Acute Physiology and Chronic Health Evaluation II Score as a Predictor of Hospital Mortality in Patients of Coronavirus Disease 2019

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Objectives: Coronavirus disease 2019 has emerged as a major global health threat with a great number of deaths in China. We aimed to assess the association between Acute Physiology and Chronic Health Evaluation II score and hospital mortality in patients with coronavirus disease 2019, and to compare the predictive ability of Acute Physiology and Chronic Health Evaluation II score, with Sequential Organ Failure Assessment score and Confusion, Urea, Respiratory rate, Blood pressure, Age 65 (CURB65) score.

Design: Retrospective observational cohort.

Setting: Tongji Hospital in Wuhan, China.

Subjects: Confirmed patients with coronavirus disease 2019 hospitalized in the ICU of Tongji hospital from January 10, 2020, to February 10, 2020.

Interventions: None.

Measurements and Main Results: Of 178 potentially eligible patients with symptoms of coronavirus disease 2019, 23 patients (12.92%) were diagnosed as suspected cases, and one patient (0.56%) suffered from cardiac arrest immediately after admission. Ultimately, 154 patients were enrolled in the analysis and 52 patients (33.77%) died. Mean Acute Physiology and Chronic Health Evaluation II score (23.23 ± 6.05) was much higher in deaths compared with the mean Acute Physiology and Chronic Health Evaluation II score of 10.87 ± 4.40 in survivors ($p < 0.001$). Acute Physiology and Chronic Health Evaluation II score was independently associated with hospital mortality (adjusted hazard ratio, 1.07; 95% CI, 1.01–1.13). In predicting hospital mortality, Acute Physiology and Chronic Health Evaluation II score demonstrated better discriminative ability (area under the curve, 0.966; 95% CI, 0.942–0.990) than Sequential Organ Failure Assessment score (area under the curve, 0.867; 95% CI, 0.808–0.926) and CURB65 score (area under the curve, 0.844; 95% CI, 0.784–0.905). Based on the cut-off value of 17, Acute Physiology and Chronic Health Evaluation II score could predict the death of patients with coronavirus disease 2019 with a sensitivity of 96.15% and a specificity of 86.27%. Kaplan-Meier analysis showed that the survivor probability of patients with coronavirus disease 2019 with Acute Physiology and Chronic Health Evaluation II score less than 17 was notably higher than that of patients with Acute Physiology and Chronic Health Evaluation II score greater than or equal to 17 ($p < 0.001$).

Conclusions: Acute Physiology and Chronic Health Evaluation II score was an effective clinical tool to predict hospital mortality in patients with coronavirus disease 2019 compared with Sequential Organ Failure Assessment score and CURB65 score. Acute Physiology and Chronic Health Evaluation II score greater than or equal to 17 serves as an early warning indicator of death and may provide guidance to make further clinical decisions. (*Crit Care Med* 2020; XX:00–00)

Key Words: Acute Physiology and Chronic Health Evaluation II score; coronavirus disease 2019; mortality; risk factor; severe acute respiratory syndrome coronavirus 2

In December 2019, a cluster of acute pneumonia infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), now known as coronavirus disease 2019 (COVID-19), occurred in Wuhan, China (1–3). The disease has rapidly spread throughout China and many other countries. A total of 79,251 cases and 2,835 deaths have been reported in China, whereas 4,767 cases and 68 deaths have been reported in 53 countries and regions outside China by February 28, 2020. The mortality of hospitalized patients was 4.3–11% (4, 5). The 28-day mortality of the critical patients was reported to be 61.5%, which was considerable (6). COVID-19 has emerged as a major global health threat; however, no clinical scoring

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system was reported to identify patients with a potentially unfavorable prognosis quickly.

During the clinical practice of patients' treatment, we observed that some patients rapidly deteriorated, developing respiratory failure, acute respiratory distress syndrome (ARDS), and even multiple organ failure, leading to death. Evaluation of various organ functions may predict the mortality of patients with COVID-19. Acute Physiology and Chronic Health Evaluation (APACHE) II score and Sequential Organ Failure Assessment (SOFA) score are commonly used to assess disease severity and estimate hospital mortality in general critical illnesses (7, 8). Confusion, Urea, Respiratory rate, Blood pressure, Age 65 (CURB65) score is commonly used to assess the severity and mortality of pneumonia (9). These scoring system may also be used to assess the mortality of COVID-19.

In this study, we aimed to describe the difference of epidemiologic and clinical characteristics between survivors and deaths, and we attempt to provide an effective clinical tool to predict the probability of death among patients with COVID-19.

MATERIALS AND METHODS

Study Design and Participants

This single-center, retrospective study was done at Tongji hospital. Tongji hospital, located in Wuhan, Hubei Province, the endemic areas of COVID-19, is one of the major tertiary teaching hospitals and is responsible for the treatments for patients with severe COVID-19 assigned by the government. We recruited inpatients cared in the ICU from January 10, 2020, to February 10, 2020, who have been diagnosed as COVID-19, according to World Health Organization interim guidance (10). Laboratory confirmation of COVID-19 was performed by the local health authority as previously described (11). Data of the patients were achieved by reviewing the admission logs and histories from all available electronic medical records and patient care resources. The patients were followed up to February 25, 2020. This study was approved by the Ethics Commission of Tongji Hospital (TJ-IRB20200225).

Data Collection

Data extraction was performed by physicians using a standardized form to collect data about demographic characteristics, exposure history to Huanan seafood market, delay time from illness onset to hospitalization, underlying chronic medical conditions, symptoms from onset to admission, vital signs, laboratory finding, complications, and outcomes. The date of disease onset was defined as the day when the symptom was noticed. For all patients, the Glasgow Coma Score (GCS), SOFA score, CURB65 score, and APACHE II score were assessed within 24 hours of admission. The length of hospitalization and outcome state of each patient were recorded.

ARDS was defined according to the Berlin definition (12). Acute kidney injury was identified according to the Kidney Disease: Improving Global Outcomes definition. The cardiac injury was defined if the serum levels of cardiac biomarkers (e.g., troponin I) were above the 99th percentile upper reference limit or new abnormalities were shown in electrocardiography and echocardiography (11).

Statistical Analysis

Based on the clinical implications of laboratory indices, we identified the cut-off value of these indicators to be the upper or lower limits of their normal range. Values are presented as mean ± SD or as number and percentage for continuous variables and categorical variables, respectively. The difference of categorical variables between the survivors and deaths groups was compared by chi-square test or Fisher exact test when appropriate, whereas continuous variables were compared using Student *t* test. Spearman correlation analysis was performed among significant variables in the univariate analysis. Univariate and multivariate Cox regression analysis was used to explore the effect of APACHE II score, SOFA score, and CURB65 score on the occurrence of death. Taking account of the potential bias, only variables with the absolute value of a correlation coefficient less than 0.4 were included in the initial model of multivariate Cox regression analysis. Receiver operating characteristics (ROC) analyses were conducted to evaluate and compare the predictive value of these three scoring systems. The scoring system with largest area under the curve (AUC) of ROC curve was selected for further analysis. The cut-off value of the selected scoring system was determined based on the maximum Youden index. Then the patients with COVID-19 were classified into two groups: low risk, less than cut-off point value and high risk, greater than or equal to cut-off point value. Kaplan-Meier method was used to compare the survival between these two groups with log-rank test. A p value of less than 0.05 was considered statistically significant. All analyses were performed with SAS 9.4 (SAS Institute, Cary, NC) and R Project version 3.6.2 (R Project for Statistical Computing, Vienna, Austria; http://cran.r-project.org).

RESULTS

From January 10, 2020, to February 10, 2020, 178 inpatients with symptoms of COVID-19 had been admitted to ICU of Tongji hospital. Of these patients, 23 patients (12.92%) were diagnosed as suspected cases and one patient (0.56%) suffered from cardiac arrest immediately after admission. Therefore, only 154 patients, including 102 survivors and 52 deaths, were enrolled in this study. Most of these patients (92.86%) were admitted to ICU directly, and 11 patients were transferred from other wards. The days stay in the ward before ICU admission were 5.27 ± 2.87.

Baseline Characteristics, Treatments, and Outcomes

The most common symptoms of the COVID-19 patients were fever (89.61%), cough (66.88%), and dyspnea (48.70%). Compared with survivors, there were more patients who were 60 years old or above, with coronary heart disease, and with symptoms of dyspnea or diarrhea in deaths (all $p < 0.05$). APACHE II score (23.23 ± 6.05 vs 10.87 ± 4.40; $p < 0.001$),

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TABLE 1. Baseline Characteristics and Outcome of the Patients With Coronavirus Disease 2019

Variables	All Patients (*n* = 154)	Survivors (*n* = 102)	Deaths (*n* = 52)	*p*
Age (yr), mean ± SD	60.68 ± 13.00	56.45 ± 12.64	68.98 ± 9.22	**< 0.001**
Age group (yr), *n* (%)				
< 60	63 (40.91)	55 (53.92)	8 (15.38)	**< 0.001**
≥ 60	91 (59.09)	47 (46.08)	44 (84.62)	
Male sex, *n* (%)	67 (43.51)	47 (46.08)	20 (38.46)	0.367
Huanan seafood market exposure, *n* (%)	47 (30.52)	31 (30.39)	16 (30.77)	0.962
Smoking, *n* (%)	13 (8.44)	7 (6.86)	6 (11.54)	0.496
Chronic medical illness, *n* (%)				
Any	80 (51.95)	48 (47.06)	32 (61.54)	0.089
Hypertension	47 (30.52)	26 (25.49)	21 (40.38)	0.058
Coronary heart disease	23 (14.94)	5 (4.90)	18 (34.62)	**< 0.001**
Diabetes	40 (25.97)	24 (23.53)	16 (30.77)	0.333
Chronic obstructive pulmonary disease	9 (5.84)	3 (2.94)	6 (11.54)	0.074
Malignancy	5 (3.25)	4 (3.92)	1 (1.92)	0.663
Neurologic diseases	2 (1.30)	2 (1.96)	0 (0.00)	0.550
Duration from onset to hospitalization (d), mean ± SD	9.24 ± 4.32	8.61 ± 3.72	10.48 ± 5.12	**0.011**
Symptoms at admission, *n* (%)				
Fever	138 (89.61)	94 (92.16)	44 (84.62)	0.147
Cough	103 (66.88)	69 (67.65)	34 (65.38)	0.778
Dyspnea	75 (48.70)	33 (32.35)	42 (80.77)	**< 0.001**
Hemoptysis	9 (5.84)	5 (4.90)	4 (7.69)	0.738
Diarrhea	15 (9.74)	5 (4.90)	10 (19.23)	**0.005**
Bilateral lung lesion on chest computed tomographic, *n* (%)	148 (96.10)	96 (94.12)	52 (100.00)	0.097
Heart rate (beats/min), mean ± SD	90.50 ± 14.48	89.40 ± 13.28	92.65 ± 16.53	0.189
Mean artery pressure (mm Hg), mean ± SD	93.56 ± 14.15	92.47 ± 12.19	95.71 ± 17.29	0.180
Respiratory rate (beats/min), mean ± SD	21.99 ± 5.04	20.39 ± 1.59	25.12 ± 7.50	**< 0.001**
Ratio of Pao_2/FIO_2 (mm Hg), *n* (%)				
< 300	76 (49.35)	28 (27.45)	48 (92.31)	**< 0.001**
≥ 300	78 (50.65)	74 (72.55)	4 (7.69)	
Glasgow Coma Score, mean ± SD	14.67 ± 1.32	15.00 ± 0.00	14.04 ± 2.14	**< 0.001**
Acute Physiology and Chronic Health Evaluation II score, mean ± SD	15.05 ± 7.71	10.87 ± 4.40	23.23 ± 6.05	**< 0.001**
Sequential Organ Failure Assessment score, mean ± SD	2.62 ± 2.36	1.63 ± 1.25	4.56 ± 2.81	**< 0.001**
Confusion, Urea, Respiratory rate, Blood pressure, Age 65 score, mean ± SD	0.74 ± 0.81	0.38 ± 0.51	1.44 ± 0.83	**< 0.001**
Duration of hospitalization (d), mean ± SD	12.86 ± 6.08	13.11 ± 5.59	12.38 ± 6.99	0.487
Complications, *n* (%)				
Acute respiratory distress syndrome	82 (53.25)	30 (29.41)	52 (100.00)	**< 0.001**
Acute cardiac injury	45 (29.22)	11 (10.78)	34 (65.38)	**< 0.001**
Liver dysfunction	15 (9.74)	2 (1.96)	13 (25.00)	**< 0.001**
Acute kidney injury	25 (16.23)	1 (0.98)	24 (46.15)	**< 0.001**
Co-infection	50 (32.47)	11 (10.78)	39 (75.00)	**< 0.001**
Shock	36 (23.38)	0 (0.00)	36 (69.23)	**< 0.001**
Gastrointestinal hemorrhage	4 (2.60)	0 (0.00)	4 (7.69)	**0.012**
Pneumothorax	1 (0.65)	0 (0.00)	1 (1.92)	0.338

Data are presented as mean ± SD or *n* (%).
Boldface values were considered statistically significant.

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SOFA score (4.56 ± 2.81 vs 1.63 ± 1.25; $p < 0.001$), CURB65 score (1.44 ± 0.83 vs 0.38 ± 0.51; $p < 0.001$), and respiratory rate (25.12 ± 7.50 vs 20.39 ± 1.59; $p < 0.001$) of deaths were higher than that of survivors. The proportion of deaths with Pao_2/Fio_2 less than 300 mm Hg (92.31%) was higher than that of survivors (27.45%; $p < 0.001$). The duration from onset to hospitalization was longer in deaths (10.48 ± 5.12) than in survivors (8.61 ± 3.72; $p = 0.011$) (**Table 1**).

Oxygen therapy, mechanical ventilation, empirical antibiotics, and antiviral therapy were given to 100.0%, 42.21%, 98.03%, and 83.12% of patients, respectively. More patients in deaths group received mechanical ventilation (96.63% vs 24.62%; $p < 0.001$) and continuous renal replacement therapy (26.92% vs 0.98%; $p < 0.001$) than those in survivor group. The 36 patients who received vasoactive amines treatment were all in deaths group (**Appendix Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/F516).

Of the 154 patients, 78 patients (50.65%) were critically ill, and 66.67% of critically ill patients died. About half of patients had organ dysfunction, including 82 (53.25%) with ARDS, 45 (29.22%) with cardiac injury, 25 (16.23%) with acute kidney injury, 15 (9.74%) with liver dysfunction, 50 (32.47%) with co-infection, 36 (23.38%) with shock, four (2.60%) with gastrointestinal hemorrhage, and one (0.65%) with pneumothorax. Except for pneumothorax, the occurrence rate of other complications was much higher in the deaths (all $p < 0.001$). The duration of hospitalization in deaths and survivors was similar, with 12.38 ± 6.99 days and 12.86 ± 6.08 days, respectively ($p = 0.487$) (Table 1).

Laboratory and Radiologic Findings at Admission

Laboratory abnormalities at admission were more frequently observed in deaths than in survivors. Elevated level of WBC, monocyte, D-dimer, aspartate aminotransferase, total bilirubin, lactate dehydrogenase, creatine kinase, blood urea nitrogen, creatinine, hypersensitive troponin I, and procalcitonin were observed in deaths, when compared with survivors (all $p < 0.05$). Total bilirubin of greater than 26 μmol/L was documented in seven deaths (13.46%) and three survivors (2.94%). The neutrophil-to-lymphocyte ratio (18.67 ± 16.93 vs 7.08 ± 6.86; $p < 0.001$) and platelet-to-lymphocyte ratio (315.96 ± 235.45 vs 284.00 ± 245.38; $p < 0.001$) were higher in deaths than in survivors. The prothrombin time and activated partial thromboplastin time were longer, whereas the levels of platelet and albumin were lower in deaths (all $p < 0.05$) (**Table 2**).

A total of 148 patients (96.10%) presented bilateral pneumonia, and the other six patients (3.90%) showed unilateral pneumonia (Table 1). **Appendix Figure 1** (Supplemental Digital Content 2, http://links.lww.com/CCM/F517; **legend**, Supplemental Digital Content 3, http://links.lww.com/CCM/F518) showed the CT images of a 56-year-old man with COVID-19. The lung of this patient under CT image presented bilateral ground-glass opacity at admission and then developed quickly with multiple patchy shadows and consolidated on 3 days later.

Performance of the Three Scoring Systems in Predicting Hospital Mortality

In multivariable Cox regression analyses, high APACHE II score (adjusted hazard ratio [HR], 1.07; 95% CI, 1.10–1.13) and SOFA score (adjusted HR, 1.43; 95% CI, 1.26–1.62) increased the hospital mortality risk for the patients with COVID-19 (**Table 3**). ROC analyses were used to determine the cut-off value of these three scoring systems in evaluating hospital mortality risk. The AUC was 0.966 (95% CI, 0.942–0.990), 0.867 (95% CI, 0.808–0.926), and 0.844 (95% CI, 0.784–0.905) for APACHE II, SOFA, and CURB65 scores, with the cut-off point value of 17, 3, and 1, respectively. Comparing to the other two scoring systems, APACHE II score was a better predictor for hospital mortality of COVID-19, with sensitivity and specificity to be 96.15% and 86.27%, respectively ($p < 0.001$) (**Fig. 1**).

Survival Probability of Patients Grouped by the Cut-Off Value of APACHE II Score

Patients were then divided into two groups based on the cut-off point value of APACHE II score: low risk, less than 17 and high risk, greater than or equal to 17. The median follow-up time since admission was 12 days (range, 2–17 d). Kaplan-Meier analysis showed that the survivor probability of patients with COVID-19 with low risk was significantly higher than that of patients with high risk ($p < 0.001$). The median survival time for the patients in high-risk group was 14 days (95% CI, 10–16 d) (**Fig. 2**).

DISCUSSION

This is a retrospective study on the epidemiology and clinical characteristics of the patients with COVID-19. About half of the patients had organ dysfunctions. APACHE II score was demonstrated to be independently associated with hospital mortality in patients with COVID-19. Furthermore, APACHE II score performed better to predict hospital mortality in patients with COVID-19 compared with SOFA and CURB65 scores. APACHE II score greater than or equal to 17 serves as an early warning indicator of death, which may help provide guidance to make further clinical decisions.

SARS-CoV-2 is a coronavirus that can be transmitted to humans like SARS-CoV and middle eastern respiratory syndrome (MERS)-CoV, and these viruses are all related to high mortality in patients with critical illness. In a cohort of 38 critical patients with SARS in Canada, 43% of patients had died at 28 days (13). Fifty-eight percentage of patients had died at 90 days in a Saudi Arabia cohort with 12 patients with MERS (14). Yang et al (6) reported 61.5% of critically ill patients with COVID-19 had died at 28 days. In our cohort, two thirds of critically ill patients died. The mortality of patients with COVID-2019 was higher than that previously seen in critically ill patients with SARS and MERS. Several of the reasons are as follows. First, a large number of COVID-19 cases occurred in a short period of time led to difficulty in hospitalization treatment. In our cohort, the duration from onset to hospitalization was longer in deaths

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TABLE 2. Laboratory Findings of the Patients With Coronavirus Disease 2019

Variables	All Patients (*n* = 154)	Survivors (*n* = 102)	Deaths (*n* = 52)	*p*
WBC count (× 10^9/L), *n* (%)				**< 0.001**
< 3.5	24 (15.58)	19 (18.63)	5 (9.62)	
3.5–9.5	97 (62.99)	73 (71.57)	24 (46.15)	
> 9.5	33 (21.48)	10 (9.80)	23 (44.23)	
Neutrophil-to-lymphocyte ratio, mean ± SD	10.99 ± 12.53	7.08 ± 6.86	18.67 ± 16.93	**< 0.001**
Platelet-to-lymphocyte ratio, mean ± SD	294.79 ± 241.77	284.00 ± 245.38	315.96 ± 235.45	**< 0.001**
Monocyte count (× 10^9/L), *n* (%)				**0.008**
≤ 0.6	134 (87.01)	94 (92.16)	40 (76.92)	
> 0.6	20 (12.99)	8 (8.84)	12 (23.08)	
Platelet count (× 10^9/L), *n* (%)				**0.019**
≥ 125	123 (79.87)	87 (85.29)	36 (69.23)	
< 125	31 (20.31)	15 (14.71)	16 (30.77)	
Prothrombin time (s), *n* (%)				**0.023**
≤ 16	125 (79.87)	88 (86.27)	37 (71.15)	
> 16	31 (20.31)	14 (13.73)	15 (28.85)	
Activated partial thromboplastin time (s), *n* (%)				**0.045**
≤ 45	138 (89.61)	95 (93.14)	43 (82.69)	
> 45	16 (10.39)	7 (6.86)	9 (17.31)	
Fibrinogen (g/L), *n* (%)				0.208
≤ 4	72 (46.75)	44 (43.14)	28 (53.85)	
> 4	82 (53.25)	58 (56.86)	24 (46.15)	
D-dimer (mg/L), *n* (%)				**< 0.001**
< 0.5	63 (40.91)	57 (55.88)	6 (11.54)	
≥ 0.5	91 (59.09)	45 (44.12)	46 (88.46)	
Alanine aminotransferase (U/L), *n* (%)				0.237
≤ 41	129 (83.77)	88 (86.27)	41 (78.85)	
> 41	25 (16.23)	14 (13.73)	11 (21.15)	
Aspartate aminotransferase (U/L), *n* (%)				**< 0.001**
≤ 40	96 (62.34)	76 (74.51)	20 (38.46)	
> 40	58 (37.66)	26 (25.49)	32 (61.54)	
Total bilirubin (μmol/L), *n* (%)				**0.031**
≤ 26	144 (93.51)	99 (97.06)	45 (86.54)	
> 26	10 (6.49)	3 (2.94)	7 (13.46)	
Albumin (g/L), *n* (%)				**< 0.001**
< 35	76 (49.35)	38 (37.5)	38 (74.15)	
≥ 35	78 (50.65)	64 (62.75)	14 (26.92)	
Lactate dehydrogenase (U/L), *n* (%)				**< 0.001**
106–245	39 (25.32)	35 (34.31)	4 (7.69)	
> 245	115 (74.68)	67 (65.69)	48 (92.31)	

(*Continued*)

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TABLE 2. (*Continued*). Laboratory Findings of the Patients With Coronavirus Disease 2019

Variables	All Patients (*n* = 154)	Survivors (*n* = 102)	Deaths (*n* = 52)	*p*
Creatine kinase (U/L), *n* (%)				**< 0.001**
≤ 171	112 (72.73)	85 (83.33)	27 (51.92)	
> 171	42 (27.27)	17 (16.67)	25 (48.08)	
Blood urea nitrogen (mmol/L), *n* (%)				**< 0.001**
1.7–8.3	109 (70.78)	88 (86.27)	21 (40.38)	
> 8.3	45 (29.22)	14 (13.73)	31 (59.62)	
Creatinine (μmol/L), *n* (%)				**< 0.001**
≤ 115	138 (89.61)	99 (97.06)	39 (75.00)	
> 115	16 (10.39)	3 (2.94)	13 (25.00)	
Serum sodium (mmol/L), *n* (%)				**< 0.001**
< 136	48 (31.17)	33 (32.35)	15 (28.85)	
136–145	97 (62.99)	69 (67.65)	28 (53.85)	
> 145	9 (5.84)	0 (0.00)	9 (17.31)	
Serum potassium (mmol/L), *n* (%)				< 0.001
< 3.5	17 (11.04)	15 (14.85)	2 (3.85)	
3.5–5.1	122 (79.22)	83 (82.18)	38 (73.08)	
> 5.1	15 (9.74)	3 (2.97)	12 (23.08)	
Hypersensitive troponin I (ng/mL), *n* (%)				**< 0.001**
≤ 0.1	121 (78.57)	97 (95.10)	24 (46.15)	
> 0.1	33 (21.43)	5 (4.90)	28 (53.85)	
Procalcitonin (ng/mL), *n* (%)				**< 0.001**
< 0.05	66 (42.86)	58 (56.86)	8 (15.38)	
≥ 0.05	88 (57.14)	44 (43.14)	44 (84.62)	

Data are presented as mean ± SD or *n* (%).

Boldface values were considered statistically significant.

TABLE 3. Univariate and Multivariate Cox Analysis for the Mortality Risk of the Patients With Coronavirus Disease 2019

	Univariate Analysis		Multivariate Analysis	
Variables	HR (95% CI)	*p*	HR[a] (95% CI)	*p*[a]
Acute Physiology and Chronic Health Evaluation II score	1.14 (1.11–1.18)	**< 0.001**	1.07 (1.01–1.13)	**< 0.001**
Sequential Organ Failure Assessment score	1.40 (1.28–1.54)	**< 0.001**	1.43 (1.26–1.62)	**< 0.001**
Confusion, Urea, Respiratory rate, Blood pressure, Age 65 score	2.35 (1.83–3.02)	**< 0.001**	1.40 (0.96–2.05)	0.080

HR = hazard ratio.

[a]Adjusted for variables including duration from onset to hospitalization, diarrhea, monocyte count, prothrombin time, activated partial thromboplastin time, D-dimer, aspartate aminotransferase, lactate dehydrogenase, and creatine kinase.

Boldface values were considered statistically significant.

than that in survivors. Second, as an emerging infectious disease, the clinical characteristics and pathophysiologic features of the patients with COVID-19 have been known little at the start of the epidemic. Although the shortage of medical staff has been improved with assistance from other provinces from all over the country, the number of doctors and nurses of critical care

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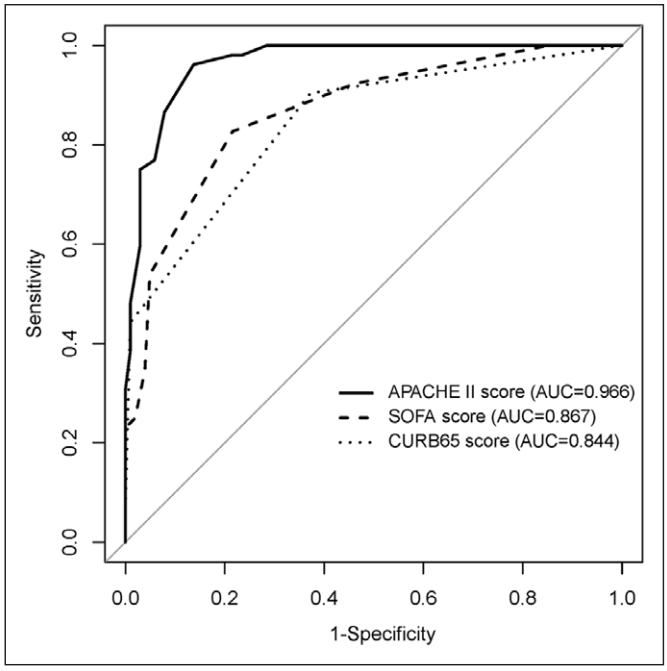

Figure 1. Receiver operating characteristic curve for the predicted value of Acute Physiology and Chronic Health Evaluation (APACHE) II, Sequential Organ Failure Assessment (SOFA) score, and Confusion, Urea, Respiratory rate, Blood pressure, Age 65 (CURB65) scores for the mortality of coronavirus disease 2019 patients. AUC = area under the curve.

medicine remains inadequate. Because of the considerable mortality of patients with COVID-19, a clinically predictive system for early warning of mortality risk is urgently needed.

The cut-off value of APACHE II score in COVID-19 is much lower to predict mortality. Several reasons may explain it. First, GCS is an important component of APACHE II score. Direct damage to the nervous system by SARS-CoV-2 was rarely reported. Only a few patients had a disturbance of consciousness in the study. Most of them suffered from hypoxemia-induced ischemic hypoxic encephalopathy and one was attributed to underlying cerebral hemorrhage. Second, APACHE II score was assessed according to the characteristics of the patients on the first day of ICU admission. Abnormal levels of serum sodium and potassium were observed in some patients, but only a few patients got scores for the corresponding part in APACHE II score. Finally, according to our observation, several patients deteriorated during their stay in the hospital in a few days and quickly died. Although timely given powerful empirical treatments including glucocorticoid, immunoglobulin, mechanical ventilation, etc, the patients were still hard to recover from COVID-19. A recent study showed the median APACHE II score of survivors and deaths in critically ill patients with COVID-19 were 14 and 18, respectively (6). This indicated that COVID-19 might be more variable and mortal, compared with pneumonia caused by other pathogens. Further studies are needed to confirm our findings.

APACHE II score, SOFA score, and CURB65 score are commonly used to describe multiple organ function for assessing disease severity and estimate hospital mortality (7, 9, 15). According to recent reports, any underlying disorder was significantly more common in severe cases when compared with non-severe cases. The medical history of coronary heart disease was an independent determinant of critical illness of the patients with COVID-19 (16), and it was also associated with a higher risk of mortality in patients with COVID-19 (17). In this cohort, about half of patients had one or more underlying comorbidities, and coronary heart disease was more common in deaths than in survivors. It suggested that comorbidities played an important role in the death of the patients with COVID-19. Age has also been identified to be associated with the severity and death in patients with COVID-19 based on the present and previous studies (18–20). Of the three score systems, only APACHE II score includes comorbidities and age, whereas CURB65 score takes into account only age, and SOFA score takes into account neither of them. These may explain why APACHE II score performed better than the other two for predicting mortality in patients with COVID-19.

Notably, SARS-CoV-2 mainly caused lung lesions, but

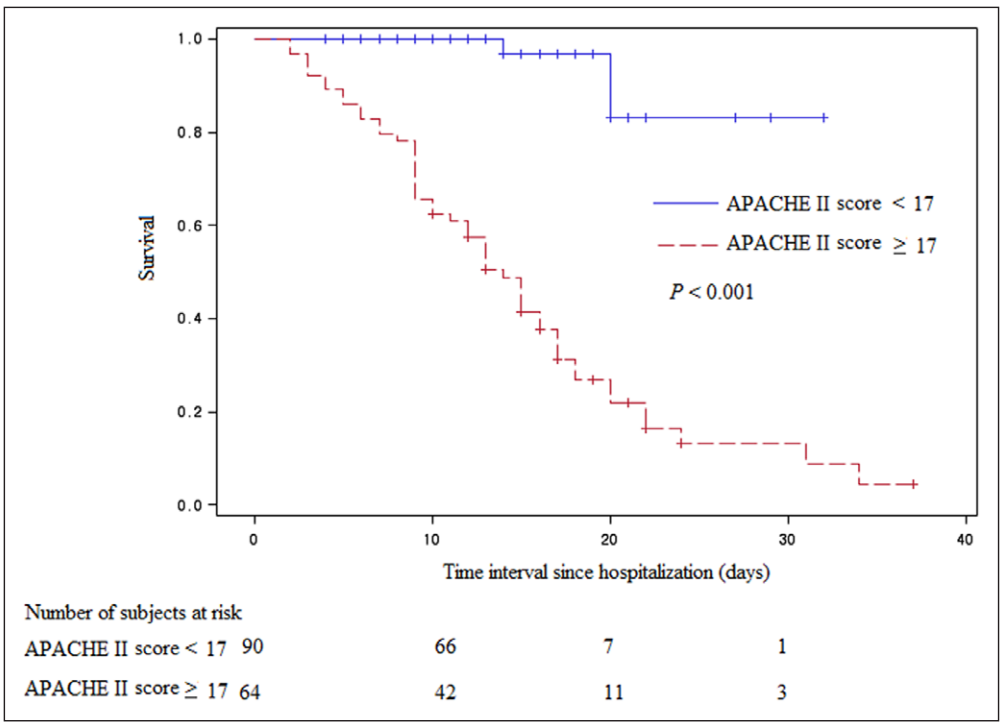

Figure 2. Kaplan-Meier survival curves of the coronavirus disease 2019 patients stratification by Acute Physiology and Chronic Health Evaluation (APACHE) II score.

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other organs injury cannot be neglected. In the present study, we found that the platelet-to-lymphocyte ratio was higher in deaths than that in survivors. Qu et al (21) also demonstrated that high platelet-to-lymphocyte ratio was associated with severe illness in patients with COVID-19. Platelet-to-lymphocyte ratio mainly reflects the level of systemic inflammation, and high value may lead to adverse outcome. Recent studies have shown that the proportion of developing liver injury in patients with severe COVID-19 was significantly higher than that in mild patients (22–24). Our study also found that the proportion of liver dysfunction was higher in the deaths group than that in the survivors group, consistent with the other study (25). Currently, studies on the mechanisms of SARS-CoV-2–related liver injury are limited. It has been shown that SARS-CoV-2 also uses angiotensin converting enzyme 2 as its entry receptor as SARS-Cov does (26). Whether it results in liver damage in patients remains to be investigated. Troponin I was significantly increased in patients with severe COVID-19 compared with those with milder illness (16). The mechanisms may be similar to that of myocardial injury in other severe respiratory illnesses in which myocardial oxygen demand is heightened and inflammation is rampant (27). Further studies are need to confirm the mechanisms underlying these findings.

There were still some limitations in our study. First, the present study was a retrospective, single-center study with a relatively small sample size. Second, all patients were enrolled from the ICU in Tongji hospital. Most patients were transferred from other hospitals or isolation units. These patients were more likely to progress to adverse outcomes. Therefore, the mortality of patients with COVID-19 in this study may be much higher than general population (28) and may be not generalized. Third, the treatments may influence the outcomes of patients with COVID-19. But in this study, we aimed to apply the characteristics of the patients at the first day admitted to ICU to predict the outcome of the patients with COVID-19. Additional research is needed to understand the role of APACHE II score in the risk stratification of patients with COVID-19.

CONCLUSIONS

APACHE II score was identified to be an effectively clinical tool to predict mortality in patients with COVID-19 compared with SOFA score and CURB65 score. Future researches are needed to explore whether the application of APACHE II score in patients with COVID-19 could reduce mortality and improve patient outcomes.

Drs. Zou, Li, Fang, and Huang conceived the study idea, analyzed the data, and prepared the article. Dr. Hu, Bian, Ling, Yu, Jing, and Li acquired the data and revised the article critically for important intellectual content. All authors contributed to the interpretation of the data and approved the final version of the article.

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