

A nomogram for predicting mortality of patients initially diagnosed with primary pulmonary tuberculosis in Hunan province, China: a retrospective study.

Dan Li

Central South University

Linqi Li

University of South China

Siyuan Tang (✉ sytang263@csu.edu.cn)

Central South University

Sheng Lei

Hunan Chest Hospital

Hebing Xie

University of South China

Research Article

Keywords: Initially diagnosed with primary PTB, Mortality, Prognostic, Nomogram

Posted Date: April 13th, 2023

DOI: <https://doi.org/10.21203/rs.3.rs-2717271/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: According to the Global Tuberculosis Report for three consecutive years, tuberculosis (TB) is the second leading infectious killer. Primary pulmonary tuberculosis (PTB) leads to the highest mortality among TB diseases. Regrettably, no previous studies targeted the PTB of a specific type or in a specific course, so models established in previous studies cannot be accurately feasible for clinical treatments. This study aimed to construct a nomogram prognostic model to quickly recognize death-related risk factors in patients initially diagnosed with PTB to intervene and treat high-risk patients as early as possible in the clinic to reduce mortality.

Methods: We retrospectively analyzed the clinical data of 1,809 in-hospital patients initially diagnosed with primary PTB at Hunan Chest Hospital from January 1, 2019, to December 31, 2019. Binary logistic regression analysis was used to identify the risk factors. A nomogram prognostic model for mortality prediction was constructed using R software and was validated using a validation set.

Results: Univariate and multivariate logistic regression analyses revealed that drinking, hepatitis B virus (HBV), body mass index (BMI), age, albumin (ALB), and hemoglobin (Hb) were six independent predictors of death in in-hospital patients initially diagnosed with primary PTB. Based on these predictors, a nomogram prognostic model was established with high prediction accuracy, of which the area under the curve (AUC) was 0.881 (95% confidence interval [CI]: 0.777-0.847), the sensitivity was 84.7%, and the specificity was 77.7%. Internal and external validations confirmed that the constructed model fit the real situation well.

Conclusion: The constructed nomogram prognostic model can recognize risk factors and accurately predict the mortality of patients initially diagnosed with primary PTB. This is expected to guide early clinical intervention and treatment for high-risk patients.

Background

According to the Global Tuberculosis Report for three consecutive years, tuberculosis (TB) is the second leading infectious killer after COVID-19, with higher mortality than human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). It is also noted that 2022 is the first year when TB incidence and death rates have increased. Impacted by COVID-19 pandemic, the effects of TB prevention and treatment can be interrupted or changed over the years (1, 2). In 2021, China ranked third worldwide, with TB incidence (new cases per 100,000 population) estimated at 55 and TB mortality at 4% (3). Moreover, in 2021, there were 780,000 new TB cases in China, of which new pulmonary tuberculosis (PTB) cases accounted for 95%. These results indicate the high TB burden in China. In the new era of COVID-19 pandemic, China has faced huge challenges in TB prevention and treatment. Recently, high-sensitivity tools have been introduced to screen out, intervene, and treat TB to reduce TB mortality (4).

The lungs are the most common site of TB infection, and PTB leads to the highest mortality among TB diseases. Patients with different types of PTB or with different courses of PTB will differ in various

aspects, such as clinical symptoms, hematologic manifestations, treatment methods, intervention methods, and even treatment outcomes (5–7). Regrettably, in previous TB prognostic studies, the research objects were classified mainly based on: 1) drug resistance; 2) HIV status; 3) comorbidities; 4) PTB or extrapulmonary TB (EPTB) (8–10). No previous studies targeted the PTB of a specific type or in a specific course, so models established in previous studies cannot be accurately feasible for clinical treatments.

This study aimed to construct a nomogram prognostic model to identify the risk factors for in-hospital patients initially diagnosed with primary PTB to offer the most effective therapeutic schemes, the most appropriate case management, and the optimal resource allocation for patients who are the least likely to be cured but most likely to benefit from the intervention measures. The study breaks through the limitations of the same type of study in terms of the lack of segmentation of the target population and the lack of clinical usefulness of the selection of predictors. To precisely move the intervention study population forward, patients with a primary diagnosis of tuberculosis were selected, and statistically significant risk factors for mortality were screened. A prognostic intervention model for death was then constructed, which was suitable for clinical applications. This study's findings have three significant advantages. First, primary TB patients account for 95% of new TB cases annually, and the model is highly targeted and applicable to a wide range of targets. Second, risk predictors of mortality prognosis are easily accessible and identifiable in the clinical setting. Third, internal model validation was performed; the model fit and predictive value were better, and the prediction method was simple and fast.

Methods

The retrospective case-control method included 1,809 in-hospital patients initially diagnosed with primary PTB at Hunan Chest Hospital from January 1, 2019, to December 31, 2019. In China, patients are received and treated at designated points and can obtain partial subsidies from health insurance (11). Hunan Chest Hospital is one of the provincial-level designated points for TB treatment in China, which has received and treated the most TB patients in Hunan province. Therefore, TB cases in Hunan Chest Hospital reflect the epidemiological trends and disease characteristics of TB throughout Hunan province.

Research objects

The research objects were included based on the following criteria. 1) The patients were diagnosed with primary PTB based on the Health Industry Standard of the People's Republic of China—Diagnosis for pulmonary tuberculosis (WS 288–2017) (12). 2) The patients never took anti-TB drugs or received irregular chemotherapy within one month after being diagnosed with primary PTB (13). 3) During the hospital stay and after discharge, the patients received standardized chemotherapy for initially diagnosed primary PTB according to the recommendations of WHO and Technical Specifications for TB Prevention and Control in China (14). 4) The patients were equal to or older than 18 years old with a hospital stay of more than three days. 5) Before a hospitalization, the patients never took cortin or drugs that affected the lab-tested albumin (ALB), lymphocyte count, and other indicators for the long term. 6) The patients were

not pregnant or lactating women. 7) The patients were not severe with HIV/AIDS, benign or malignant tumors, organ failure, or other diseases. 8) The clinical baseline data of patients were complete.

The study was conducted in accordance with the Declaration of Helsinki. As this study was based on retrospective research of patient data from a case management system, with visa-free informed consent for ethical approvals, and oral knowledge with respondents during telephone surveys with respondents. This visa-free informed consent for ethical approvals was approved by the Nursing and Behavioral Medicine Research Ethics Review Committee, Xiangya Nursing School of Central South University (ID: E2022104).

Data collection

This study collected data on in-hospital PTB patients from the case management system in Hunan Chest Hospital, including general demographic data (gender, age, marital status, type of health insurance, smoking history, drinking history, and dust exposure history), in-hospital comorbidity data [hypertension, diabetes, chronic gastritis, and coronary heart disease (CHD)], clinic-related data, and experimental parameters [height, weight, ALB, lymphocyte count, creatinine, cholinesterase (CHE), total cholesterol, C-reactive protein (CRP), hemoglobin (Hb), and platelet (PLT)]. The above data are from the first week of admission of patients initially diagnosed with primary PTB. Smoking no less than 20 cigarettes per week was considered a smoking history. Drinking no less than five times or 500 mL weekly was considered to have a drinking history. Exposure to an extremely dusty environment of no less than five times was considered to have a dust exposure history. In-hospital comorbidity data were obtained from the chief complaints of patients, which is consistent with the review results after admission to the hospital. For reflecting the nutritional status of research objects, this study converted the height and weight into the body mass index (BMI) according to *Medical Nutrition Treatment of Overweight/Obesity in China (2021)*, where BMI values less than 18.5 kg/m² are considered underweight, BMI values from 18.5 to 24.99 kg/m² are normal weight. BMI values > 25 kg/m² were overweight or obese (15, 16).

This study obtained follow-up data from the research subjects and understood patient death on a phone visit from September 1, 2022, to September 31, 2022. The outcomes were collected from the first hospitalized treatment upon initial diagnosis of primary PTB to the end of the phone visit, the average duration of which was three years. According to WHO classification standards, this study classified the treatment results of research subjects into non-survivor group (died) and survivor group (cured, drug-resistant, and relapsing) (17).

Statistical analysis

R software V4.2.2 (<http://www.R-project>) was used for data input and statistical analysis. Continuous variables were normally distributed and described as mean and standard deviation (SD), whereas categorical variables were expressed as frequency percentages. The confidence interval (CI) was 95% ($\alpha = 0.05$), and $p < 0.05$ (bilateral) is statistically significant. The *t*-test was conducted to compare the continuous variables with the research results, and *chi-square* (χ^2) test was adopted to compare the

categorized variables with research results. Binary logistic regression was used for univariate analysis, and backward stepwise logistic regression was used for multivariate analysis to screen for statistically significant prognostic risk factors for patients initially diagnosed with primary PTB. R software was used to construct the nomogram prediction model based on independent risk factors in the training set and to validate the constructed model using the validation set.

Results

Characteristics of research objects

This study included 1,809 in-hospital patients initially diagnosed with primary PTB who were screened, as presented in Fig. 1. The research objects were randomly split into a training set (n = 1449) and a validation set (n = 360) at a ratio of 8:2 and a random seed of 1314.

Among 1,809 research subjects, 83 patients (4.6%) died within three years of treatment, including 72 patients (4.9%) in the training set and 11 patients (3.1%) in the validation set. In this study, 22 variables were analyzed, the results of which were as follows. 1) The average age of the research subjects was 48 years. 2) The number of male patients (64%) was higher than that of female patients (37%). 3) Smokers (65.2%) and drinkers (76.2%) accounted for relatively high proportions. 4) Patients with comorbidities accounted for 25.5%, including 8.9% hypertension, 10.6% diabetes, 2.9% HBV, 5.7% chronic gastritis, and 5.7% CHD. 5) Bachelordom represented 24.6% of the participants. 6) Patients without health insurance accounted for 13.9% of the patients. 7) Underweight patients accounted for 24.5%, and overweight patients accounted for 9.3%, for details about the demographic variables and clinical characteristics of the research subjects (Table 1).

Table 1

Baseline characteristics of included in-hospital patients initially dragonized with primary PTB.

Variable	Total cohort (n = 1809)	Training set (n = 1449)	Validation set (n = 360)
	number (percentage)	number (percentage)	number (percentage)
Treatment outcomes			
Survivors	1726 (95.4%)	1377 (95.1%)	348 (96.9%)
Non-survivors	83 (4.6%)	72 (4.9%)	12 (3.1%)
Gender			
Male	1157 (64.0%)	942 (65.0%)	215 (59.7%)
Female	652 (36.0%)	507 (35.0%)	145 (40.3%)
Smoking			
No	1179 (65.2%)	947 (65.4%)	232 (64.4%)
Yes	630 (34.8%)	502 (34.6%)	128 (35.6%)
Drinking			
No	1378 (76.2%)	1107 (76.4%)	271 (75.3%)
Yes	431 (23.8%)	342 (23.6%)	89 (24.7%)
Dust exposure			
No	1688(93.3%)	1358 (93.7%)	33 (91.7%)
Yes	121 (6.7%)	91 (6.3%)	30 (8.3%)
Hypertension			
No	1648(91.1%)	1319 (91.0%)	329 (91.4%)
Yes	161 (8.9%)	130 (9.0%)	31 (8.6%)
Diabetes			
No	1618 (89.4%)	1304 (90.0%)	314 (87.2%)
Yes	191 (10.6%)	145 (10.0%)	46 (12.8%)
Hepatitis B virus (HBV)			
No	1756 (97.1%)	1406 (97.0%)	350 (97.2%)
Yes	53 (2.9%)	43 (3.0%)	10 (2.8%)
Gastritis			

Variable	Total cohort (n = 1809)	Training set (n = 1449)	Validation set (n = 360)
	number (percentage)	number (percentage)	number (percentage)
No	1706 (94.3%)	1369 (94.5%)	337 (93.6%)
Yes	103 (5.7%)	80 (5.5%)	23 (6.4%)
Coronary heart disease (CHD)			
No	1706 (94.3%)	1369 (94.5%)	337 (93.6%)
Yes	103 (5.7%)	80 (5.5%)	23 (6.4%)
Comorbidity			
No	1348 (74.5%)	1087 (75.0%)	261 (72.5%)
Yes	461 (25.5%)	362 (25.0%)	99 (27.5%)
Bachelordom			
No	445 (24.6%)	361 (24.9%)	84 (23.3%)
Yes	1364 (75.4%)	1088 (75.1%)	276 (76.7%)
Health insurance			
No	251 (13.9%)	199 (13.7%)	52 (14.4%)
Yes	1558 (86.1%)	1250 (86.3%)	308 (85.6%)
BMI (kg/m ²)			
Normal	1196 (66.1%)	937 (64.7%)	259 (71.9%)
Underweight	444 (24.5%)	372 (25.7%)	72 (20%)
Overweight	169 (9.3%)	140 (9.6%)	29 (8.1%)
Age, years	47.59 ± 17.65	47.44 ± 17.62	48.18 ± 16.55
Albumin (ALB) (g/L)	40.90 ± 5.61	40.95 ± 5.55	40.74 ± 5.22
Creatinine (Cr) (µmol/L)	69.26 ± 25.31	69.43 ± 24.93	68.60 ± 25.16
Cholinesterase (CHE) (U/L)	7964.37 ± 2453.63	7960.79 ± 2426.87	7981.94 ± 2479.55
Total cholesterol (TC) (mmol/L)	4.29 ± 1.02	4.28 ± 1.00	4.32 ± 0.99
C-reactive protein (CRP) (mg/L)	25.99 ± 43.04	25.85 ± 43.78	26.56 ± 38.18

Variable	Total cohort (n = 1809)	Training set (n = 1449)	Validation set (n = 360)
	number (percentage)	number (percentage)	number (percentage)
Lymphocyte count (Lym) (*10 ⁹ /L)	1.60 ± 0.66	1.59 ± 0.67	1.63 ± 0.65
Hemoglobin (Hb) (g/L)	122.32 ± 17.66	122.40 ± 17.42	122.20 ± 18.14
Platelet count (PLT) (*10 ⁹ /L)	253.73 ± 91.58	255.70 ± 91.40	245.80 ± 88.97

Univariate analysis was performed for 1,448 cases in the training set. The results demonstrated that 13 variables, including sex, smoking, drinking, hypertension, HBV, comorbidity, BMI, age, ALB, CHE, CRP, lymphocyte count, and Hb, were statistically different between the survivor and non-survivor group ($p < 0.05$), as illustrated in Table 2.

Table 2

Demographics and clinical characteristics of the population of in-hospital patients initially dragonized with primary PTB

Variable	Total (n = 1449)	Survivors (n = 1377)	Non-survivors (n = 72)	P value
		number (percentage)	number (percentage)	
Gender				
Male	942	884 (64.2%)	58 (80.6%)	0.007
Female	507	493 (35.8%)	14 (19.4%)	
Smoking				
No	947	914 (66.4%)	33 (45.8%)	0.001
Yes	502	463 (33.6%)	39 (54.2%)	
Drinking				
No	1107	1065 (77.3%)	42 (58.3%)	0.001
Yes	342	312 (22.7%)	30 (41.7%)	
Dust exposure				
No	1358	1291 (93.8%)	67 (93.1%)	1.000
Yes	91	86 (6.2%)	5 (6.9%)	
Hypertension				
No	1319	1259 (91.4%)	60 (83.3%)	0.033
Yes	130	118 (8.6%)	12 (16.7%)	
Diabetes				
No	1304	1244 (90.3%)	60 (83.3%)	0.084
Yes	145	133 (9.7%)	12 (16.7%)	
Hepatitis B virus (HBV)				
No	1406	1340 (97.3%)	66 (91.7%)	0.017
Yes	43	37 (2.7%)	6 (8.3%)	
Gastritis				
No	1369	1300 (94.4%)	69 (95.8%)	0.801
Yes	80	77 (5.6%)	3 (4.2%)	

Variable	Total (n = 1449)	Survivors (n = 1377)	Non-survivors (n = 72)	P value
		number (percentage)	number (percentage)	
Coronary heart disease (CHD)				
No	1369	1300 (94.4%)	69 (95.8%)	0.801
Yes	80	77 (5.6%)	3 (4.2%)	
Comorbidity				
No	1087	1045 (75.9%)	42 (58.3%)	0.001
Yes	362	332 (24.1%)	30 (41.7%)	
Bachelordom				
No	361	348 (25.3%)	13 (18.1%)	0.215
Yes	1088	1029 (74.7%)	59 (81.9%)	
Health insurance				
No	199	185 (13.4%)	14 (19.4%)	0.205
Yes	1250	1192 (86.6%)	58 (80.6%)	
BMI (kg/m²)				
Normal	937	905 (65.7%)	32 (44.4%)	< .001
Underweight	372	337 (24.5%)	35 (48.6%)	
Overweight	140	135 (9.8%)	5 (6.9%)	
Age, years	47.4 ± 17.6	46.4 ± 17.3	67.2 ± 12.5	< .001
Albumin (ALB) (g/L)	40.9 ± 5.6	41.3 ± 5.4	35.0 ± 5.4	< .001
Creatinine (Cr) (μmol/L)	69.4 ± 24.9	69.2 ± 24.1	73.4 ± 32.0	0.273
Cholinesterase (CHE) (U/L)	7960.8 ± 2426.9	8066.1 ± 2422.0	5933.6 ± 2745.4	< .001
Total cholesterol (TC) (mmol/L)	4.3 ± 1.0	4.3 ± 1.0	4.2 ± 1.4	0.438
C-reactive protein (CRP) (mg/L)	25.9 ± 43.8	24.9 ± 41.8	43.4 ± 51.6	0.004
Lymphocyte count (Lym) (*10⁹/L)	1.6 ± 0.7	1.6 ± 0.6	1.3 ± 0.8	0.002
Hemoglobin (Hb) (g/L)	122.4 ± 17.4	123.1 ± 17.3	108.1 ± 17.2	< .001

Variable	Total (n = 1449)	Survivors (n = 1377)	Non-survivors (n = 72)	P value
		number (percentage)	number (percentage)	
Platelet count (PLT) (*10 ⁹ /L)	255.7 ± 91.4	254.4 ± 91.2	280.2 ± 126.8	0.093

Risk predictors for in-hospital patients initially diagnosed with primary PTB

Statistically significant variables were included in multivariate binary logistic regression analysis. The results in Fig. 2 indicate that drinking ($p = 0.03$; OR = 1.97; 95% CI: 1.07–3.60), HBV ($p = 0.02$; OR = 3.58; 95% CI: 1.14–9.95), BMI ($p = 0.04$; OR = 1.79; 95% CI: 1.01–3.16), age ($p = 0.001$; OR = 1.08; 95% CI: 1.06–1.11), ALB ($p = 0.003$; OR = 0.90; 95% CI: 0.84–0.96), and Hb ($p = 0.035$; OR = 0.98; 95% CI: 0.96–1.00) were independent risk predictors for death ($p < 0.05$) in the prognosis of in-hospital patients initially diagnosed with primary PTB (Fig. 2).

With drinking, HBV, BMI, age, ALB, and Hb included in the prognosis of in-hospital patients initially diagnosed with primary PTB as independent risk predictors for death, R software established the nomogram prognostic model for mortality prediction to obtain the points corresponding to every predictor. The sum of these points was considered the death probability of in-hospital patients initially diagnosed with primary PTB, as described in Fig. 3.

The nomogram model was adopted to obtain the points corresponding to every predictor and then calculate the total points considered as the death probability of in-hospital patients initially diagnosed with primary PTB. The total number of points is then calculated.

The area under the receiver operating characteristic (ROC) curve (AUC) was used to evaluate the predictive accuracy of the constructed nomogram model. In the training set, AUC of the model was 0.881, with a sensitivity of 84.7% and specificity of 77.7% (Fig. 4). In the validation set, AUC of the model was 0.907 (Fig. 4). Consequently, the internal and external validation results were relatively consistent (Fig. 4). R software was adopted to establish the calibration curves (1,000 bootstrapping samples) of the training set (Fig. 5A) and the validation set (Fig. 5B), where X-axis represents the predicted death probability of in-hospital patients initially diagnosed with primary PTB and Y-axis represents the observed death probability of in-hospital patients initially diagnosed with primary PTB. The calibration curves determined that the model effectively fitted the actual situation and had a high predictive value. Moreover, R software was used to draw the clinical decision curves for the training set (Fig. 6A) and validation set (Fig. 6B), the area of which was greater than 0, indicating that the model had high clinical effectiveness.

Discussion

Mycobacterium tuberculosis (MTB) infection is a dynamic process in which the systemic immune response is passively activated. The damaging immune and inflammatory responses of human tissues

are subject to the infection site, infection cycle, and bacterial aggregation (18). Based on the *Health Industry Standard of the People's Republic of China—Classification of Tuberculosis (WS 196–2017)*, PTB is categorized into primary PTB, hematogenous PTB, secondary PTB, tuberculous pleurisy, and EPTB. From the perspective of histology, the organs of patients with any of the five types of PTB generate granulomatous inflammation (2). However, because of different immune and inflammatory responses, there will be a significant difference in aspects such as imaging, clinical course, test indicators, and therapeutic scheme (19, 20). Previous studies generally selected a wide range of research objects to establish TB-related prediction models, especially prognosis prediction models, reducing the practicability of these models in the clinic (21–24).

Numerous studies have confirmed that different types and courses of PTB have different immune mechanisms, treatment outcomes, outcome probabilities, and risk factors (25–30). Based on this, this study accurately selected the patients initially diagnosed with primary PTB as the research objects to construct the prediction model and selected the predictors by combining the sensitive indicators and commonly used clinical indicators from previous relevant studies. These predictors can be routinely acquired in the clinical setting. Therefore, the constructed nomogram prediction model is highly operable to quickly predict the outcomes of patients initially diagnosed with primary PTB for accurate and targeted intervention in the clinic.

The selection of a follow-up period was a peculiarity in this study because the survival cycle of PTB patients varies greatly from country to country. A previous study on 8,240 TB patients in Andhra Pradesh, southern India, demonstrated that the death frequency in the four-year follow-up period was even (31). Another previous study on time-related death factors of the 604 TB patients in southwestern Ethiopia indicated that the average time to death was five months (32). A survival analysis of TB deaths from the Tuberculosis Disease and Mortality Surveillance Information System in Zhejiang province, China, concluded that 71.1% of 283 deaths caused by TB occurred within three years of diagnosis and treatment (33). The main reason for this difference is that TB is closely related to body nutrition as a type of immune disease, and individual nutritional status is closely related to individual economic and socioeconomic status (34–36). Therefore, we discovered that the results of a prognostic model are different for TB patients in different regions. Therefore, accurately matching the characteristics of the clinical application population is the first step toward constructing a prognostic model. The regions of patients with TB and their influence on their survival cycle by region must be considered. Combining case studies on PTB patients in China and the estimated probability of TB death in China, this study found that over the 3-year follow-up period, 4.89% of patients who had been initially diagnosed with primary PTB died. This indicated that the selection of the follow-up period reduced the bias error and greatly increased the clinical applicability of the model.

Compared with the treatment outcome prediction model for adult patients with the same type of PTB, age and BMI are common predictive risk factors affecting treatment outcomes. On the one hand, older PTB patients have a higher death possibility than younger patients (24). According to the statistical data in PTB case reports (2006–2020) from the Tuberculosis Information Management System (TBIMS) in

China, PTB incidence and mortality in China increased with age (37). On the other hand, undernutrition is a risk factor for immunodeficiency and an important risk factor for PTB incidence and adverse outcomes (38). BMI is the macro indicator of human nutritional status, and ALB and Hb are the biomarkers to reflect human nutritional status (39). Therefore, BMI, ALB, and Hb are mutually the cause and effect, also reflected in TB patients in China (40–42). Therefore, this study considered age, BMI, ALB, and Hb as the core and easy-to-quantify indicators in the prediction model. These are important monitoring indicators for quantifying the intervention effects in high-risk patients initially diagnosed with primary PTB.

In demographic characteristics, drinking and HBV infection are also important risk predictors for death in the prognosis of in-hospital patients initially diagnosed with primary PTB because chronic alcohol and HBV reduce the expression of immune proteins in infected patients, further decreasing their immune function (43). HBV infection cycle and the amount or frequency of drinking are positively correlated with TB susceptibility, indicating that both drinking and HBV infection are high-risk factors for the death of TB patients (44–47). In the later stage of standard anti-TB chemotherapy, as prescribed, the anti-TB drugs such as isoniazid (INH), rifampicin (RIF), and pyrazinamide (PZA) have hepatotoxic side effects for patients initially diagnosed with primary PTB. Drinking and HBV infection can exacerbate liver damage and increase fatality (48, 49). Accordingly, to reduce the prognostic mortality of patients initially diagnosed with primary PTB, it is necessary to conduct routine lifestyle surveys and HBV screening before treatment to facilitate early clinical recognition, adjustment of therapeutic schemes, and disease management, further improving anti-TB treatment and reducing death outcomes.

Limitations of the study

One limitation of this study was that the evidence level of this retrospective study was relatively inferior. Second, the clinically relevant data and experimental parameters adopted in this study are only part of the clinical data of the patients, and other meaningful data may not be included. Further studies are required to widen the scope of these variables.

Conclusion

The constructed nomogram prognostic model verified that drinking, HBV, BMI, age, ALB, and Hb were the six independent risk predictors of death in hospital patients with primary PTB who were initially diagnosed. Consequently, the six risk predictors of in-hospital patients initially diagnosed with primary PTB must be screened, recognized, and intervened as early as possible to reduce patient mortality.

Abbreviations

TB
Tuberculosis
PTB
Pulmonary Tuberculosis

EPTB
Extrapulmonary TB
MTB
Mycobacterium Tuberculosis
HIV
Human Immunodeficiency Virus
AIDS
Acquired Immunodeficiency Syndrome
BMI
Body Mass Index
BV
Hepatitis B Virus
ALB
Albumin
Hb
Hemoglobin
CHD
Coronary Heart Disease
CHE
Cholinesterase
CRP
C-reactive Protein
PLT
Platelet
SD
Standard Deviation
AUC
Area Under the Curve
CI
Confidence Interval.

Declarations

Ethics approval and consent to participate:

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by The Nursing and Behavioral Medicine Research Ethics Review Committee, Xiangya Nursing School of Central South University (ID: E2022104). The Nursing and Behavioral Medicine Research Ethics Review Committee, Xiangya Nursing School of Central South University exempted the acquisition of informed consent because this was a retrospective study. Patients' data confidentiality was fully respected during data collection and the preparation of the manuscript.

Consent for publication:

Not applicable.

Availability of data and materials:

The data that support the findings of this study are not openly available due to clinical data, and are available from the corresponding author upon reasonable request.

Competing interests:

The authors declare that they have no competing interests.

Ethics approval and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations or Declaration of Helsinki

Funding:

The Science and Technology Program Foundation of Changsha (No. kq2004169); the Natural Science Foundation of Hunan Province (No. 2020JJ8044); the Scientific Research Funds of Health Commission of Hunan Province (No. 20201936).

Authors' contributions:

Dan Li and Siyuan Tang contributed to the conception of the study protocol and study design. Dan Li wrote the first draft of the manuscript. All authors contributed to subsequent drafts and gave final approval of the version to be published

Acknowledgements:

We are grateful to Hunan Chest Hospital for its approval to search its clinical database.

Authors' information:

¹Xiangya Nursing School, Central South University, Changsha, Hunan, China;

²Hunan Open University, Changsha, Hunan, China;

³Hunan Chest Hospital, Changsha, Hunan, China;

⁴ Department of Drug Clinical Trial Institutions, The Affiliated Changsha Central Hospital, Hengyang Medical School, University of South China, Changsha, Hunan, China;

⁵School of Public Health, University of South China, Hengyang, China.

Additional Files: none

References

1. Dheda K, Perumal T, Moultrie H, Perumal R, Esmail A, Scott AJ, et al. The intersecting pandemics of tuberculosis and COVID-19: population-level and patient-level impact, clinical presentation, and corrective interventions. *The Lancet Respiratory medicine*. 2022;10(6):603–22.
2. Acharya B, Acharya A, Gautam S, Ghimire SP, Mishra G, Parajuli N, et al. Advances in diagnosis of Tuberculosis: an update into molecular diagnosis of *Mycobacterium tuberculosis*. *Mol Biol Rep*. 2020;47(5):4065–75.
3. WHO. Global Tuberculosis Report 2022 Factsheet. 2022.
4. Chakaya JPE, Nantanda R, Mungai BN, Migliori GB, Amanullah F, Lungu P, Ntoumi F, Kumarasamy N, Maeurer M, Zumla A. The WHO Global Tuberculosis 2021 Report - not so good news and turning the tide back to End TB. *Int J Infect Dis*. 2022;Nov;124.
5. Kheirandish M, Catanzaro D, Crudu V, Zhang S. Integrating landmark modeling framework and machine learning algorithms for dynamic prediction of tuberculosis treatment outcomes. *J Am Med Inf Association: JAMIA*. 2022;29(5):900–8.
6. Sauer CM, Sasson D, Paik KE, McCague N, Celi LA, Sánchez Fernández I, et al. Feature selection and prediction of treatment failure in tuberculosis. *PLoS ONE*. 2018;13(11):e0207491.
7. Mohidem NA, Osman M, Muharam FM, Elias SM, Shaharudin R, Hashim Z. Prediction of tuberculosis cases based on sociodemographic and environmental factors in gombak, Selangor, Malaysia: A comparative assessment of multiple linear regression and artificial neural network models. *Int J mycobacteriology*. 2021;10(4):442–56.
8. Liu K, Li T, Vongpradith A, Wang F, Peng Y, Wang W, et al. Identification and Prediction of Tuberculosis in Eastern China: Analyses from 10-year Population-based Notification Data in Zhejiang Province, China. *Sci Rep*. 2020;10(1):7425.
9. Jamal S, Khubaib M, Gangwar R, Grover S, Grover A, Hasnain SE. Artificial Intelligence and Machine learning based prediction of resistant and susceptible mutations in *Mycobacterium tuberculosis*. *Sci Rep*. 2020;10(1):5487.
10. Li JYT, Hong C, Yang Z, Wu L, Gao Q, Yang H, Tan W. Whole-Genome Sequencing for Resistance Level Prediction in Multidrug-Resistant Tuberculosis. *Microbiol Spectr*. 2022;022 Jun 29;10(3):e0271421.
11. Liu X, Lin KH, Li YH, Jiang JN, Zhong ZD, Xiong YB, et al. Impacts of Medical Security Level on Treatment Outcomes of Drug-Resistant Tuberculosis: Evidence from Wuhan City, China. *Patient Prefer Adherence*. 2022;16:3341–55.
12. China NHaFPCotPsRo. National Health and Family Planning Commission of the People's Republic of China. 2017. p. 2017 11 009.

13. CMA. Tuberculosis Branch of Chinese Medical Association Tuberculosis Diagnosis and Treatment Guidelines. Chinese Journal of Tuberculosis and Respiratory; 2001.
14. WHO. Treatment of Tuberculosis Guidelines. 4th edition. 2010.
15. Sahile Z, Tezera R, Haile Mariam D, Collins J, Ali JH. Nutritional status and TB treatment outcomes in Addis Ababa, Ethiopia: An ambi-directional cohort study. PLoS ONE. 2021;16(3):e0247945.
16. Chen C, Lu FC, Department of Disease Control Ministry of Health PRC. The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed Environ Sci. 2004;17 Suppl:1–36.
17. WHO. Definitions and reporting framework for tuberculosis – 2013 revision. 2014.
18. Natarajan A, Beena PM, Devnikar AV, Mali S. A systemic review on tuberculosis. Indian J Tuberc. 2020;67(3):295–311.
19. Hunter RL. The Pathogenesis of Tuberculosis: The Early Infiltrate of Post-primary (Adult Pulmonary) Tuberculosis: A Distinct Disease Entity. Front Immunol. 2018;9:2108.
20. Cohen SB, Gern BH, Urdahl KB. The Tuberculous Granuloma and Preexisting Immunity. Annu Rev Immunol. 2022;40:589–614.
21. Tangri NKD. Toward a modern ern in clinical prediction:the TRIPOD sintement for reporting prediction models. Ame Kidney Dis. 2015;65(4):530–3.
22. Peetluk LS, Ridolfi FM, Rebeiro PF, Liu D, Rolla VC, Sterling TR. Systematic review of prediction models for pulmonary tuberculosis treatment outcomes in adults. BMJ open. 2021;11(3):e044687.
23. Kuan MM. Applying SARIMA, ETS, and hybrid models for prediction of tuberculosis incidence rate in Taiwan. PeerJ. 2022;10:e13117.
24. Bert-Dulanto A, Alarcón-Braga EA, Castillo-Soto A, Escalante-Kanashiro R. Predicting mortality in pulmonary tuberculosis: A systematic review of prognostic models. Indian J Tuberc. 2022;69(4):432–40.
25. Koo HK, Min J, Kim HW, Lee J, Kim JS, Park JS, et al. Prediction of treatment failure and compliance in patients with tuberculosis. BMC Infect Dis. 2020;20(1):622.
26. Peetluk LS, Rebeiro PF, Ridolfi FM, Andrade BB, Cordeiro-Santos M, Kritski A, et al. A Clinical Prediction Model for Unsuccessful Pulmonary Tuberculosis Treatment Outcomes. Clin Infect Dis. 2022;74(6):973–82.
27. Li R, Nordio F, Huang CC, Contreras C, Calderon R, Yataco R, et al. Two Clinical Prediction Tools to Improve Tuberculosis Contact Investigation. Clin Infect diseases: official publication Infect Dis Soc Am. 2020;71(8):e338–e50.
28. Zhao D, Zhang H, Cao Q, Wang Z, He S, Zhou M, et al. The research of ARIMA, GM(1,1), and LSTM models for prediction of TB cases in China. PLoS ONE. 2022;17(2):e0262734.
29. Ali MH, Khan DM, Jamal K, Ahmad Z, Manzoor S, Khan Z. Prediction of Multidrug-Resistant Tuberculosis Using Machine Learning Algorithms in SWAT, Pakistan. J Healthc Eng. 2021;2021:2567080.

30. Williams V, Vos A, Otwombe K, Grobbee DE, Klipstein-Grobusch K. Epidemiology and Control of diabetes - tuberculosis comorbidity in Eswatini: protocol for the prospective study of tuberculosis patients on predictive factors, treatment outcomes and patient management practices. *BMJ Open*. 2022;12(6):e059254.
31. Ramakrishnan J, Sarkar S, Chinnakali P, Lakshminarayanan S, Sahu SK, Reshma A, et al. Risk factors for death during treatment in pulmonary tuberculosis patients in South India: A cohort study. *Indian J Tuberc*. 2021;68(1):32–9.
32. Jabir YN, Aniley TT, Bacha RH, Debusho LK, Chikako TU, Hagan JE Jr et al. Time to Death and Associated Factors among Tuberculosis Patients in South West Ethiopia: Application of Shared Frailty Model. *Diseases (Basel, Switzerland)*. 2022;10(3).
33. Liu K, Ai L, Pan J, Fei F, Chen S, Zhang Y, et al. Survival Analysis and Associated Factors for Pulmonary Tuberculosis Death: Evidence from the Information System of Tuberculosis Disease and Mortality Surveillance in China. *Risk Manage Healthc policy*. 2022;15:1167–78.
34. Guo X, Yang Y, Zhang B, Cai J, Hu Y, Ma A. Nutrition and clinical manifestations of pulmonary tuberculosis: A cross-sectional study in Shandong province, China. *Asia Pac J Clin Nutr*. 2022;31(1):41–8.
35. Sinha P, Lakshminarayanan SL, Cintron C, Narasimhan PB, Locks LM, Kulatilaka N, et al. Nutritional Supplementation Would Be Cost-Effective for Reducing Tuberculosis Incidence and Mortality in India: The Ration Optimization to Impede Tuberculosis (ROTI-TB) Model. *Clin Infect diseases: official publication Infect Dis Soc Am*. 2022;75(4):577–85.
36. Muttamba W, Tumwebaze R, Mugenyi L, Batte C, Sekibira R, Nkolo A, et al. Households experiencing catastrophic costs due to tuberculosis in Uganda: magnitude and cost drivers. *BMC Public Health*. 2020;20(1):1409.
37. Dong Z, Wang QQ, Yu SC, Huang F, Liu JJ, Yao HY, et al. Age-period-cohort analysis of pulmonary tuberculosis reported incidence, China, 2006–2020. *Infect Dis poverty*. 2022;11(1):85.
38. Ma L, Chen X, Gao M. Analysis on the Risk Factors of Malnutrition in Type 2 Diabetes Mellitus Patients with Pulmonary Tuberculosis. *Infect drug Resist*. 2022;15:7555–64.
39. Du ZX, Chang FQ, Wang ZJ, Zhou DM, Li Y, Yang JH. A risk prediction model for acute kidney injury in patients with pulmonary tuberculosis during anti-tuberculosis treatment. *Ren Fail*. 2022;44(1):625–35.
40. Ashenafi S, Bekele A, Aseffa G, Amogne W, Kassa E, Aderaye G et al. Anemia Is a Strong Predictor of Wasting, Disease Severity, and Progression, in Clinical Tuberculosis (TB). *Nutrients*. 2022;14(16).
41. Kamruzzaman M. Is BMI associated with anemia and hemoglobin level of women and children in Bangladesh: A study with multiple statistical approaches. *PLoS ONE*. 2021;16(10):e0259116.
42. Jiang G, Du X, Zhu Y, Zhang M, Qin W, Xiong T, et al. Value of Postoperative Serum Albumin to Predict Postoperative Complication Severity in Spinal Tuberculosis. *Biomed Res Int*. 2022;2022:4946848.

43. Wigger GW, Khani D, Ahmed M, Sayegh L, Auld SC, Fan X, et al. Alcohol impairs recognition and uptake of Mycobacterium tuberculosis by suppressing toll-like receptor 2 expression. *Alcohol Clin Exp Res.* 2022;46(12):2214–24.
44. Imtiaz S, Shield KD, Roerecke M, Samokhvalov AV, Lönnroth K, Rehm J. Alcohol consumption as a risk factor for tuberculosis: meta-analyses and burden of disease. *The European respiratory journal.* 2017;50(1).
45. Chen J, Hubbard A, Bagley L, Shiao R, Wong RJ, Chitnis AS. Prevalence of Latent Tuberculosis Infection Among Persons with Chronic Hepatitis B Virus Infection: A Systematic Review and Meta-Analysis. *Dig Dis Sci.* 2022;67(6):2646–54.
46. Echazarreta A, Zerbini E, De Sandro J, Sáenz C, Yessi L, Saad R, et al. Tuberculosis and comorbidities in urban areas in Argentina. A gender and age perspective. *Biomedica: revista del Instituto Nacional de Salud.* 2018;38(2):180–8.
47. Kang W, Du J, Yang S, Yu J, Chen H, Liu J, et al. The prevalence and risks of major comorbidities among inpatients with pulmonary tuberculosis in China from a gender and age perspective: a large-scale multicenter observational study. *Eur J Clin Microbiol Infect diseases: official publication Eur Soc Clin Microbiol.* 2021;40(4):787–800.
48. Chou C, Veracruz N, Chitnis AS, Wong RJ. Risk of drug-induced liver injury in chronic hepatitis B and tuberculosis co-infection: A systematic review and meta-analysis. *J Viral Hepatitis.* 2022;29(12):1107–14.
49. Khan AF, Sajjad A, Mian DA, Tariq MM, Jadoon UK, Abbas M, et al. Co-infection With Hepatitis B in Tuberculosis Patients on Anti-tuberculosis Treatment and the Final Outcome. *Cureus.* 2021;13(4):e14433.

Figures

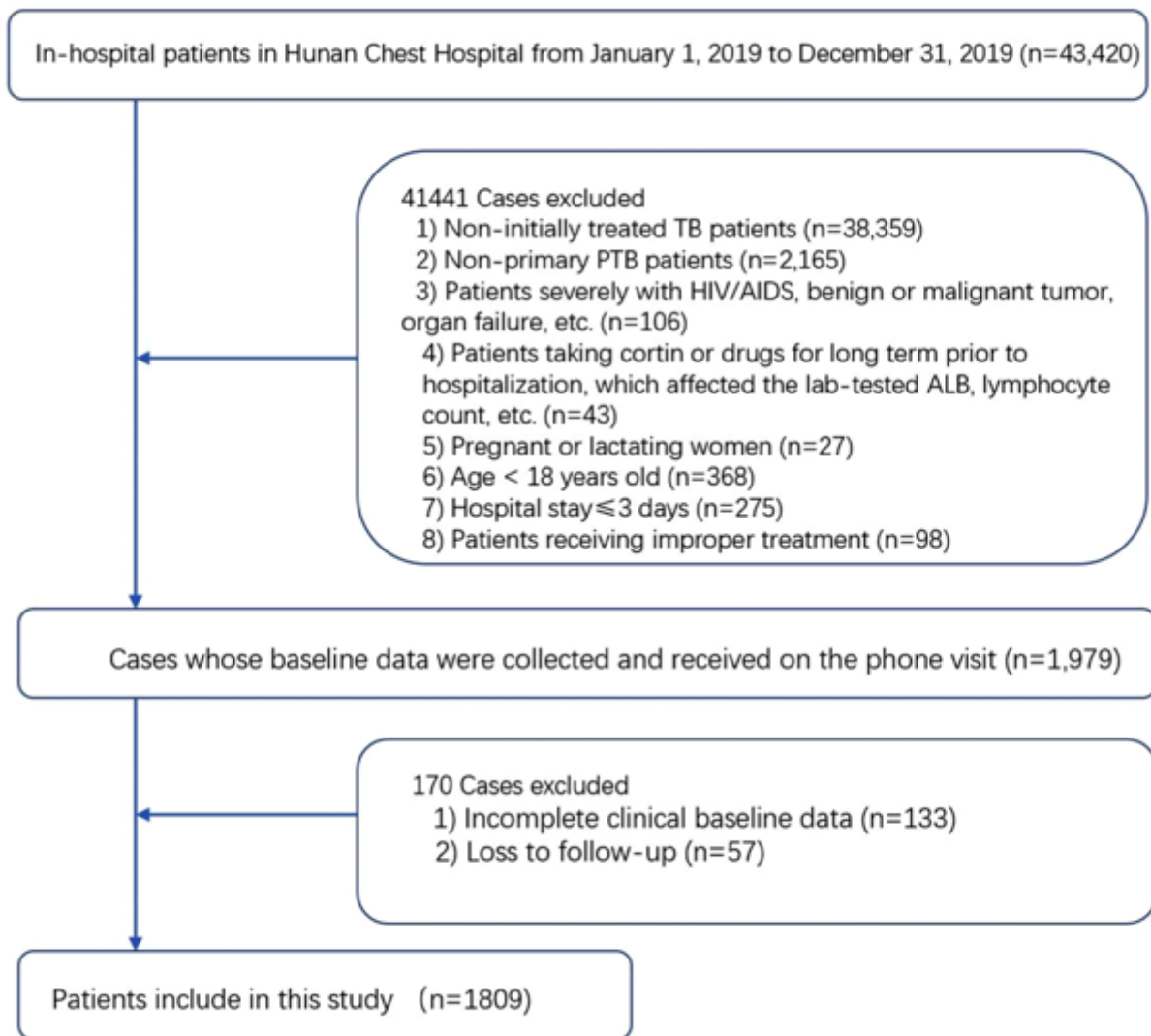


Figure 1

Study design. 1809 in-hospital patients initially diagnosed with primary PTB were enrolled in this study

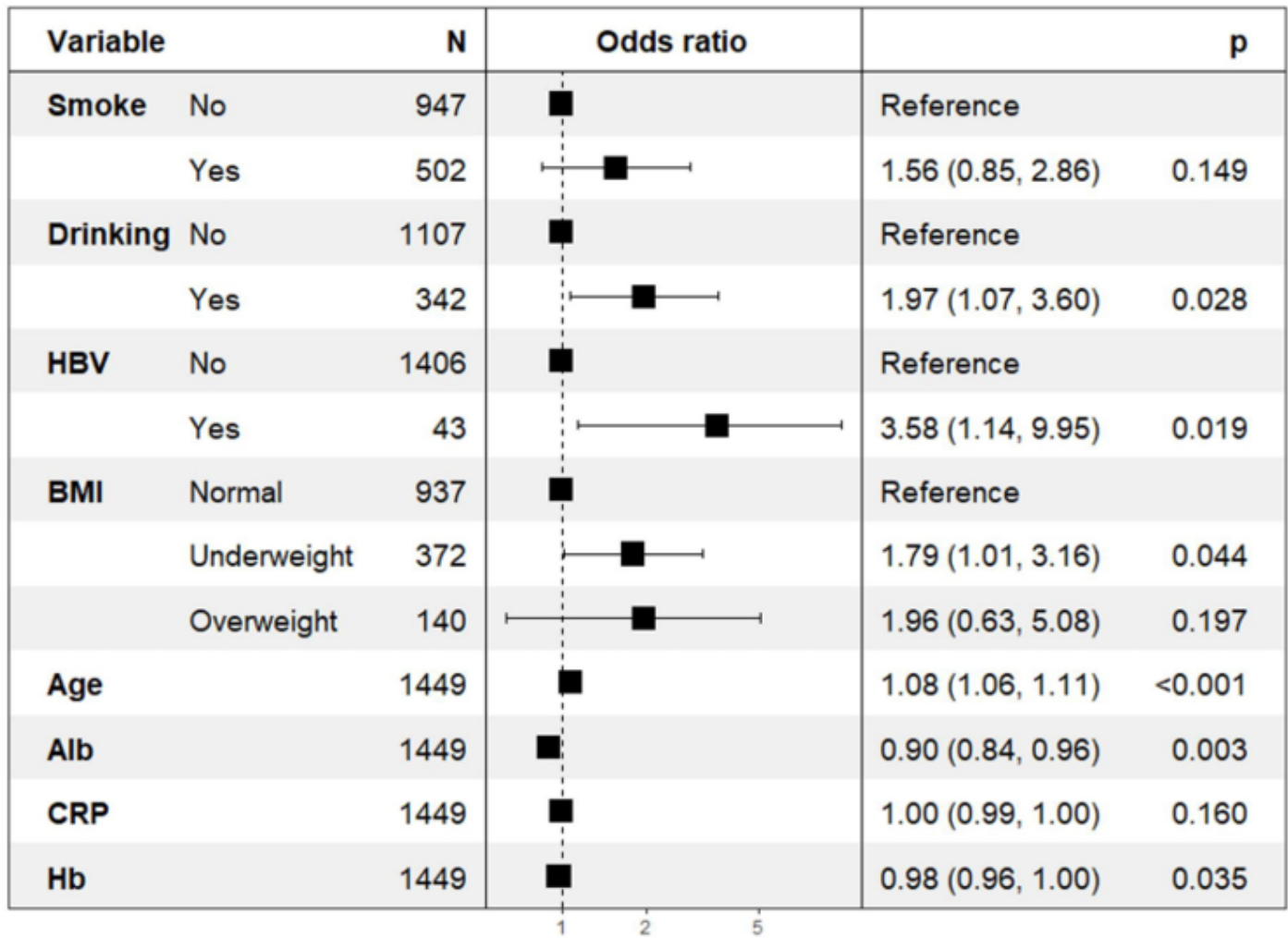


Figure 2

Backward logistic regression of the training set of in-hospital patients initially diagnosed with primary PTB

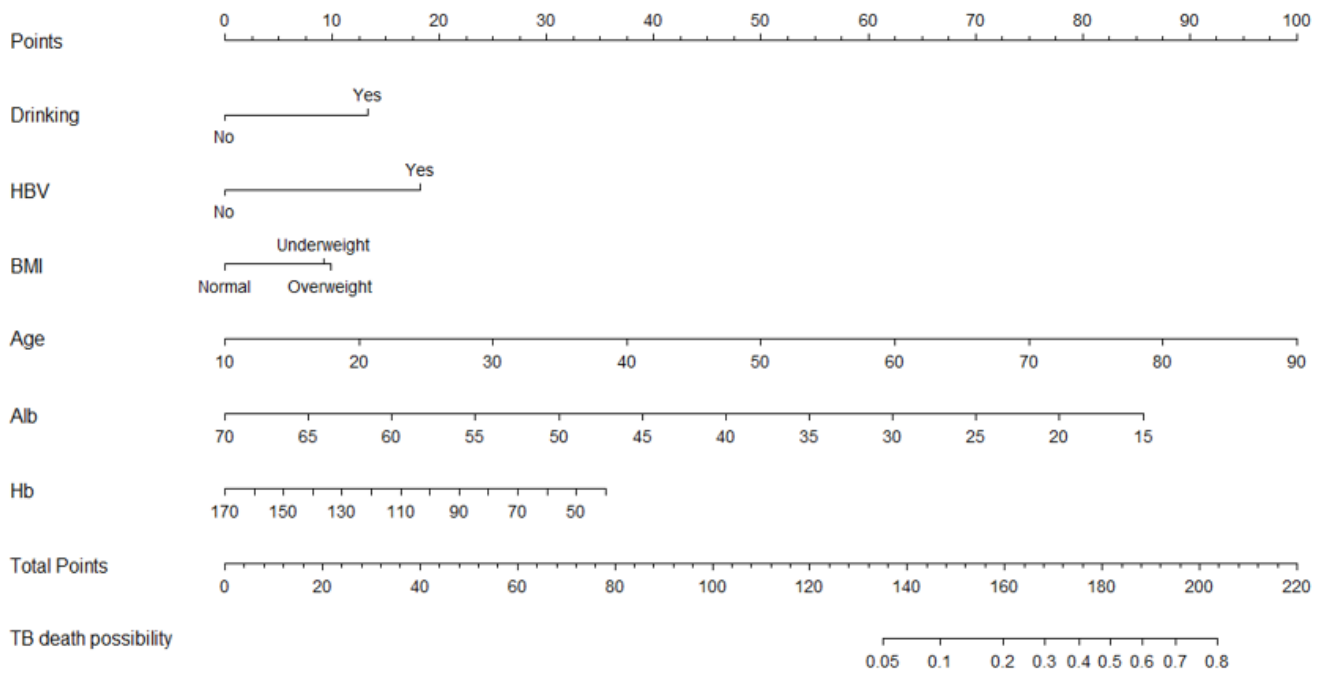


Figure 3

Nomogram to predict the outcome of patients initially diagnosed with primary PTB

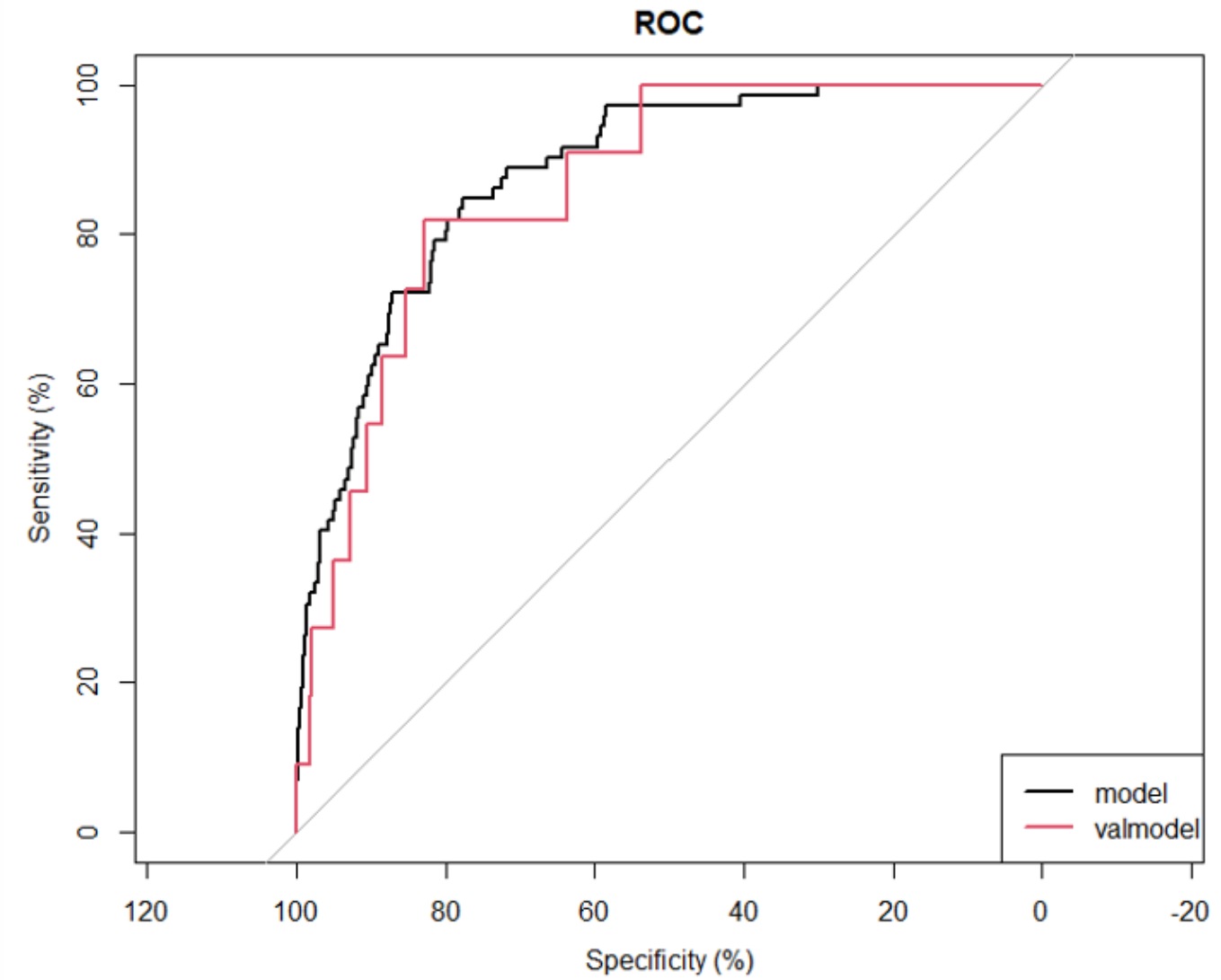
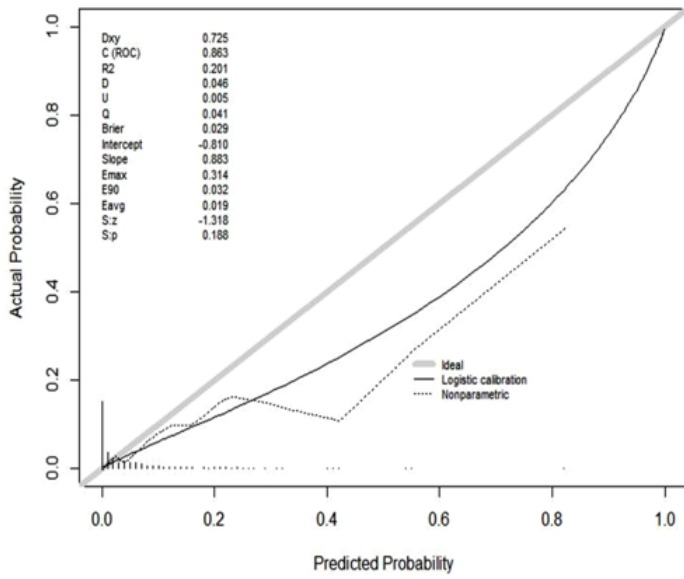


Figure 4

Calibration curves of the nomogram in training set and validation set

(A)



(B)

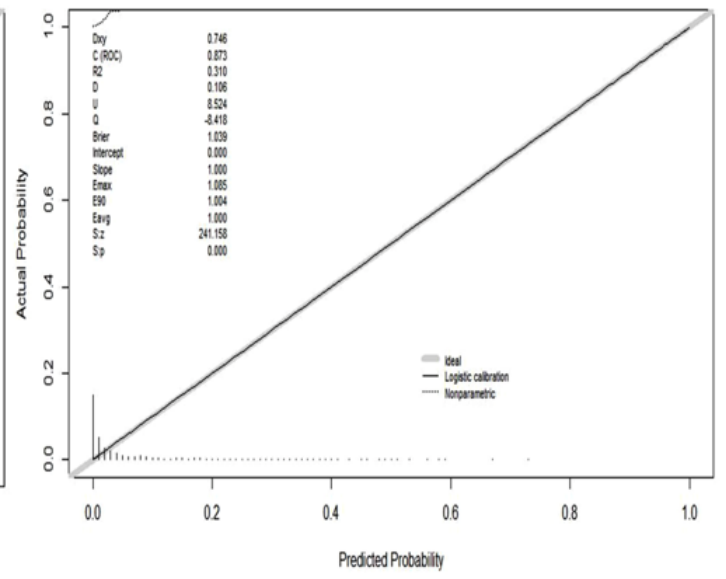
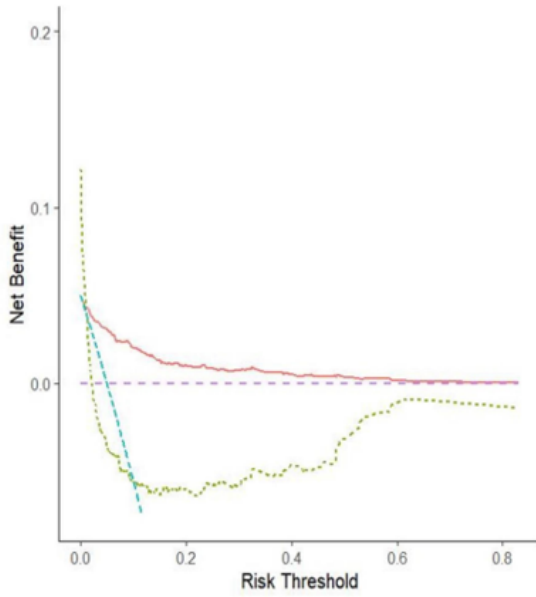


Figure 5

Calibration curves of the nomogram to predict death in training set(A) and validation set(B)

A



B

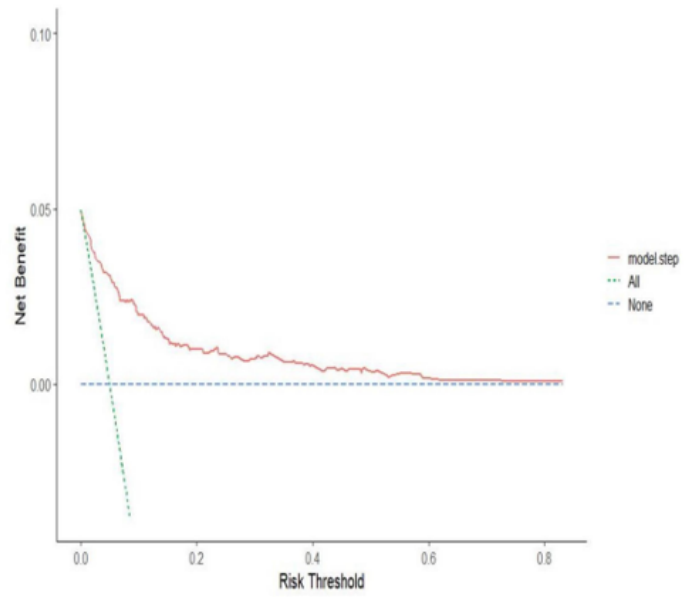


Figure 6

Decision cure analysis (DCA) for the nomogram in the training set(A) and validation set(B)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [AdditionalFile1.xlsx](#)