A predictive model for thirty-day mortality of fungemia in ICUs

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Abstract

Background: Few predictive models have been established to predict the risk of thirty-day mortality from fungemia. This study aims to create a nomogram to predict the 30-day mortality of fungemia in ICUs.

Methods: Data of ICU patients with fungemia from both the Medical Information Mart for Intensive Care (MIMIC-III) database and the Grade-III Class-A hospital in China were collected. The data extracted from the MIMIC-III database functioned as the training dataset, which was used to construct the predictive model for 30-day mortality risk in ICU patients with fungemia; the data from the hospital functioned as the validation dataset, which was used to validate the model. The predictive model for 30-day mortality risk in ICU patients with fungemia was then built based on R software. Such indicators as C-index and calibration curve were utilized to evaluate the prediction ability of the model. The data of ICU patients with fungemia from the hospital were used as the validation dataset to validate the model.

Results: Predictive models were constructed by age, international normalized ratio (INR), renal failure, liver disease, respiratory rate (RR), glucocorticoid therapy, antifungal therapy, and platelets. The C-index value of the models was 0.838 (95% CI: 0.79096-0.88504). Attested by the external validation results, the model has satisfactory predictive ability.

Conclusions: The 30-day mortality risk predictive model for ICU patients with fungemia constructed in this study has good predictive ability, and may hopefully provide a 30-day mortality risk screening tool for ICU patients with fungemia.

Introduction

Fungemia is a highly lethal disease, and Candida is the major pathogen[1].Candidemia can be defined as the presence of any species of Candida in the blood[2].Recently, because of the widespread use of active immunosuppressive therapy and increasing use of invasive devices, such as central venous catheters[3],the incidence of intensive care unit admission (ICU admission) has increased significantly among patients with fungemia[4].Candidemia is the fourth most common cause of nosocomial bloodstream infection (BSI) in the United States[5].The meta-analysis by P. Koehler et al.[6]shows that the highest pooled incidence rate is observed in ICUs (5.5/1000 admissions; 30-day mortality: 37%).The mortality of candidemiacan be 35–80%[7], with prolonged hospital stay and increased treatment cost[8], [9].Treatment cost increase may worsen the doctor-patient relationship[10].Therefore, accurate prediction of an illness and its mortality rate may improve both the prognosis and the relationship between doctors and patients.

Although there are many models which can predict the possibility of candidemia[11, 12], only few can predict the mortality of fungemia.This study aims to establish a simple model to predict the 30-day mortality of fungemia in ICUs by using the known clinical vital signs and laboratory physiological and biochemical variables of patients with positive blood cultures. The model may reduce uncertainty in clinical decision-making and help doctors and patients' families to predict the mortality.

Methods

Study design

This retrospective study was based on the MIMIC-III Database[13].The inclusion criteria were positive fungal blood cultures and age over 18 years old, while the exclusion criterion was incomplete data.This large open database consists of about 53,000 adult ICU patients' de-identified health-related data from 2001 to 2012 at Beth Israel Deaconess Medical Center in Boston, MA. It was jointly established by Massachusetts Institute of Technology, Phillips Healthcare and Beth Israel Deaconess Medical Center. Access to and use of it were granted after "Human Research (Curriculum Group)", a course of the Collaborative Institutional Training Initiative (CITI) Program, was finished (Certification Number: 29641289). Using database was subject to approval by the institutional review boards of Massachusetts Institute. Based on the Medical Information Mart for Intensive Care (MIMIC-III) database, which served as the training dataset to construct a 30-day mortality risk predictive model for ICU patients with fungemia. The data from ICU of a Grade-III Class-A hospital in China are selected as the validation dataset of the model. This study was reviewed and approved by the ethics committee of the hospital (Version No. 2021 Review (No. 103)). The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to.

Data collection

The variables extracted from the MIMIC-III Database and a Grade-III Class-A hospital in China were age on the day of blood culture test, sex, and major underlying diseases, such as diabetes mellitus(diabetes), congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), renal failure,liver disease and solid tumors. The variables of blood test results were plasma albumin(albumin, g/dL),serum bilirubin (bilirubin, mg/dL),serum creatinine (creatinine, mg/dL), blood urea nitrogen (BUN, mg/dL),blood lactate (lactate,mmol/L), platelet count (platelet, /L), international normalized ratio(INR) and pulse oxygen saturation(SpO2)on the day of blood culture test.The variables of vital signs were heart rate (HR,beats/min),respiratory rate (RR,breaths/min), mean arterial pressure (MAP, mmHg)and temperature(Temp,℃)on the day of blood culture test.The severity of fungemia was estimated using the sequential organ failure assessment(SOFA) score on the day of blood culture test.The worst value of a variable was taken if repeated tests were done.Data about immunosuppressive agents, glucocorticoids, renal replacement therapy,antifungal therapy within 36 hours of blood culture test and fungus types were extracted.

Statistical analysis

The count data were expressed as case numbers (n).Shapiro-Wilk normality test showed that some data did not conform to a normal distribution ($P < 0.05$). Therefore, the measurement data in this study were described asP50 (P25,P75).Analyses were performed using SPSS (IBM SPSS Statistics 25).Leastabsolute shrinkage and selection operator(LASSO) regression analysis and multivariable

logistic regression analysis were conducted and a nomogram was created with R software (Version 3.5.1).

Predictors was selected via LASSO with R software.Multivariable logistic regression analysis was performed to develop a predictive model for the30-day ICU mortality of fungemia based on the predictors selected via LASSO. The odd ratios(ORs) demonstrated the correlations between the factors and the mortality of fungemia. P values of less than 0.05 were considered to indicate statistical significance. The nomogram was created based on the results of multivariable analysis.The predictors whose P values were less than 0.05 were included.

The receiver operating characteristic (ROC) curve was created by plotting the true positive rate (sensitivity)against the false positive rate (specificity) at various threshold settings of the analyses. The concordance index (C-index) was used to assess the discriminative capacity of the nomogram. The calibration curve was plotted to evaluate the agreement between the results and the predicted mortalities of fungemia using the rms package.A diagonal line of 45° was considered to indicate a qualified model.Bootstrapping with 1,000 resamples was performed to calculate a relatively accurate C-index for validation.Decision curve analysis (DCA) was conducted to assess the clinical use of the prediction nomogram for mortalities of fungemia risk by quantifying the net benefits of different threshold probabilities in the data[14, 15]. External validation of the nomogram was performed on the validation data set.

Results

The 322 patients met the inclusion and exclusion criteria in the MIMIC-III database and the ICU of a tertiary hospital in China. The data of 267 patients in the MIMIC-III database were used as in the training dataset to construct a 30-day mortality risk predictive model for ICU patients with fungemia and the data of 55 ICU patients with fungemia in a Grade-III Class-A hospital in China were used as the validation dataset to verify the model. The basic characteristics of the training and validation dataset of ICU patients with fungemia were shown in the Table 1.The 267 ICU patients (151 males and 116 females) in the MIMIC-III database were assigned into two groups: the group of patients who survived 30 days(n = 138) and the group of patients who did not (n = 129). The 30-day mortality rate was 48.3%.The patients’characteristics are listed in Table 2.

Table 1
basic conditions of patients in training dataset and validation dataset

Variable	Total(n = 322)	Training dataset (n = 267)	Validation dataset (n = 55)
Gender(Female)	134 (41.6%)	116 (43.4%)	18 (32.7%)
Age (years)	65.7(52.08, 76.6)	64.3(51.4, 75.7)	71(55, 81)
18–49(years)	65 (20.2%)	57 (21.3%)	8 (14.5%)
50–70(years)	132 (41.0%)	113 (42.3%)	19 (34.5%)
>70(years)	125 (38.8%)	97 (36.3%)	28 (50.9%)
SOFA	5 (1, 9)	4 (0, 9)	6 (4, 9)
Underlying conditions			
Diabetes	79 (24.5%)	66 (24.7%)	13 (23.6%)
CHF	85 (26.4%)	81 (30.3%)	4 (7.2%)
COPD	56 (17.4%)	48 (18%)	8 (14.5%)
Liver disease	86 (26.7%)	82 (30.7%)	4 (7.2%)
Renal failure	59 (18.3%)	55 (20.6%)	4 (7.2%)
Solid tumor	17 (5.2%)	9 (3.4%)	8 (14.5%)
Previous treatment			
Immunosuppressant	27 (834%)	24 (9%)	3 (5.5%)
Glucocorticoid therapy	143 (44.4%)	126 (47.1%)	17 (30.9%)
CRRT	23 (7.1%)	14 (5.2%)	9 (16.4%)
Antifungal therapy	252 (78.2%)	204 (76.4%)	48 (87.3%)
Type of fungus			
C. albicans	136 (42.2%)	105 (39.3%)	31 (56.4%)
C. glabrata	77 (23.9%)	73 (27.3%)	4 (7.2%)
C. parapsilosis	39 (12.1%)	34 (12.7%)	5 (9.1%)
C. tropicalis	28 (8.7%)	21 (3.4%)	7 (12.%)
Other fungi	42 (13%)	34 (12.7%)	8 (14.5%)
Monitoring value			
Albumin(g/dL)	2.5(1.7, 2.9)	2.3 (1.5, 2.7)	3.1(2.8, 3.6)

Variable	Total(n = 322)	Training dataset (n = 267)	Validation dataset (n = 55)
Bilirubin(mg/dlL)	0.9(0.4, 3.2)	1 (0.4, 4.6)	3.1(2.7, 3.6)
Creatinine(mg/dl)	1.6(0.9, 2.9)	1.8 (1.0, 3.1)	1.0(0.6, 2.0)
Bun(mg/dl)	41.7(24, 69)	45 (26, 72)	30.1(19.6, 46.7)
Lactate(mmol/L)	2.4(1.6, 4.2)	2.4 (1.4, 4.4)	2.5 (1.7, 3.3)
PLT(10^9/L)	123(49, 225)	129(53, 238)	91 (40, 196)
<100	139 (43.2%)	110 (41.2%)	29 (52.7%)
100–300	136 (42.2%)	114 (42.7%)	22 (40%)
>300	47 (14.6%)	43 (16.1%)	4 (7.3%)
INR	1.4 (1.2, 2.1)	1.5 (1.3, 2.3)	1.2(1.1, 1.6)
HR(beats/min)	81 (67, 118)	77 (66, 117)	99 (89, 120)
<60	46 (14.3%)	40 (15%)	6 (10.9%)
60–100	177 (55%)	154 (57.8%)	23 (41.8%)
>100	99 (30.7%)	73 (27.3%)	26 (47.3%)
RR(times/min)	28 (18, 33)	29 (17, 34)	24(18, 27)
<10	50 (15.5%)	49 (18.4%)	1 (1.8%)
44856	47 (14.6%)	24 (9%)	23 (41.8%)
>22	225 (69.8%)	194 (72.6%)	31 (56.4%)
MAP(mmHg)	58 (50, 67)	56 (48, 63)	75(67, 79)
T(℃)	37.5(36, 38.2)	37 (35.6, 38)	37.8(37.4, 38.5)
<36.0	76 (23.6%)	76 (28.5%)	0 (0%)
36.0-37.2	74 (23%)	61 (22.8%)	13 (23.6%)
>37.2	172 (53.4%)	130 (48.7%)	42 (76.4%)
SPO_2(%)	93 (90, 96)	93 (90, 96)	95(92, 96)

Table 2
Characteristics of ICU patients with fungemia (training data set)

Variable	Survived(n = 137)	unsurvive (n = 130)
Gender(Female)	58 (42.3%)	58 (44.6%)
Age (years)	60.7 (49.7, 72.6)	67.8 (55.6, 77.9)
18–49岁	35 (25.5%)	22 (16.9%)
50–70岁	61 (44.5%)	52 (40.0%)
>70岁	41 (29.9%)	56 (43.1%)
SOFA	3 (0, 6)	7 (3, 12)
Underlying conditions		
Diabetes	31(22.6%)	35(26.9%)
CHF	34(24.8%)	47(32.2%)
COPD	27(19.78%)	21(16.2%)
Renal failure	18(13.1%)	37(28.5%)
Liver disease	26(19.0%)	56(43.1%)
Solid tumor	8 (5.8%)	1 (0.8%)
Previous treatment		
Immunosuppressant	13 (9.5%)	11 (8.5%)
Glucocorticoid therapy	55 (40.1%)	71 (54.6%)
CRRT	4 (2.9%)	10 (7.7%)
Antifungal therapy	119(86.8%)	85 (65.4%)
Type of fungus		
C. albicans	57 (41.6%)	48 (36.9%)
C. glabrata	40 (29.2%)	33 (25.4%)
C. parapsilosis	17 (12.5%)	17 (13.1%)
C. tropicalis	8 (5.8%)	13 (10.0%)
Other fungi	15 (10.9%)	19 (14.6%)
Monitoring value		
Albumin(g/dL)	2.4 (1.4, 2.8)	2.2 (1.5, 2.6)
Bilirubin(mg/dlL)	0.6 (0.3, 2.2)	1.8 (0.6, 8.5)

Variable	Survived(n = 137)	unsurvive (n = 130)
Creatinine(mg/dl)	1.3 (0.8, 221)	2.2 (1.3, 3.7)
Bun(mg/dl)	35 (20, 56.7)	54 (39, 86)
Lactate(mmol/L)	2 (1.3, 2.2)	2.8 (1.6, 5.8)
PLT(10^9/L)	185 (100, 296)	77 (33.5, 146)
<100	32 (23.9%)	78 (59.7%)
100–300	74 (53.6%)	40 (31.0%)
>300	31 (22.5%)	12 (27.9%)
INR	1.3 (1.2, 1.8)	1.9 (1.4, 2.75)
HR(beats/min)	78 (66, 118)	76 (65, 99.5)
<60	18 (13.0%)	22 (17.1%)
60–100	77 (56.5%)	77 (48.9%)
>100	42 (30.4%)	31 (24.0%)
RR(times/min)	25 (12, 35)	29 (14, 33)
<10	20 (14.5%)	29 (22.5%)
44856	18 (13.0%)	6 (4.7%)
>22	99 (72.5%)	95 (72.9%)
MAP(mmHg)	57 (50, 65)	55 (47, 60)
T(℃)	38 (36, 38)	36 (35, 38)
<36.0	30 (21.7%)	46 (35.7%)
36.0-37.2	27 (19.6%)	34 (26.4%)
>37.2	80 (58.7%)	50 (38.0%)
SPO_2(%)	94 (91, 96)	92 (89, 95)

According to the results of the LASSO regression analysis, 24 of the 26 features were considered as the potential predictors (Fig. 1), and they were sex, age, diabetes, CHF,COPD, renal failure, liver disease, solid tumors, immunosuppressants, glucocorticoid therapy, antifungal therapy, fungus type, bilirubin, creatinine, lactate, platelet, INR,BUN,HR,RR, MAP, Temp and SPO2. The logistic regression analysis results of these predictors are shown in Table 3. There were statically significant differences in age, diabetes,renal failure, glucocorticoid therapy,antifungal therapy,platelet and RR between the two groups ($P < 0.05$). Thus, the predictive model was developed and presented as the nomogram (Fig. 2) by

incorporating age, renal failure, liver disease,glucocorticoid therapy,antifungal therapy,platelet, INR and RR as the variables. The scores in the nomogram were are displayed in the Table 4.

Table 3
Potential predictors of 30-day mortality in patients in ICU patients with fungemia

Variable	β	Odds ratio	(95% CI)	*p*
Intercept	-0.456	0.633	0.072–5.378	0.676
Gender(male)	-0.573	0.563	0.273–1.138	0.113
Age(50-70years)	0.656	1.927	0.691–5.555	0.214
Age(>70years)	1.71	5.577	1.894–17.660	0.002
SOFA	0.058	1.06	0.432–2.560	0.89
Diabetes(YES)	0.792	2.208	0.976–5.160	0.06
CHF(YES)	0.382	1.466	0.674–3.243	0.336
COPD(YES)	-0.339	0.712	0.277–1.779	0.471
Renal failure(YES)	1.366	3.921	1.568–10.383	0.004
Liver disease(YES)	1.099	3.002	1.117–8.335	0.03
Solid tumor(YES)	-1.629	0.196	0.009–1.470	0.168
Immunosuppressant(YES)	-0.927	0.395	0.099–1.550	0.182
Glucocorticoid therapy(YES)	0.976	2.656	1.225–5.925	0.014
Antifungal therapy(YES)	-2.096	0.122	0.045–0.305	<0.001
Type of fungus(C. glabrata)	-0.259	0.771	0.315–1.857	0.564
Type of fungus(C. parapsilosis)	0.733	2.081	0.676–6.597	0.204
Type of fungus(C. tropicalis)	0.253	1.288	0.374–4.579	0.689
Type of fungus(Other fungi)	0.077	1.08	0.370–3.200	0.887
Bilirubin(>1.1mg/dlL)	0.391	1.478	0.606–3.591	0.385
Creatinine(>1.3mg/dl)	-0.007	0.992	0.428–2.259	0.98
Lactate(≥2mmol/L)	0.116	1.123	0.509–2.461	0.77
Platelet(100–300×109/L)	-1.324	0.266	0.105–0.645	0.003
Platelet(>300×10^9/L)	1.815	0.162	0.046–0.533	0.003
INR(≥1.5)	0.803	2.234	1.062–4.758	0.034
BUN(>21mg/dl)	0.374	1.454	0.477–4.683	0.516
HR(60-100beats/min)	-0.603	0.546	0.201–1.44	0.227

Variable	β	Odds ratio	(95% CI)	*p*
HR(>100beats/min)	-0.992	0.37	0.116–1.134	0.086
RR(10-22times/min)	-1.343	0.26	0.072–0.892	0.035
RR(>22times/min)	0.625	1.869	0.721–4.899	0.198
MAP(<65mmHg)	0.331	1.393	0.588–3.341	0.451
T (36.0-37.2℃)	-0.067	0.934	0.351–2.488	0.891
T (>37.2℃)	-0.189	0.827	0.346–1.983	0.668
SPO_2(<93%)	0.447	1.564	0.766–3.242	0.221

Table 4
Score of predictive factors in predictive model of 30-day mortality in ICU patients with fungemia

Risk factor	Score
Age(years)	
18–49	0
50–70	46
>70	100
INR	
≤ 1.5	0
> 1.5	52
Renal failure	
□	0
□	69
Liver disease	
NO	0
YES	59
RR(times/min)	
< 10	74
10–22	0
> 22	88
Glucocorticoid therapy	
NO	0
YES	40
Antifungal therapy	
NO	98
YES	0
PLT(109/L)	
< 100	85

Risk factor	Score
100–300	19
> 300	0

The calibration curve showed that the nomogram was very reliable(Fig. 3). It showed good correspondence between the actual incidences and the predicted 30-day mortality of fungemia.The value of AUC (the area under the ROC curve) was 0.8272319(Fig. 3). The C-index value of the predictive nomogram was 0.838 (95% CI: 0.79096–0.88504). The C-index value of interval validation was 0.8118919, suggesting that the model did well in discrimination and prediction. DCA of the nomogram is presented in Fig. 4. It showed that within the range of 1–91%, the net benefit rate of the model was higher than that of those models for “all patients” or “none”. The area under the ROC curve and calibration results of external validation (Fig. 5) suggesting that the nomogram did well in terms of discrimination and prediction.

Discussion

Although new antifungal drugs such as caspofungin have been widely used in clinical treatment[16], the mortality of fungemia has not been significantly reduced[6], A predictive model for the 30-day mortality of fungemia in ICUs was developed, incorporating the following variables: age, renal failure, liver disease, glucocorticoid therapy, antifungal therapy, RR, INR and platelet count.

Patients with fungemia have an increased risk of death with age. Aging is a natural process which involves multiple factors and is characterized by “the accumulation of degenerative processes that are in turn underpinned by multiple alterations and damage within molecular pathways[17].Although many theories have been proposed to explain aging as a phenomenon, none of them has been able to fully explain the mechanisms that drive the fundamental process(es)[18].

Infectious diseases are considered important complications of renal failure[19].Fungemia is a serious BSI for patients with renal failure.Central venous catheterization is the only risk factor independently associated with BSIs due to non-albicans Candida species. Impairment of the innate and adaptive immunity predisposes patients with chronic kidney disease to BSIs.[20]In patients with fungemia, renal failure leads to difficulties in infection control and increases the mortality.Glucocorticoids reduce inflammation and immune activation[21] and are high risk factors for fungemia.Treatment of mice with mycosis using glucocorticoids leads to multiplying of fungi in large numbers and an increased mortality[22].

In this study, liver disease. is a risk factor for dying of fungemia within 30 days.The liver has important functions in the human body, including material metabolism, protein synthesis, detoxification, immune regulation and so on[23]. Liver disease may lead to pathological changes in other organs, such as hepatopulmonary syndrome and hepatorenal syndrome; on the other hand, metabolic syndrome and glucose intolerance in fatty liver can lead to cardiovascular disease[23]. When infection such as

fungemia occurs, it can induce liver tolerance and desensitization to lipopolysaccharide and endotoxin, leading to immunosuppression[24, 25].

This study showed that the use of glucocorticoids in ICU patients with fungemia increased 30-day mortality. There is a consensus that glucocorticoid therapy is a high risk factor for invasive fungal infections[26]. Glucocorticoids are standard therapy for the control of inflammation and immunosuppression in patients with various immune diseases, such as allergy□asthma□arthritis□ inflammatory bowel disease and so on[21, 27]. However, they have many side effects, including osteoporosis, hyperglycemia, insulin resistance, hypertension, muscle atrophy, severe infection, Cushing's syndrome, peptic ulcer and neuropsychiatric disorder[21]. High-dose and prolonged systemic glucocorticoid therapy is associated with a high risk of invasive fungal and poor outcomes[26].

In this study, antifungal therapy improved the prognosis, however,the mortality was still high.SiriluckAnunnatsiriet et al.[28]reported that there was no difference in the mortality rate between patients receiving antifungal treatment and those not.Zengli Xiaoet al.[29]reported that there was no difference in the mortality among patients receiving antifungal treatment. Garnacho-Montero, J et al[30].found that the empirical use of an echinocandin in critically ill patients with documented candidemia reduced the 30-day and 90-day mortality rates significantly.Current antifungal therapies for fungemia are still controversial and have not been proved to be effective by randomized controlled trials.

This study shows that RR provides important information about the prognosis of fungemia.It is the first time for RR to be identified as a prognostic marker of fungemia.Our data indicate that its prognostic significance remains unchanged in the modern era of acute treatment.RR increases after acute lung injury to compensate for insufficient ventilation. During the critical stage, respiration is suppressed through the central nervous system and peripheral receptors.RR is an indicator of the severity of the damages to the respiratory system.It can also predict the outcome after acute myocardial infarction[31].

In this study, thrombocytopenia is associated with an increased mortality. Thrombocytopenia is common among critically ill patients, and has been reported to be associated with a poor prognosis[32].An acute reduction in platelet count is seen during the early phase of many diseases.Some mechanisms may lead to thrombocytopenia in patient with fungemia. Platelet production may be impaired by bone marrow depression caused by infectious fungi. Besides,ongoing consumption of platelets, for example, in the framework of disseminated intravascular coagulation and sepsis, may also play an important role. International normalized ratio (INR) was a risk factor for mortality in ICUs patients with fungemia. Coagulopathy is strongly associated with the severity and mortality of sepsis, and mortality increases with prolonged INR[33]. Platelets also play an important role in sepsis, where platelets and INR co-locate at the intersection of the immune system, the coagulation cascade, and endothelial cells[33].

There are three limitations in this study. Firstly, the sample size is relatively small because the data are from a single center and the incidence of fungemia is low, which may lead to nonuniversal findings.Secondly, this study is a retrospective study rather than a randomized controlled trial, which inevitably leads to bias. Lastly,death from candidemia was not differentiated from that from deterioration

of underlying diseases because it could be very difficult to determine the exact cause of death in critically ill patients.

The 30-day mortality risk predictive model for ICU patients with fungemia constructed in this study has good predictive ability.Attested by the external validation results, this predictive nomogram boasts a relatively high accuracy in early identification of high-risk patients.Therefore, it is able to help control the risk of death from fungemia within 30 days in ICUs and may hopefully provide a 30-day mortality risk screening tool for ICU patients with fungemia.

Declarations

Author's contribution

Maolong dong was responsible for the design and revision of papers. Peng Xie was responsible for extracting data from MIMIC-III database performed statistical analysis and writed paper. Wenqiang Wang was responsible for checking data and statistical analysis. All authors contributed to the writing of the final manuscript.

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Figures

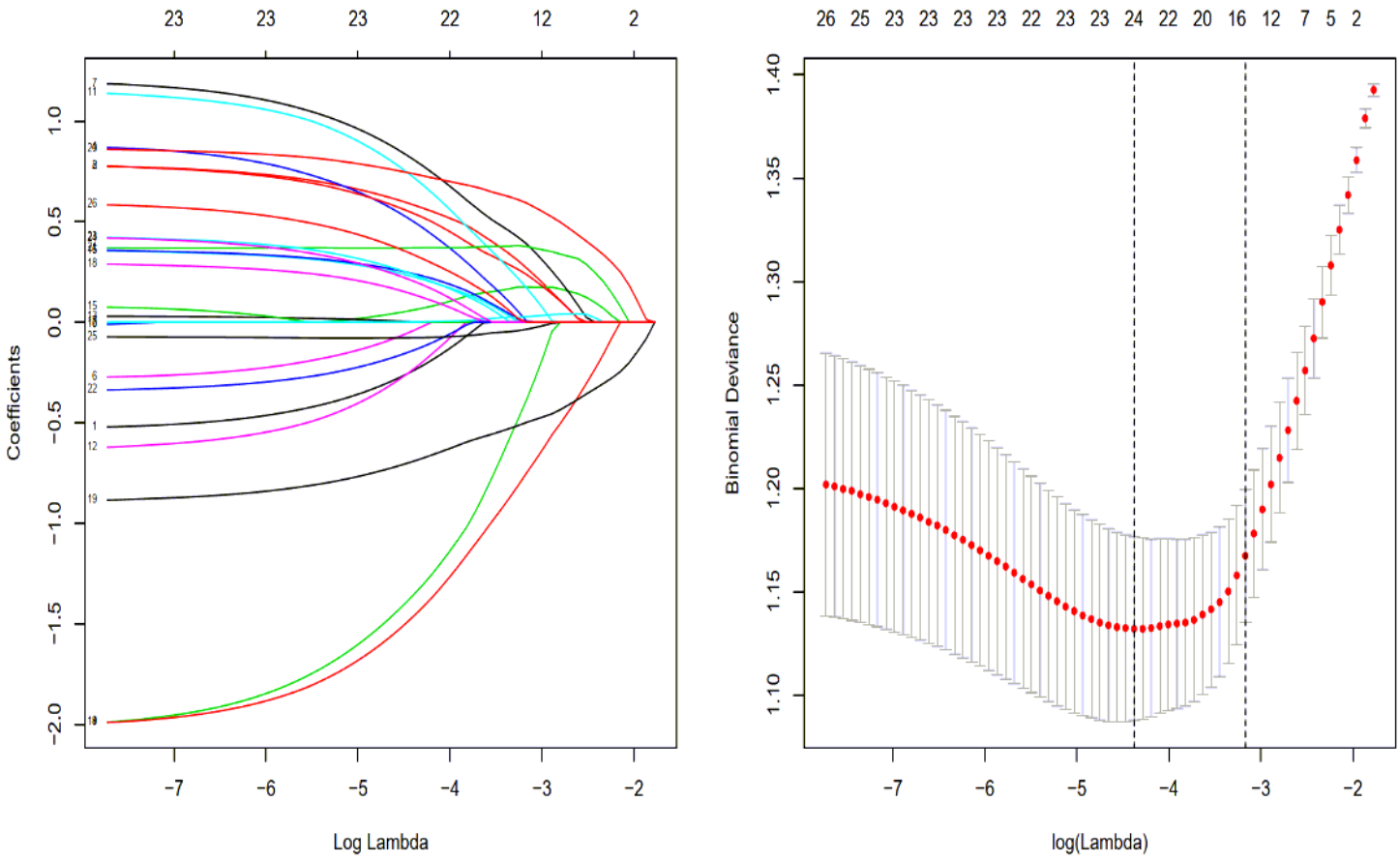

Figure 1

According to the results of the LASSO regression analysis, 25 of the 28 features were considered as the potential predictors.

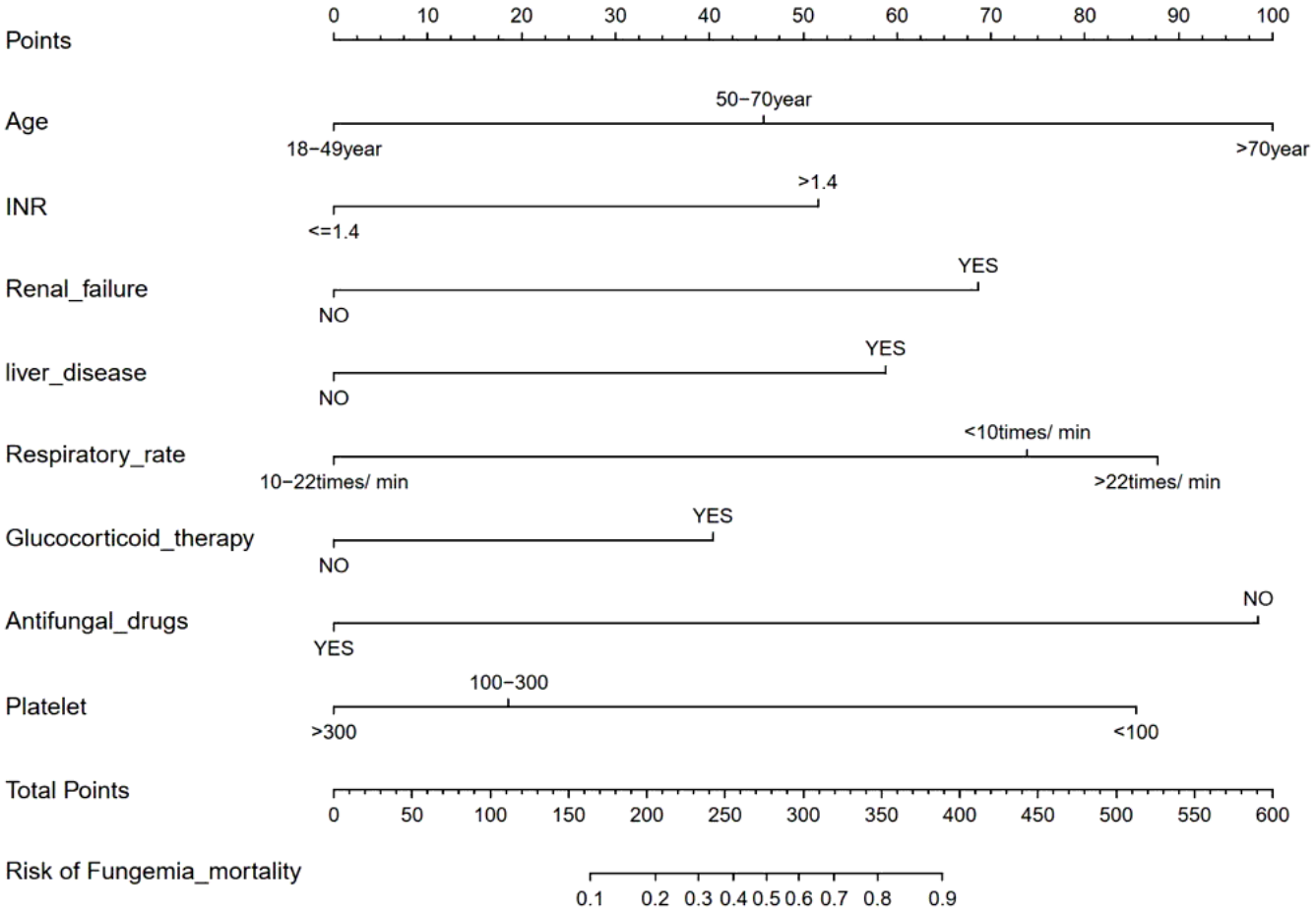

Figure 2

The predictive model was developedand presented as the nomogram.

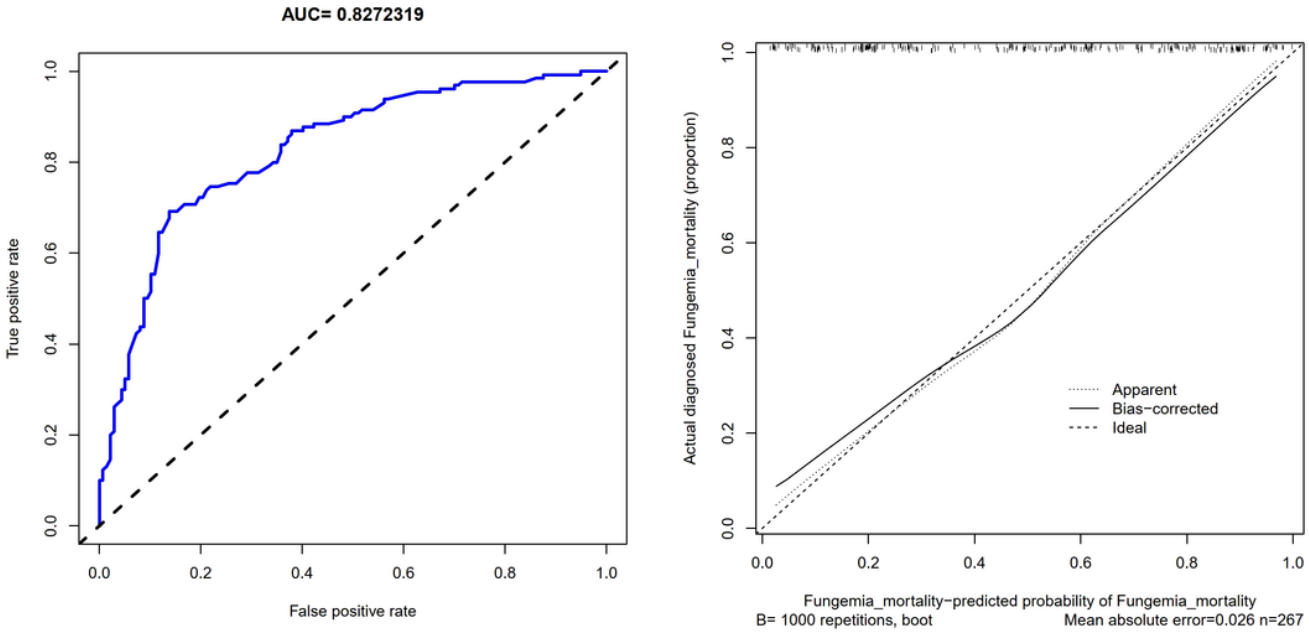

Figure 3

The calibration curve showed that the nomogram and . the area under the ROC curve.

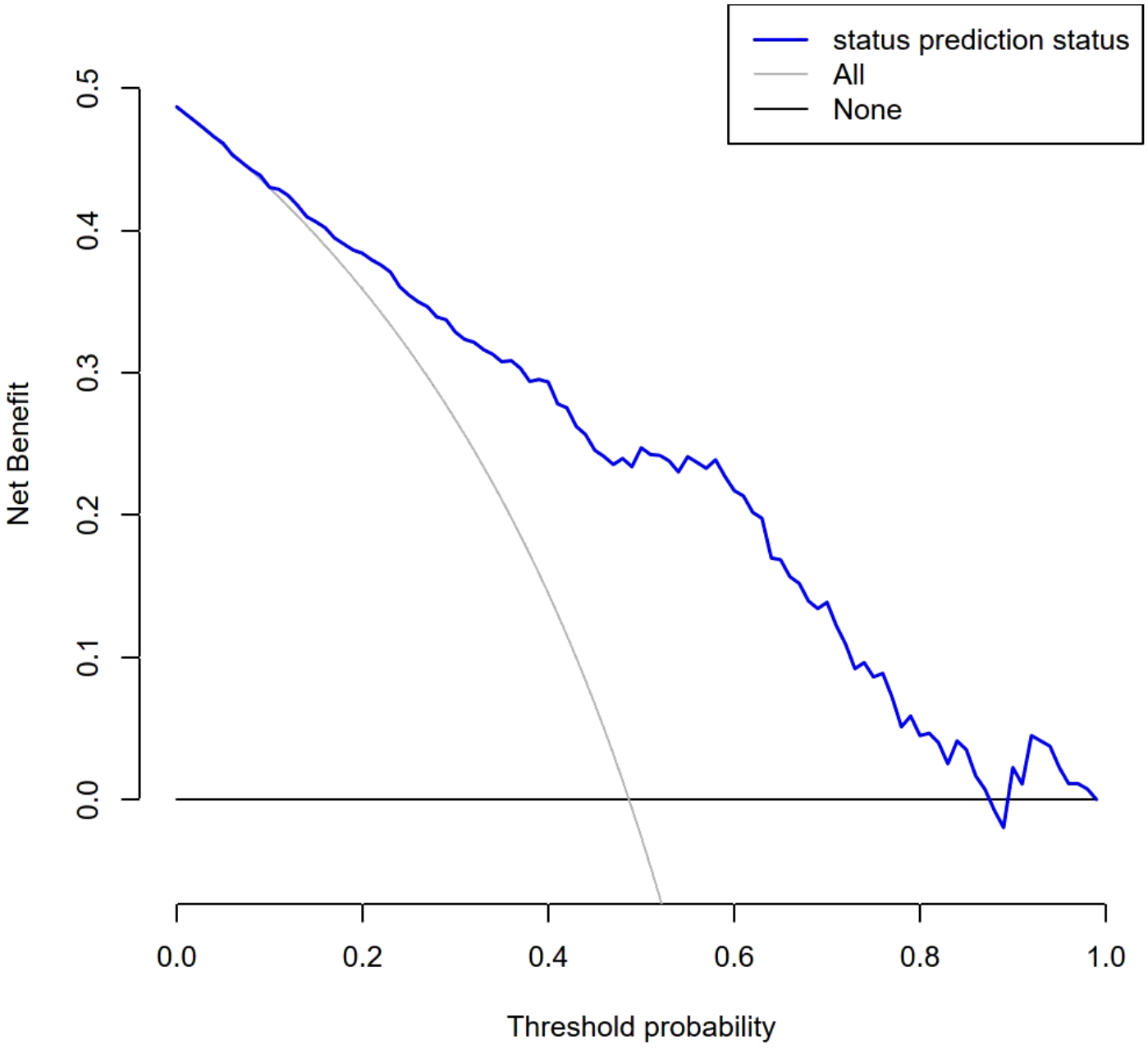

Figure 4

Decision curve analysis for fungemia risk predictive nomogram.

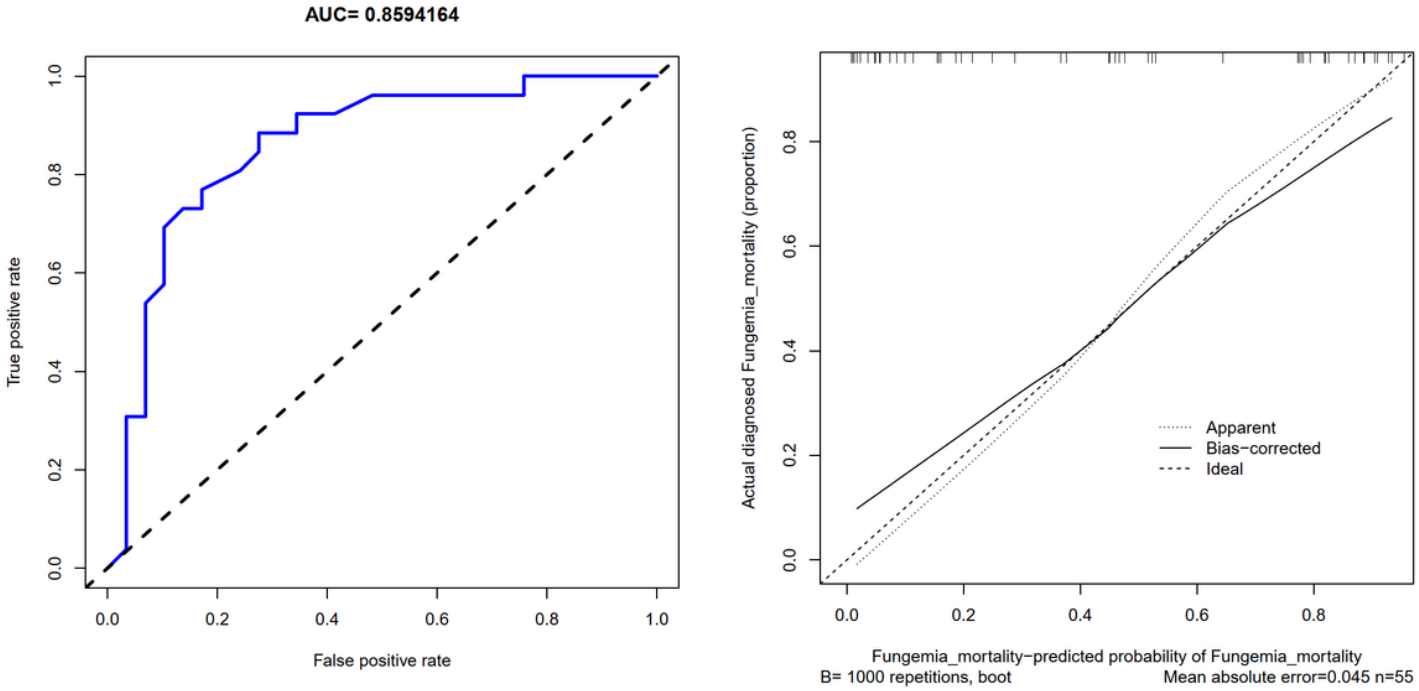

Figure 5

Legend not included with this version.