A diagnostic and classification model integrating cTnI, CK-MB, MYO and NT-proBNP for cardiovascular diseases

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Abstract. Cardiovascular diseases (CVD) are among the leading causes of mortality worldwide and accurate diagnosis is important for treatment and prognosis. The present study intended to develop a model for diagnosing and classifying cardiovascular diseases to improve early diagnosis precision. The present retrospective study analyzed 116 cases of coronary artery disease (CAD), 26 cases of structural heart disease (SHD), and 58 cases of arrhythmias, along with 200 healthy controls. The present study analyzed the differences in demographic characteristics, clinical symptoms, cardiovascular biomarker levels and electrocardiogram results across these four groups. Multivariate logistic regression and random forests were used to identify significant factors in cardiovascular disease. A diagnostic model was constructed based on the selected factors, and its ability to diagnose cardiovascular diseases and differentiate between CAD, SHD and arrhythmias was evaluated. Patients with CVD showed significant differences compared with the healthy control group in demographic characteristics, including age, sex and family history. Different types of patients with CVD showed varying degrees of symptoms such as pain, dyspnea, and dizziness and there are significant differences in the levels of cardiovascular biomarkers. Cardiac Troponin I, creatine kinase MB, myoglobin and N-terminal pro B-type natriuretic peptide were identified as significant predictors of CVD. The diagnostic model for CVD achieved an Area Under the Curve (AUC) of 0.719, outperforming the use of individual biomarkers. The model differentiated arrhythmias from SHD with an AUC of 0.771 and SHD from CAD with an AUC of 0.715. The diagnostic model offers improved predictive ability for early cardiovascular disease diagnosis compared with standard methods and demonstrates clear advantages when distinguishing between CAD, SHD, and arrhythmias, supporting improved clinical decision-making.

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Abbreviations: CVD, cardiovascular disease; CAD, coronary artery disease; SHD, structural heart disease; ECG, electrocardiogram; hs-CRP, high-sensitivity C-reactive protein; LDH, lactate dehydrogenase; FIB, fibrinogen; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BNP, B-type natriuretic peptide; MYO, myoglobin; NT-proBNP, N-terminal pre-B natriuretic peptide; cTnT, cardiac troponin T; cTnI, cardiac troponin I; CK-MB, creatine kinase-MB

Key words: cardiovascular disease, coronary artery disease, structural heart disease, arrhythmias, diagnostic model

Introduction

Cardiovascular disease (CVD) is one of the deadliest diseases in the world (1,2). According to data from the World Health Organization, ~17 million individuals succumb to CVD each year, accounting for 31% of all mortalities worldwide, forming a significant threat to public health (3,4). Cardiovascular diseases not only affect the physical health of patients but also impose a heavy burden on the social economy (5,6). With the aging of the global population, the number of individuals suffering from CVD continues to increase and the burden of the disease is gradually increasing. With the westernization of lifestyle, unhealthy eating habits and lack of exercise, the incidence rate of CVD among young individuals is also growing at an alarming rate (7,8).

At present, the diagnosis of CVD mainly relies on clinical symptoms, physical examination, ECG (9,10), imaging examination (11) and detection of cardiovascular disease biomarkers (12,13). However, these methods are not well-suited for short-term risk prediction. Different types of cardiovascular diseases, such as coronary artery disease (CAD), structural heart disease (SHD), heart failure and various types of arrhythmias, may have highly similar clinical manifestations and some patients may not have obvious symptoms in the early stages, making early diagnosis a difficult task. At present, one or more biomarkers are commonly used to diagnose specific cardiovascular disease (14,15) and this single diagnosis often cannot meet the needs of clinical diagnosis. Therefore, the present study intended to construct a diagnostic auxiliary model combining multiple biomarkers to predict short-term cardiovascular disease risk at an early stage, support clinical decision-making, and optimize early treatment strategies.

Materials and methods

Research design. The present study included a retrospective cohort of patients who underwent routine physical examinations at Beijing Fengtai You'anmen Hospital between January 2023 and June 2024. A total of 400 participants were included. The median age of all participants was 50 years (range: 21-81 years). The sex distribution was 67.5% male (270 individuals) and 32.5% female (130 individuals). Patients diagnosed with cardiovascular disease were selected as the case group, while healthy individuals without cardiovascular disease were selected as the control group. The inclusion criteria were: Age ≥18 years; the case group data should include physiological and biochemical indicators of the patient collected within the first 6 months before the onset of the disease. The exclusion criteria were: Women who were pregnant or within 6 months postpartum; severe liver and kidney dysfunction; suffering from malignant tumors and other serious systemic diseases; and laboratory inspection data incomplete.

The diagnostic criteria for CAD were coronary angiography showing ≥50% luminal stenosis in at least one major coronary artery, clinical manifestations such as chest pain, chest tightness, or precordial discomfort and electrocardiographic findings showing ST-segment changes or T-wave abnormalities. The diagnostic criteria for SHD include structural abnormalities of the heart detected by echocardiography, including valvular, myocardial and chamber abnormalities. The diagnosis of arrhythmias was based on electrocardiographic examination results, including standard 12-lead ECG or Holter monitoring. When the electrocardiogram showed an abnormal cardiac rhythm, an arrhythmia was diagnosed. The manifestations included abnormal or absent P waves, irregular RR intervals, abnormal heart rate (tachycardia or bradycardia), prematurely occurring ectopic beats and atrioventricular conduction block and other electrocardiographic changes.

Data collection. Baseline information was collected from the six months prior to the onset of cardiovascular disease and from the normal group, including age, sex, BMI, family history of cardiovascular disease, smoking, drinking and exercise habits. The disease types of all patients with CVD were collected and divided into three categories: CAD, SHD and arrhythmia. Symptom manifestations (such as pain, dyspnea, dizziness, nausea and vomiting, fever) and electrocardiogram changes (ST segment changes, T wave changes) were collected in patients with CVD. Biomarker levels in patients with CVD were measured 6 months prior to onset and in the normal control group. High-sensitivity C-reactive protein (hs-CRP), B-type natriuretic peptide (BNP), myoglobin (MYO), and N-terminal pro B-type natriuretic peptide (NT-proBNP) were detected using chemiluminescence immunoassay and enzyme-based measurement of lactate dehydrogenase (LDH), detection of cardiac troponin T (cTnT), cardiac troponin I (cTnI), creatine kinase-MB (CK-MB), fibrinogen (FIB), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were measured using immunoturbidimetry. To ensure data validity and comparability, all biomarker measurements were performed in the clinical laboratory of Beijing Fengtai You'anmen Hospital using the same testing methods and equipment. All samples were collected in the morning under fasting conditions.

Statistical analysis. The present study used R software (version 4.4.1; https://www.R-project.org/) for statistical analysis and graphical visualization. The Shapiro-Wilk test was used for normality assessment, $P>0.05$ was considered approximately normally distribution, whereas $P<0.05$ was considered non-normally distribution. Continuous data were summarized by median (minimum, maximum) and inter-group comparisons are performed using unpaired tests, Specifically, an independent-samples unpaired t-test or a nonparametric test (Mann-Whitney U test, Kruskal-Wallis test) was used, as appropriate. Categorical variables are expressed in frequency (percentage) and intergroup comparisons performed using the chi-square test or Fisher's exact test. Multiple logistic regression analysis and random forest screening were used to identify significant factors for CVD. The random forest used the out-of-bag error (OOB Error) method to select the optimal parameters (16), The OOB Error method uses the characteristics of random forests, During training, each tree uses only a subset of the dataset, while the remaining samples serve as 'out of bag' samples. It already has a similar cross validation function, so there is no need to split the data into training and test sets. The factors that were significant in the multiple logistic regression and had a higher Gini scores in the random forest were selected as diagnostic factors for CVD. Since these two indicators differ in scale and range, Z-score standardization was first applied to both the regression coefficients and the Gini index to eliminate scale differences and ensure comparability. A diagnostic model based on the coefficients of these significant diagnostic factors was constructed.
The specific formula was as follows:

$$\text{Diagnostic model} = Coef_{[1]} x Factor_{[1]} + Coef_{[2]} x Factor_{[2]} + Coef_{[3]} x Factor_{[3]} + \ldots\ldots Coef_{[n]} x Factor_{[n]}$$

Where Coef was the coefficients of the multivariable Logistic regression and the Gini index from random forest are standardized using Z-score and then summed.

ROC curve analysis was performed to evaluate the ability of the diagnostic models to distinguish between the normal population and patients with CVD, as well as between different CVD subtypes.

An independent external validation cohort (n=120) was obtained from a different time period than the training cohort, with patients enrolled between July 2024 and December 2024.

A post hoc power analysis for the ROC analysis was performed using the pROC package (version 1.19.0.1) in R (version 4.4.1). The pROC package is available at https://cran.r-project.org/package=pROC.

Results

Demographic characteristics of patients with CVD and the normal population. The median BMI was 25.4 (range: 19.5-30.8). A total of 25.25% (101 individuals) had a family history of cardiovascular disease. The proportion of patients with CVD who had a family history of CVD was significantly

Table I. Demographic characteristics of patients with cardiovascular disease and healthy controls.

Characteristic	All (n=400)	Patients with cardiovascular disease (n=200)	Healthy population (n=200)	P-value
Age, years (range)	50 (21-81)	54 (21-81)	48 (21-81)	0.0252
Sex				0.3367
Male	270 (67.5%)	140 (70%)	130 (65%)	
Female	130 (32.5%)	60 (30%)	70 (35%)	
BMI [a]	25.4 (19.5-30.8)	25.3 (19.6-30.8)	25.5 (19.5-30.7)	0.573
Family history of cardiovascular disease				0.0057
Yes	101 (25.25%)	63 (31.5%)	38 (19%)	
No	299 (74.75%)	137 (68.5%)	162 (81%)	
Smoking				0.2592
Mild or none	183 (45.75%)	90 (45%)	93 (46.5%)	
Moderate	91 (22.75%)	52 (26%)	39 (19.5%)	
Heavy	126 (31.5%)	58 (29%)	68 (34%)	
Drinking				0.3021
Mild or none	198 (49.5%)	95 (47.5%)	103 (51.5%)	
Moderate	128 (32%)	62 (31%)	66 (33%)	
Heavy	74 (18.5%)	43 (21.5%)	31 (15.5%)	
Exercise habits				0.0982
Sedentary	262 (65.5%)	140 (70%)	122 (61%)	
Moderate exercise	102 (25.5%)	47 (23.5%)	55 (27.5%)	
Intensive exercise	36 (9%)	13 (6.5%)	23 (11.5%)	

[a]Student's t-test. Continuous variables without superscripts were compared using the Mann-Whitney U test.

higher than that in the healthy control group (31.5 vs. 19%, P value 0.0057). A total of 45.75% (183 individuals) were mild or non-smokers (0-9 cigarettes/day), 22.75% (91 individuals) were moderate smokers (10-19 cigarettes/day), and 31.5% (126 individuals) were heavy smokers (≥20 cigarettes/day). A total of 49.5% (198 individuals) consumed light or no alcohol (≤1 time/week), 32% (128 individuals) moderately consumed alcohol (2-3 times/week), and 18.5% (74 individuals) heavily consumed alcohol (≥4 times/week). In terms of exercise habits, 65.5% (262 individuals) hardly exercised (≤1 time/week), 25.5% (102 individuals) engaged in moderate intensity exercise (2-3 times/week), and 9% (36 individuals) engaged in vigorous-intense exercise (≥4 times/week; Table I).

Differences in clinical symptoms and physiological manifestations among patients with different types of cardiovascular diseases. Among all patients with CVD, 56% (112 individuals) had no or mild pain, 36% (72 individuals) had moderate pain, and 8% (16 individuals) had severe pain. A total of 59.5% (119 individuals) of patients with CVD had mild or no respiratory distress, 31.5% (63 individuals) had moderate respiratory distress, and 9% (18 individuals) had severe respiratory distress. The proportion of moderate through severe respiratory distress in SHD patients (38.46%) was significantly higher than in other groups (6.03% in patients with CHD, 5.17% in arrhythmia patients; P=0.0012), with the highest proportion of mild or no respiratory distress among patients with coronary heart disease being 62.07%. As to dizziness, 59% of patients with CVD had mild or no dizziness and the proportion of severe dizziness in patients with arrhythmia was significantly higher compared with the other two groups (13.79 vs. 5.17% in patients with coronary heart disease and 3.85% in patients with arrhythmia; P=0.0234). As to nausea and vomiting, 54% (108 individuals) of patients with CVD had mild or no nausea and vomiting, 37% (74 individuals) had moderate nausea and vomiting and 9% (18 individuals) had severe nausea and vomiting. A total of 87% (174 individuals) of patients with CVD had mild or no fever and 13% (26 individuals) had moderate fever. A total of 71.5% (143 individuals) of patients with CVD had normal ST segments, 19% (38 individuals) had ST segment elevation and 9.5% (19 individuals) had ST segment depression. A total of 76.5% (153 individuals) of patients with CVD had normal T waves, 20% (40 individuals) had T wave inversion, and 3.5% (7 individuals) had T-wave spikes. The proportion of normal T waves in patients with SHD and arrhythmia was significantly higher than that in patients with coronary heart disease (P=0.0020; Table II).

Differences in levels of cardiovascular disease biomarkers between patients with different types of cardiovascular diseases and the normal population. The levels of hs-CRP and BNP were markedly higher in patients with SHD than in the other three groups. The levels of cTnT, cTnI, LDH, CK-MB, FIB, MYO and N-terminal pre-B natriuretic peptide (NT proBNP) were markedly higher in patients with coronary heart disease than in the other three groups. There were no

Table II. Differences in clinical symptoms and physiological manifestations among patients with different types of cardiovascular disease.

Clinical symptoms and physiological manifestation	Patients with cardiovascular disease (n=200)	Coronary artery disease (n=116)	Structural heart disease (n=26)	Arrhythmias (n=58)	P-value
Pain					0.1875321
Mild or none	112 (56%)	59 (50.86%)	15 (57.69%)	38 (65.52%)	
Moderate	72 (36%)	47 (40.52%)	7 (26.92%)	18 (31.03%)	
Heavy	16 (8%)	10 (8.62%)	4 (15.38%)	2 (3.45%)	
Dyspnea					0.001220462
Mild or none	119 (59.5%)	72 (62.07%)	10 (38.46%)	37 (63.79%)	
Moderate	63 (31.5%)	37 (31.9%)	8 (30.77%)	18 (31.03%)	
Heavy	18 (9%)	7 (6.03%)	8 (30.77%)	3 (5.17%)	
Dizziness					0.02343554
Mild or none	118 (59%)	77 (66.38%)	11 (42.31%)	30 (51.72%)	
Moderate	67 (33.5%)	33 (28.45%)	14 (53.85%)	20 (34.48%)	
Heavy	15 (7.5%)	6 (5.17%)	1 (3.85%)	8 (13.79%)	
Nausea and Vomiting					0.109
Mild or none	108 (54%)	64 (55.17%)	16 (61.54%)	28 (48.28%)	
Moderate	74 (37%)	46 (39.66%)	8 (30.77%)	20 (34.48%)	
Heavy	18 (9%)	6 (5.17%)	2 (7.69%)	10 (17.24%)	
Fever					0.073
Mild or none	174 (87%)	106 (91.38%)	20 (76.92%)	48 (82.76%)	
Moderate	26 (13%)	10 (8.62%)	6 (23.08%)	10 (17.24%)	
ST Segment Changes					0.1759263
Normal	143 (71.5%)	77 (66.38%)	18 (69.23%)	48 (82.76%)	
ST Elevation	38 (19%)	27 (23.28%)	6 (23.08%)	5 (8.62%)	
ST Depression	19 (9.5%)	12 (10.34%)	2 (7.69%)	5 (8.62%)	
T-Wave Changes					0.002042715
Normal	153 (76.5%)	78 (67.24%)	25 (96.15%)	50 (86.21%)	
Inverted T-Wave	40 (20%)	34 (29.31%)	1 (3.85%)	5 (8.62%)	
Peaked T-Wave	7 (3.5%)	4 (3.45%)	0 (0%)	3 (5.17%)	

significant differences in LDL and HDL between the four groups (Table III).

Multivariate logistic regression (MLR) screening for significant factors of cardiovascular disease. The results showed that cTnI was a significant predictor (P=0.000), with an odds ratio (OR) of 1.597, indicating that the higher cTnI levels were associated with a higher the risk of cardiovascular disease. CK-MB was also a significant predictor (P=0.000), with an OR of 1.254, indicating that higher CK-MB levels were associated with a higher the risk of cardiovascular disease. MYO was a significant predictor (P=0.000) with an OR of 1.028, indicating that the higher the level of MYO, the higher the risk of cardiovascular disease. NT proBNP was also a significant predictor (P=0.000), with an OR of 1.001, indicating that the higher the level of NT proBNP levels were associated with a higher risk of cardiovascular disease (Table IV).

Random forest screening for significant factors of CVD. The random forest results showed that the Gini indices of CK-MB, NT-proBNP, cTnI and MYO were relatively high, indicating that these indicators were crucial for the occurrence of cardiovascular disease (Fig. 1).

External validation. The model's generalizability was further evaluated in the external validation cohort using ROC curves and calibration plots. The results showed that the Area Under the Curve (AUC) values for the MLR and random forest models were 0.675 [95% (CI): 0.578-0.771] and 0.688 (95% CI: 0.593-0.782), respectively. The calibration plots demonstrated good agreement between the predicted probabilities and the measured outcomes, indicating acceptable calibration performance of the models (Fig. S1A-D).

Construction of the diagnostic model. According to the aforementioned results, CK-MB, NT-proBNP, cTnI, and MYO were both significant in MLR and ranked high in random forest visualization analysis, so these four factors were selected to construct the model. The formula of the diagnostic model is:

Table III. Differences in cardiovascular disease biomarkers among patients with different types of cardiovascular disease.

Cardiovascular disease biomarker	Coronary artery disease (n=116)	Structural heart disease (n=26)	Arrhythmias (n=58)	Healthy population (n=200)	P-value
High-sensitivity C-reactive protein, mg/l (range)	2.4 (1.0-3.5)	2.9 (1.7-3.2)	1.7 (1.2-2.3)	0.5 (0.3-0.8)	$4.230x10^{-5}$
B-type Natriuretic Peptide, pg/ml, (range)	49.8 (11.8-99.8)	69.2 (40.3-81.9)	54.8 (22.5-81.5)	32.8 (29.7-36.3)	$1.560x10^{-7}$
Cardiac troponin T, μg/l (range)[a]	0.10 (0.02-0.15)	0.09 (0.03-0.15)	0.09 (0.02-0.15)	0.07 (0.02-0.12)	$5.830x10^{-4}$
Cardiac troponin I, μg/l (range)	0.027 (0.002-0.043)	0.023 (0.006-0.043)	0.023 (0.002-0.041)	0.020 (0.001-0.033)	$3.770x10^{-2}$
Lactate dehydrogenase, U/l (range)	193.86 (117.75-254.84)	186.55 (122.19-252.23)	186.07 (115.27-248.75)	174.07 (114.64-254.99)	$1.810x10^{-2}$
Creatine kinase-MB, ng/ml (range)[a]	3.92 (0.14-6.52)	3.84 (0.82-6.54)	3.18 (0.08-6.49)	3.03 (0.02-6.50)	$3.700x10^{-2}$
Fibrinogen, g/l (range)	3.45 (2.23-4.40)	3.39 (2.25-4.24)	3.29 (2.24-4.39)	3.13 (2.21-4.39)	$4.250x10^{-2}$
Low-density lipoprotein, g/l (range)[a]	1.13 (0.60-1.60)	1.13 (0.60-1.54)	1.12 (0.60-1.60)	1.06 (0.60-1.60)	$5.650x10^{-1}$
High-density lipoprotein, mg/dl (range)	38.41 (22.42-57.79)	39.41 (28.78-53.65)	40.24 (20.75-56.96)	42.14 (20.53-57.75)	$8.650x10^{-1}$
Myoglobin, ng/ml (range)	57.29 (28.78-75.93)	57.10 (33.25-76.45)	56.66 (28.88-75.97)	52.86 (28.68-76.45)	$1.960x10^{-2}$
N-terminal pre-B natriuretic peptide, pg/ml (range)	172.37 (29.96-279.01)	161.02 (35.55-276.71)	157.09 (34.46-278.99)	131.97 (30.61-277.71)	$1.510x10^{-2}$

[a] Student's t-test. Continuous variables without superscripts were compared using the Mann-Whitney U test.

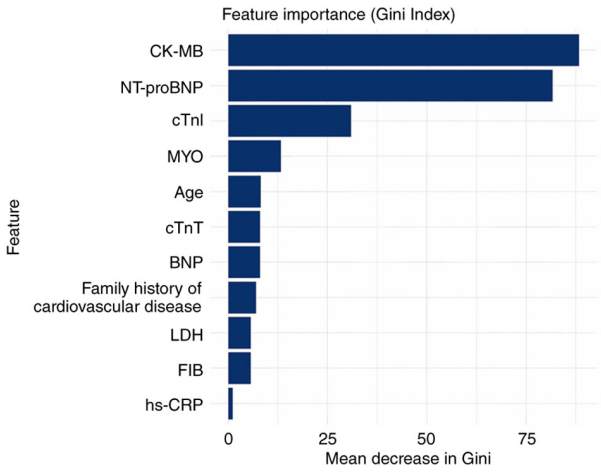

Figure 1. Gini index of random forest model. CK-MB, creatine kinase-MB; NT-proBNP, N-terminal pre-B natriuretic peptide; cTnI, cardiac troponin I; MYO, myoglobin; cTnT, cardiac troponin T; BNP, B-type natriuretic peptide; LDH, lactate dehydrogenase; FIB, fibrinogen; hs-CRP, high-sensitivity C-reactive protein.

Diagnostic score = 0.801 x cTnI +1.275 x CK.MB - 0.027 x NT - proBNP - 2.049 x MYO.

The performance of the model was measured using the ROC curve. The results showed that the AUC value performance of the model was highest at 0.719 (95% CI: 0.670-0.769), with a sensitivity of 0.855 and a specificity of 0.510. This performance substantially outperformed the individual biomarkers cTnI, CK-MB, MYO and NT-proBNP (Fig. 2A-E; Table V). To evaluate the model's robustness, we sequentially removed each biomarker to perform a sensitivity analysis. The results showed that after removing any biomarker, the model's AUC decreased by 0.033-0.044 (Fig. S2A-D), and still remained at a similar level, indicating that the model had good stability.

Diagnostic model for differentiating different types of CVD. The diagnostic model can also differentiate between arrhythmias, SHD and coronary artery disease, with AUC values of 0.771 (95% CI: 0.702-0.840) and 0.715 (95% CI: 0.631-0.798), respectively When the diagnostic model value is between 3.870 and 4.077, it indicates arrhythmias; between 4.077 and 4.916, it indicates SHD; and above 4.916, it indicates coronary artery disease (Table V; Fig. 3A and B).

The statistical power of the ROC curves for both the overall cardiovascular disease diagnosis and the discrimination of disease subtypes was >0.9. This indicated that the present study had sufficient statistical power to demonstrate that the observed AUC was significantly greater than 0.5 (random classification).

Discussion

Although CAD, SHD and arrhythmias differ in their pathophysiological mechanisms, they all essentially belong to

Table IV. Multivariate logistic regression to screen cardiovascular disease biomarkers in cardiovascular disease and normal populations.

Term	Estimate	Standard error	Statistic	P-value	Odds ratio	Confidence interval-lower	Confidence interval-upper
Age	0.000	0.000	0.814	0.416	1.000	1.000	1.001
Family history of cardiovascular disease	-0.001	0.013	-0.042	0.967	0.999	0.974	1.026
High-sensitivity C-reactive protein	0.002	0.005	0.456	0.649	1.002	0.992	1.013
B-type natriuretic peptide	0.000	0.000	1.268	0.206	1.000	1.000	1.000
Cardiac troponin T	-0.004	0.005	-0.933	0.351	0.996	0.987	1.005
Cardiac troponin I	0.468	0.109	4.289	0.000	1.597	1.289	1.978
Lactate dehydrogenase	0.000	0.000	-0.221	0.825	1.000	1.000	1.000
Creatine kinase-MB	0.226	0.021	10.839	0.000	1.254	1.204	1.306
Fibrinogen	0.002	0.006	0.323	0.747	1.002	0.990	1.013
Myoglobin	0.028	0.003	10.359	0.000	1.028	1.022	1.034
N-terminal pre-B natriuretic peptide	0.001	0.000	13.478	0.000	1.001	1.001	1.002

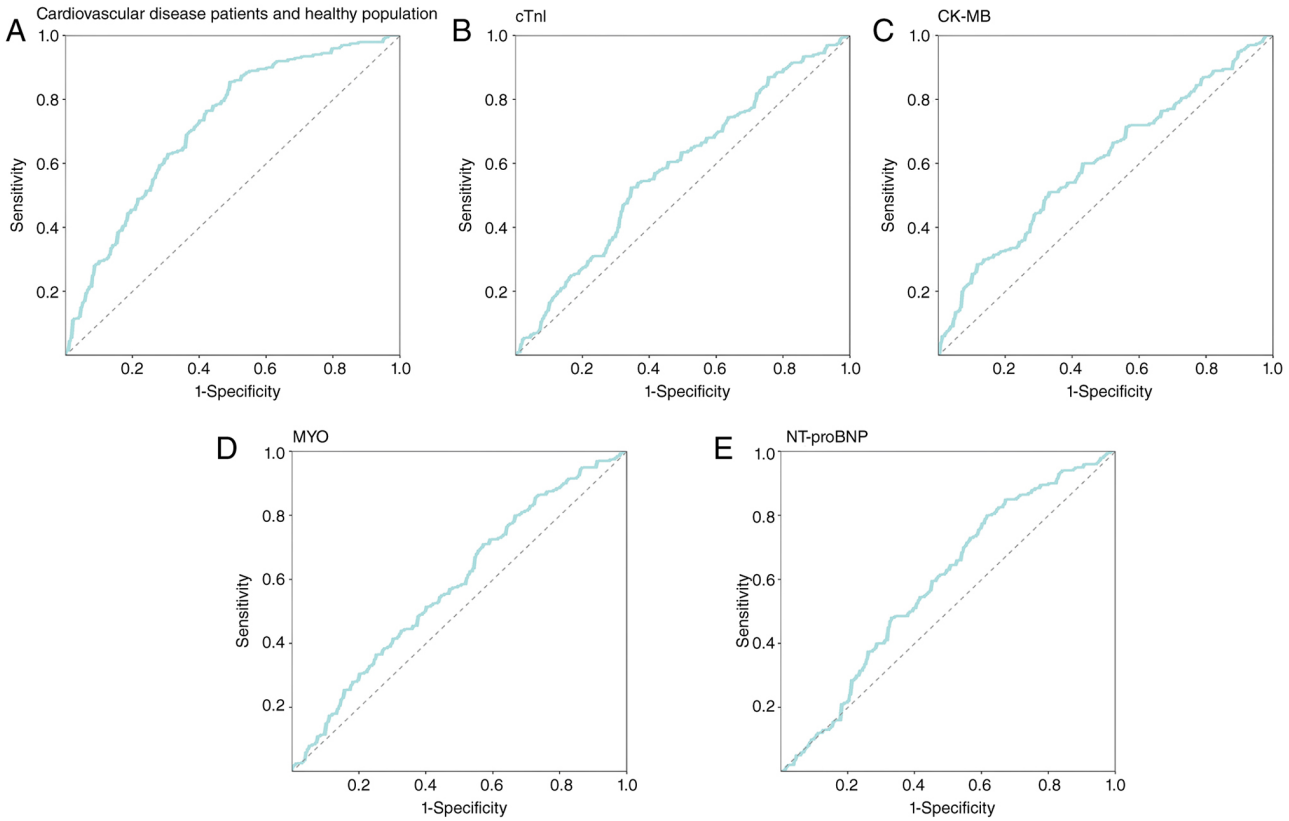

Figure 2. ROC curve for diagnosing cardiovascular diseases. (A) Diagnostic model (B) cTnI, (C) CK-MB, (D) MYO and (E) NT-proBNP in diagnosing cardiovascular diseases. cTnI, cardiac troponin I; CK-MB, creatine kinase-MB; NT-proBNP, N-terminal pre-B natriuretic peptide.

the broader category of CVD. Therefore, the present study hypothesized that these conditions may share certain overlapping changes in biomarkers. Some studies support this view, showing that myocardial injury biomarkers such as cTnI and NT-proBNP are closely associated with CAD (17,18) and are also related to SHD and arrhythmias (19,20). This suggests that these biomarkers may reflect common pathological processes shared across different CVD, such as subclinical myocardial injury, cardiac stress, or early hemodynamic alterations. Therefore, changes in these indicators may serve as cross-disease biological signals for cardiovascular risk assessment or preliminary screening.

The present study identified CK-MB, NT-proBNP, cTnI and MYO as essential diagnostic biomarkers for cardiovascular disease. CK-MB is an enzyme primarily found in myocardial tissue (21). When myocardial damage occurs, CK-MB is released into the bloodstream, resulting in elevated CK-MB levels. Therefore, CK-MB serves as an important biomarker

Table V. ROC curve parameters.

	AUC	AUC-CI-lower	AUC-CI-upper	Best-threshold	Youden	Sensitivity	Specificity
Cardiovascular Disease	0.719	0.670	0.769	3.870	0.365	0.855	0.510
Structural Heart Disease	0.771	0.702	0.840	4.077	0.495	0.888	0.607
Coronary Artery Disease	0.715	0.631	0.798	4.916	0.341	0.824	0.517
Cardiac troponin I	0.583	0.527	0.639	1.591	0.180	0.525	0.655
Creatine kinase-MB	0.601	0.546	0.657	8.797	0.180	0.510	0.670
Myoglobin	0.582	0.527	0.638	98.445	0.140	0.710	0.430
N-terminal pre-B natriuretic peptide	0.587	0.531	0.643	359.604	0.185	0.800	0.385

AUC, area under the curve; CI, confidence interval.

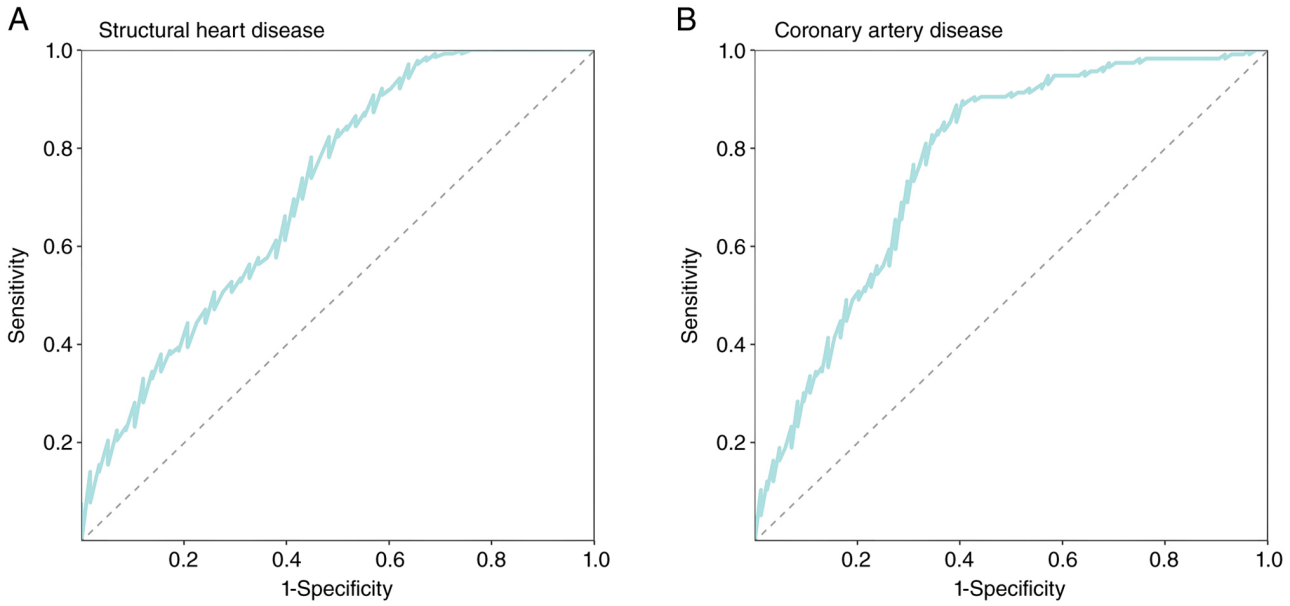

Figure 3. ROC curves for differentiating different types of cardiovascular diseases. (A) Arrhythmias and structural heart disease. (B) Structural heart disease and coronary artery disease.

for diagnosing myocardial injury (22). In patients with CAD, CK-MB is commonly used to evaluate the degree of myocardial ischemia or injury. Following stent implantation, CK-MB can also be used to monitor treatment response (23). In patients with arrhythmia, since there is no significant myocardial damage, the clinical utility of CK-MB is relatively limited. For patients with SHD, CK-MB is commonly used to evaluate myocardial injury, monitor treatment response to percutaneous coronary intervention or stent placement and assess complications such as worsening heart failure or myocardial ischemia.

NT-proBNP is a precursor of BNP, primarily secreted by ventricular myocytes to assess cardiac function (24). In coronary artery disease (CAD), elevated NT-proBNP may indicate left ventricular dysfunction, myocardial ischemia, or decreased efficacy of drug therapy. In SHD, increased NT-proBNP is frequently associated with elevated ventricular wall stress, myocardial fibrosis, or poor treatment outcomes, implying the need for treatment optimization (25). In arrhythmias, NT-proBNP elevation may be associated with left atrial dilation and atrial remodeling. Additionally, NT-proBNP levels can help assess treatment efficacy, significant reductions following antiarrhythmic drug therapy or catheter ablation suggest successful intervention.

cTnI is one of the most sensitive and specific biomarkers for detecting myocardial injury and is a key component of the cardiac troponin complex (26,27), cTnI is also valuable for detecting CAD, particularly in patients with acute coronary syndrome, where its levels rise markedly (28). In SHD, elevated cTnI may indicate progressive myocardial damage and an increased risk of heart failure. Additionally, cTnI serves an essential function in arrhythmia diagnosis. Severe arrhythmias, such as atrial fibrillation or ventricular arrhythmias, can lead to myocardial hypoxia, often accompanied by ischemia or mild myocardial injury, resulting in increased cTnI levels. This makes cTnI a valuable marker for assessing the severity and impact of arrhythmias on cardiac health.

MYO is an oxygen-binding protein found in skeletal muscle and myocardium, primarily responsible for storing

and transporting oxygen to support cellular respiration during hypoxia or intense exercise. MYO is commonly used as a biomarker for acute myocardial infarction and skeletal muscle injury (29). When myocardial cells are damaged, MYO is rapidly released into the bloodstream. Due to its early release and quick clearance, it functions as an early indicator of myocardial injury. However, its low specificity necessitates the use of additional biomarkers to ensure accurate diagnosis.

The main innovation of the present study consisted in the development of a diagnostic model intended as an auxiliary tool to help identify CVD at an early stage and assist in differentiating between CAD, SHD and arrhythmia. Health examination data from 6 months prior to diagnosis to was used build the model, enabling short-term prediction of cardiovascular disease risk and illustrating its potential as an auxiliary tool for timely clinical intervention. Unlike previous studies, which typically focused on a single disease type, few have extensively addressed multiple cardiovascular conditions within an integrated framework. This model may have clinical utility, as it could assist physicians at the early diagnostic stage by providing additional information to differentiate cardiovascular conditions. However, the present model integrated multiple cardiovascular diseases and no previously reported diagnostic models that differentiated between CAD, SHD and arrhythmias was found. Therefore, a direct comparison of AUC values with existing studies was not feasible.

The present study also had several limitations. First, this was a retrospective study, which may have introduced selection bias into data. Second, the sample size was relatively small and the data were collected at a single center. In addition, CVD was simply categorized into three major groups, possibly overlooking some complex disease subtypes. In the future, larger-scale, multicenter prospective randomized controlled studies are needed, and these classifications should be further refined to improve the precision and usability of the model. The diagnostic model shows relatively limited specificity but high sensitivity, showing a good ability to identify true patients. Therefore, the model may be more suitable as an auxiliary tool for screening or early detection rather than as a standalone method for clinical confirmation. The cardiac biomarkers included in the present study are all indicators reported in previous studies. Therefore, the novelty of the present study consisted mainly in the combined modeling of multiple biomarkers. rather than the discovery of novel biomarkers. Due to differences in prediction horizon and study objectives, the model developed in the present study was not directly compared with existing long-term cardiovascular risk prediction models. Future studies with longer follow-up periods might be conducted to allow comparisons with established risk scoring systems. Although all biomarkers were collected within six months prior to diagnosis, the exact sampling times varied, which may have introduced some heterogeneity. Future studies may benefit from more precisely defining the sampling time intervals.

In conclusion, CK-MB, NT-proBNP, cTnI and MYO play important roles in the diagnosis of cardiovascular diseases. The diagnostic model constructed based on this can not only effectively diagnose cardiovascular disease as well as accurately distinguish coronary artery disease, SHD and arrhythmia. It has potential clinical application value in increasing diagnostic accuracy and individualized therapy.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

HZ was responsible for conceptualization, collection of raw data and preprocessing of the raw data, methodology, software and writing the original draft. JW and QL were responsible for formal analysis, project administration, the preparation of figures, writing, reviewing and editing. TZ and XC were responsible for selecting study participants according to the inclusion and exclusion criteria and completing the collection of clinical samples, supervision, the external validation of the diagnostic model and verification of the results, writing, reviewing and editing. HZ and JW confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the Beijing Fengtai You'anmen Hospital (approval number: LL-8701) The present study was conducted in strict accordance with the Declaration of Helsinki and relevant ethical guidelines. The research content involved in this research meets the requirements of medical ethics and academic morality of our hospital, and the research content is reasonable, the risks are controllable, and there are no violations. The relevant research performed was in line with the safe, standardized and true scientific research guiding principles, and in line with the requirements of the clinical research ethics code. The requirement for informed consent was waived by the Ethics Committee due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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