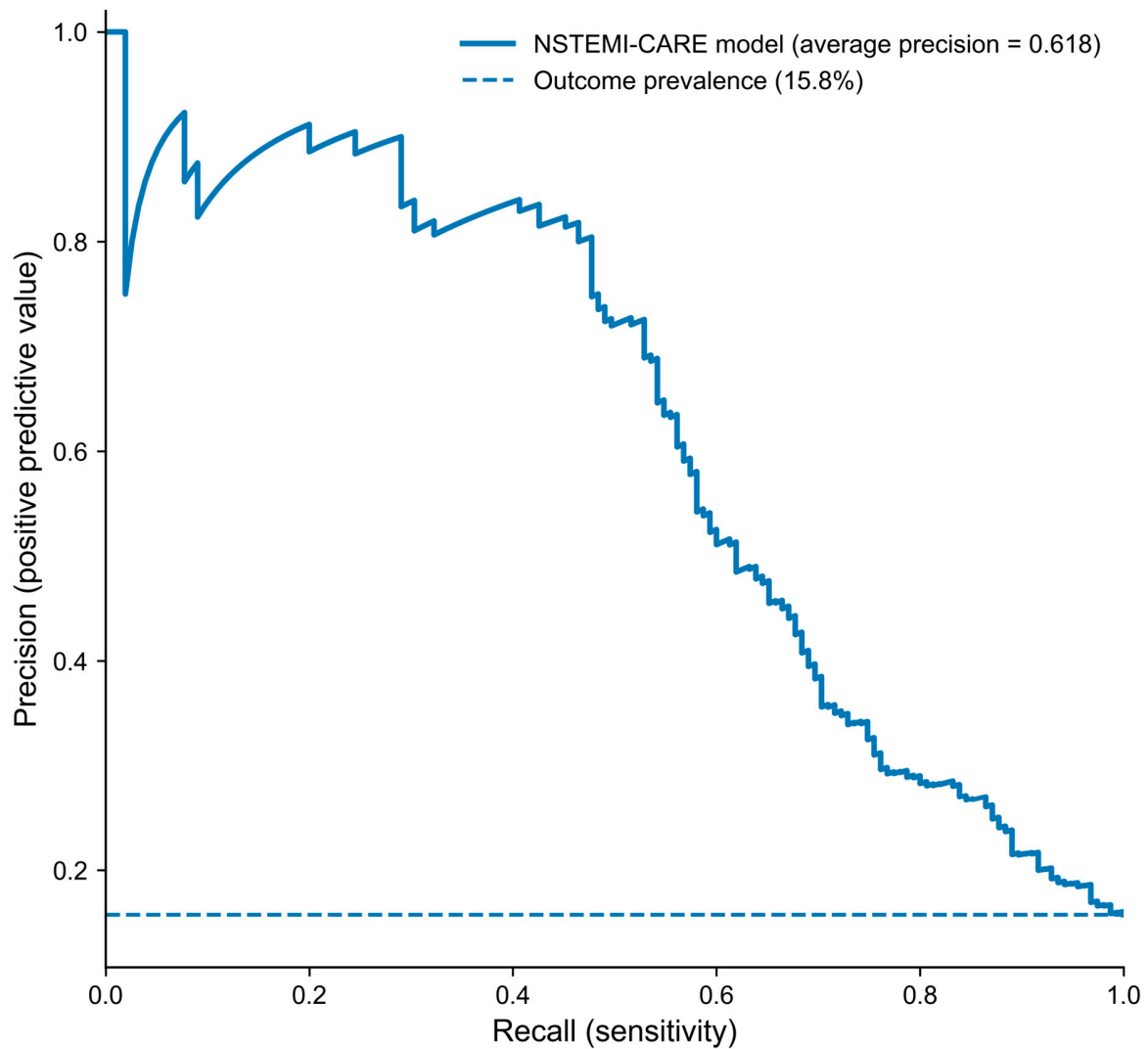
Candidate bedside variables retained in the final Gray-Zone decision rule and their observed event rates within the intermediate-risk cohort. Panel B summarizes the performance of the secondary decision rule after final patient assignment. Abbreviations. ICU = intensive care unit.

Table S5. Comparative Performance of NSTEMI-CARE and ACTION-ICU for ICU Triage

Performance metric	NSTEMI-CARE	ACTION-ICU ≥3	ACTION-ICU ≥5
Sensitivity	88.4%	89.0%	69.7%
Specificity	54.0%	15.0%	48.1%
Positive predictive value	26.5%	16.4%	20.1%
Negative predictive value	96.1%	87.9%	89.4%
False-negative classifications	18	17	47
Area under ROC curve (AUC)	0.821 (95% CI 0.777–0.861)	0.645 (95% CI 0.595–0.694)	Same continuous ACTION score
AUC comparison	Reference	DeLong p < 0.001	—

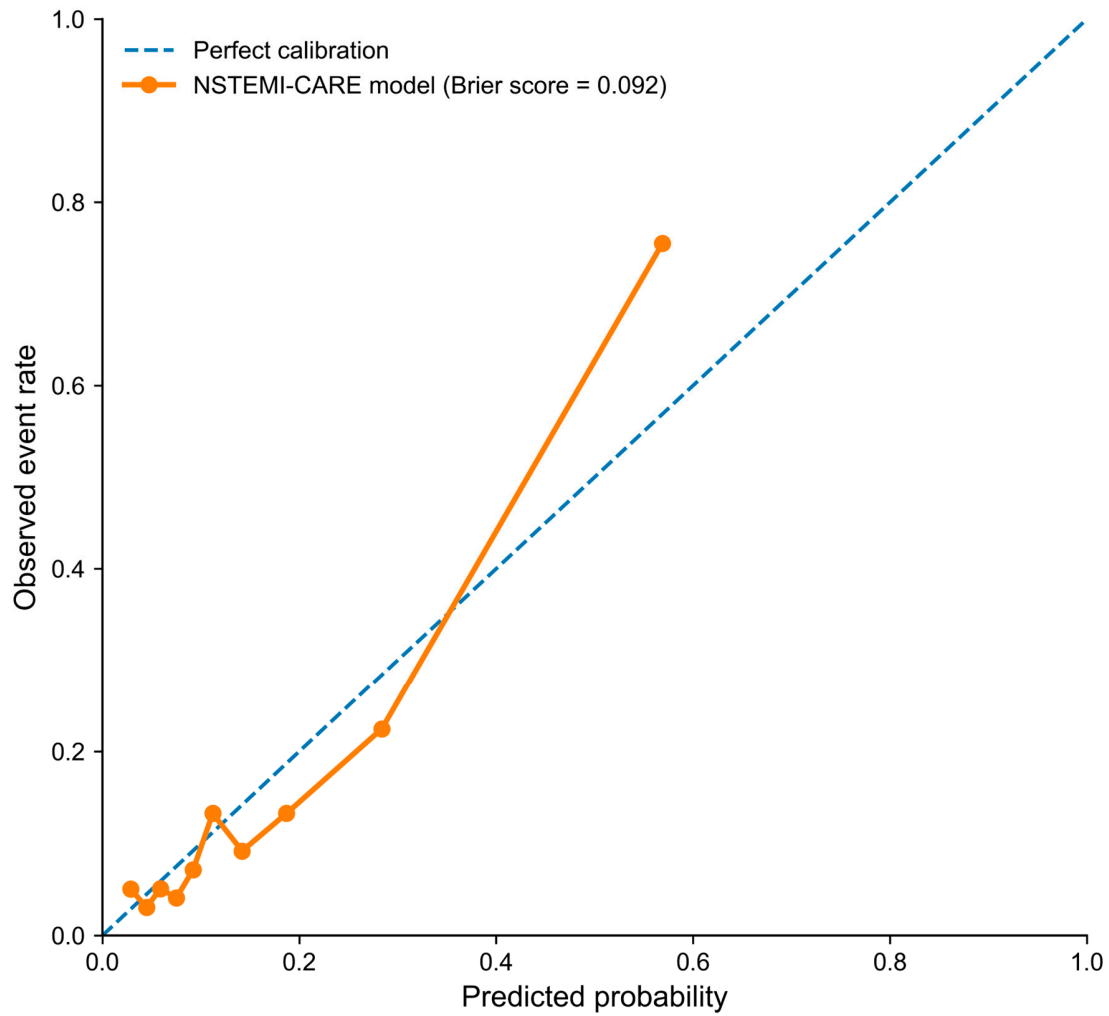
Comparison of the final NSTEMI-CARE algorithm with the ACTION-ICU score evaluated at the recommended thresholds (≥3 and ≥5 points). Continuous-score discrimination was compared using the DeLong test. Abbreviations. AUC = area under the receiver operating characteristic curve; CI = confidence interval; ICU = intensive care unit; NPV = negative predictive value; PPV = positive predictive value.

Figure S1. Precision–Recall Curve of the Final NSTEMI-CARE Probabilistic Model



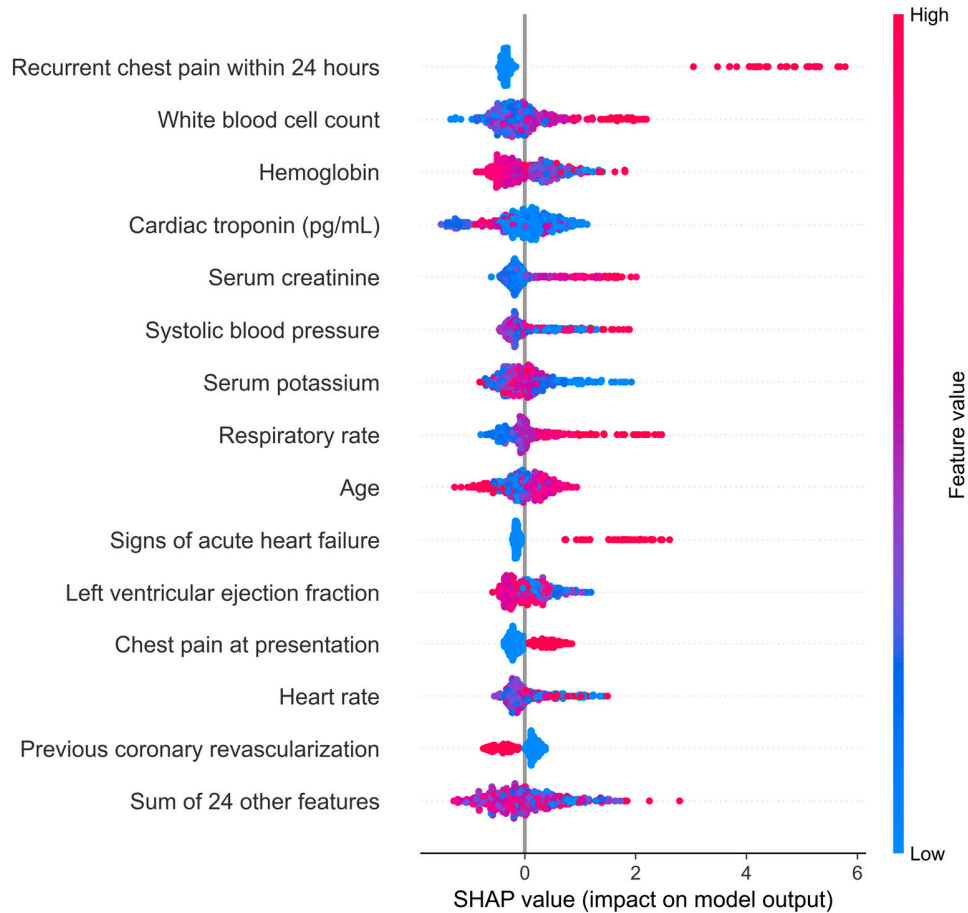
Precision–recall curve of the final isotonic-calibrated HistGradientBoosting probabilistic model generated using five-fold out-of-fold predictions. The average precision was 0.618. The dashed horizontal line represents the prevalence of the primary outcome (15.8%) in the study cohort.

Figure S2. Calibration Plot of the Final NSTEMI-CARE Probabilistic Model



Calibration plot of the final isotonic-calibrated HistGradientBoosting probabilistic model using five-fold out-of-fold predictions. The dashed diagonal line represents perfect calibration. Observed event rates are plotted against predicted probabilities across risk groups, demonstrating overall agreement between predicted and observed risks (Brier score = 0.092).

Figure S3. SHAP Summary Plot of the Final Probabilistic Model



SHAP (Shapley Additive Explanations) summary plot illustrating the global contribution of individual predictors to the final isotonic-calibrated HistGradientBoosting model. Predictors are ranked according to their overall importance based on the mean absolute SHAP value. Each point represents an individual patient, with color indicating the predictor value (blue = lower values; red = higher values) and the horizontal position representing the magnitude and direction of each variable's contribution to the predicted risk of the primary outcome. Positive SHAP values indicate an increased predicted risk, whereas negative values indicate a reduced predicted risk.