Exploiting an Early Warning Nomogram for Predicting the Risk of ICU Admission in COVID-19 patients: A Multi-Center Study in China

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Abstract

Background

Novel corona virus disease 2019 (COVID-19) is an urgent event in the worldwide. We aimed to develop and validate a practical model for early identifying and predicting which patients will be admitted to intensive care unit (ICU) based on a multi-center cohort in China.

Methods

Data from 1087 patients of laboratory-confirmed COVID-19 were collected from 49 sites between January 2 and February 28 2020 in Sichuan and Wuhan. Patients were randomly divided into the training and validation cohorts (7:3). The least absolute shrinkage and selection operator (LASSO) analysis and logistic regression analysis were employed for the development account. The performance of the nomogram was evaluated for the C-index, calibration, discrimination, and clinical usefulness. The nomogram was further assessed in a different cohort as external validation.

Results

The individualized prediction nomogram included 6 predictors, including age, respiratory rate, systolic blood pressure, smoking status, fever and chronic kidney disease. The model showed high discrimination ability in the training cohort (C-index = 0.829), which was confirmed in the external validation cohort (C-index = 0.776). In addition, the calibration plots confirmed good concordance for prediction the risk of ICU admission. Decision curve analysis showed that the prediction nomogram was clinically useful.

Conclusion

We established an early prediction model incorporating clinical characteristics that could be quickly obtained on hospital admission even in community health center. This model can be conveniently used to facilitate predicting the individual risk for ICU admission of COVID-19 patients and optimizing use of limited resources.

Background

Novel Coronavirus disease 2019 (COVID-19) is a newly discovered contagious disease which first reported in Wuhan, Hubei, China and rapidly spreading outbreak[1, 2]. By May 23, 2020, according to the World Health Organization announcement, there are more than 4,993,470 confirmed cases reported worldwide in almost all countries and regions around the world, and more than 327,738 infected patients' death[3]. In recent days, the number of cases has risen rapidly in the United States, Europe, Russia, and Latin America. COVID-19 spread by human-to-human transmission via droplets, aerosols, fecal, or direct contact, and has an incubation period estimated at 1 to 14 days or longer. COVID-19 infection has been reported in all ages, and a higher mortality rate in older adults and those with comorbidities such as hypertension, cardiovascular disease, chronic kidney disease (CKD), diabetes, and chronic respiratory

disease[4]. Obesity may also be a risk factor for respiratory failure leading to invasive mechanical ventilation in COVID-19 patients[5]. The disease manifested at the presentation was generally similar, and most symptoms were mild and flu-like and the most common symptoms in the general population are fever, cough, dyspnea, and myalgias or fatigue. But some patients might rapidly develop acute respiratory failure, multiple organ failure, and other fatal complications. So far, no specific treatment for COVID-19 has been fully developed.

Despite public health responses aimed at containing the disease and delay its spread, the outbreak has led to an increase in the demand for medical resources, while medical staff themselves could also get infected. In order to reduce the burden on the health care system and provide optimal care for patients, an effective prognosis assessment of the disease is needed. A predictive model that combines multiple variables or features to estimate the risk of an infected person's poor outcomes can help healthcare staff classify patients' severity when allocating limited medical resources[6]. In present studies, it showed that the rate of severe cases had significant regional difference[7]. Hence, the aim of our study was to describe the clinical characteristics with confirmed COVID-19 in different cities of China where the outbreak risk levels are different, and construct an early warning prediction nomogram model incorporating clinical characteristics to identify the risk of patients with poor prognosis. It may help provide appropriate supportive treatment in advance and reduce the probability of severe COVID-19.

Methods

Patients

This retrospective, multicenter study was approved by the Ethics Committee of West China Hospital. Written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases. This study included consecutive patients with laboratory-confirmed hospitalized COVID-19 cases reported to the National Health Commission between January 2, 2020, and February 28, 2020. The data cutoff for the study was March 14, 2020. COVID-19 diagnosis was confirmed by high-throughput sequencing or real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) of nasal and pharyngeal swab specimens[8]. All study patients were diagnosed with COVID-19 according to the WHO interim guidance[9]. These patients in the primary cohort were subsequently randomly assigned, using a simple random splitting method, in a ratio of 7 to 3 to the training or validation sets, using R version 3.5.1 and the “caret” package.

Demographical And Risk Variables

The following data were obtained from electronic medical records: demographics, clinical signs on admission, clinical symptoms, clinical risk factors, and exposure to infection. Demographics collected from this study included age, gender, drinking status, smoking status, obesity and time between onset of symptoms to admission. Clinical symptoms were defined as the interval between the onset of clinical

symptoms and the data of admission. Exposure to infection was defined as exposure to Wuhan (including Wuhan residency, travel history to Wuhan, or contact with people from Wuhan), or other COVID-19 affected areas (including residency, travel history or contact with people from these areas), or COVID-19 patients. The risk of exposure to infection changed as the relevant definitions in the COVID-19 guidelines of the National Health Commission of the People's Republic of China changed. If data were missing from the records or clarification was needed, data were obtained by direct communication with attending physicians and other health care providers. A team of experienced clinicians reviewed, abstracted and cross-checked the data. Each record was checked independently by 2 clinicians. The clinical and demographic features in our cohort are summarized in Table 1.

Table 1
Baseline characteristics of patients infected with COVID-19

	Training Cohort (%)			Validation Cohort (%)		
Characteristic	ICU (N = 68)	Non-ICU (N = 695)	*P*	ICU (N = 29)	Non-ICU (N = 295)	*P*
Age, median (IQR), years	66.5(51–76)	50(36–63)	0.000	65(51–76)	49(38–63)	0.000
Gender			0.016			0.066
Male	43(63.2)	328(47.2)		19(65.5)	135(45.8)	
Female	25(36.8)	367(52.8)		10(34.5)	160(54.2)	
Temperature on Admission			0.317			0.021
≤ 36.1	3(0.6)	45(6.5)		6(20.7)	14(4.7)	
36.2–38	56(82.4)	593(85.3)		19(65.5)	251(85.1)	
≥ 38.1	9(1.2)	57(8.2)		4(13.8)	30(10.2)	
Heart Rate, bmp			0.370			0.001
< 100	52(76.5)	568(81.7)		16(55.2)	242(82)	
≥100	16(23.5)	127(18.3)		13(44.8)	53(18)	
Respiratory Rate			0.000			0.000
< 22	36(52.9)	605(87.1)		14(48.3)	235(79.7)	
≥ 22	32(47.1)	90(12.9)		15(51.7)	60(20.3)	
Systolic Blood Pressure, mmHg			0.322			0.554
≤ 100	4(5.9)	20(2.9)		0(0)	12(4.1)	
> 100	64(94.1)	675(97.1)		29(100)	283(95.9)	
Drinking			0.311			1.000
Former and/or Current	54(79.4)	590(84.9)		25(86.2)	251(85.1)	
Never	14(20.6)	105(15.1)		4(13.8)	44(14.9)	
Smoking			0.005			0.766
Former and/or Current	49(72.1)	596(85.8)		26(89.7)	253(85.8)	
Never	19(27.9)	99(14.2)		3(10.3)	42(14.2)	

	Training Cohort (%)			Validation Cohort (%)		
Time interval from the onset of symptoms to admission			0.306			1.000
> 7	16(23.5)	123(17.7)		5(17.2)	51(17.3)	
≤ 7	52(76.5)	572(82.3)		24(82.8)	244(82.7)	
Obesity			1.000			1.000
Yes	0(0)	4(0.6)		0(0)	2(0.7)	
No	68(100)	691(99.4)		29(100)	293(99.3)	
Symptoms						
Fever			0.005			0.580
Yes	54(79.4)	427(61.4)		21(72.4)	193(65.4)	
No	14(20.6)	268(38.6)		8(27.6)	102(34.6)	
Cough			0.075			1.000
Yes	48(70.6)	408(58.7)		19(65.5)	192(65.1)	
No	20(29.4)	287(41.3)		10(34.5)	103(34.9)	
Dyspnea			0.000			0.004
Yes	26(38.2)	126(18.1)		12(41.4)	51(17.3)	
No	42(61.8)	569(81.9)		17(58.6)	244(82.7)	
Fatigue			0.029			0.336
Yes	34(50)	249(35.8)		14(48.3)	110(37.3)	
No	34(50)	446(64.2)		15(51.7)	185(62.7)	
Sore Throat			1.000			0.205
Yes	8(11.8)	78(11.2)		0(0)	25(8.5)	
No	60(88.2)	617(88.8)		29(100)	270(91.5)	
Nasal Discharge			0.501			0.471
Yes	1(1.5)	27(3.9)		0(0)	14(4.7)	
No	67(98.5)	668(96.1)		29(100)	281(95.3)	
Wheeze			0.285			0.000
Yes	10(14.7)	68(9.8)		10(34.5)	26(8.8)	
No	58(85.3)	627(90.2)		19(65.5)	269(91.2)	

	Training Cohort (%)			Validation Cohort (%)		
Chest Distress			0.687			1.000
Yes	13(19.1)	114(16.4)		7(24.1)	68(23.1)	
No	55(80.9)	581(83.6)		22(75.9)	227(76.9)	
Muscle and Joint Pain			0.848			1.000
Yes	8(11.8)	71(10.2)		3(10.3)	31(10.5)	
No	60(88.2)	624(89.8)		26(89.7)	264(89.5)	
Headache			0.749			0.794
Yes	3(4.4)	43(6.2)		3(10.3)	21(7.1)	
No	65(95.6)	652(93.8)		26(89.7)	274(92.9)	
Nausea and Vomiting			1.000			1.000
Yes	2(2.9)	25(3.6)		1(3.4)	13(4.4)	
No	66(97.1)	670(96.4)		28(96.6)	282(95.6)	
Diarrhea			1.000			1.000
Yes	6(8.8)	64(9.2)		4(13.8)	36(12.2)	
No	62(91.2)	631(90.8)		25(86.2)	259(87.8)	
Comorbidities						
Asthma			0.790			1.000
Yes	0(0)	8(1.2)		0(0)	3(1)	
No	68(100)	687(98.8)		29(100)	292(99)	
Chronic Obstructive Pulmonary Disease			0.112			0.934
Yes	4(5.9)	14(2)		1(3.4)	4(1.4)	
No	64(94.1)	681(98)		28(96.6)	291(98.6)	
Hypertension			0.011			0.410
Yes	26(38.2)	163(23.5)		9(31)	66(22.4)	
No	42(61.8)	532(76.5)		20(69)	229(77.6)	
Chronic Respiratory Disease			0.003			0.165
Yes	7(10.3)	19(2.7)		2(6.9)	4(1.4)	
No	61(89.7)	676(97.3)		27(93.1)	291(98.6)	

	Training Cohort (%)			Validation Cohort (%)		
Cardiovascular System Disease			0.000			0.566
Yes	14(20.6)	43(6.2)		3(10.3)	17(5.8)	
No	54(79.4)	652(93.8)		26(89.7)	278(94.2)	
Chronic Kidney Disease			0.000			0.000
Yes	6(8.8)	8(1.2)		4(13.8)	3(1)	
No	62(91.2)	687(98.8)		25(86.2)	292(99)	
Chronic Liver Disease			1.000			0.624
Yes	5(7.4)	50(7.2)		3(10.3)	18(6.1)	
No	63(92.6)	645(92.8)		26(89.7)	277(93.9)	
Cerebrovascular Disease			0.326			-
Yes	2(2.9)	6(0.9)		-	-	
No	66(97.1)	689(99.1)		-	-	
Autoimmune Disease			0.013			1.000
Yes	4(5.9)	8(1.2)		0(0)	5(1.7)	
No	64(94.1)	687(98.8)		29(100)	290(98.3)	
Hematological Disease			0.149			0.425
Yes	1(1.5)	0(0)		1(3.4)	1(0.3)	
No	67(98.5)	695(100)		28(96.6)	294(99.7)	
Stroke History			0.015			0.802
Yes	5(7.4)	13(1.9)		1(3.4)	3(1)	
No	63(92.6)	682(98.1)		28(96.6)	292(99)	
Malignancy			0.341			1.000
Yes	3(4.4)	13(1.9)		1(3.4)	8(2.7)	
No	65(95.6)	682(98.1)		28(96.6)	287(97.3)	
Diabetes			0.064			0.812
Yes	14(20.6)	83(11.9)		2(6.9)	30(10.2)	
No	54(79.4)	612(88.1)		27(93.1)	265(89.8)	

	Training Cohort (%)			Validation Cohort (%)		
Exposure to source of transmission within past 14 days						
Recently visited COVID-affected area			0.266			0.921
Yes	63(92.6)	606(87.2)		26(89.7)	257(87.1)	
No	5(7.4)	89(12.8)		3(10.3)	38(12.9)	
Contact history of COVID-19			0.019			0.044
Yes	12(17.6)	224(32.2)		3(10.3)	88(29.8)	
No	56(82.4)	471(67.8)		26(89.7)	207(70.2)	

Definition Of Outcomes

The severity of COVID-19 during hospitalization was according to the American Thoracic Society guidelines for community-acquired pneumonia[10]. The primary outcome was defined as admission to the intensive care unit (ICU) which were serious outcomes of COVID-19 and other serious infectious diseases reported in previous studies[10, 11].

Features Selection

In the training cohort, there were 763 patients hospitalized with COVID-19 including for variable selection and risk model development. As described, 37 variables were entered into the selection process. The least absolute shrinkage and selection operator (LASSO) method, which is suitable for analyzing high-dimensional data, was used to select the most significant predictive features[12, 13]. Features with non-zero coefficients in the LASSO regression model were selected in the forward stepwise logistic regression model[14]. The features were considered as odds ratio (OR) with 95% confidence interval and two-tailed p-values. Variables with p-values smaller than 0.1 in the univariate analysis and potentially significant in the multivariate analysis were included in the logistic regression analysis, and the forward selection procedure was used to develop a parsimonious model for predicting ICU admission of COVID-19 in our cohort.

Development And Validation Of An Individualized Prediction Model

Nomogram is a statistical model useful for risk assessment. A predictive nomogram was developed using the independent factors selected by LASSO to generate a combined indicator for estimating ICU admission of COVID-19, and provided a quantitative tool for physicians to assess the individual

probability of ICU admission. The created nomogram was used for external validation, and the total score for each nodule was calculated. The nomogram was constructed using the total score as a factor.

Apparent performance of the nomogram in the training cohort and validation cohort

Adequate discrimination and calibration were performed to test and validate the prognostic accuracy of the nomogram model[15]. Discrimination was quantified using Harrell's concordance index (C-index), in which an absolute value close to 1 indicated that the model had strong predictive ability. The nomogram was further validated by bootstrapping (1000 bootstrap replicates) to calculate the corrected C-index. Calibration plots were developed to assess the predictive accuracy and agreement between predicted and observed severity. Decision curve analyses (DCAs) were performed to assess the clinical usefulness of the nomogram. The net benefit was calculated by subtracting the proportion of patients with false-positive results from the proportion of patients with true-positive results and by weighing the relative risk of an intervention compared with the adverse effects of an unnecessary intervention. The precision of the predictions was evaluated using the area under the receiver-operating characteristic curve (AUC). Two-sided p-values of less than 0.05 were considered to indicate a statistically significant difference.

Statistical analysis

Continuous variables were expressed as median and interquartile range. Categorical variables were expressed as absolute values and percentages. The medians of continuous variables were compared using independent group *t*-tests for normally distributed data and the Mann-Whitney test for non-normally distributed data. The chi-square test or Fisher's exact test was used to compare proportions between the training and validation cohort. Statistical analyses were performed using R software version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS version 25.0 (IBM Corporation, Armonk, NY).

Results

Clinical characteristics

Until February 28, 2020, 1087 patients with COVID-19 who had been hospitalized in 47 regions of Sichuan and 2 regions of Wuhan were enrolled. Of these patients, 763 and 324 were assigned as the training and validation cohorts, respectively. The demographic and clinical characteristics of our cohort are shown in Table 1. A total of 97 patients eventually were admission to ICU (8.9%). The median age was 51 years (interquartile range, 37–65) in training cohort and 50 years (interquartile range, 38–64) in validation cohort. More than half of patients were female (51.4% in training cohort, 52.5% in validation cohort). Fever (63.0% in training cohort, 66.0% in validation cohort), cough (59.8% in training cohort, 65.1% in validation cohort) and fatigue (37.1% in training cohort, 38.3% in validation cohort) were the most common symptoms. Hypertension (24.8% in training cohort, 23.1% in validation cohort), diabetes (12.7%

in training cohort, 10.2% in validation cohort) and cardiovascular system disease (7.5% in training cohort, 6.2% in validation cohort) were top 3 comorbidities.

Among those patients with admission to ICU, most were drinking (79.4% in training cohort, 86.2% in validation cohort), smoking (72.1% in training cohort, 89.7% in validation cohort) and without obesity (100% in training cohort and validation cohort). Patients with ICU admission were older than those without ICU admission by a median of 6 years both in training cohort and validation cohort. Most patient with admission to ICU had systolic blood pressure greater than 100 mmHg, heart rate less than 100 bmp, and temperature on admission between 36.2 and 38.0℃. Nearly 90% patients among admission to ICU exposured to Wuhan or other COVID-affected areas in the past 14 days.

Selection Of Independent Predictive Factors

Based on demographics, clinical signs on admission, clinical symptoms, clinical risk factors, and exposure to infection, 19 potential predictors with non-zero coefficients were selected in the LASSO logistic regression model (Fig. 1). Inclusion of these 19 variables in a logistic regression model resulted in 6 variables that were independently statistically significant predictors of admission to ICU.

The selected predictors were age, respiratory rate, systolic blood pressure, smoking status, fever and chronic kidney disease. The results of the logistic regression analysis are shown in Table 2.

Table 2
Logistic analysis of each factor's ability in predicting the risk of severe disease with COVID-19

	Prediction model		
	β	Odds ratio (95%CI)	P-value
Intercept	8.409	4485.633 (0.000-NA)	0.997
Age	**-1.650**	**0.192(0.102–0.356)**	**0.000**
Gender	-0.548	0.578(0.312–1.055)	0.077
Respiratory rate	**-1.516**	**0.220(0.120–0.403)**	**0.000**
Systolic Blood Pressure	**-1.466**	**0.231(0.067–0.966)**	**0.029**
Smoking	**0.974**	**2.647(1.308–5.245)**	**0.006**
Fever	**-0.912**	**0.402(0.186–0.808)**	**0.014**
Cough	-0.172	0.842(0.438–1.583)	0.599
Dyspnea	-0.489	0.613(0.325–1.177)	0.134
Fatigue	-0.419	0.658(0.362–1.192)	0.166
Sore Throat	-0.725	0.484(0.205–1.249)	0.112
Asthma	14.989	32340(0.000-NA)	0.984
Chronic Respiratory Disease	-0.405	0.667(0.206–2.347)	0.509
Chronic Kidney Disease	**-2.043**	**0.130(0.031–0.582)**	**0.005**
Cardiovascular System Disease	-0.465	0.628(0.275–1.516)	0.283
Autoimmune Disease	-1.132	0.322(0.075–1.544)	0.135
Hematological Disease	-16.456	0.000(NA-Inf)	0.995
Stroke History	-0.780	0.458(0.130–1.955)	0.251
Chronic Liver Disease	0.041	1.042(0.361–3.854)	0.945
Contact history of COVID-19	0.450	1.569(0.748–3.537)	0.252

Building And Validating A Prediction Nomogram Model

The nomogram used for predicting ICU admission of COVID-19 was formulated using significant independent factors, including age, respiratory rate, systolic blood pressure, smoking status, fever and chronic kidney disease. The nomogram showed that the best predictor was chronic kidney disease, age, and respiratory rate. Each variable was assigned a score according to the demographic and clinical

characteristics of each patient, and the total score was computed by summing individual scores. The ICU admission probabilities were also obtained from the nomogram (Fig. 2).

The C-index of the nomogram was 0.829 (95% CI, 0.779–0.879) in training cohort and 0.776 (95% CI, 0.684–0.868) in validation cohort, suggesting that the model had good discriminative ability. The calibration plots of the nomogram showed that the agreement between predicted and observed severity was optimal in training cohort and validation cohort (Fig. 3). In addition, DCA showed that the predictive model had significant net benefits for almost all threshold probabilities at different time points in training cohort and validation cohort, demonstrating the potential clinical benefit of the predictive model (Fig. 4). The AUC of the nomogram was 0.829 in training cohort and 0.776 in validation cohort, indicating improved survival prediction compared with the nomogram model (Fig. 5).

Discussion

Our study enrolled 1087 patients with COVID-19 who were registry from a multi-center of Sichuan and Wuhan provinces where the outbreak risk levels are different. In primary study, based on patents' demographic and clinical characteristics obtained on first admission, we established and validated a nomogram predicting the risk for admission to ICU through the LASSO and logistic regression analysis. The independently statistically significant factors including in the prediction model were age, respiratory rate, systolic blood pressure, smoking status, fever and chronic kidney disease. The validation of the model demonstrated its great performance using different statistical methods. As those factors could be obtained easily when first on admission, our nomogram is a convenient and valuable clinical warning tool for predicting ICU admission of COVID-19, especially in emergency department and even in community health center.

Most COVID-19 cases have mild disease with good prognosis, but some patients may develop severe respiratory distress syndrome and poor prognosis[16]. To mitigate the burden on the healthcare system and provide the best care for patients, it is necessary to effectively predict the prognosis of the disease[17]. A predictive model that combines multiple variables or features to estimate the risk of an infected person's poor outcomes can help healthcare staff classify patients' severity when allocating limited medical resources[18]. Previous studies have reported prediction models for diagnosing and prognosis of COVID-19, and for detecting the risk of being admitted to hospital for COVID-19. Chen *et al* constructed a diagnosis prediction models with 10 clinical factors based on 136 participants[19]. Wang *et al* enrolled 296 in-hospital COVID-19 patients and developed a clinical model for predicting the mortality of in-hospital COVID-19 patients[17]. Dong *et al* developed a scoring model to predict the progression risk with COVID-19 pneumonia base on 209 patients[20]. However, those proposed models are poorly reported and at high risk of bias, raising concern that their predictions could be unreliable when applied in daily practice for diagnosing. In a recent study, a risk score was reported to estimate the risk of critical illness of patients with COVID-19 based on 10 variables[21]. Although the study has modest sample size and satisfying performance, this scoring system was complicated with some laboratory examination data which cannot be obtained before admission or as soon as possible on admission. It is

necessary to develop and validate a convenient prediction model for healthcare staff or emergency staff to use quickly and easily. Based on multi-center study from different cities and different severity of outbreak in Wuhan and Sichuan province, we constructed a warning model for predicting the risk of ICU admission. In our model, the independently statistically significant factors were age, respiratory rate, systolic blood pressure, smoking status, fever and comorbidity with chronic kidney disease, which could be obtained simply, practically, reliability, and fast. This prediction model could be used in prehospital care or emergency department, allowing medical staff to intervene at an early stage and determine their treatment location and the type of intervention. Our model showed a good discriminative ability and potential clinical benefit using different statistical methods. This prediction model is more practical to evaluate COVID-19 patients than other scoring tools and greatly improve the applicability and robustness of prediction models in routine care.

It identified that comorbidities played a key role in the prognosis of COVID-19. Cardiovascular system disease, especially hypertension, was reported to be one of the most important independent risk factors[22]. In this study, we observed the patients with presence of kidney disease more likely to be admitted to the ICU and it was an independent risk factor for ICU admission of COVID-19, suggesting that the patients with comorbidity of kidney disease on admission might have a high risk of deterioration[23, 24]. Previous study showed that kidney injury was associated with an increased risk of death in patients with influenza A virus subtype H1N1 and SARS[25–27]. Multiple organ involvement including the liver, gastrointestinal tract, and kidney have been reported during the course of SARS in 2003 and very recently in patients with COVID-19[28]. In our hypothesis, such patients might have a proinflammatory state with functional defects in innate and adaptive immune cell populations and were known to have a higher risk for upper respiratory tract infection and pneumonia. The 2019-nCoV itself may also cause kidney injury through multiple mechanisms: the 2019-nCoV may uses angiotensin converting enzyme 2 (ACE2) as a cell entry receptor and exert direct cytopathic effects on kidney tissue. It has been reoprted ACE2 expression in urinary organs (kidney) was nearly 100-fold higher than in respiratory organs (lung)[28]. Viral antigens or virus-induced specific immune effect mechanisms (specific T-cell lymphocytes or antibodies) deposits of immune complexes may damage the kidneys[29]. Early detection and treatment of renal abnormalities, including assess volume status and renal transplantation pressure, avoidance of nephrotoxic drugs and adequate hemodynamic support may help to improve the vital prognosis of COVID-19.

In most prognosis prediction models published, elder age, comorbidities, lactate dehydrogenase, lymphocyte and C-reactive protein were reported as risk factors for poor prognosis[20]. Some other indicators such as heart rate, breath rate, oxygen saturation, procalcitonin, procalcitonin, direct bilirubin, albumin, D-dimer levels, activated partial thromboplastin time, glomerular filtration rate, chest radiography (CXR) abnormality have controversial conclusions[30, 31]. Our study also demonstrated that the COVID-19 infected patients with elder age, especially greater than 65 years, would have worse prognosis than younger patients. In our study, fever (63.0% in training cohort, 66.0% in validation cohort), cough (59.8% in training cohort, 65.1% in validation cohort) and fatigue (37.1% in training cohort, 38.3% in validation cohort) were the most common symptoms. But of all the symptoms, only fever is an

independent risk factor for prognosis, which is different from other studies. The reasons for the inconsistent reports of these models may be related to the risk of bias caused by the sample size and geographical differences of each model.

Our study has some limitations. First, the design was retrospective. Second, some cases had incomplete data on symptoms, laboratory tests, and imaging examinations, given the variation in the structure of electronic databases across different participating hospitals and an urgent data extraction schedule. Third, Sample size limit, future studies with larger sample sizes are warranted to validate our results. Fourth, severe patients were older than non-severe patients, and this difference in age may be a confounding factor. Fifth, although the study is multicenter, the results cannot be generalized to other populations. Sixth, we did not collect treatment-related data which may be critical to patient's outcome. However, all patients received treatment in accordance with the guidelines issued by the National health commission of China.

Conclusions

We established an early prediction model incorporating clinical characteristics that could be quickly obtained on hospital admission even on community health center. This model can be conveniently used to facilitate predicting the individual risk for ICU admission of COVID-19 patients and optimizing use of limited resources.

Abbreviations

COVID-19, coronavirus disease 2019; ICU, intensive care unit; LASSO, least absolute shrinkage and selection operator; AUC, area under the curve; RT-PCR, real-time reverse-transcriptase-polymerase-chain-reaction; OR, odds ratio; C-index, concordance index; DCAs, decision curve analyses; ROC, receiver operating characteristic; 95% CI, 95% confidence interval; SARS, Severe Acute Respiratory Syndrome; MERS, Middle East Respiratory Syndrome;

Declarations

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

Author's contributions

Conception and design: Yiwu Zhou, Yanqi He, Yao Rong and Zongan Liang, Collection and assembly of data: Huan Yang, He Yu and Zhu Chen. Data analyses and interpretation: Yanqi He and Ting Wang. Manuscript preparation: Yiwu Zhou and Yanqi He. Manuscript proofing: all authors. Final approval of the manuscript: all authors.

Competing interests

The authors have no conflict of interest to declare.

Ethics approval and consent to participate

After institutional review board approval was provided at each institution, written informed consent was obtained from each patient or the patient's legally authorized surrogate prior to conduct of study-specific procedures.

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Figures

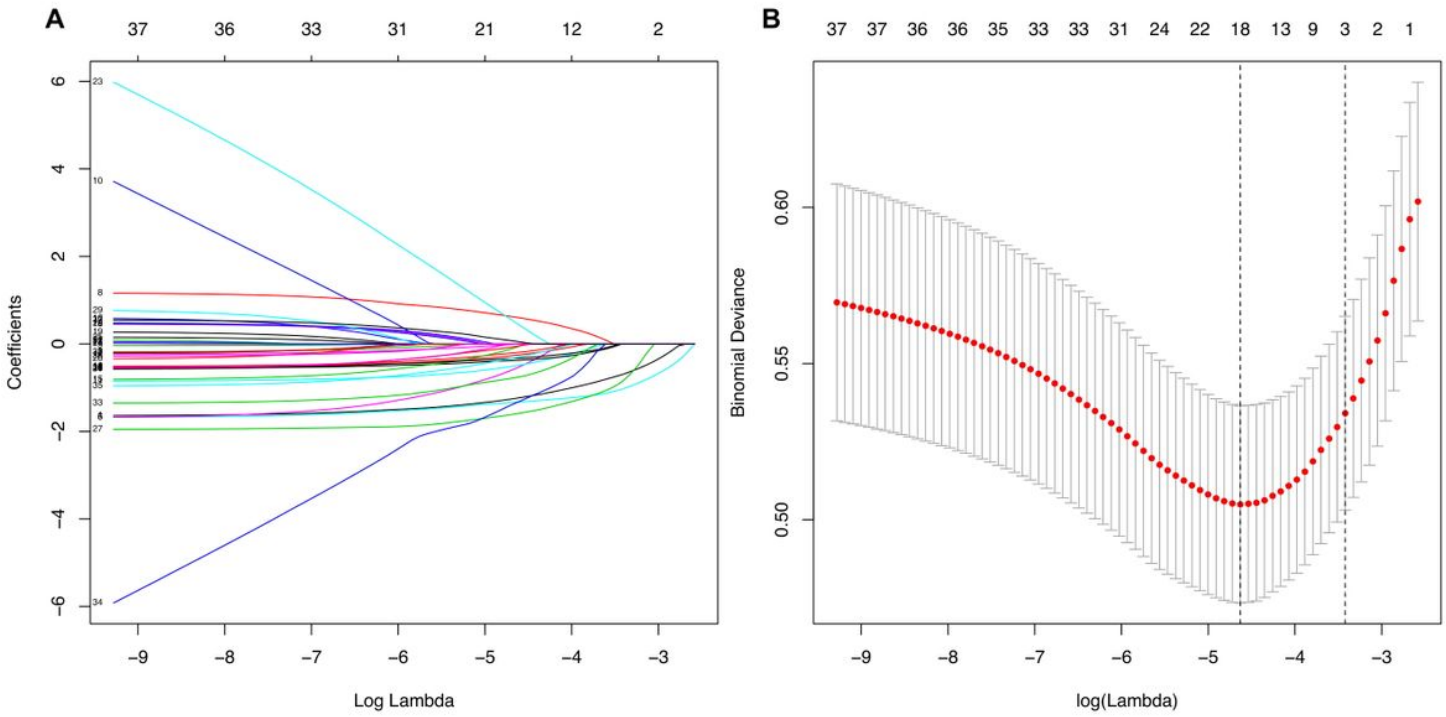

Figure 1

Selection of demographic and clinical features using the least absolute shrinkage and selection operator (LASSO) logistic regression model. (A). LASSO coefficient profiles of 19 features. (B). Selection of optimal parameters (lambda) from the LASSO model using five-fold cross-validation and minimum criteria.

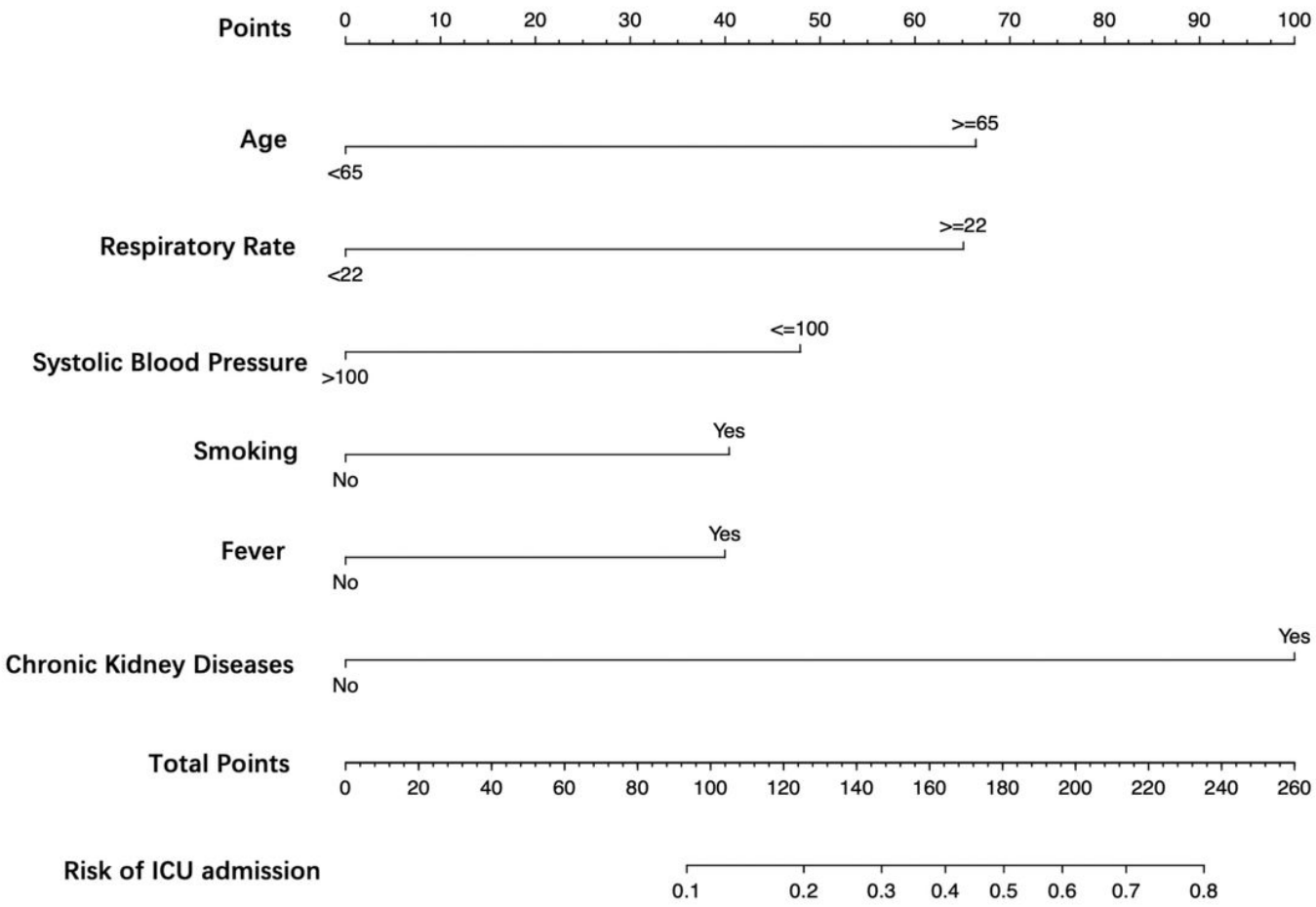

Figure 2

Development of a nomogram for predicting the risk of ICU admission in COVID-19 patients. The nomogram included age, respiratory rate, systolic blood pressure, smoking status, fever and chronic kidney disease. The nomogram summed the scores for each scale and variable. The total score on each scale indicated the risk of ICU admission.

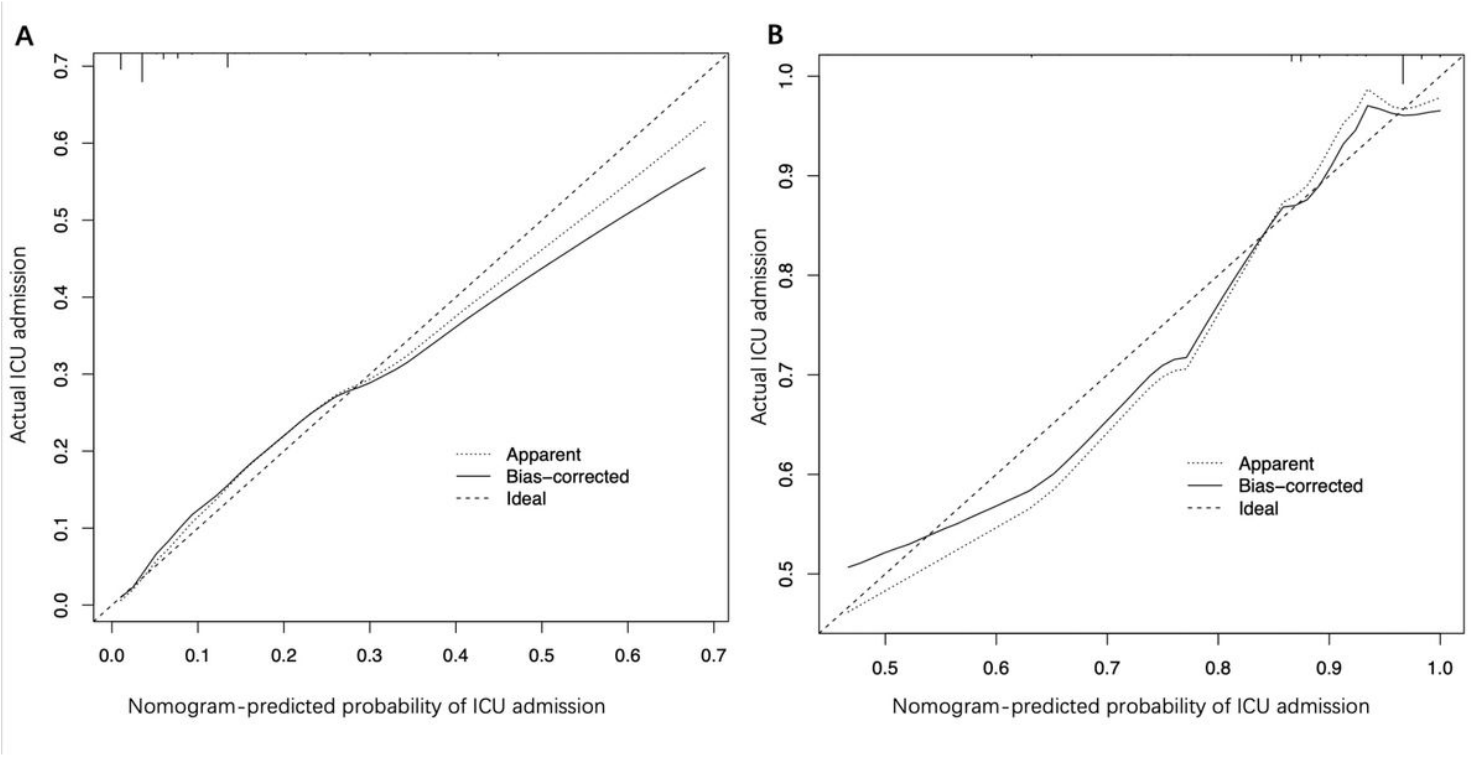

Figure 3

Calibration curves of the nomogram for predicting the risk of ICU admission in training (A) and validation cohort (B). Data on predicted and actual disease severity were plotted on the x- and y-axis, respectively. The diagonal dotted line indicates the ideal nomogram, in which actual and predicted probabilities are identical. The solid line indicates the actual nomogram, and a better fit to the dotted line indicates a better calibration.

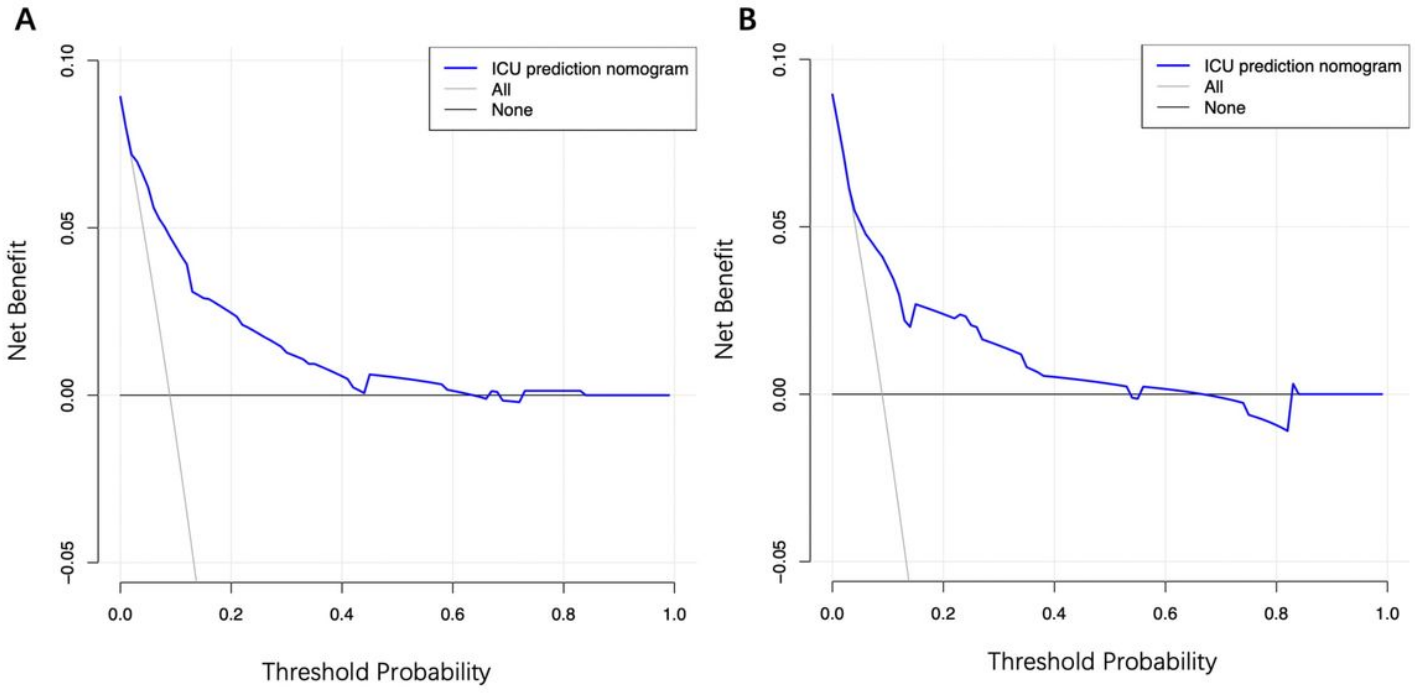

Figure 4

Decision curves of the nomogram predicting the risk of ICU admission in training (A) and validation cohort (B). The x-axis represents threshold probabilities and the y-axis measures the net benefit calculated by adding true positives and subtracting false positives.

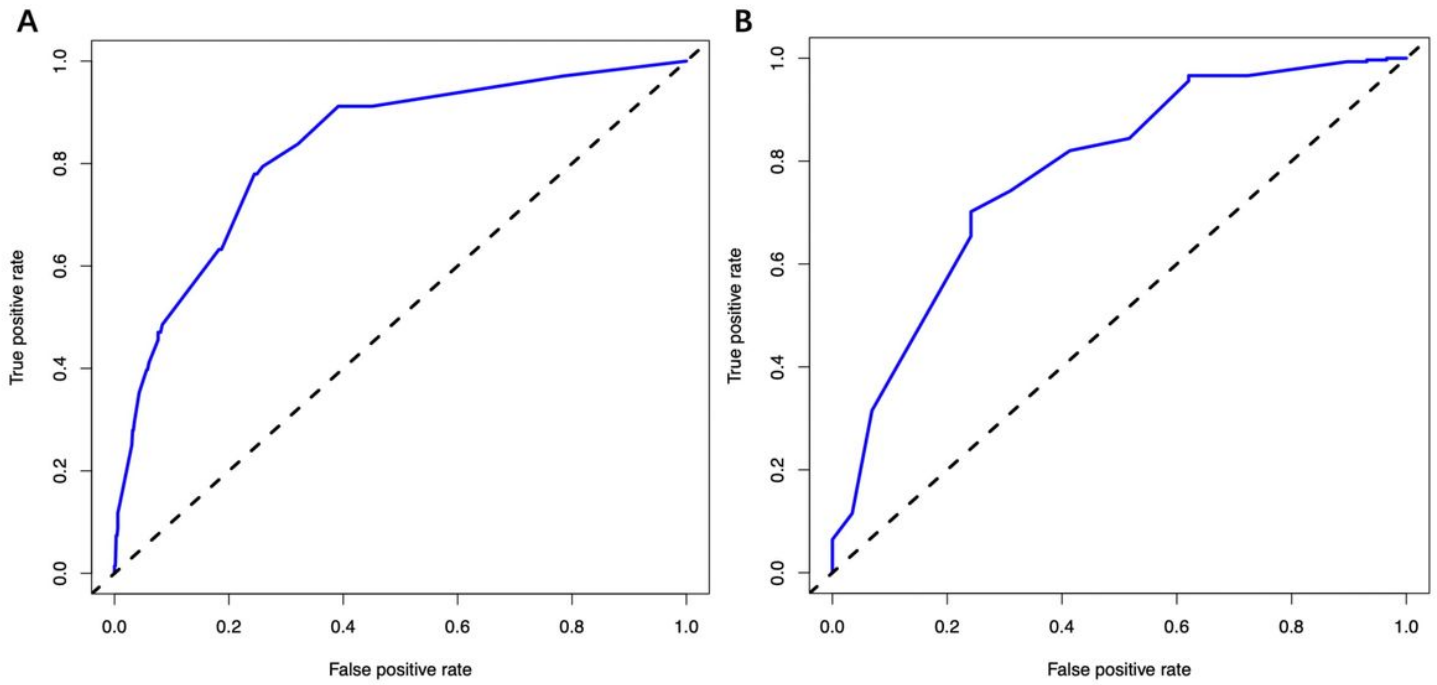

Figure 5

Receiver-operating characteristic curve of the nomogram for predicting the risk of ICU admission in training (A) and validation cohort (B).