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http://jept.ir
doi 10.34172/jept.2022.28

Journal of Emergency Practice and Trauma
Volume 9, Issue 1, 2023, p. 19-24

Original Article

Prognostic value of intensive care scores concerning the prediction of 30-day mortality in COVID-19

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Received: September 6, 2022
Accepted: December 11, 2022
Published online: December 24, 2022

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Citation: Kalani N, Tavasolian M, Dehghani K, Mousavi SR, Ghanbarzadeh E, Shakeri M, et al. Prognostic value of intensive care scores concerning the prediction of 30-day mortality in COVID-19. Journal of Emergency Practice and Trauma 2023; 9(1): 19-24. doi: 10.34172/jept.2022.28.

Abstract

Objective: The goal of our study was to determine the prognostic value of CURB-65, Sequential Organ Failure Assessment (SOFA), pneumonia severity index (PSI), MuLBSTA, and Acute Physiology and Chronic Health Evaluation (APACHE) II upon admission in patients with coronavirus disease 2019 (COVID-19, as well as the prediction cut-off value for death regarding these parameters.

Methods: This observational retrospective study was performed in COVID-19 triage in Peymaniyeh hospital in Jahrom in 2021. In order to calculate SOFA, APACHE II, PSI, MuLBSTA, and CURB-65, data were collected from patients who were selected by available sampling method from PCR-confirmed COVID-19 patients. Thirty-day mortality was assessed as the primary outcome. ROC analysis was conducted using the STATA software to evaluate the prognostic value of the scoring systems. DeLong test was utilized to compare AUC of scores using a web based tool.

Results: Ninety-two patients were included in this study with the mean age of 51.02 ± 17.81 years (male to female ratio was 1:1). SOFA had an AUC of 0.656 ($P = 0.130$), but other indices had statistically significant values of AUC. Based on the comparison of the AUCs, SOFA was the worst scoring system in COVID-19 as it had significantly lower AUC than PSI and APACHE II ($P < 0.05$); while its comparison with MULBSTA and CURB65 was not statistically significant ($P > 0.05$).

Conclusion: It seems that APACHE II and PSI are the best prognostic factors in our study with no statistical difference compared together ($P > 0.05$). The sensitivity of APACHE II and PSI was 0.857 with the specificity of 0.927 and 0.976, respectively. The optimal cut-off point was 13 and 50 for APACHE II and PSI, respectively.

Keywords: COVID-19, SARS-CoV-2, Mortality, APACHE II

Introduction

Coronavirus disease 2019 (COVID-19) manifestations may range from asymptomatic to mild symptoms and sometimes contribute to severe forms of pneumonia, extrapulmonary manifestations, intensive care unit (ICU) admission, and even death (1-4). Multiple research works have been conducted to predict the severity of the disease and its prognosis (5). However, there is no standardized scoring system for COVID-19 to assess the prognosis of the disease and the risk of death. Such measures can be easily used to better control pandemics and reduce mortality in primary care (6). Understanding the severity of the disease is essential to determine the best management approach, including whether admission to an ICU or the ward is required (7). Therefore, a straightforward approach for quick patient triage that can anticipate serious illness is considered as a prerequisite. The pneumonia severity index (PSI) is a method for categorizing patient groups according to their features and mortality risk (8). Even though it is difficult to utilize and necessitates the calculation of a score based on 20 criteria, it might not be appropriate for frequent usage in congested hospital emergency rooms (8). So far, many other mortality prediction tools have been developed to predict the mortality rate in ICU admitted patients and patients with severe respiratory diseases as well as Sequential Organ Failure Assessment (SOFA) score (9), SOFA score (10), CURB-65 score (11,12), MuLBSTA

score (13,14), and the Acute Physiology and Chronic Health Evaluation (APACHE) II system (15) that all have been investigated in COVID-19 era. The aim of our study was to analyze the prognostic value of CURB-65, SOFA, PSI, MuLBSTA, and APACHE II at admission in patients with COVID-19.

Methods

This observational retrospective study was performed in COVID-19 triage in Peymaniyeh Hospital in Jahrom in 2021. All patients' information remained confidential and Ethical Approval related to human studies (according to the Helsinki Declaration) were considered (ethical code: IR.JUMS.REC.1400.098).

All cases confirmed by Reverse transcription polymerase chain reaction (RT-PCR) COVID-19 at COVID-19 care center were included in this study. Inclusion criteria were admission to hospital, confirmation of COVID-19 diagnosis by RT-PCR or CT scan of lung, and informed consent to participate in the study. Patients transferred from other hospitals to Peymaniyeh hospital, pediatric cases, incomplete medical records, and self-request for discharge from the hospital were considered as exclusion criteria.

Based on the WHO report of mortality rate of COVID-19 in Iran (1.9%) (16), and the study conducted by Baud et al. in which the crude mortality rate was 7%, we estimated our sample size to be 90 patients by considering the alpha of 0.05 and power of 80%,. Available simple sampling method was performed accordingly.

Selected patients' medical records were queried and different clinical, paraclinical and radiological findings were extracted. Outcomes of the disease were followed up from the hospital. Five criteria of SOFA, APACHE II, PSI, MuLBSTA and CURB-65 were calculated using MDCalc online calculator (https://www.mdcalc.com); the components of each scoring scale are summarized in Table 1.

A detailed history of the patient (past medical/surgical history, and drug history) and physical examination (including the vital signs of heart rate, respiratory rate, blood pressure, and oxygen saturation) were taken by the physician in an interview. Blood samples (5 cc) were taken and then sent for laboratory analysis. Upon the request of the treating physician, a culture was sent for the simultaneous bacterial infection. Then, for each patient, computed tomography of the chest was performed. All data were collected and mentioned scores were calculated. Data about the intubation or non-invasive ventilation (NIV) use were collected if these methods of oxygen supplementation were applied later during the admission; while other data were recorded upon arrival to the hospital. Data were collected using a pre-designed Excel spreadsheet, containing all study variables completed by researchers.

The collected data were entered into the computer and after data processing and exclusion of incomplete records; data were analyzed using STATA software version 17. Chi-square test for classified data was used to evaluate the significance of the proposed hypothesis. Mortality rate was predicted by ROC analysis. easyROC tool, a web-tool for ROC curve analysis was used to determine the cut-off using the Youden index formula (17). DeLong test was used to compare AUC of scores. *P* value less than 0.05 was considered statistically significant.

Results

In this study, 92 patients were included with a mean age of 51.02 ± 17.81 years (male to female ratio was 1:1). Most patients received O_2 supplementation using a mask and 19.57% were on mechanical ventilation (NIV or intubation). Also, 23.91% of patients had diabetes and 16.3% had hypertension. Other baseline characteristics are reported in Table 2. Mortality was recorded for 7 (7.60%) patients.

The calculated value of CURB-65, SOFA, PSI, MuLBSTA and APACHE II are presented in Figure 1. ROC analyses for predicting mortality are shown in Figure 2.

Table 1. Components of the scoring systems

SOFA	MuLBSTA		APACHE II		PSI		CURB65
PaO_2	Multi-lobe infiltrate	FiO_2	Organ failure or Immunocompromised	Pleural effusion	Neoplastic disease	Age	Age
FiO_2	Lymphocyte count	GCS	White blood cell count	The partial pressure of oxygen	Liver disease history	Sex	Blood pressure
Mechanical ventilation	Coinfection	Hematocrit	Acute renal failure	Hematocrit	Chronic heart failure		Respiratory rate
Platelets	Smoking	Potassium	Sodium	Glucose	Cerebrovascular disease history		Blood urea nitrogen
GCS	Hypertension	Respiratory rate	Heart rate	Sodium	Renal disease history		Confusion
Bilirubin	Age ≥ 60	pH	Age	Blood urea nitrogen	Altered mental status		
Mean arterial pressure		Temperature	Mean arterial pressure	Pulse	Respiratory rate		
Creatinine		Creatinine	Temperature < 35°C		Systolic blood pressure < 90 mm Hg		

Abbreviation: GCS, Glasgow Coma Scale; FiO_2, fraction of inspired oxygen; PaO_2, Partial pressure of oxygen

Table 2. Baseline characteristics of the studied participants

Variable	value
Male, No. (%)	46 (50)
Age, mean ± SD	51.02 ± 17.81
O2 supplementation method, No. (%)	
Mask	74 (80.43)
Intubation	8 (8.7)
NIV	10 (10.87)
Diabetes, No. (%)	22 (23.91)
Hypertension, No. (%)	15 (16.3)
Smoking, No. (%)	5 (5.43)
O2 saturation without O2 supplementation, mean ± SD	89.84 ± 6.96
O2 saturation with O2 supplementation, %, mean ± SD	95.71 ± 2.52
CRP levels, mg/L, mean ± SD	26.85 ± 27.91
Respiratory rate, count per minute, mean ± SD	20.1 9 ± 1.7
BUN, mg/dL, mean ± SD	18.6 ± 17.84
SBP, mm Hg, mean ± SD	108.43 ± 15.39
DBP, mm Hg, mean ± SD	66.57 ± 13.27
PO2, kPa, mean ± SD	42.37 ± 25.31
Hematocrit, %, mean ± SD	38.22 ± 5.26
Platelet, count per microliter, mean ± SD	230.24 ± 87.94
Bilirubin, mg/dL, mean ± SD	0.72 ± 1.04
Serum creatinine, mg/dL, mean ± SD	1.22 ± 0.75
Lymph %	20.87 ± 11.83
Heart rate, count per minute, mean ± SD	77.86 ± 15.77
Potassium, mmol/L, mean ± SD	4.07 ± 0.59
GCS, score, mean ± SD	14.95 ± 0.27
Temperature (°C), mean ± SD	36.92 ± 0.84
MAP, mm HG, mean ± SD	78.77 ± 17.03
HCO3, mEq/L, mean ± SD	23.39 ± 4.67
Ph, scale, mean ± SD	7.34 ± 0.42
Sodium, mEq/L, mean ± SD	135.68 ± 4.73
WBC, count × 10^9/L, mean ± SD	7.87 ± 3.8

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; CRP, C-reactive protein; PO2, partial pressure of oxygen; GCS, Glasgow Coma Scale; MAP, mean arterial pressure; WBC, white blood count; NIV, Non-invasive ventilation; BUN, blood urea nitrogen

The value of each ROC analysis is presented in Table 3. As shown in this table, SOFA does not seem to be predictive of COVID-19; while other scores can be used to predict mortality in COVID-19. Based on the comparison of the AUCs, SOFA was the worst scoring system in COVID-19 as it had significantly lower AUC than PSI and APACHE II ($P<0.05$); while its comparison with MULBSTA and CURB65 was not statistically significant based on Table 4. Thus, we conclude that APACHE II and PSI are the best prognostic factors in our study with no statistical difference compared together ($P>0.05$). Sensitivity of APACHE II and PSI was 0.857 with the specificity of 0.927 and 0.976, respectively. The optimal cut-off point was 13 and 50 for APACHE II and PSI, respectively.

Numbers in the Table 4 show the *P* values of pairwise comparison of the prediction scores. Bolded numbers indicate a statistically significant difference, $P<0.05$; Comparisons are made based on the AUC of each tests with each other and the red flashes show the scoring system with higher AUC.

The 30-day mortality rate was compared based on the quantiles of each score to estimate the odds ratio (OR). Only patients with APACHE II of higher than 13 had an increased risk of death by 77 times (7.92-748.43) and patients with PSI scores higher than 50 had an increased risk of death by 243 times (19.17-3080.1), as shown in Table 5. Categorizing data in quartiles did not help in finding any significant relationships.

Discussion

Given that it is not clear how the prognosis of COVID-19 patients would go on at the time of hospitalization and having proper prognostic information can help implement timely measures and interventions to prevent the death of patients who may be at greater risk during hospitalization, it will be helpful to identify patients who have a serious illness or who may have a serious illness in the future. For this purpose, various methods have been proposed, including the mentioned scoring criteria. However, the diagnostic power of these criteria and the appropriate incision point for their use for the Iranian patient population is not clear. Consequently, we designed this study to present these cut-off points and evaluate the best criteria for use in hospitals. Our study revealed that APACHE II and PSI were the best predictive indicators, with no statistical difference when compared with each other ($P>0.05$). APACHE II and PSI had a sensitivity of 0.857 and a specificity of 0.927 and 0.976, respectively. For APACHE II and PSI, the optimal cut-off point was 13 and 50, respectively. To compare our study results with other studies, in the study by Chen et al, the role of CURB-65, PSI, and APACHE II scores in determining the severity of COVID-19 pneumonia mortality was investigated. They included 167 patients with COVID-19. They used the 30-day mortality for the study outcome. Their comparison showed usability of all three scores (CURB-65, PSI, and APACHE II); while our study did not confirm this for CURB-65. Patients with PSI ≤ 90 scores, and APACHE II-I all survived their study. Their findings show that PSI and CURB-65 may be useful in predicting the severity and mortality of COVID-19 (18); while our study confirms PSI and APACHE II. In the study conducted by Preetam and Anurag, 122 patients were evaluated. Their study showed that participants with MuLBSTA scores of more than 11 would have a higher chance of mortality (19); while in our study, MuLBSTA ≥ 4 was predicting mortality, but we do not prefer it to PSI and APACHE II. Cheng et al concluded that the APACHE- score II is a strong predictor of the

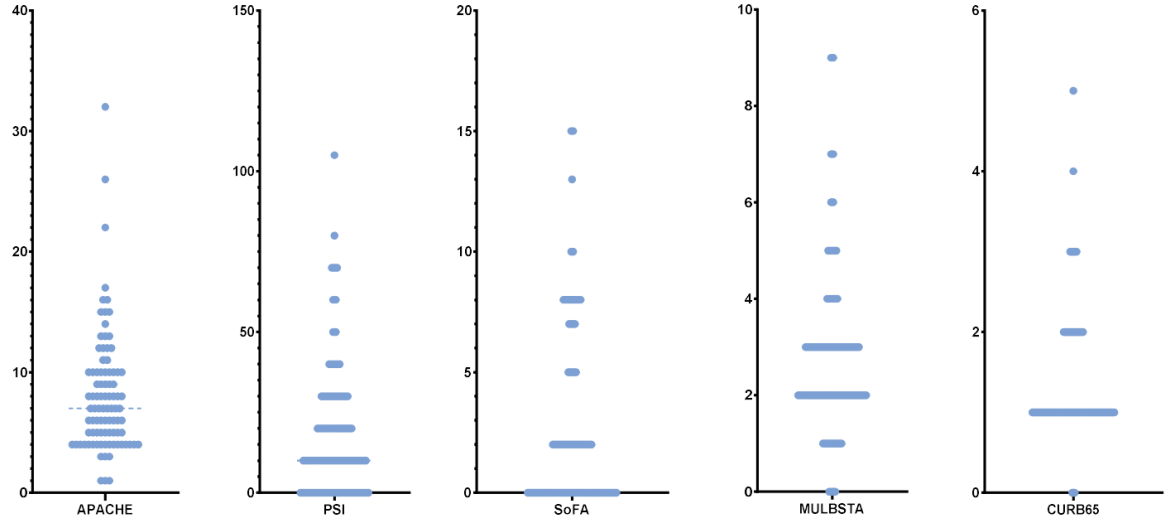

Figure 1. The histogram of distribution of scoring values

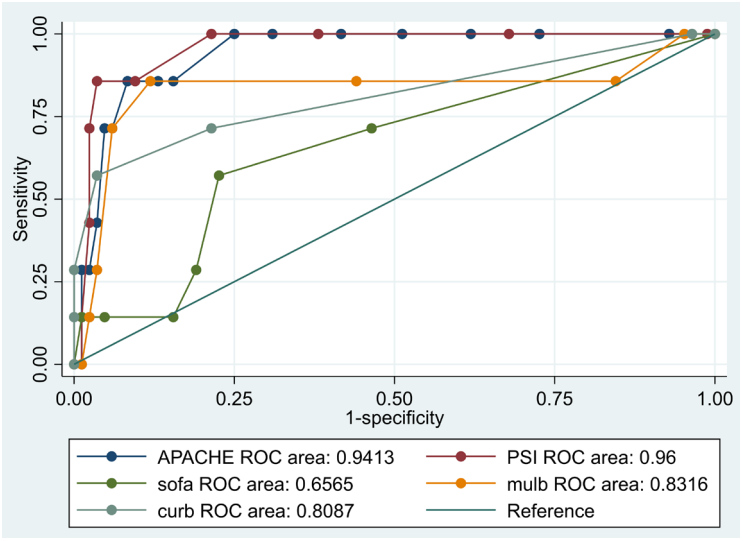

Figure 2. AUC curve of different scoring systems

Table 3. Sensitivity and specificity of the results

	APACHE II	PSI	SOFA	MULBSTA	CURB65
AUC	0.9413*	0.96*	0.656	0.836*	0.808*
P value	<0.001	<0.001	0.13035	0.00694	0.00279
Optimal cut-off point	13	50	5	4	3
Sensitivity	0.857	0.857	0.571	0.857	0.571
Specificity	0.927	0.976	0.793	0.89	0.976
Positive predictive value	0.5	0.75	0.19	0.4	0.667
Negative predictive value	0.987	0.988	0.956	0.986	0.964
Positive likelihood ratio	11.714	35.143	2.756	7.81	23.429
Negative likelihood ratio	0.154	0.146	0.541	0.16	0.439

* Statistically significant.
AUC, area under curve.
Note: Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratioare calculated based on the Receiver operating characteristic (ROC) test suggested cut-off points.

severity and mortality of COVID-19; but they suggested that it is a complex score and it contains many variables. In addition, it is not easy to manipulate and it is not specific to the respiratory system disorders (20).

These criteria are also used in other respiratory diseases. In the study by Akhter et al, retrospective data from patients with chronic obstructive pulmonary disease (COPD) were collected over two months. The results of their analysis showed that the total number of hospitalizations was 103 with 28% mortality. Of the three APACHE II, SOFA, and CURB-65 scores, CURB-65 showed the greatest difference between survivors and non-survivors. They concluded that CURB-65 compared to APACHE and SOFA has a significant ability to predict the mortality of hospitalized patients with COPD (21). As their study population had different diseases, we can see how different these scoring systems can be in various

Table 4. Pairwise comparison of prediction power of each score based on the DeLong test

	CURB-65	SOFA	PSI	MuLBSTA	APACHE II
CURB-65	-	0.207	0.106	0.848	0.128
SOFA	0.207	-	↑ **0.028**	0.108	↑ 0.041
PSI	0.106	←**0.028**	-	0.217	0.174
MuLBSTA	0.848	0.108	0.217	-	0.274
APACHE II	0.128	←**0.041**	0.174	0.274	-

Table 5. The prediction of 30-day mortality based on the intensive care scores

	Value	Survived	Death	OR	*P*
APACHE II	Q1 (<4)	6	0	Reference	-
	Q2 (4-7)	35	0	NE	0.999
	Q3 (≥7)	42	7	NE	0.997
	<13 (Cut point)	77	1	Reference	-
	>13 (Cut point)	6	6	77 (7.92-748.43)	>0.0001
SOFA	<5	65	3	Reference	-
	5 to 10	14	3	0.18(0.02-2.2)	0.181
	≥10	4	1	0.86 (0.07-10.67)	0.904
PSI	Q1 (<10)	77	0	Reference	-
	Q2 (10-30)	39	0	NE	0.999
	Q3 (≥30)	17	7	NE	0.999
	<50 (Cut point)	81	1	Reference	-
	Cut point>50	2	6	243 (19.17-3080.1)	>0.0001
MuLBSTA	0	4	0	Reference	-
	1	9	1	NE	0.999
	2	34	0	NE	0.999
	3	27	0	NE	0.999
	4	5	1	NE	0.999
	5	2	3	NE	1
	6	1	1	NE	0.999
	7	1	1	NE	0.999
CURB65	0	3	0	Reference	-
	1	63	2	NE	0.999
	2	15	1	NE	0.999
	3	2	2	NE	0.999
	4	0	1	NE	0.999
	5	0	1	NE	1

Abbreviations: OR, Odds ratio. NE, not estimated.
Where number of observations is low, ORs are not calculated. ORs are crude odds of each category of intensive care scores for death compared to reference groups. Two grouping methods (based on the quartiles or cut off point of 13) are used for APACHE II and two for PSI (based on the quartiles or cut off point of 50).

medical conditions.

There are many research studies performed in Jahrom city, in the same study setting as the current study, 15.54% of patients in a study were admitted to ICU (22) which was high as well as our study. This necessitates the proper risk stratification of patients at arrival in the emergency department to decrease the rate of ICU admissions and death.

Limitations

All evaluated intensive care scores change through the time of admission and are time-varying values. We justified this issue by calculating scores at the admission time in the emergency department. But many factors as well as late referral would affect the intensive care scores. Also, we evaluated the 30-day mortality in COVID-19 patients and many other known and unknown factors as well as the different medications would act as confounding factors. Besides, a larger sample size might reveal different results. While we powered our study sample size based on the mortality rates in Iran according to WHO statistics, this measure might be affected by time/place varying changes in mortality rate and non-reported mortalities.

Conclusion

Our study revealed that APACHE II and PSI were the best predictive indicators of thirty-day mortality for COVID-19 patients. But APACHE II application may be hard due to multiple necessary indices needed to be calculated; while PSI calculation only needs underlying disease list and routine medical investigations. We suggest healthcare policy providers to bring these prediction scores available for physicians who visit the patients in user interfaces like electronic devices to help determine patients with poor prognosis.

Acknowledgments

We would like to thank the Clinical Research Development Unit of Peymaniyeh Educational and Research and Therapeutic Center of Jahrom University of Medical Sciences for providing facilities for this work.

Authors' Contribution

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Writing – review & editing: Seyed Reza Mousavi, Erfan Ghanbarzadeh, Elahe Rahmanian.

Competing Interests

None.

Ethical Approval

Ethical licenses were obtained from the relevant authorities and ethics committee of Jahrom University of medical sciences with

code number: IR.JUMS.REC.1400.098. Informed consent was obtained from all participants.

Funding
None.

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