Prognostic Value of Charlton's Weighted Index of Capabilities Combined with Chronic Health Evaluation II Score in COVID-19：a retrospective cohort study

Yali Qian
Children's Hospital Of Nanjing Medical University
Zhuo Li (Zhuoli0415@163.com)
Ziqiang Du
Children's Hospital Of Nanjing Medical University
Yanfang Zhu
Huangshi Hospital Of TCM(Infectious Desease Hospital)
Hongjun Miao
Children's Hospital Of Nanjing Medical University

Research article

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Abstract

Background: Since December 2019, coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread across the world. Age and underlying diseases have been reported as predictors of mortality in 2019-nCoV infection. Charlson's weighted index of comorbidities (WIC) and acute physiology and chronic health evaluation (APACHE) II are two frequently-used measures of comorbidity. In this study, we have assessed the performance of WIC and APACHE II in predicting the mortality of COVID-19 patients.

Methods: A total of 76 adult patients with COVID-19 were admitted to a designated hospital in Huangshi province from 1 January 2020 to 29 February 2020. Clinical data including age, gender, underlying diseases, and hospital mortality were collected. The APACHE II and WIC scores were assessed within the first 24 hours of admission. Univariate and multiple logistic regression analyses were used to compare the performance of WIC, APACHE II, and joint detection. The area under the receiver operating characteristic curve (AUC) was used to predict the hospital mortality.

Results: Of the 76 enrolled patients, 57 patients survived, and 19 died. The surviving patients had significantly lower WIC and APACHE II than the non-surviving patients (p-value < 0.05). The AUC for the hospital mortality was 0.814 (95% confidence interval (CI) 0.705-0.923) of WIC, 0.854 (95% CI 0.705-0.956) of APACHE II and 0.891(95% CI 0.830-0.966) for the joint detection. The diagnostic value of the joint detection was found to be better than that of WIC (p-value= 0.002) or APACHE II (p-value = 0.042).

Conclusions: The WIC and APACHE II scores might serve as independent determinants for the hospital mortality associated with COVID-19 patients. The combined use of WIC and APACHE II is more predictive than individuals

Background

The new coronavirus disease (COVID-19), started in Wuhan in December 2019, has now been considered as a pandemic and is rapidly spreading throughout China and the world [1, 2]. There were a total of 80864 accumulated confirmed cases of 2019-nCoV infections till March 6, 2020, in the mainland of China. Of these, a total of 3101 patients had died, 57355 had been discharged and 5264 remained in hospital [3]. The outbreak spreads rapidly and within 4 months, the World Health Organization(WHO) increased the risk of spread and impact of COVID-19 to very high at a global level on February 28th[4]. Although the epidemic rate in China appears to be decreasing, the number of confirmed cases in South Korea, Iran, Italy, France, and the United States is increasing rapidly.

As per the available reports, the COVID-19 patients admitted to ICU are often older and more likely to have underlying diseases like hypertension or diabetes[1]. At present, there is no vaccine or specific drug for COVID-19 patients, so it is critical to understand the nature of the virus and its clinical characteristics. Charlton’s weighted index of comorbidities (WIC) is a scoring system based on 19 basic diseases[5]. This has been widely employed in clinical practice. Previous studies have shown that the WIC score can be

used as a prognostic evaluation index for critically ill patients[6]. Acute physiology and chronic health status score (APACHE) were proposed by the American scholar Knaus in the 1980s. It includes the acute physiology score (APC) reflecting the severity of the acute disease and the chronic health condition (CHS) before the illness, this has been widely used in mortality prediction and criticality assessment[7]. The present study is focused on exploring the values WIC and APACHE II scores for the condition assessment, treatment and prognosis of COVID-19 patients.

Methods

Study population

We performed a retrospective study on 76 severe and critical COVID-19 patients (> 18 years) in Huangshi Hospital of TCM (Infectious Disease Hospital), Hubei Province between January 1 to February 28, 2020. All cases were confirmed by the Local Center for Disease Control and Prevention through a nucleic acid test. The clinical types were classified as mild, common, severe, and critically severe infection according to "Recommendations for the diagnosis and prevention of new coronavirus infection 2019 (edition 5)" [8] The diagnostic criteria for severe cases was one of the following: respiratory distress, RR ≥ 30 beats/min; means oxygen saturation ≤ 93% in resting-state; arterial blood oxygen partial pressure (PaO2) /oxygen concentration (FiO2) ≤ 300 mmHg. For critical severe cases it was one of the following: respiratory failure requiring mechanical ventilation; shock state; combined failure of other organs requiring ICU monitoring and treatment. The basic information such as age, gender, weight, basic treatment and outcome of the patients were recorded.

Clinical Information

In addition to the general epidemiological characteristics, we specifically documented chronic conditions that were suspected risk factors for COVID-19 patients. This primarily included autoimmune diseases, diabetes, hypertension, cardiovascular disease, and respiratory disorders. Most of the patients admitted to the hospital had chest imaging examinations. Clinical symptoms upon admission and during the illness were also recorded.

Laboratory Variables On Admission

Information about levels of serum glucose, serum creatinine, sodium, phosphate, phosphorus, hemoglobin, neutrophil count, white blood count, C-reactive protein (CRP), lymphocyte count, lymphocyte percentage, and serum albumin were obtained from the medical records.

Statistical Methods

Categorical variables were presented as number and percentage (%) and were compared using the Chi-squared test or Fisher's exact test. Continuous variables with normal distribution were presented as mean ± standard deviation (SD). Variable without normal distribution were represented as median (interquartile range [IQR]). They were compared using either Student's t-test or the Mann-Whitney U test. The correlation between the indicators was analyzed by Spearman rank correlation. The relationship between each variable and the patient's prognosis was analyzed by the multivariate logistic regression model. The receiver operating characteristic curve (ROC) was used to evaluate the value of different scoring methods on the prognosis of the COVID-19. Two-sided p-values < 0.05 were considered significant. All the analyses were performed using SPSS (version 21.0).

Results

A total of 76 severe COVID-19 patients (age 63.5 ± 14.7 years) were included in the study. Among these 45 (59%) were males and 31 (41) were female (p-value = 0.89). Among the dead, all the subjects were older than 50 years (72.6 ± 12.1 years). This also included 6 patients that were 50–65 years old (31.5%). A total of 13 patients were over 65 years (68.5%) and approximately half of the patients had at least one chronic disease on admission. The most common diseases were hypertension (n = 29,38%), cardiovascular disease (n = 14,18%), diabetes (n = 11,15%), lung disease (n = 3,4%), tumor (n = 3,4%), tuberculosis (n = 3,4%), hepatic disease (n = 4,5%), cerebrovascular disease (n = 1,1%), connective tissue diseases (n = 1,1%).

The most common symptoms at the onset of illness were fever (53 [70%] of 76 patients), cough (36 [47%]), and myalgia or fatigue (4 [5%]). Relatively less common symptoms were headache (1 [1%]), diarrhea (3[4%]). Fourteen (14) patients (18%) had developed dyspnea.

Peripheral white blood cell counts were normal in severe and critically severe patients (p-value > 0.05). A decrease in the number of lymphocytes was noted in non-survivors but not in survivors (p-value > 0.05). The value of c-reactive protein for all the patients was above the normal range (p-value > 0.05). The average levels of platelets, blood potassium, blood calcium, blood phosphorus and blood glucose in 76 patients were normal (p-value > 0.05). All the patients on admission showed hyponatremia (p-value > 0.05) and hypoalbuminemia (average 36.74 g/L). These values were lower in non-survivors as compared to the survivors (p-value = 0.006) (Table 1).

Table 1
Demographic, Clinical and Laboratory Findings of Patients on Admission

Characteristics	All patients (n = 76)	Survivors(n = 57)	Nonsurvivors(n = 19)	p value
Age(years, mean ± SD)	63.5 ± 14.7	60.5 ± 14.4	72.6 ± 12.1	0.001
Sex				0.89
Male	45(59%)	34(60%)	11(58%)	
Female	31(41%)	23(40%)	8(42%)	
Charlton's weighted index of capabilities (Median□Quartile low, Quartile up)□[a]	3(2,3)	2(0,3)	4(3,6)	0.000
Acute physiology and chronic health evaluation II score (mean ± SD)[b]	9.4 ± 4.8	8.2 ± 4.4	13.3 ± 3.9	0.000
Comorbidity				
Hypertension	29(38%)	21(36%)	8(42%)	0.68
Lung disease	3(4%)	2(4%)	1(5%)	0.73
Hepatic disease	4(5%)	3(5%)	1(5%)	1
Diabetes	11(15%)	10(18%)	1(5%)	0.19
Cerebrovascular disease	1(1%)	0	1(5%)	0.08
Connective tissue diseases	1(1%)	0	1(5%)	0.08
Tumor	3(4%)	1(2%)	2(10%)	0.09
Tuberculosis	3(4%)	2(4%)	1(5%)	0.73
Cardiovascular disease	14(18%)	9(16%)	5(26%)	0.34
Signs and symptoms				
Fever	53(70%)	39(63%)	14(74%)	0.67
Cough	36(47%)	28(49%)	8(42%)	0.59
Myalgia or fatigue	4(5%)	4(7%)	0	0.24
SD = standard deviation.				
Data are median (IQR), n (%), or n/N (%).				
[a]Charlton's weighted index of Capabilities was assessed within 24 hr of admission to hospital				
[b]Acute Physiology and Chronic Health Evaluation II score was assessed within 24 hr of admission to hospital				

Characteristics	All patients (n = 76)	Survivors(n = 57)	Nonsurvivors(n = 19)	p value
Headache	1(1%)	1(2%)	0	0.56
Diarrhea	3(4%)	1(2%)	2(10%)	0.09
Dyspnea	14(18%)	9(16%)	5(26%)	0.31
> 24 breaths per min	36(47%)	23(40%)	13(68%)	0.03
Mean arterial pressure, mm Hg	97.6 ± 10.2	97.3 ± 10.2	96.6 ± 10.4	0.79
Laboratory parameters				
Lymphocyte count(10^9/L)	0.85 ± 0.65	0.89 ± 0.71	0.71 ± 0.44	0.29
Albumin,g/L	36.74 ± 4.93	37.45 ± 4.43	34.60 ± 5.80	0.02
Creatinine,μmol/L	65.47 ± 20.85	63.16 ± 20.08	72.41 ± 22.08	0.09
White blood cell count, × 10 per L	5.4 ± 2.68	5.08 ± 2.03	6.35 ± 3.98	0.07
Neutrophil count, × 10^9 per L	4.11 ± 2.54	4.39 ± 2.76	3.25 ± 1.50	0.09
Hemoglobin, g/L	129.63 ± 30.04	126.68 ± 23.19	138.47 ± 44.45	0.13
Platelet count, × 10 per L	150.80 ± 57.79	157.72 ± 58.82	130.05 ± 50.48	0.07
C-reactive protein, mg/L	57.72 ± 36.48	55.55 ± 37.86	64.22 ± 32.03	0.37
Potassium, mmol/L	4.01 ± 0.55	3.99 ± 0.53	4.05 ± 0.61	0.65
Sodium, mmol/L	130.95 ± 30.93	130.96 ± 30.67	131.46 ± 32.53	0.93
Phosphate, mmol/L	0.97 ± 0.23	0.95 ± 0.21	1.04 ± 0.26	0.15
Blood sugar,mmol/L	9.58 ± 15.20	10.19 ± 17.49	7.73 ± 2.61	0.55
SD = standard deviation.				
Data are median (IQR), n (%), or n/N (%).				
[a]Charlton's weighted index of Capabilities was assessed within 24 hr of admission to hospital				
[b]Acute Physiology and Chronic Health Evaluation II score was assessed within 24 hr of admission to hospital				

The survivor group had a median WIC of 2 (0,3) while the median for the non-survivor group was 4(3,6). 14 patients (18.4%) had WIC of 0 and survived, 2 patients (2.6%) had WIC of 1, 20 patients (26.3%) had WIC of 2, 22 patients (28.9%) had WIC of 3, 7 patients (9.2%) had WIC of 4, and 4 patients (5.3%) had WIC of 5. The group with WIC greater than or equal to 6 had 7 patients and all of them died. An increasing WIC was found to be associated with higher mortality. (Fig. 1)

The group whose APACHE score ranged from 0 to 5 had 21 patients and only one died. There were 28 patients with APACHE scores ranging from 6 to 10. A total of 20 patients were part of the group with APACHE II values ranging from 11 to 15 and 6 patients in the group with values ranging from 16 to 20. Only one patient had score higher than 20 and he/she did not survive. (Fig. 2)

We also found a correlation (Medium) between the APACHE score and WIC score ($r = 0.565$; p-value < 0 .000). Multivariate Logistic regression analysis was performed using age, WIC score, APACHE score, albumin and respiratory rate > 24 breaths per min. These were indicated as covariates by univariate logistic regression (variable inclusion criteria p-value < 0.05). The multivariate logistic regression model identified APACHE score and the WIC as independent risk factors of COVID-19 death. (Table 2)

Table 2
Risk Factors Associated with In-hospital Death

Demographics and clinical characteristics	Univariable OR(95% CI)	p value	Multivariable OR (95% CI)	p value
Age(years)	1.07(1.02–1.12)	0.003	0.98(0.91–1.06)	0.681
Female sex(vs male)	0.93(0.324–2.667)	0.890	-	-
Comorbidity present (vs not present)				
Hypertension	0.80(0.28–2.31)	0.683	-	-
Lung disease	0.66(0.06–7.65	0.735	-	-
Hepatic disease	1(0.09–10.23)	1.000	-	-
Diabetes	3.83(0.46–32.11)	0.216	-	-
Tumor	0.15(0.01–1.78)	0.133	-	-
Tuberculosis	0.66(0.06–7.65)	0.735	-	-
Cardiovascular disease	0.53(0.15–1.82)	0.310	-	-
> 24 breaths per min	0.312(0.10–0.94)	0.039	2.31(0.51–4.19)	0.277
Charlton's weighted index of capabilities	2.53(1.54–4.16)	0.000	2.18(1.14–4.19)	0.019
Acute physiology and chronic health evaluation II score	1.30(1.13–1.49)	0.000	1.28(1.08–1.51)	0.004
laboratory parameters				
Lymphocyte count(10^9/L)	0.32(0.07–1.49)	0.146	-	
Albumin	0.88(0.78–0.99)	0.034	1.04(0.89–1.22)	0.558
Creatinine,μmol/L	1.02(0.99–1.05)	0.097	-	-
White blood cell count,x10^9 per L	1.13(0.88–1.44)	0.336	-	-
Neutrophil count, × 10^9 per L	0.76(0.55–1.04)	0.090	-	-
Haemoglobin, g/L	1.01(0.99–1.03)	0.190	-	-

Univariable and multivariate logistic regression analysis of risk factors associated with hospitalized patients.

OR = Odds Ratio.CI = Confidence Interval.

Demographics and clinical characteristics	Univariable OR(95% CI)	p value	Multivariable OR (95% CI)	p value
Platelet count, × 10 per L	0.99(0.98-1.00)	0.077	-	-
C-reactive protein, mg/L	1.01(.099-1.02)	0.369	-	-
Potassium, mmol/L	1.25(0.49–3.19)	0.645	-	-
Sodium, mmol/L	1.00(0.98–1.02)	0.933	-	-
Phosphate, mmol/L	5.26(0.55–50.63)	0.151	-	-
Blood sugar,mmol/L	0.97(0.874–1.09)	0.630	-	-
Univariable and multivariate logistic regression analysis of risk factors associated with hospitalized patients.				
OR = Odds Ratio.CI = Confidence Interval.				

When the WIC score and the APACHE score were substituted into Logit (P) =-5.724 + 0.814xWIC + 0.199xAPACHE and the predicted probability of the equation was saved as the combined value of the two scores. The area under the ROC curve (AUC) of the WIC score, APACHE score, and their combined predicted probabilities were 0.814, 0.854, and 0.891, respectively. This further indicates that they are highly valuable to predict the prognosis of the COVID-19. The AUC of joint detection was the largest indicating that the accuracy rate of predicting survival outcomes was greater than any single indicator (Fig. 3).

The cutoff value for Charlton's WIC as revealed by the ROC curve was 2.5 while the APACHE was 10.5. The sensitivity and specificity of Charlton's WIC were 84.2% and 57.9% while the APACHE was 84.2% and 64.9%, respectively. The ROC curve of the joint detection is 0.891. The sensitivity and specificity were 94.7% and 68.4%, respectively (Table 3). The diagnostic value of the joint detection was better than WIC (p-value = 0.002) and APACHE II (p-value = 0.042).

Table 3
Cut-off Value,95% CI, P value, Cut-off value, Sensitivity and Specificity of Predictors of Mortality

Predictors of Mortality	AUC[a]	95% CI	P value	cut-off value	sensitivity(%)	specificity(%)
WIC[b]	0.814	0.705–0.923	0.000	2.5	84.2	57.9
APACHE Ⅱ[c]	0.854	0.753–0.963	0.000	10.5	84.2	64.9
Joint detection[d]	0.891	0.818–0.966	0.000	0.947	94.7	68.4
[a]AUC= Area under the receiver operating characteristic curves.						
[b]Charlton's weighted index of Capabilities were assessed within 24 hr of admission to hospital						
[c]Acute Physiology and Chronic Health Evaluation (APACHE) II score was assessed within 24 hr of admission to hospital. WIC = Charlton's weighted index of comorbidities						
[d] Predicted probability of the equation by substituting WIC score and the APACHE Ⅱ score into Logit (P) =-5.724 + 0.814xWIC + 0.199xAPACHE Ⅱ						

Discussion

The 2019-nCoV emerged at the end of 2019 from Wuhan and has already spread across the world. The 2019-nCoV is a newly discovered virus and no effective antiviral treatments have been identified yet. Here we report a cohort of 76 2019-nCoV infection patients and identified several risk factors of death in severe patients. Furthermore, we found a prediction model that can help to identify critical patients early and give them more attention.

Older age has been reported as an important independent predictor of mortality in 2019-nCoV infections [9]. Our study confirmed that the risk of death may increase with age in patients with COVID-19. We also confirmed that many critically ill patients have evidence of an underlying illness such as cardiovascular disease, liver disease or malignant tumors. Findings suggest that we should pay more attention to the patients who have comorbidity and the prevention of multiorgan injuries in the treatment of COVID-19. We observed a lower albumin level in dead COVID-19 cases. It was consistent with previous reports suggesting lower serum albumin is associated with higher mortality in critically ill patients [10, 11]. In the context of oxidative stress, serum albumin plays an important role as it binds to variety of substances such as fatty acids and homocysteine lipoproteins and protect them from oxidation [12].

WIC is a scoring system developed by Charlson[5] to assess the severity of patients with underlying diseases. It evaluates 19 chronic diseases and gives different scores as per the severity of the disease to obtain a quantification of the underlying diseases. Many studies have reported that the WIC scoring system can predict prognosis accurately in patients with malignant tumors [13], sepsis [14], long-term

mechanical ventilation [15]. Some studies found that the WIC score can also predict hospital mortality in critical patients [16]. APACHE II score contains 12 routine physiological measurements, previous health status, recent surgery, history of severe organ insufficiency, immunocompromised state and age [17]. It is one of the most commonly used scoring systems to evaluate the critical patients and has shown to be an accurate measurement of disease severity and strongly correlates with outcome in critical patients [18]. In this study, we analyzed clinical characteristics and laboratory examination of survivors and non-survivors of COVID-19. The predictors were explored through univariate analyses and multivariate linear and logistic regression. We also found that it is possible to combine the WIC score with the APACHE II score by establishing a logistic regression model. The area under the curve (AUC) of joint detection was 0.891 while the individual AUCs for WIC and APACHE II were 0.814 and 0.854, respectively. This indicates an improvement in the forecasting ability on the sensitivity of the 76 COVID-19 patients with hospital mortality.

Our research has some limitations. First, all the patients did not undergo laboratory tests for lactate dehydrogenase, PCT, and hematologic values. Due to the retrospective study design their role in predicting in-hospital mortality may be overestimated. Prospective studies may help to decrease this influence. Second, the retrospective, correlational study design limits possible conclusions to those of available data. The generalizability of results may be limited due to the demographics of the available population and the fact that we used a single hospital to obtain the data. The next step would be to conduct a multicenter study with a larger sample size.

Conclusions

In addition to age and basic diseases, the WIC and APACHE □ scores might be independent determinants for hospital mortality among patients with COVID-19 infections. The combined use of WIC and APACHE II was found to be more predictive.

Abbreviations

COVID-19: Coronavirus disease 2019; WIC: Charlson's weighted index of comorbidities; APACHE: Acute physiology and chronic health evaluation; AUC: Area under the receiver operating characteristic curve; CI: Confidence interval; APC: Acute physiology score; CHS: Chronic health condition; SD: Standard deviation; ROC: Receiver operating characteristic curve;

Declarations

Ethics approval and consent to participate: The study protocol was approved by the Institutional Review Board of Huangshi Hospital of TCM (Infectious Disease Hospital).

Consent for publication: Not applicable.

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: YLQ wrote the paper. ZL commented on the manuscript and approved the final version. All authors contributed to the design of the study.ZQD and YFZ participated in data collection. HJM performed the statistical analyses. All authors read and approved the final manuscript.

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Authors' information (optional): [1]Department of Emergency / Critical Medicine, Children's Hospital of Nanjing Medical University, Nanjing, Jiangsu, China;[2]Department of Critical Medicine, Huangshi Hospital of TCM (Infectious Disease Hospital), Hubei, China.

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Figures

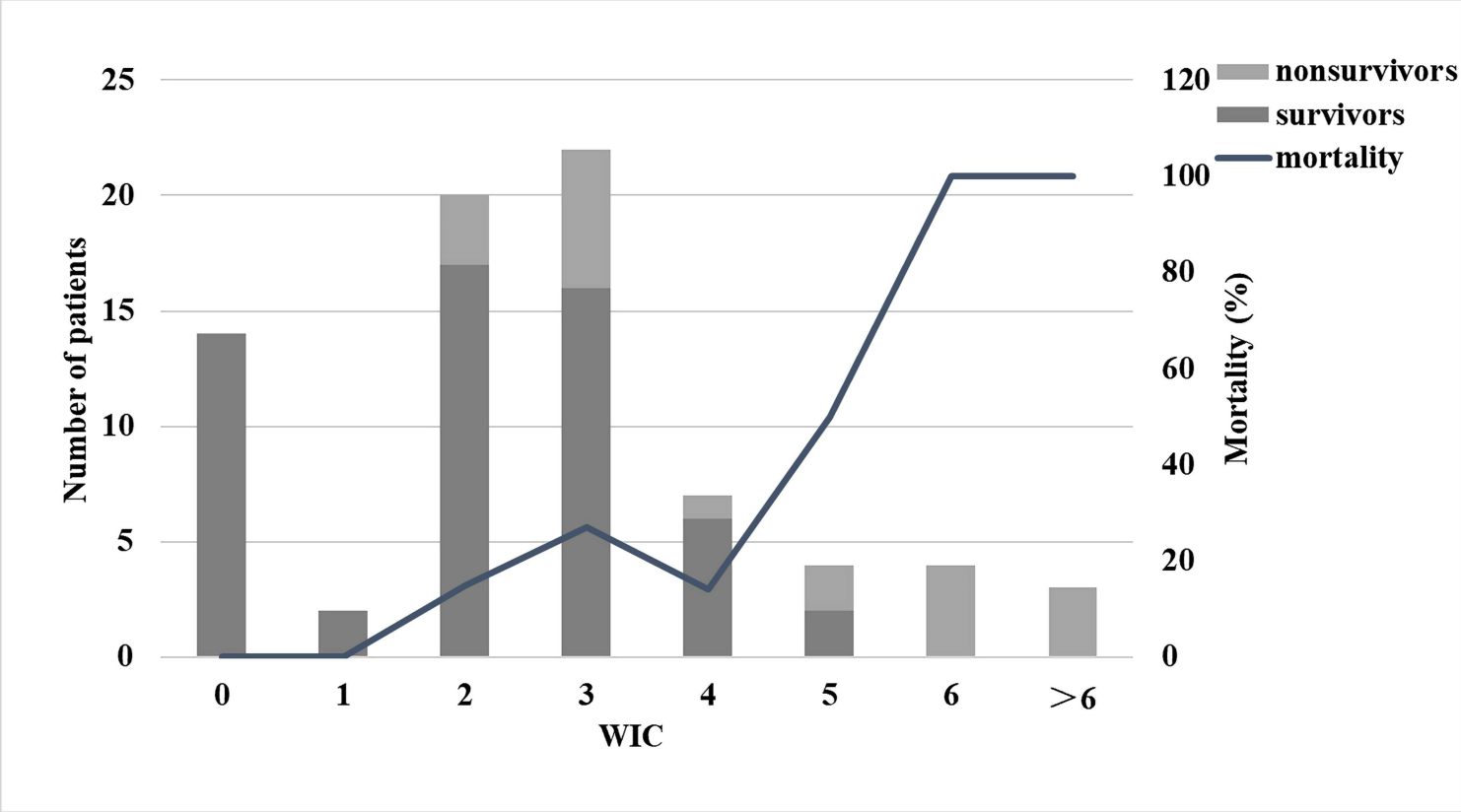

Figure 1

The number of survivors and nonsurvivors for each Charlton's weighted index of Capabilities score level (left Y axis) and the corresponding mortality (right Y axis).

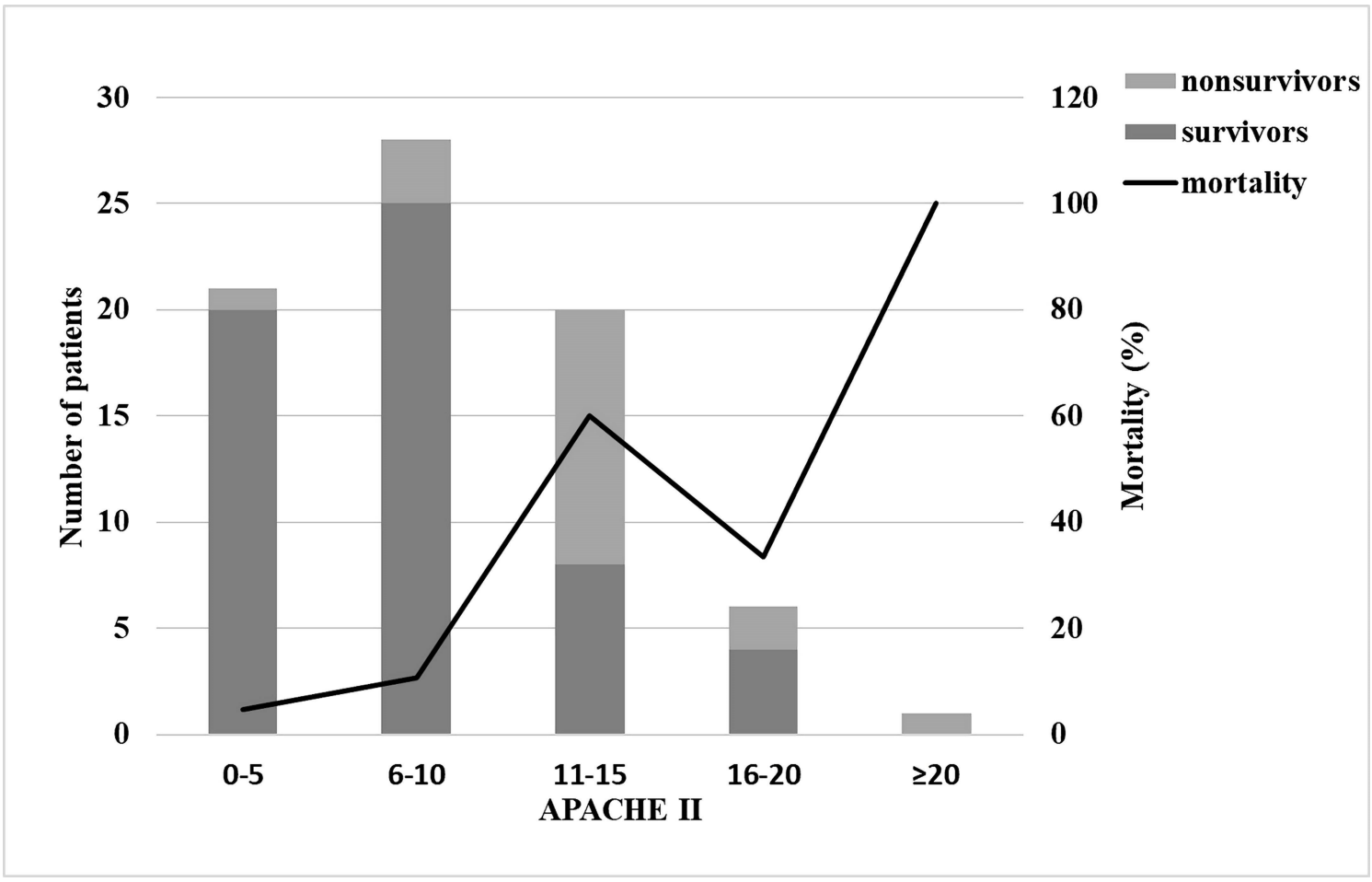

Figure 2

The number of survivors and nonsurvivors for each APACHE level (left Y axis) and the corresponding mortality (right Y axis)

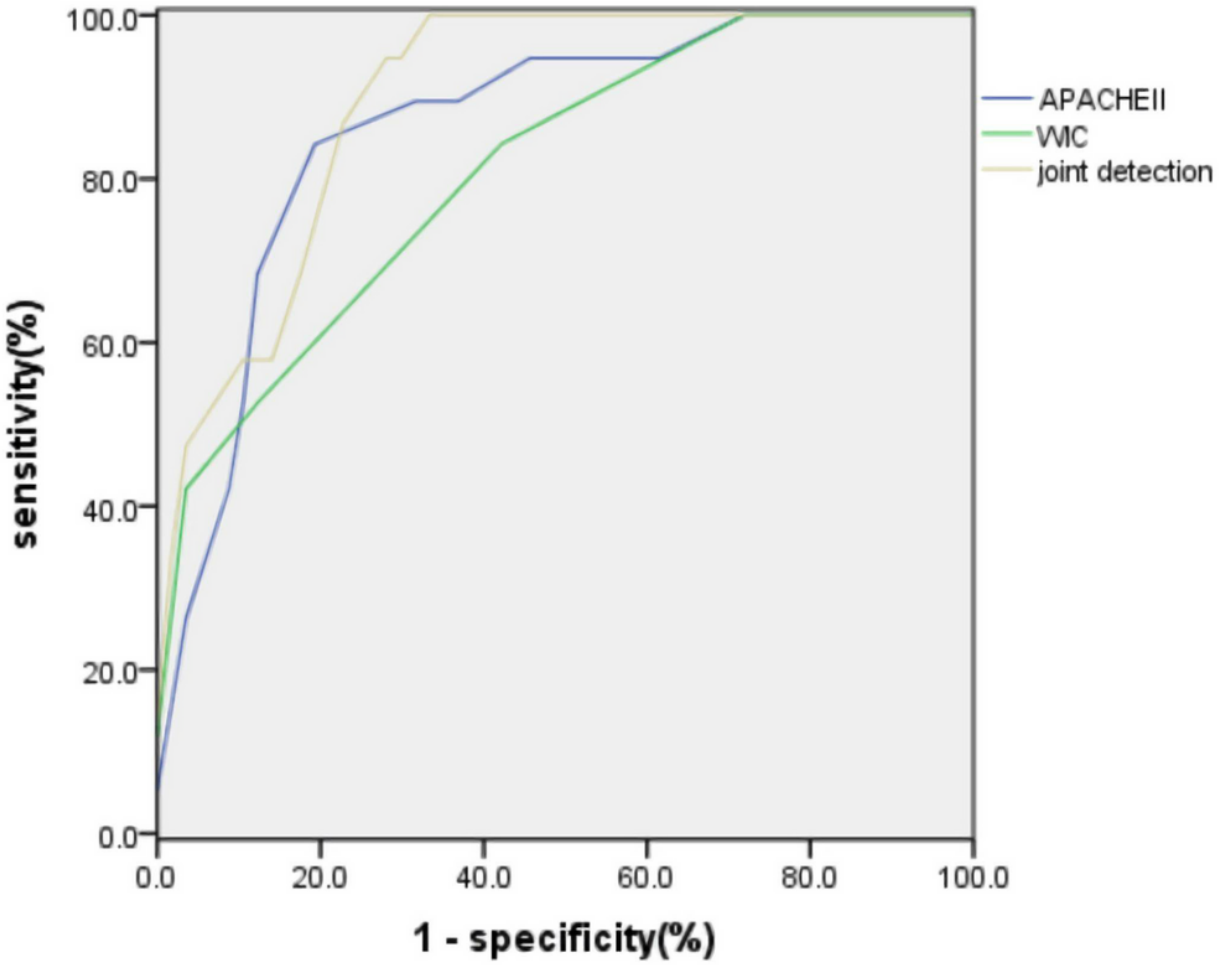

Figure 3

Receiver operating characteristic curves of Charlson's WIC and APACHE Ⅱ for predicting hospital mortality.