

# Diagnosis of Tuberculous Pericarditis in Zhejiang, China: A Diagnostic Prediction Model Based on LASSO Logistic Regression

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**Background and Aims:** Tuberculous pericarditis (TBP) is a severe, life-threatening complication, yet its diagnosis is highly challenging due to the lack of sufficient diagnostic tools. The aim of this study was to develop and validate a diagnostic prediction model suitable for primary healthcare institutions to predict the risk of TBP.

**Methods:** We collected detailed medical histories, imaging examination results, laboratory test data, and clinical characteristics of patients and used the Least Absolute Shrinkage and Selection Operator (LASSO) technique combined with logistic regression analysis to construct a predictive model. The diagnostic efficacy of the model was assessed using the Receiver Operating Characteristic (ROC) curve, calibration curve, and Decision Curve Analysis (DCA).

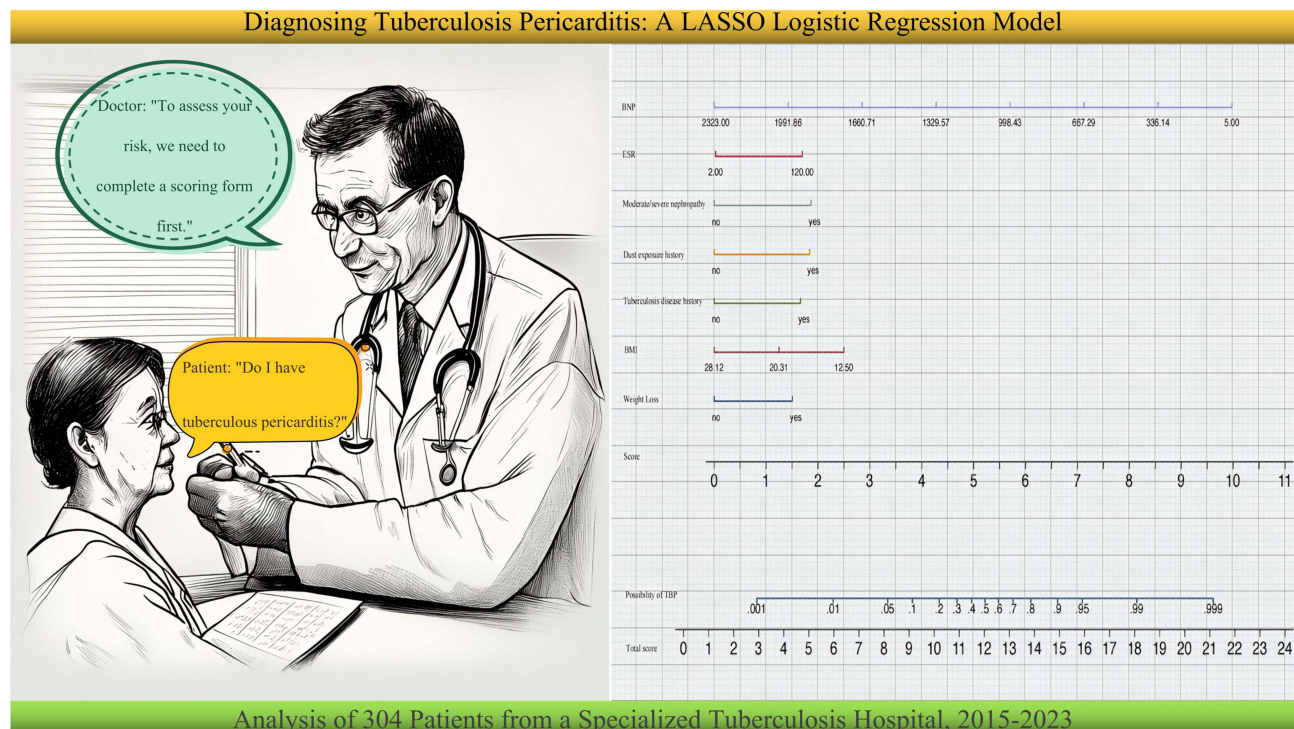
**Results:** A total of 304 patients were included in the study, with a median age of 64 years, of which 144 were diagnosed with tuberculous pericarditis. Patients were randomly assigned to the training and validation sets in a 7:3 ratio. LASSO logistic regression analysis revealed that weight loss ( $P=0.011$ ), body mass index (BMI) ( $P=0.061$ ), history of tuberculosis ( $P=0.022$ ), history of dust exposure ( $P=0.03$ ), moderate to severe kidney disease ( $P=0.005$ ), erythrocyte sedimentation rate (ESR) ( $P=0.084$ ), and B-type natriuretic peptide (BNP) ( $P<0.001$ ) are independent risk factors for TBP. Based on these factors, we constructed a nomogram with an Area Under the Receiver Operating Characteristic Curve (AUC) of 0.757 in both the training and validation sets, indicating high discriminative ability of the model. Calibration curve analysis showed good consistency of the model. DCA results indicated that the model has significant clinical application value when the threshold probability is set between 1–100% (training set) and 30–100% (validation set).

**Conclusion:** We successfully developed a nomogram model for predicting tuberculous pericarditis, which can assist clinicians in improving diagnostic accuracy and reducing misdiagnoses and missed diagnoses in primary healthcare settings.

**Plain Language Summary:** Imagine you have a tool that helps doctors figure out if someone has a serious heart issue called tuberculous pericarditis, which is tough to detect. Our team collected data from 304 patients, looking at everything from their medical history to lab results. We used a smart method to pinpoint key risk factors like weight loss, body mass index, past tuberculosis, exposure to dust, moderate or severe kidney disease, a measure of inflammation called erythrocyte sedimentation rate, and a heart failure marker known as B-type natriuretic peptide. From there, we crafted a simple scoring tool that predicts the likelihood of having this heart problem. When we put our tool to the test, it did a great job, especially when we set the risk level just right. This means we have developed a helpful guide for doctors, especially in places with limited resources, to diagnose this condition more accurately and avoid mistakes. In simple terms, our research has led to a better way to spot a dangerous heart condition that can be tricky to find. This not only helps patients get the right treatment but also raises awareness about the importance of medical research and its impact on public health.

**Keywords:** tuberculous pericarditis, diagnostic prediction model, primary healthcare, LASSO logistic regression

## Graphical Abstract



## Introduction

Tuberculosis is a very serious disease, often becoming the leading cause of death from a single infectious disease worldwide. Over the past three years, it was dethroned by COVID-19, but now it is poised to reclaim its position at the top.<sup>1</sup> Among the various forms of tuberculosis, tuberculous pericarditis (TBP) stands out as a particularly severe manifestation. Without prompt and effective treatment, TBP can lead to severe complications such as constrictive pericarditis, cardiac tamponade, and even death.<sup>2,3</sup> Due to its rapid progression and potential for fatality, in some developing countries, the mortality rate among patients with untreated TBP within six months of onset ranges from 17% to 40%.<sup>4</sup> In Zhejiang Province, China, a recent survey report<sup>5</sup> indicated that the region's implementation of tuberculosis health management service projects was generally good, partly due to the application of new diagnostic technologies such as the molecular diagnostic technique Xpert MTB/RIF. However, despite these advancements, the rapid and accurate diagnosis of TBP still faces significant challenges. The low number of mycobacteria in pericardial effusion not only poses a problem for traditional microbiological methods, such as acid-fast bacilli (AFB) smears and culture methods, which suffer from low sensitivity,<sup>6</sup> but also limits the effectiveness of molecular diagnostic techniques like Xpert MTB/RIF. These technologies require sufficient pathogen DNA to produce reliable results, and the high cost of repeat testing can exacerbate the economic burden on patients. Pericardial biopsy, while a diagnostic option, is an invasive procedure that demands specialized clinical skills and may impose both psychological and physical burdens on patients.

In primary healthcare facilities in Zhejiang Province, the diagnosis of TBP faces significant challenges due to the uneven distribution of medical resources. Particularly in small primary healthcare service sites, the lack of key imaging tools such as radiological equipment, along with a deficiency in professional knowledge about TBP diagnosis among medical staff, makes rapid and accurate diagnosis even more difficult. This situation not only limits the effective management of tuberculosis in these areas but is also commonly found in primary healthcare facilities in other countries.<sup>7</sup> There is an urgent need for a clinical diagnostic model based on easily accessible data such as demographic characteristics, clinical presentations, and common laboratory results to assist clinicians in rapidly and effectively diagnosing TBP.

Addressing this need, we conducted a retrospective study and developed a diagnostic prediction model presented in the form of a nomogram. In this study, we integrated clinical characteristics, laboratory indicators, and imaging data of patients to develop a novel diagnostic prediction model. The model is designed to provide an effective diagnostic tool for clinicians, especially in primary healthcare institutions and healthcare environments with limited medical resources, to improve the diagnostic accuracy of tuberculous pericarditis (see Graphical Abstract for a visual representation of the model's framework).

## Methods

### Ethical Statement and Data Source

This study, a single-center retrospective cohort study conducted at Hangzhou Red Cross Hospital from January 2015 to August 2023, aimed to establish a predictive model for the diagnosis of tuberculous pericarditis. Hangzhou Red Cross Hospital serves as a provincial tuberculosis treatment center, treating patients with tuberculosis from various regions of Zhejiang Province, China. The study involved patients with tuberculous pericarditis and non-specific pericarditis who were consecutively hospitalized for treatment during this period. In accordance with the ethical standards of the Declaration of Helsinki, the World Medical Association, and the Council for International Organizations of Medical Sciences (CIOMS) guidelines for international ethics in human biomedical research, the Ethics Committee of Hangzhou Red Cross Hospital reviewed and approved this study. A waiver for the requirement of informed consent was granted by the Ethics Committee due to the retrospective nature of the study (Ethics Application Number: 2024YS90). The study strictly adheres to the principles outlined in the Declaration of Helsinki and ensures the protection of participants' rights and welfare. We pledge to keep confidential all patient information gathered from the electronic medical records database. The raw data supporting the results of this study have been uploaded to Zenodo and are accessible upon reasonable request at the following link: <https://zenodo.org/records/13822455>.

### Patient Selection

**Inclusion Criteria:** The diagnosis of TBP is based on any of the following criteria: 1. Mycobacterium tuberculosis is isolated from pericardial effusion or pericardial biopsy specimens, confirmed by positive acid-fast staining or tuberculosis culture. 2. Histological examination of pericardial biopsy samples shows granulomatous inflammation. 3. In the presence of clinical and radiological evidence of tuberculosis, there is a positive response to standardized anti-tuberculosis treatment, and Mycobacterium tuberculosis is isolated from sputum or non-pericardial exudate.<sup>8</sup> The diagnosis of non-specific pericarditis is based on: patients presenting with clinical manifestations of pericarditis, but without clear evidence of pathogen infection in clinical tests, and postoperative pathological diagnosis shows non-specific pericardial inflammatory changes. **Exclusion Criteria:** Patients with incomplete clinical data.

### Data Collection

During the model development process, we documented the following age-adjusted Charlson Comorbidity Index (CCI)<sup>9</sup> and a series of clinically common indicators that may suggest TBP: demographic characteristics: age, gender, height, and weight (used to calculate body mass index (BMI)), marital status, level of education, immigration status; lifestyle factors: smoking status, history of alcohol consumption; clinical symptoms: chest pain, fever, night sweats, cough, difficulty breathing, weight loss; past medical history: chronic infections, history of tuberculosis, history of dust exposure, hypertension, diabetes, connective tissue diseases, liver diseases, moderate to severe kidney diseases, tumors, leukemia, lymphoma, acquired immune deficiency syndrome (AIDS); clinical examination results: pericardial friction rub, electrocardiogram changes, amount of pericardial effusion; laboratory test results: neutrophil count, lymphocyte count, monocyte count, hemoglobin level, platelet count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), creatine kinase (CK), creatine kinase isoenzyme MB (CK-MB), B-type natriuretic peptide (BNP). All biochemical indicators were selected and recorded based on the patients' first set of biochemical test results after admission. Detailed diagnostic criteria can be found in [Appendix 1](#).

## Model Development and Validation

Initially, the dataset was randomly divided into a training set and a validation set in a 7:3 ratio. The training set was used to develop the diagnostic model and prepare the nomogram, while the validation set was utilized for the model's verification process. Subsequently, the Least Absolute Shrinkage and Selection Operator (LASSO) method was employed for preliminary variable screening. To compare the fit of seven logistic regression modeling strategies, we evaluated them based on the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC). The results revealed that, aside from the enter method, the remaining six strategies showed consistency in model fit, and all displayed lower AIC and BIC values compared to the enter method ([Supplementary Table 1](#)). Consequently, we selected any one of these six strategies for modeling in this study. Ultimately, we employed the backward likelihood ratio (LR) method for multivariate logistic regression analysis to identify independent risk factors in the model. Based on the results of the multivariate regression model, a nomogram for diagnosing tuberculous pericarditis was constructed. The model's discriminative ability was assessed using the Area Under the Receiver Operating Characteristic Curve (AUC). The Hosmer-Lemeshow test was used to evaluate the model's calibration.

## Clinical Decision Analysis and Model Application

To evaluate the clinical utility of the model, we used clinical decision curve analysis (DCA) to assess the model's performance in both the training and validation sets. Based on the results of the validation set and the Youden index, the total score of the nomogram was used to stratify patients with tuberculous pericarditis into low-risk, medium-risk, and high-risk categories. In clinical practice, due to the lack of precise diagnostic tools, physicians often rely on clinical experience to diagnose tuberculous pericarditis. To assess the practical application value of the model, we compared the model's risk assessment with that of physicians based on clinical experience, including: misdiagnosis - analyzing non-TBP patients in the validation set to evaluate the proportion of TBP misdiagnosed by physicians' clinical experience and the proportion misdiagnosed as TBP based on the model's high-risk group threshold, and comparing the misdiagnosis rates between the two; missed diagnosis - analyzing TBP patients in the validation set to evaluate the proportion of TBP missed by physicians' clinical experience and the proportion incorrectly excluded as TBP based on the model's low-risk group threshold, and comparing the missed diagnosis rates between the two; overuse of anti-tuberculosis treatment - assessing non-TBP patients in the validation set to observe the proportion given anti-tuberculosis treatment in actual clinical practice.

## Statistical Analysis

In this study, continuous variables were summarized using medians and interquartile ranges (IQR), and the Mann-Whitney *U*-test was utilized to compare statistical differences between the two groups. For categorical variables, we conducted analyses using Pearson's chi-squared test. To address missing data, we employed the Expectation-Maximization (EM) algorithm for estimating and imputing missing values, thereby enhancing the completeness of the data analysis. Odds ratios (OR) and their corresponding 95% confidence intervals (CI) were obtained from multivariate logistic regression models. Data analysis was primarily conducted using SPSS software version 27 and STATA software version 15.

## Results

### Patient Characteristics

A total of 304 patients were ultimately included in this study, with a median age of 64 years, ranging from a minimum age of 16 years, and 29.28% were female ([Table 1](#)). They were randomly assigned to the training and validation sets in a 7:3 ratio ([Supplementary Figure 1](#)). Comparisons between the training and validation sets revealed no statistically significant differences in most indicators, except for a history of dust exposure, moderate to severe kidney disease, and weight loss, which showed significant differences between the two groups. Compared to patients with non-specific pericarditis, those with TBP in both the training and validation sets exhibited the following characteristics: lower BMI, a higher proportion of weight loss, lower hemoglobin levels, and a higher proportion of tuberculosis history and dust exposure history ([Supplementary Table 2](#)). For the handling of missing data, we used the EM algorithm to estimate and impute the following variables: BMI, neutrophils, lymphocytes, monocytes, hemoglobin, platelets, ESR, CRP, BNP, CK, CK-MB, electrocardiogram, and pericardial effusion.

**Table 1** Baseline Features of Training and Validation Datasets

Characteristics	Whole Cohort (N=304)	Training Dataset (N=222)	Validation Dataset (N=82)	P Value
Age, median (quartile), years	64 (54–71)	64 (54–71)	65 (54–72)	0.204
Female, no. (%)	89 (29.28)	65 (29.3)	24 (29.3)	0.999
BMI, median (quartile), kg/m <sup>2</sup>	17.65 (15.77–19.44)	17.68 (15.81–19.47)	17.49 (15.43–19.20)	0.467
Marital status, no. (%)				0.204
Married	275 (90.5)	203 (91.4)	72 (87.8)	
Unmarried	10 (3.3)	6 (2.7)	4 (4.9)	
Divorce	5 (1.6)	5 (2.3)	0 (0)	
Widowed	14 (4.6)	8 (3.6)	6 (7.3)	
Education status, no. (%)				0.908
≥ High school	47 (15.46)	34 (15.3)	13 (15.9)	
< High school	257 (84.54)	188 (84.7)	69 (84.1)	
Migrant, no. (%)	3 (0.99)	3 (1.4)	0 (0)	0.290
Smoking, no. (%)	92 (30.26)	69 (31.1)	23 (28)	0.610
Consumed alcohol no. (%)	76 (25)	60 (27)	16 (19.5)	0.179
Chest pain, no. (%)	43 (14.14)	28 (12.6)	15 (18.3)	0.207
Fever, no. (%)	108 (35.5)	75 (33.8)	33 (40.2)	0.296
Night sweat, no. (%)	30 (9.87)	22 (9.9)	8 (9.8)	0.968
Cough, no. (%)	157 (51.64)	121 (54.5)	36 (43.9)	0.101
Dyspnea, no. (%)	248 (81.58)	181 (81.5)	67 (81.7)	0.972
Weight loss, no. (%)	58 (19.08)	36 (16.2)	22 (26.8)	0.037
Chronic infection, no. (%)	37 (12.17)	26 (11.7)	11 (13.4)	0.687
Pericardial friction sound, no. (%)	1 (0.33)	1 (0.5)	0 (0)	0.543
Changes in electrocardiogram, no. (%)	4 (1.3)	2 (0.9)	2 (2.4)	0.403
Pericardial effusion, no. (%)				0.078
< 5mm	172 (56.58)	129 (58.1)	43 (52.4)	
5–10mm	80 (26.32)	50 (22.5)	30 (36.6)	
10–20mm	38 (12.5)	30 (13.5)	8 (9.8)	
>20mm	11 (3.62)	10 (4.5)	1 (1.2)	
Neutrophils, median (quartile), ×10 <sup>9</sup> /L	3.60 (2.70–4.76)	3.60 (2.78–4.70)	3.54 (2.38–4.90)	0.261
Lymphocyte, median (quartile), ×10 <sup>9</sup> /L	0.80 (0.59–1.10)	0.80 (0.60–1.10)	0.8 (0.054–1.06)	0.642
Monocyte, median (quartile), ×10 <sup>9</sup> /L	0.50 (0.40–0.60)	0.50 (0.40–0.64)	0.50 (0.31–0.60)	0.277
Hemoglobin, median (quartile), g/L	119.50 (109–131)	120 (110–131)	119 (108–130.50)	0.535
Platelet, median (quartile), ×10 <sup>9</sup> /L	176 (130.75–246.50)	178.5 (132.25–243.21)	165.5 (129.75–269.75)	0.665

(Continued)

**Table 1** (Continued).

Characteristics	Whole Cohort (N=304)	Training Dataset (N=222)	Validation Dataset (N=82)	P Value
ESR, median (quartile), mm/h	38.76 (23.11–57.89)	38 (23.34–58)	41.10 (22–57.50)	0.916
CRP, median (quartile), mg/L	20.6 (9.91–46.44)	21.76 (9.48–48.18)	19.57 (12.16–34.18)	0.474
CK, median (quartile), U/L	55 (35–75.58)	55.66 (34–79)	51.5 (35.75–69.02)	0.730
CK-MB, median (quartile), U/L	10 (8–13)	10.25 (8–13)	10 (7–11.87)	0.190
BNP, median (quartile), pg/mL	250.5 (145.19–361.25)	250.05 (148.75–357.81)	249 (129–401.75)	0.797
Tuberculosis history, no. (%)	35 (11.51)	24 (10.8)	11 (13.4)	0.528
Dust exposure history, no. (%)	31 (10.20)	15 (6.8)	16 (19.5)	0.001
Hypertension, no. (%)	74 (24.34)	50 (22.5)	24 (29.3)	0.224
Diabetes, no. (%)	46 (15.13)	36 (16.2)	10 (12.2)	0.385
Connective tissue disease, no. (%)	3 (0.99)	1 (0.5)	2 (2.4)	0.120
Liver dysfunction, no. (%)	82 (26.97)	66 (29.7)	16 (19.5)	0.075
Moderate or severe nephropathy, no. (%)	49 (16.12)	29 (13.1)	20 (24.4)	0.017
Cancer, no. (%)	9 (2.96)	8 (3.6)	1 (1.2)	0.276
Leukemia, no. (%)	0 (0)	0 (0)	0 (0)	–
Lymphoma, no. (%)	0 (0)	0 (0)	0 (0)	–
AIDS, no. (%)	0 (0)	0 (0)	0 (0)	–

**Note:** Values are numbers (%) or medians (quartile).

**Abbreviations:** AIDS, acquired immune deficiency syndrome; BMI, body mass index; BNP, B-type natriuretic peptide; CK, creatine kinase; CK-MB, creatine kinase isoenzyme MB; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; TBP, Tuberculous pericarditis.

The proportions of missing data imputed for these variables were 21.7%, 0.3%, 0.3%, 0.3%, 0.3%, 16.4%, 0.7%, 15.5%, 15.5%, 15.5%, 0.7%, and 1.0%, respectively ([Supplementary Table 3](#)).

### Variable Selection and Nomogram Construction

Based on the principle of the maximum allowable lambda value within one standard error of the minimum loss, after triple cross-validation of the LASSO coefficient distribution for 39 features, lambda=13.145167 was selected as the standard for this LASSO regression. A total of 8 variables were retained, including weight loss, BMI, history of tuberculosis, history of dust exposure, moderate to severe kidney disease, platelets, ESR, and BNP ([Supplementary Figure 2](#)). The aforementioned variables were further subjected to multivariate logistic regression, ultimately determining that weight loss [OR, 3.131, (95% CI, 1.305–7.511), P=0.011], BMI [OR, 0.886, [95% CI, 0.780–1.006), P=0.061], previous tuberculosis history [OR, 3.529, (95% CI, 1.197–10.406), P=0.022], history of dust exposure [OR, 4.036, (95% CI, 1.144–14.245), P=0.030], moderate to severe kidney disease [OR, 4.121, (95% CI, 1.539–11.031), P=0.005], ESR [OR, 1.011, (95% CI, 0.999–1.023), P=0.084], and BNP [OR, 0.997, (95% CI, 0.995–0.999), P<0.001] were independently associated factors for diagnosing tuberculous pericarditis ([Table 2](#)). These factors were used to construct a nomogram model to visualize the model ([Figure 1](#)).

### Model Validation

The AUC of the diagnostic model for TBP was 0.757 (95% CI, 0.694–0.820) in the training set and 0.757 (95% CI, 0.651–0.862) in the validation set ([Figure 2A and B](#)). The Hosmer–Lemeshow goodness-of-fit test showed P=0.863 in the training dataset and P=0.084 in the validation dataset, and the calibration curves demonstrated good consistency between predicted and observed values ([Figure 2C and D](#)).

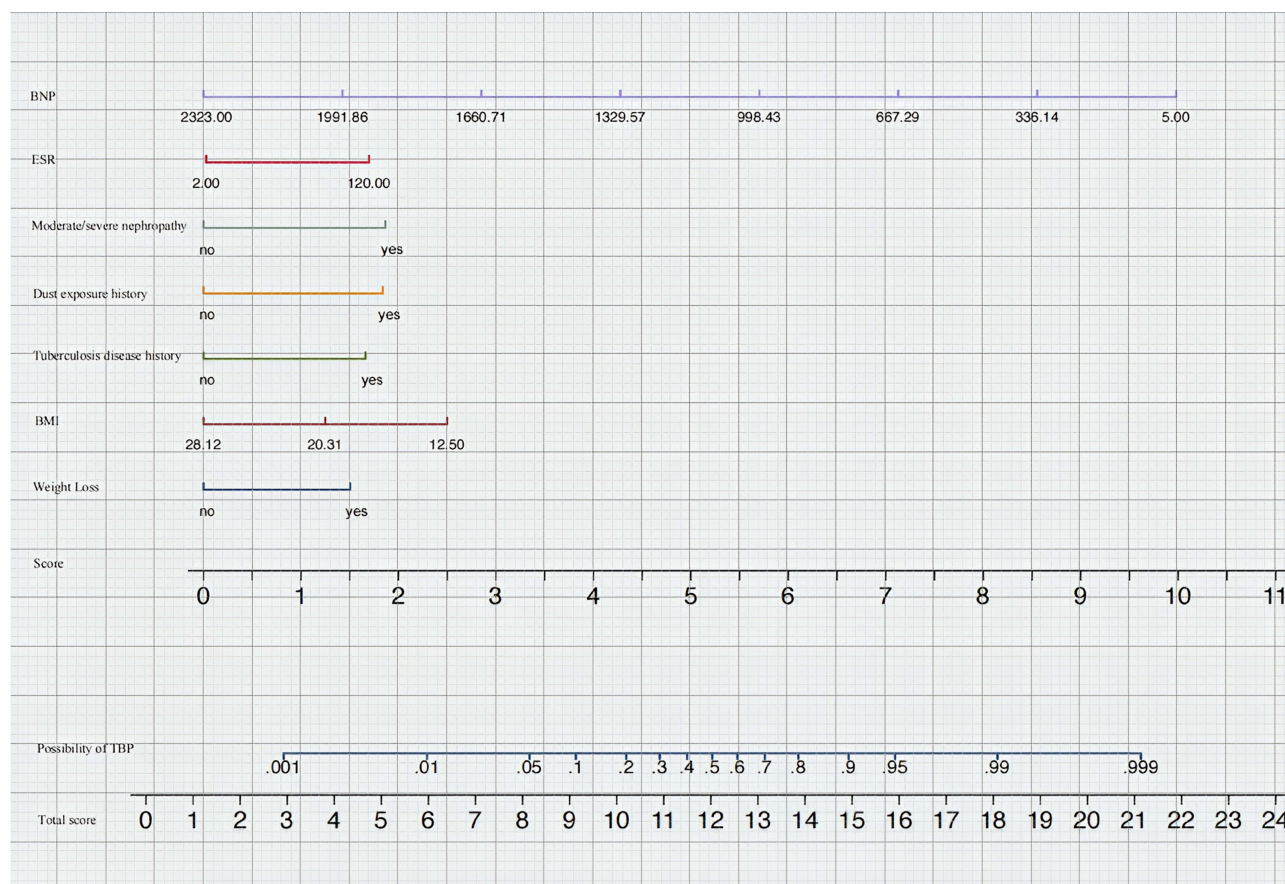
**Table 2** Multivariate Logistic Regression

Predictors	OR (95% CI)	P Value
BMI	0.886 (0.780–1.006)	0.061
Weight loss	3.131 (1.305–7.511)	0.011
Tuberculosis history	3.529 (1.197–10.406)	0.022
Dust exposure history	4.036 (1.144–14.245)	0.030
Moderate or severe nephropathy	4.121 (1.539–11.031)	0.005
ESR	1.011 (0.999–1.023)	0.084
BNP	0.997 (0.995–0.999)	<0.001
Platelet	–	0.721

**Abbreviations:** BMI, body mass index; BNP, B-type natriuretic peptide; ESR, erythrocyte sedimentation rate; CI, confidence intervals; OR, odds ratio.

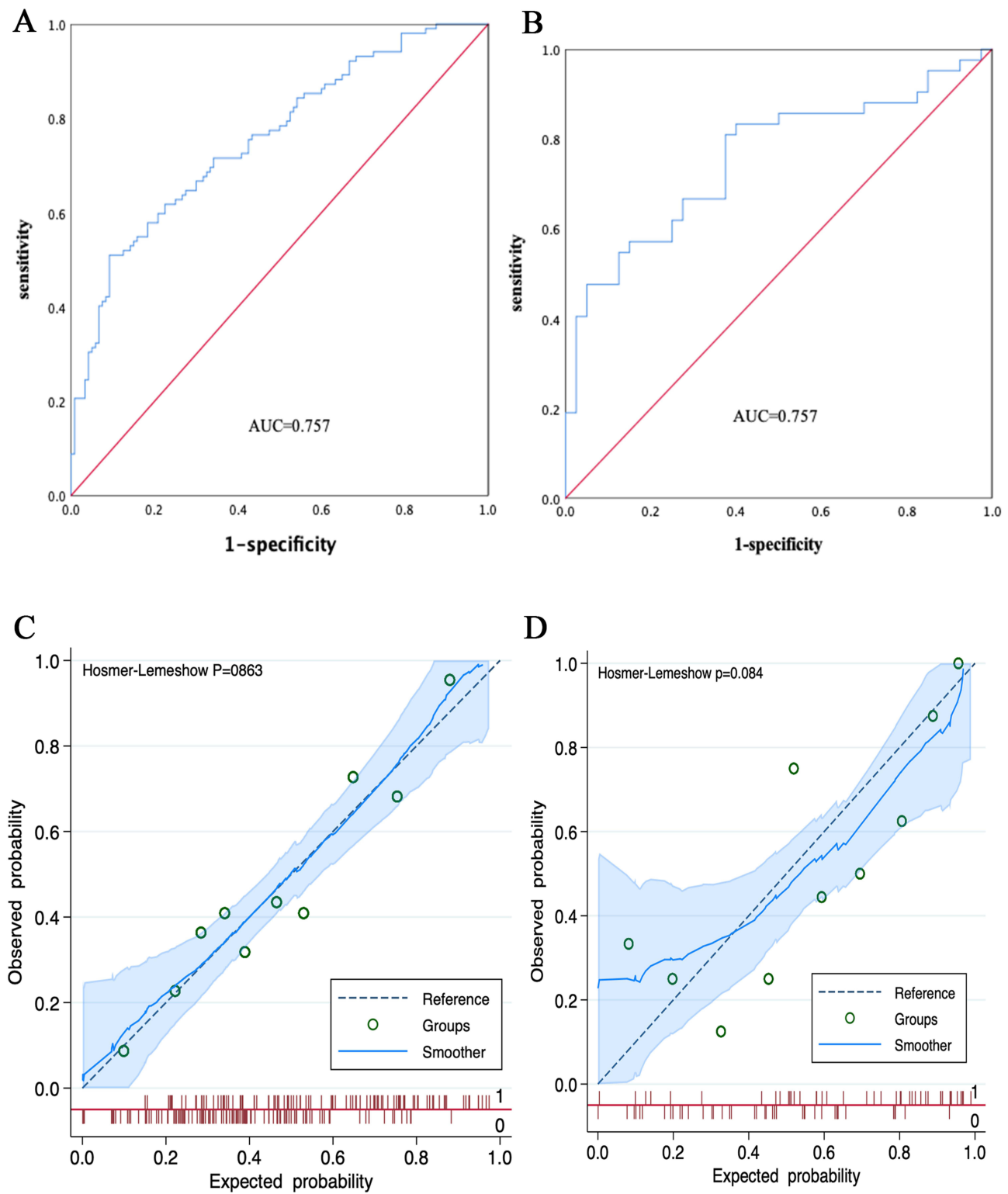
### Clinical Application

Results from the DCA indicated that the model achieved the maximum clinical net benefit when the threshold probabilities were set from 1–100% in the training cohort and 30–100% in the validation cohort (Figure 3A and B). Based on the DCA from the validation set, we first identified the optimal threshold for low risk at 11 points and then set the optimal threshold between medium and high risk at 14 points according to the Youden index, thereby stratifying



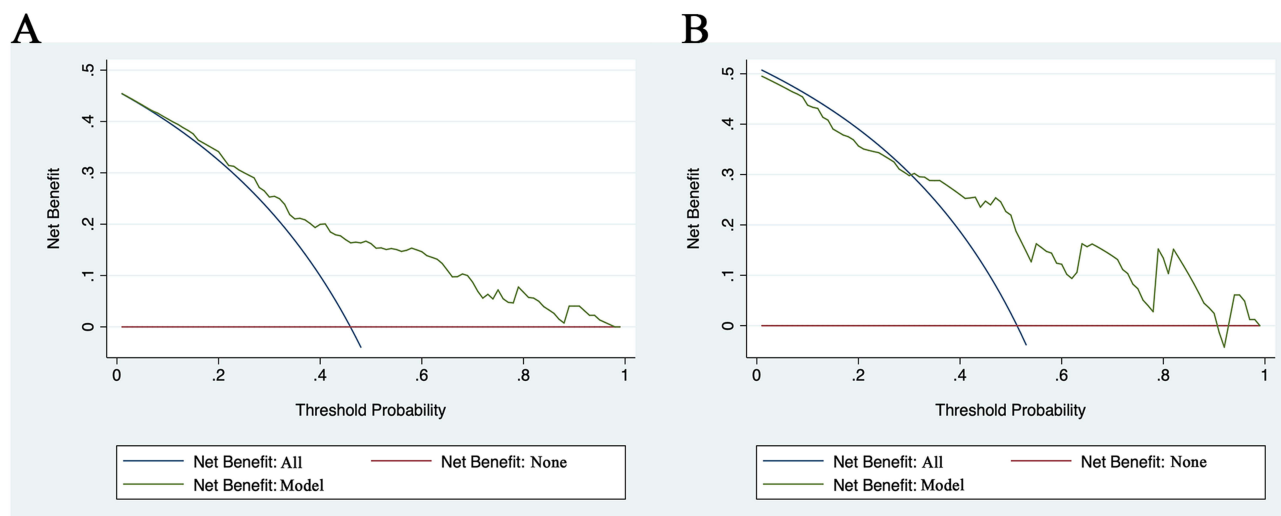
**Figure 1** Nomogram Developed from the LASSO Logistic Regression Model.

**Abbreviations:** BMI, body mass index; BNP, B-type Natriuretic Peptide; ESR, erythrocyte sedimentation rate; TBP, Tuberculous pericarditis.



**Figure 2** Analysis of the ROC and Calibration Plots. **(A)** Model performance in diagnosing tuberculous pericarditis within the training set. **(B)** Model performance in diagnosing tuberculous pericarditis within the validation set. **(C)** Calibration of the model for diagnosing tuberculous pericarditis within the training set. **(D)** Calibration of the model for diagnosing tuberculous pericarditis within the validation set. The sawtooth pattern in red above represents patients diagnosed with tuberculous pericarditis (coded as 1), while the sawtooth pattern below represents patients diagnosed with non-specific pericarditis (coded as 0).  
**Abbreviations:** AUC, Area Under the ROC Curve; ROC, Receiver Operating Characteristic.





**Figure 3** Decision Curve Analysis of the Nomogram. **(A)** Decision curve analysis for the nomogram in the training set. **(B)** Decision curve analysis for the nomogram in the validation set.

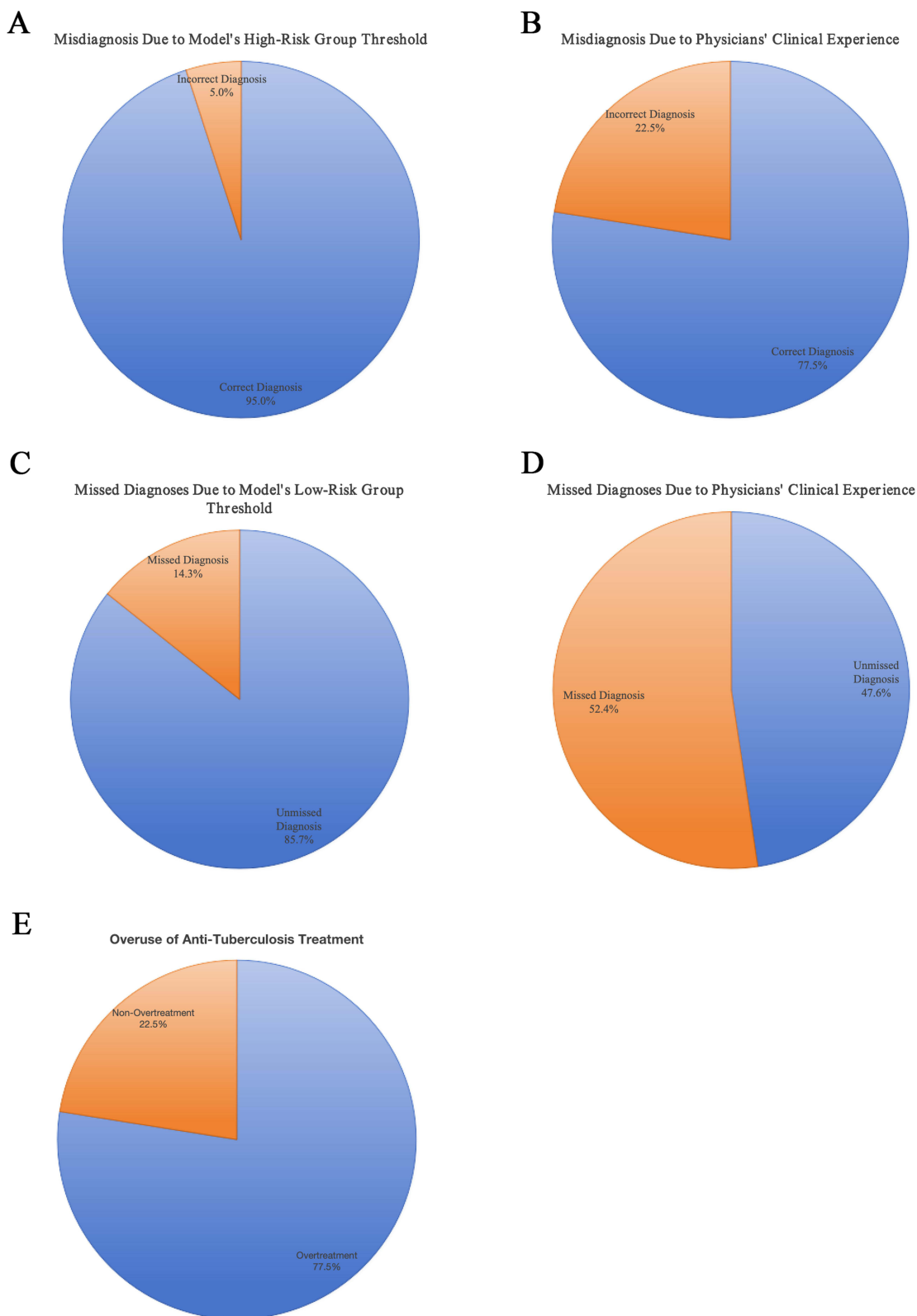
patients into low-, medium-, and high-risk groups. Based on decisions made with a high-risk threshold, the misdiagnosis rate was 5.0% (2/40), while the misdiagnosis rate based on physicians' initial clinical decisions was 22.5% (9/40), with a statistically significant difference ( $P=0.023$ ) (Figure 4A and B). The missed diagnosis rate based on decisions made with a low-risk threshold was 14.3% (6/42). In contrast, the missed diagnosis rate for physicians' initial clinical decisions was 52.4% (22/42), also showing a statistically significant difference ( $P<0.001$ ) (Figure 4C and D). The rate of overuse of anti-tuberculosis treatment was 77.5% (31/40) (Figure 4E).

## Discussion

In this cohort study, we assessed the value of constructing a diagnostic model for TBP based on indicators such as demographic characteristics, clinical manifestations, and common laboratory results. This diagnostic model can effectively and rapidly identify patients with TBP. Compared to the preliminary clinical decisions made by tuberculosis specialists based on experience, this model significantly reduced the rates of misdiagnosis and missed diagnosis. Based on this model, we recommend that clinicians immediately refer high-risk patients identified for TBP diagnosis to specialized tuberculosis hospitals. Considering the increase in global migration, the spectrum of cardiovascular diseases in developed countries is changing, and physicians in these regions may also have insufficient awareness of tuberculous pericarditis.<sup>10</sup> Therefore, this model can not only play a role in primary healthcare facilities in developing countries but may also provide a powerful tool for physicians in developed countries to diagnose TBP, helping them better meet this challenge.

This study ultimately identified seven variables. Weight loss, history of tuberculosis, history of dust exposure, moderate to severe kidney disease, and ESR are positively correlated with the risk of developing TBP, while BMI and BNP are negatively correlated with the risk of the disease. Nutritional status is considered closely related to the occurrence of tuberculosis. Weight loss reflects the recent rate of nutritional decline, and a low BMI also reflects a state of weakened nutritional status. Malnutrition can impair the human immune system, thereby increasing the risk of tuberculosis infection. A Study have found that individuals with a BMI  $<18.5$  have an estimated risk ratio of 12.4 for developing tuberculosis.<sup>11</sup> At the same time, Mycobacterium tuberculosis infection leads to the activation of TNF- $\alpha$ .<sup>12</sup> TNF- $\alpha$  acts on muscle cells, promoting protein loss through nuclear factor- $\kappa$ B and activating the ubiquitin-proteasome pathway, which further leads to muscle degradation, exacerbating the progression of tuberculosis.<sup>13</sup>

Individuals with a history of tuberculosis are at a significantly higher risk of developing the disease again compared to those without such a history. This increased risk may be due to the reactivation of Mycobacterium tuberculosis present in the body. The bacteria can exist in a dormant state within tissues for months to years, yet still possess the capability to resume growth and cause disease. Immunocompromised states, such as malnutrition, use of corticosteroids, or other



**Figure 4** Comparison of Clinical Application Based on the Model and Clinical Experience. **(A)** Misdiagnosis Due to Model's High-Risk Group Threshold. **(B)** Misdiagnosis Due to Physicians' Clinical Experience. **(C)** Missed Diagnoses Due to Model's Low-Risk Group Threshold. **(D)** Missed Diagnoses Due to Physicians' Clinical Experience. **(E)** Overuse of Anti-Tuberculosis Treatment.

immunosuppressive agents, can lead to the reactivation of these latent infections.<sup>14,15</sup> Another explanation may be that previous tuberculosis can result in reduced immunity to certain *Mycobacterium tuberculosis* epitopes, primarily because these epitopes have high homology with bacteria in the microbiome. Anti-tuberculosis treatment may further alter immune responses to these epitopes by affecting the balance of the microbiome.<sup>16</sup> Individuals with a history of dust exposure may exhibit varying degrees of structural changes in lung tissue, such as fibrosis, as well as a reduction in immune defense functions, making them more susceptible to tuberculosis infection.<sup>17,18</sup>

Patients with chronic kidney disease may have impaired functions of various immune cells, including B and T cells, neutrophils, and monocytes. This immune dysfunction not only makes patients more vulnerable to *Mycobacterium tuberculosis* infection but also may reactivate tuberculosis they may have contracted during childhood or adolescence, turning it into active tuberculosis.<sup>19–22</sup> Consequently, the risk of tuberculosis in patients with chronic kidney disease is much higher than in the general population. The ESR, a method for measuring the sedimentation speed of red blood cells in the blood, is a non-specific test for inflammation and infection. Traditionally used in the diagnosis and assessment of tuberculosis,<sup>23</sup> it reflects the active state of the disease. Patients with active tuberculosis have significantly higher ESR levels than healthy individuals.<sup>24</sup>

BNP, primarily secreted by myocardial cells, is a 32-amino acid residue polypeptide that not only regulates blood pressure and blood volume homeostasis but also has diuretic effects. It is considered the gold standard biomarker for heart dysfunction<sup>25,26</sup> and has a clear diagnostic and prognostic role in heart failure patients.<sup>27</sup> Interestingly, this study found a negative correlation between BNP and the risk of tuberculous pericarditis, which contradicts our usual understanding of cardiopulmonary comorbidities. A possible explanation is that this model compares tuberculous pericarditis with non-specific pericarditis; while tuberculous pericarditis may lead to pericardial effusion, it does not necessarily directly affect cardiac pump function. In contrast, non-specific pericarditis may be more likely to cause cardiac dysfunction, leading to heart failure.<sup>28</sup> Another explanation is that inflammation itself is involved in biological processes including tissue remodeling and metabolism,<sup>29–31</sup> which could affect the secretion of BNP. TBP, as a chronic inflammatory state, may affect the secretion of BNP through different mechanisms, distinct from the acute inflammatory response caused by non-specific pericarditis.

Previous studies<sup>8</sup> have focused on developing diagnostic models for tuberculous pericarditis using indicators such as gamma interferon (IFN- $\gamma$ ), adenosine deaminase (ADA) levels, *Mycobacterium tuberculosis* polymerase chain reaction detection, and sputum smear and culture. However, many of these indicators are difficult to obtain and time-consuming in primary healthcare settings, making their application scenarios different from the screening model in this study.

The advantage of this study is that the predictive model used predictors that are easily obtainable clinical characteristics and routine laboratory indicators. Compared to traditional microbiological methods, this model not only saved diagnostic time but also may be more cost-effective for high-risk patients in areas with limited access to precision diagnostic tools and economic constraints. However, our study has some limitations. Firstly, this study was a single-center, small-sample study, but it still had good predictive value after internal validation. Additionally, our study lacked external data validation. We plan to conduct prospective studies with multiple centers to further verify the effectiveness of the model.

## Conclusions

In summary, our model accurately identifies high-risk individuals, reduces the misuse of anti-tuberculosis drugs due to misdiagnosis, and lowers the diagnostic delays and associated adverse outcomes caused by missed diagnoses. We recommend the implementation of this model in primary care to enhance early and accurate diagnosis of TBP, thereby improving patient outcomes and alleviating the burden of this disease in resource-limited or economically underdeveloped regions.

## Data Sharing Statement

The raw data supporting the results of this study was uploaded to zenodo (<https://zenodo.org/records/13822455>) and accessed upon reasonable request.

## Ethical Approval and Consent to Participate

All procedures performed in studies involving human participants were following the ethical standards of the institutional and national research committee and with the 1964 helsinki declaration and its later amendments or comparable ethical standards.

## Consent for Publication

This study was a retrospective cohort study, and an exemption from the informed consent requirement was approved by the ethics committee of Hangzhou Red Cross Hospital (Ethical Application Ref: 2024YS90).

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. All authors approved the final version of the manuscript.

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