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DEVELOPMENT AND VALIDATION OF AN EARLY DIAGNOSTIC PREDICTION MODEL FOR ACUTE CORONARY SYNDROME IN PATIENTS WITH CHEST PAIN

<i>Objective</i>	To develop and validate an early diagnostic prediction model for acute coronary syndrome (ACS) in patients with chest pain; thus providing scientific evidence for clinical decision-making.
<i>Material and methods</i>	A retrospective cohort study design was employed, including 480 chest pain patients who presented to the emergency department from January 2020 to January 2025. The patients were randomly divided into a modeling set (336 cases) and a validation set (144 cases) at a 7:3 ratio. Data collected included demographic characteristics, clinical symptoms and signs, medical history, laboratory tests, electrocardiogram, and imaging examinations. Univariate and multivariate logistic regression analyses were used to screen independent predictors and establish the prediction model. Model performance was evaluated through receiver operating characteristic (ROC) curves, Hosmer-Lemeshow test, and Bootstrap resampling, and a simplified risk scoring system was established.
<i>Results</i>	Multivariate logistic regression analysis showed that elevated cTnI (OR=17.231), ST-segment changes (OR=8.451), typical chest pain (OR=4.047), age ≥ 60 years (OR=2.441), smoking history (OR=2.103), sweating (OR=1.931), male sex (OR=1.799), and pain duration >30 min (OR=1.689) were independent predictors of ACS (all $p < 0.05$). The area under the curve (AUC) of the model in the modeling set and validation set were 0.921 (95%CI: 0.890–0.952) and 0.908 (95%CI: 0.857–0.959), respectively, with sensitivities of 86.4% and 82.9%, and specificities of 89.7% and 87.4%, respectively. The Hosmer-Lemeshow test indicated good model calibration (modeling set $p=0.609$, validation set $p=0.776$). The established risk scoring system (0–20 points) classified patients into four risk stratifications: low risk (0–4 points, ACS incidence 3.8%), moderate risk (5–8 points, 23.1%), high risk (9–12 points, 62.2%), and very high risk (13–20 points, 91.9%), with an optimal cutoff value of 8 points (Youden index 0.716).
<i>Conclusion</i>	The ACS early diagnostic prediction model established in this study incorporated eight readily accessible clinical variables and demonstrated good discrimination and calibration. The risk scoring system based on this model is simple and practical. This scoring system can effectively perform risk stratification and provide a valuable clinical tool for early diagnosis and risk assessment of chest pain patients.
<i>Keywords</i>	Acute coronary syndrome; chest pain; prediction model; risk score; early diagnosis
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SUPPLEMENTARY MATERIALS

Table 1 (beginning). Comparison of patient baseline characteristics

Variable	Overall (n=480)	ACS diagnosis group (n=144)	Non-ACS diagnosis group (n=336)	Test Statistic	p-value
Basic Information					
Age (yrs)	58.2±12.7	63.2±11.4	56.1±12.8	t=5.836	<0.001
Male sex	289 (60.2)	102 (70.8)	187 (55.6)	$\chi^2=8.731$	0.003
BMI (kg/m ²)	24.8±3.2	25.4±3.1	24.5±3.3	t=2.674	0.008
Clinical Symptoms					
Typical chest pain	312 (65.0)	118 (81.9)	194 (57.7)	$\chi^2=23.916$	<0.001
Pain location					
Retrosternal	287 (59.8)	108 (75.0)	179 (53.3)	$\chi^2=17.891$	<0.001
Precordial	156 (32.5)	52 (36.1)	104 (31.0)	$\chi^2=1.066$	0.302
Left chest	89 (18.5)	18 (12.5)	71 (21.1)	$\chi^2=4.327$	0.038
Other locations	43 (9.0)	8 (5.6)	35 (10.4)	Fisher's exact test	0.098
Pain duration >30min	267 (55.6)	98 (68.1)	169 (50.3)	$\chi^2=11.745$	0.001
Pain activity-induced	198 (41.3)	79 (54.9)	119 (35.4)	$\chi^2=14.086$	<0.001
Pain relief factors					
Relief with rest	234 (48.8)	89 (61.8)	145 (43.2)	$\chi^2=12.685$	<0.001
Relief with nitroglycerin	156 (32.5)	67 (46.5)	89 (26.5)	$\chi^2=16.147$	<0.001
No obvious relief factors	178 (37.1)	43 (29.9)	135 (40.2)	$\chi^2=4.158$	0.041
Accompanying Symptoms					
Dyspnea	156 (32.5)	62 (43.1)	94 (28.0)	$\chi^2=9.532$	0.002
Nausea and vomiting	89 (18.5)	38 (26.4)	51 (15.2)	$\chi^2=7.649$	0.006
Sweating	147 (30.6)	67 (46.5)	80 (23.8)	$\chi^2=22.438$	<0.001
Dizziness	112 (23.3)	41 (28.5)	71 (21.1)	$\chi^2=2.632$	0.105
Vital Signs					
Systolic BP (mmHg)	138.6±24.3	142.8±26.1	136.9±23.4	t=2.406	0.017
Diastolic BP (mmHg)	84.2±12.8	86.7±13.5	83.1±12.4	t=2.727	0.007
Heart rate (beats/min)	79.4±16.8	83.7±18.2	77.6±15.9	t=3.558	<0.001
Respiratory rate (breaths/min)	18.6±3.2	19.8±3.7	18.1±2.9	t=4.906	<0.001
Temperature (°C)	36.7±0.5	36.8±0.6	36.6±0.4	t=2.339	0.02
Oxygen saturation (%)	97.2±2.1	96.8±2.5	97.4±1.9	t= - 2.674	0.008
Medical History					
Hypertension	256 (53.3)	92 (63.9)	164 (48.8)	$\chi^2=8.374$	0.004
Diabetes	134 (27.9)	52 (36.1)	82 (24.4)	$\chi^2=6.118$	0.013
Dyslipidemia	189 (39.4)	71 (49.3)	118 (35.1)	$\chi^2=7.681$	0.006
Smoking history	187 (39.0)	74 (51.4)	113 (33.6)	$\chi^2=11.937$	0.001
Family history	98 (20.4)	41 (28.5)	57 (17.0)	$\chi^2=7.344$	0.007
Laboratory Tests					
Myocardial Injury Markers					
Elevated cTnI	127 (26.5)	98 (68.1)	29 (8.6)	$\chi^2=138.762$	<0.001
CK-MB (U/l)	18.7±24.3	35.2±31.4	11.2±12.8	Z= -8.742*	<0.001
Inflammatory Markers					
CRP (mg/l)	8.9±12.4	13.7±15.8	6.8±9.7	Z= -4.832*	<0.001
White blood cells (×10 ⁹ /l)	7.8±2.4	8.7±2.8	7.4±2.1	t=5.127	<0.001

Table 1 (ending). Comparison of patient baseline characteristics

Variable	Overall (n=480)	ACS diagnosis group (n=144)	Non-ACS diagnosis group (n=336)	Test Statistic	p-value
Lipids					
Total cholesterol (mmol/l)	4.8±1.2	5.2±1.4	4.6±1.1	t=4.586	<0.001
Low-density lipoprotein (mmol/l)	3.1±0.9	3.5±1.1	2.9±0.8	t=5.934	<0.001
High-density lipoprotein (mmol/l)	1.2±0.3	1.1±0.3	1.3±0.3	t= - 4.261	<0.001
Triglycerides (mmol/l)	1.8 (1.2–2.6)	2.1 (1.4–3.1)	1.7 (1.1–2.4)	Z= - 3.124*	0.002
Biochemical Indicators					
Blood glucose (mmol/l)	6.8±2.1	7.4±2.5	6.5±1.9	t=4.017	<0.001
Liver and Kidney Function					
ALT (U/l)	28.4±18.7	31.2±21.3	27.1±17.4	t=2.032	0.043
AST (U/l)	32.6±22.1	38.9±26.8	29.8±19.2	t=3.773	<0.001
Creatinine (μmol/l)	82.3±24.6	89.7±28.1	78.9±22.4	t=4.161	<0.001
Blood urea nitrogen (mmol/l)	5.8±2.1	6.4±2.4	5.5±1.9	t=4.123	<0.001
Coagulation Function					
PT (s)	12.1±1.4	12.4±1.6	12.0±1.3	t=2.677	0.008
APTT (s)	28.9±4.2	29.8±4.7	28.5±3.9	t=2.841	0.005
D-dimer (mg/l)	0.8±1.2	1.1±1.5	0.7±1.0	Z= - 2.963*	0.003
Electrocardiogram Changes					
ST-segment changes	149 (31.0)	89 (61.8)	60 (17.9)	$\chi^2=75.827$	<0.001
ST-segment elevation	67 (14.0)	52 (36.1)	15 (4.5)	$\chi^2=69.527$	<0.001
ST-segment depression	82 (17.1)	37 (25.7)	45 (13.4)	$\chi^2=9.631$	0.002
T-wave changes	132 (27.5)	74 (51.4)	58 (17.3)	$\chi^2=48.852$	<0.001
T-wave inversion	89 (18.5)	52 (36.1)	37 (11.0)	$\chi^2=35.617$	<0.001
T-wave flattening	43 (9.0)	22 (15.3)	21 (6.3)	$\chi^2=8.619$	0.003
Pathological Q waves	43 (9.0)	31 (21.5)	12 (3.6)	$\chi^2=32.894$	<0.001
Arrhythmias	67 (14.0)	28 (19.4)	39 (11.6)	$\chi^2=4.758$	0.029
Atrial arrhythmias	34 (7.1)	16 (11.1)	18 (5.4)	$\chi^2=4.507$	0.034
Ventricular arrhythmias	21 (4.4)	9 (6.3)	12 (3.6)	Fisher's exact test	0.216
Conduction block	12 (2.5)	3 (2.1)	9 (2.7)	Fisher's exact test	0.739
Imaging Examinations					
Abnormal echocardiography	187 (39.0)	89 (61.8)	98 (29.2)	$\chi^2=39.607$	<0.001
Wall motion abnormality	134 (27.9)	76 (52.8)	58 (17.3)	$\chi^2=49.947$	<0.001
Ejection fraction <50%	78 (16.3)	45 (31.3)	33 (9.8)	$\chi^2=27.948$	<0.001
Valvular abnormality	56 (11.7)	23 (16.0)	33 (9.8)	$\chi^2=3.318$	0.069
Abnormal chest X-ray	89 (18.5)	38 (26.4)	51 (15.2)	$\chi^2=7.649$	0.006
Cardiac enlargement	67 (14.0)	32 (22.2)	35 (10.4)	$\chi^2=10.428$	0.001
Pulmonary edema	23 (4.8)	12 (8.3)	11 (3.3)	Fisher's exact test	0.027
Pleural effusion	12 (2.5)	6 (4.2)	6 (1.8)	Fisher's exact test	0.149

Statistical analysis: Continuous variables are presented as mean ± standard deviation or median (interquartile range) and were compared using the independent-samples t test or Mann–Whitney U test, as appropriate. Categorical variables are presented as number (percentage) and were compared using the chi-square (χ^2) test or Fisher's exact test when expected cell counts were small. Z values represent standardized statistics from non-parametric tests.

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index; BP, blood pressure; cTnI, cardiac troponin I; CK-MB, creatine kinase – MB; CRP, C-reactive protein; PT, prothrombin time; APTT, activated partial thromboplastin time; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 2. Performance of the ACS prediction model in the modeling and validation sets

Indicator	Modeling Set (n=336)	Validation Set (n=144)
AUC	0.921 (0.890–0.952)	0.908 (0.857–0.959)
Sensitivity (%)	86.4	82.9
Specificity (%)	89.7	87.4
Positive predictive value (%)	78.8	72.3
Negative predictive value (%)	93.2	92.8
Accuracy (%)	88.7	86.1
Positive likelihood ratio	8.39	6.58
Negative likelihood ratio	0.15	0.2
Hosmer-Lemeshow test	$\chi^2=6.342$, p=0.609	$\chi^2=4.827$, p=0.776

Abbreviations: AUC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR–, negative likelihood ratio; χ^2 , chi-square statistic.

Table 3. Evaluation of the model calibration

Predicted Probability Interval	Observed Cases	Predicted Cases	Observed ACS Cases	Observed ACS Rate (%)	Predicted ACS Rate (%)	χ^2 Value	p-value
0.00–0.10	89	89.2	2	2.2	5.1	1.41	0.234
0.10–0.20	67	65.8	7	10.4	14.8	0.82	0.367
0.20–0.40	78	79.1	19	24.4	29.2	0.58	0.445
0.40–0.60	43	41.7	21	48.8	50.1	0.02	0.889
0.60–0.80	34	35.3	23	67.6	69.7	0.05	0.821
0.80–1.00	25	24.9	22	88	90.2	0.09	0.765

Table 4. Model performance comparison at different cutoff values

Cutoff Value	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Youden Index
6 points	92.4	76.8	66.7	95.6	0.692
7 points	89.6	81.5	71.2	94.2	0.711
8 points	84.7	86.9	77.6	91.8	0.716
9 points	79.2	91.1	82.4	89.7	0.703
10 points	72.9	94.3	86.8	87.2	0.672