Validation test of sequential organ failure assessment score in predicting 28-day mortality in critically ill COVID-19

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Abstract

***Background*: Mortality predictors are often used for analyzing disease progression as a guide for disease management strategy. The sequential organ failure assessment (SOFA) score is a predictor tool used to analyze organ dysfunction in critically ill patients. This study aimed to validate the SOFA score in predicting 28-day mortality in critically ill Coronavirus disease 2019 (COVID-19) patients.**

***Methods*: Subjects included in this study were critically ill, confirmed COVID-19 cases admitted to the intensive care unit (ICU) between March and August 2020. Demographic data, clinical characteristics, and laboratory findings within the first 24 hours of ICU admission were obtained from medical records to compute the SOFA score. The 28-day outcome was recorded as alive or deceased. Validity was analyzed using the area under the curve (AUC), Hosmer-Lemeshow goodness of fit, and bivariate logistic regression. The optimal cut-off point was determined statistically.**

***Result*: From the total of 88 subjects in this study, the mortality rate was 39.8%. AUC was 0.971 (confidence interval [CI] 95% 0.943-0.999), and the goodness of fit test by using Hosmer-Lemeshow showed p=0.782. An optimal cut-off point of SOFA score was 6, with a sensitivity of 87% and specificity of 90%.**

***Discussion*: SOFA score demonstrated very strong discrimination and good calibration in predicting 28-day mortality on the critical case of COVID-19.**

***Conclusion*: The SOFA score is valid for predicting 28-day mortality in the critical case of COVID-19.**

Key words: SOFA score, mortality, COVID-19, intensive care, validation test.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), also known as Coronavirus Disease 2019 (COVID-19), has been stated as a global pandemic by the World Health Organization (WHO) since Mar 11, 2020. (1) This pandemic had been known to first enter Indonesia on Mar 2, 2020, (2) causing the first death on Mar 3, 2020, (3) and continues to spread in Indonesia, especially Jakarta as its epicenter.

There are broad clinical spectrums of COVID-19, ranging from asymptomatic, mild upper respiratory tract infection, and severe viral pneumonia, leading to respiratory failure. (4) According to the policy in Indonesia, asymptomatic patients are asked to self-isolation, and only symptomatic patients were admitted to the hospital. Among the admitted patients, the one with severe symptoms is treated in the intensive care unit (ICU). When this study began, the case fatality rate in Indonesia was high, with a value of 8.7% as of Apr 20, 2020. Limited knowledge on disease treatment and prevention, lack of test numbers, and government policy were some of the factors that contribute to this high number. The death due to COVID-19 is defined as death in previously probable and confirmed cases of COVID-19 unless there are other causes unrelated to COVID-19. (5) COVID-19 is a new disease; hence research about

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mortality prediction on COVID-19 is very limited, especially in ICU patients.

A good mortality predictor could be used to facilitate physicians in managing critical patients, analyzing disease progression, and resource allocation. Up to this moment, there was no scoring system specifically used to predict mortality in COVID-19 patients; hence the alternative was adopting the existing one. Some predictors that are commonly used in critical patients were Sequential Organ Failure Assessment (SOFA), (6) Logistic Organ Dysfunction System (LODS), (7) and Simplified Acute Physiology Score (SAPS). (8) Each of these predictors uses different data to determine a patient's prognosis. SOFA, LODS, and SAPS 3 have been proven to give accurate prognostic values in predicting mortality in the ICU. (9,10)

SOFA scoring system describes multiple organ dysfunction by six parameters: respiratory, cardiovascular, central nerve system, renal, coagulation, and hepatic. Although the SOFA score was not initially designed to predict mortality, several studies showed that the SOFA score was valid to predict mortality in critically ill patients. (11) Therefore, we aimed to validate the usage of the SOFA score in the critical case of COVID-19 and its optimum value to predict 28-day mortality.

Methods

The Faculty of Medicine Universitas Indonesia is affiliated with two leading hospitals: Cipto Mangunkusumo National General Hospital, a national referral hospital, and Universitas Indonesia Hospital. We conducted a retrospective cohort study at the two hospitals using data from medical records of COVID-19 critical cases patients. This study was conducted on COVID-19 patients admitted to the ICUs in Cipto Mangunkusumo National General Hospital and Universitas Indonesia Hospital from March to August 2020. Critical care services in both hospitals were performed by medical staff from Anesthesiology and Intensive Care Department, Universitas Indonesia. This study was reviewed and obtained ethical approval from the Committee of Research Ethics Faculty of Medicine Universitas Indonesia.

Adult patients (age >18 years) admitted to the ICU within the study duration and fulfilled the criteria of COVID-19 based on the WHO definition (March 20, 2020) with critical illness, ranging from severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock. (12) Probable cases of COVID-19 and subjects with incomplete medical record data were excluded.

The sample size was estimated using area under the curve (AUC) descriptive formula. With research precision of 10% and a generalized error of 5%, the minimum required number of subjects was 88. The consecutive sample recruitment was performed while searching through all medical records of confirmed COVID-19 patients admitted to the ICU of the particular hospitals.

The data collection was conducted using a questionnaire based on the COVID-19 case report form. (13) Only patients with polymerase chain reaction (PCR) confirmed COVID-19 were included. All the data of patients admitted to the ICU during the first 24 hours, including basic characteristics (age, gender, weight, height, body mass index, and comorbidities), vital signs, SOFA score variables (Glasgow Coma Scale [GCS], blood pressure, mean arterial pressure, vasopressor use and dose, platelet count, ratio of partial pressure of arterial oxygen [PaO2] and fraction of inspired oxygen [FiO2] [PaO2/FiO2], bilirubin count, blood creatinine levels, and urine output) were recorded. A modified SOFA score was used, we employed the Richmond Agitation Sedation Scale (RASS) for highly sedated patients and converted it to a four-point SOFA score neurological parameter.

We investigated the outcome of the 28-day mortality after being admitted to the ICU. We searched the 28-day mortality data from the medical records; if the patients were discharged before 28 days, we contacted the family and inquired about the patient's condition.

All statistical analysis was conducted using the software Statistical Package for Social Science (SPSS) 25th version. Univariate analysis was done to describe subject characteristics by using frequency distribution tables. An external validity testing of the SOFA score was conducted based on discrimination and calibration values. The discrimination value (examining the ability of SOFA score in differentiating between patients predicted to survive or die) was calculated by creating a receiver operating characteristic (ROC) curve to obtain the AUC value. The calibration value (examining the degree of correlation between mortality prediction and the actual mortality rates in all patient groups) was done using the Hosmer-Lemeshow test. The optimal cut-off point was determined using the highest Youden index based on data from the ROC curve with its specificity and sensitivity.

Results

Between March and August 2020, a total of 89 confirmed cases of COVID-19 were admitted to the ICUs of Cipto Mangunkusumo National General Hospital (38 subjects) and Universitas Indone-

sia Hospital (51 subjects), with one subject removed from the final analysis due to incomplete data (**Figure 1**).

Thirty-five patients died (39.8%) within 28 days of ICU admission. In this study, the male proportion was higher with an age mean of 52 years old (**Table 1**). The most common comorbid was hypertension (50%). The median ICU length of stay was 11 days. Discrimination of SOFA score can be seen in **Figure 2**, with an AUC value of 0.971 (95% confidence interval [CI] 0.943-0.999). Calibration performance by using the goodness of fit with the Hosmer-Lemeshow test showed a p-value of 0.782. Based on that value, the SOFA score demonstrated a very strong discrimination quality towards mortality of COVID-19 patients. To conclude, the SOFA score is suitable to predict 28-day mortality in COVID-19 patients.

The optimal cut-off points of the SOFA score to predict mortality were then extracted. Based on **Table 2** and **Figure 3**, the optimal cut-off point was 6 with 87% sensitivity and 90% specificity.

The value of mortality probability prediction was determined from a simple logistic regression test (**Table 3**) by using the formula of $1/(1+\exp(-y))$, in which $y=-6.600 + 1.070 \times$ SOFA score (**Table 4**).

Discussion

This study retrospectively investigated the performance of the SOFA score as a predictor of 28-day mortality in COVID-19 patients. We studied patients from two hospitals with different operating capabilities. Cipto Mangunkusumo General Hospital is a national referral hospital, with patients admitted commonly present with severe conditions. The Universitas Indonesia Hospital is a type B hospital that has been the referral hospital for COVID-19 during the pandemic, hence collaborating data from both hospitals enriched the patient's variability. The intensivists who worked in the two particular hospitals were the same. Therefore, there was no bias in the patient's management due to the clinician's decision.

This study showed a relatively high mortality rate, reaching 40%. There was no significant difference between gender and mortality rate due to COVID-19 based on the data from National Institute for Demographic Studies. (14) A higher case fatality rate per age was consistent with previous studies. (15) As a novel disease, the lack of knowledge and experience for clinical management contributed to high mortality rates.

A majority of subjects presented cardiovascular comorbidities, such as hypertension, a history of myocardial infarction, and congestive heart failure. However, in our study, there was no significant association between comorbidities and patient outcomes. COVID-19 seems to cause severe damage to the respiratory system, leading to fatalities in the early phase of the disease. The highest cause of death was attributed to severe respiratory failure.

The median length of stay in the ICU in deceased patients was lower when compared to the patients that survived, showing deterioration in early phases of COVID-19 may be due to cytokine storm and less healing time in critical COVID-19 patients. SOFA score >3 was obtained in approximately 63.2% of the participants, showing that most of the patients had at least one organ failure. In prolonged cases, prolonged hypoxia due to respiratory failure eventually led to severe sepsis, multiple organ dysfunction syndrome, and death.

The SOFA score is complex as it yields six variables, and not all health care facilities can examine all variables, especially laboratory parameters. Each of these parameters may have a relationship with mortality in COVID-19.

The SOFA score during the first 24-hour in ICU showed good calibration based on the Hosmer-Lemeshow test (p=0.782) and very strong discrimination performance with an AUC value of 0.971 (95% CI 0.943-0.999). This number was relatively similar to the previous study in Wuhan by Liu et al (2020). (16) The patients with very severe ARDS, might present with normal organ functions upon admission in the study. Since SARS-CoV-2 is transmitted via air droplets and invades the respiratory system, a blood gas analysis is routinely performed in COVID-19 patients admitted to the ICU to examine the severity of clinical manifestations, particularly the respiratory system. This parameter may have a prognostic value in COVID-19. This was consistent with previous studies, which showed significant differences in PaO2/FiO2 between different COVID-19 outcomes. (16-18)

Cardiovascular parameters may also affect COVID-19 mortality since lower cardiac functional status leads to higher mortality. This situation is not only found in COVID-19 cases but also in other septic patients in general. (19). The coagulation parameter can also be affected by COVID-19, but not necessarily due to low platelet count. Studies in Wuhan population showed that even though coagulopathy was commonly found in COVID-19 patients, low platelet counts were not commonly found; therefore, D-dimer testing to evaluate coagulopathy in COVID-19 was suggested. (20) For renal function parameter, Marik et al (2017) showed that in septic patients, mortality rates were higher when there was

a deterioration of renal function, and it may be applicable in COVID-19. (21)

The optimal cut-off point of the SOFA score in this study was 6 with 87% sensitivity and 90% specificity, which implied that when the SOFA score was greater than 6, COVID-19 patients had a greater tendency of mortality in 28 days. This value was greater than the study by Liu et al (2020) in Wuhan, where the cut-off point was 3. (16) The higher value from this study might be attributed due to the severity of the patients in this study. We obtained most of our samples in a national referral hospital where patients presented with more comorbidities and were referred to our ICU from lower-tier hospitals due to the severity of the cases.

We found it challenging to assess neurological dysfunction in intubated COVID-19 patients by using GCS because most patients in our study required a high dose of sedative. Therefore, we estimated the neurological dysfunction by using the Richmond Agitation Sedation Scale (RASS) when GCS evaluation was not possible and converted it to a four-point SOFA score neurological parameter. A study by Vasilevskis et al (2016) found that RASS as a replacement of GCS in the SOFA score was valid. (22) A similar condition also occurred in the liver function parameter test with bilirubin count since it was not routinely tested, especially in Universitas Indonesia Hospital, unless there was supporting evidence for impaired liver function. Therefore, we assumed that if patients did not present with jaundice, the bilirubin count was assumed to be normal. Another limitation of this study was the small sample size. During the study period, 236 patients were admitted to the COVID-19 dedicated ICU. Admission was based on clinical suspicion towards COVID-19 taking into consideration clinical symptoms, as well as radiologic and laboratory findings. Only 89 patients had the diagnosis confirmed by a positive PCR test. During the study period, the early days of the pandemic, PCR testing facilities were limited, hence results could take two to three days. A significant number of patients passed away while waiting for the PCR result, hence ineligible for the study. Poor sample processing as samples were not processed immediately may have further increased the number of false negatives, hence further hindering inclusion in the study. Selection bias might occur in this study as subjects were recruited consecutively from two hospitals. Information bias might also occur since this was a retrospective study in which data were collected from medical records.

With appropriate prognostic factors, we could predict earlier which patients will more likely perish in 28 days, so that resources could be diverted to the patients with a better-predicted outcome, leading to lower mortality rates. The SOFA score is a prognostic scoring system that has been widely used in various studies for critical care patients and yields good validity. However, studies in Indonesia are still limited since this is a new disease.

Even though the SOFA score during the first 24-hour ICU care in this study could be considered valid to predict 28-day mortality due to COVID-19, multiple evaluations will be beneficial since organ dysfunction is a dynamic process. We also recommend further multicenter study with greater populations specifically for confirmed COVID-19 patients. The use of SOFA score should also be compared with other prognostic scoring systems to evaluate which predictor is the most accurate in predicting 28-day mortality due to COVID-19.

Conclusion

The SOFA score is valid in predicting 28-day mortality in critically ill COVID-19 patients. The optimal cut-off point of SOFA score in this study was 6 with 87% sensitivity and 90% specificity. SOFA scores greater than six were associated with increased 28-day mortality.

Data availability

Data used to support the conclusions of this study could be obtained from the corresponding author by request.

Conflicts of interest

There are no conflicts of interest.

Acknowledgments

This article was presented in the 5th International Conference and Exhibition on Indonesian Medical Education and Research Institute (5th ICE on IMERI), Faculty of Medicine, Universitas Indonesia.

Table 1. Subject characteristics

	Patients	Outcome mortality	Outcome live	p-value
Sex				
- Male	66 (66.0)	34 (77.3)	32 (57.1)	0.075
- Female	34 (33.0)	10 (22.7)	24 (42.9)	
Age[a]				
- >80	5 (5.3)	4 (10.0)	1 (20.0)	0.020
- 70-79	11 (11.6)	6 (15.0)	5 (45.5)	
- 60-69	21 (22.1)	9 (22.5)	12 (21.8)	
- 50-59	22 (23.2)	11 (27.5)	11 (20.0)	
- <50	36 (37.9)	10 (25.0)	26 (47.3)	
Comorbidity[b]				
- Myocardial infarct	22 (21.4)	11 (50.0)	11 (50.0)	0.471
- Hypertension	52 (50.5)	25 (48.1)	27 (51.9)	0.307
- Congestive heart failure	15 (14.6)	10 (66.7)	5 (33.3)	0.047
- Peripheral arterial disease	4 (3.9)	3 (75.0)	1 (25.0)	0.191
- Stroke	5 (4.9)	3 (60.0)	2 (40.0)	0.439
- Dementia	15 (14.6)	11 (73.3)	4 (26.7)	0.011
- COPD	14 (13.6)	6 (42.9)	8 (57.1)	0.971
- Connective tissue disease	6 (5.8)	3 (50.0)	3 (50.0)	0.732
- Peptic ulcer	17 (16.5)	7 (41.2)	10 (58.8)	0.846
- Liver disease	9 (8.7)	3 (33.3)	6 (66.7)	0.296
- Diabetes mellitus	29 (28.2)	11 (379)	18 (62.0)	0.183
- Hemiplegia	7 (6.8)	5 (71.4)	2 (28.6)	0.119
- Chronic kidney disease	18 (17.5)	10 (55.6)	8 (44.4)	0.245
- Tumor	14 (13.6)	8 (57.1)	6 (42.9)	0.473
- Leukemic mass	2 (1.9)	1 (50)	1 (50.0)	1.000
- Lymphoma	2 (1.9)	2 (100)	0 (0)	0.185
- HIV-AIDS	1 (1.0)	0 (0)	1 (100)	1.000
ICU length of stay (days)[c]	10 (1-57)	6.5 (1-27)	11 (2-57)	0.020

Legend: COPD=chronic obstructive pulmonary disease; HIV-AIDS=human immunodeficiency virus-acquired immunodeficiency syndrome; ICU=intensive care unit.
[a]n (%), tested with Mann-Whitney.
[b]n (%), tested with chi-square.
[c]mean±standard deviation or median (min-max), tested with Mann-Whitney.

Table 2. The optimal cut-off point, sensitivity, and specificity of SOFA scores towards 28-day mortality

Cut-off	SOFA score	Sensitivity	Specificity
1.00	-1.000	1.000	0.000
2.00	0.500	1.000	0.019
3.00	1.500	1.000	0.315
4.00	2.500	1.000	0.537
5.00	3.500	1.000	0.741
6.00	4.500	1.000	0.815
7.00	5.500	0.914	0.889
8.00	6.500	0.829	0.926
9.00	7.500	0.771	0.981
10.00	8.500	0.600	0.981
11.00	9.500	0.343	1.000
12.00	10.500	0.200	1.000
13.00	11.500	0.086	1.000
14.00	13	0.029	1.000
15.00	15	0.000	1.000

Legend: SOFA=Sequential Organ Failure Assessment.

Table 3. Bivariate regression analysis of SOFA towards 28-day mortality

28-day mortality					
	B (constant coefficient)	Standard error	Adjusted OR	95% CI	p
SOFA	1.070	0.230	2.916	1.860-4.573	<0.001
Constant	-6.600	1.454	0.001		

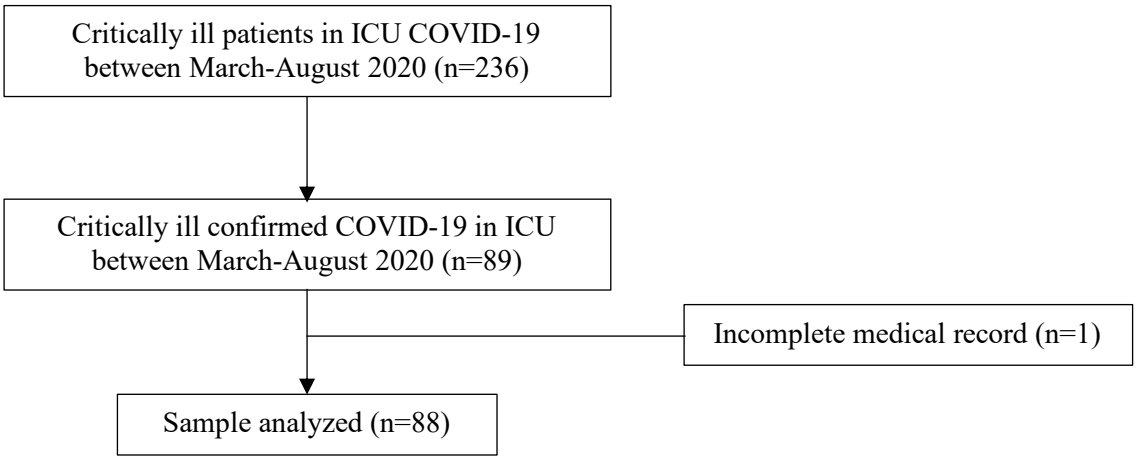
Legend: SOFA=Sequential Organ Failure Assessment; OR=odds ratio; CI=confidence interval.

Table 4. 28-day mortality on critically ill COVID-19 based on SOFA score

Constant	Coefficient	SOFA score	y	p
-2.57	0.356	1	-2.214	0.09850031
-2.57	0.356	2	-1.858	0.13493634
-2.57	0.356	3	-1.502	0.18212742
-2.57	0.356	4	-1.146	0.24122046
-2.57	0.356	5	-0.79	0.31216867
-2.57	0.356	6	-0.434	0.39317157
-2.57	0.356	7	-0.078	0.48050988
-2.57	0.356	8	0.278	0.56905583
-2.57	0.356	9	0.634	0.6533959
-2.57	0.356	10	0.99	0.72908792
-2.57	0.356	11	1.346	0.79347491
-2.57	0.356	12	1.702	0.84579577
-2.57	0.356	13	2.058	0.88675348
-2.57	0.356	14	2.414	0.91788866
-2.57	0.356	15	2.77	0.94103299
-2.57	0.356	16	3.126	0.95795257
-2.57	0.356	17	3.482	0.97017125
-2.57	0.356	18	3.838	0.97891742
-2.57	0.356	19	4.194	0.98513838
-2.57	0.356	20	4.55	0.98954329
-2.57	0.356	21	4.906	0.99265235
-2.57	0.356	22	5.262	0.99484182

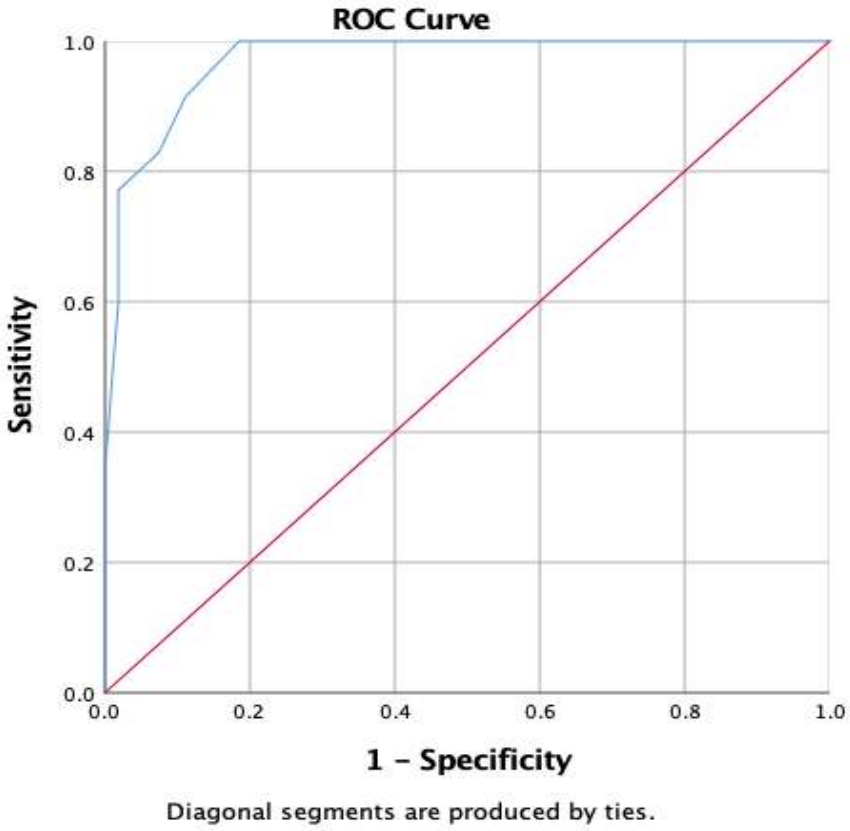
Legend: COVID-19=Coronavirus disease 2019; SOFA=Sequential Organ Failure Assessment.

Figure 1. Subject selection flowchart



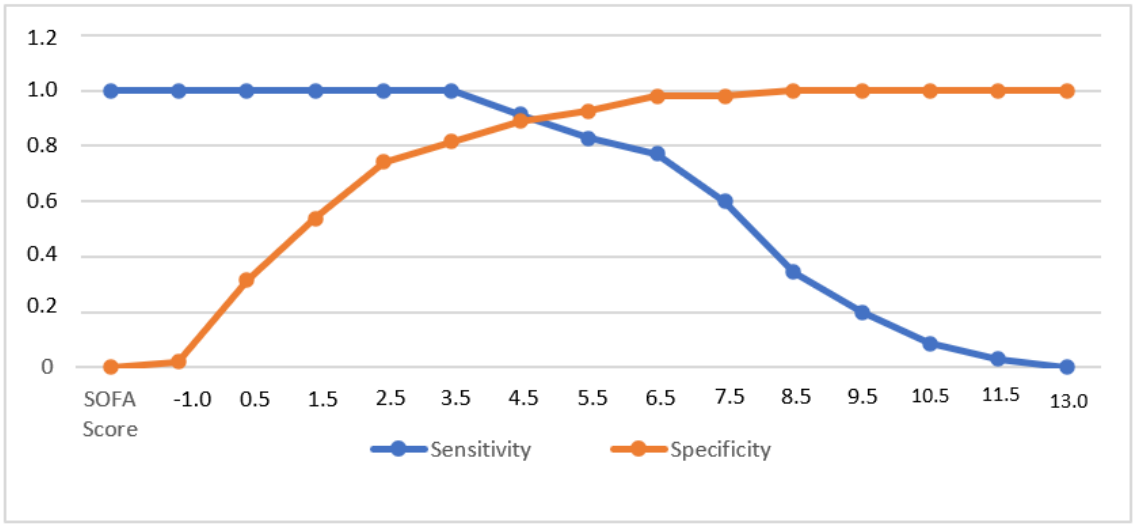
Legend: ICU=intensive care unit; COVID-19=Coronavirus disease 2019.

Figure 2. ROC curve of SOFA to predict 28-day mortality, AUC 0.83 (95% CI 0.943-0.999)



Legend: ROC=receiver operating characteristic; SOFA=Sequential Organ Failure Assessment; AUC=area under the curve; CI=confidence interval.

Figure 3. Sensitivity and specificity graph of SOFA score towards mortality with the optimal cut-off point



Legend: SOFA=Sequential Organ Failure Assessment.

References

1. World Health Organization. Director-General's opening remarks at the media briefing on COVID-19 – 11 March 2020 [Internet]. World Health Organization. 2020 Mar 11 [cited 2020 May 5]. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
2. Jokowi Umumkan Dua WNI Positif Corona di Indonesia [Internet]. 2020 Mar 2 [cited 2020 May 5]. Available from: https://www.cnnindonesia.com/nasional/20200302111534-20-479660/jokowi-umumkan-dua-wni-positif-corona-di-indonesia
3. Ridwan Kamil: Karyawan Telkom yang Meninggal di Cianjur Positif Corona [Internet]. 2020 Mar 15 [cited 2020 May 5]. Available from: https://kumparan.com/kumparannews/ridwan-kamil-karyawan-telkom-yang-meninggal-di-cianjur-positif-corona-1t1rxZr4Vt3
4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020;323: 1061-9.
5. World Health Organization (WHO). International guidelines for certification and classification (coding) of COVID-19 as cause of death. 2020 Apr 16. 14 p.
6. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 1996;22: 707-10.
7. Le Gall JR, Klar J, Lemeshow S, Saulnier F, Alberti C, Artigas A, et al. The Logistic Organ Dysfunction system. A new way to assess organ dysfunction in the intensive care unit. ICU Scoring Group. JAMA 1996;276:802-10.
8. Moreno RP, Metnitz PGH, Almeida E, Jordan B, Bauer P, Campos RA, et al. SAPS 3 - From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. Intensive Care Med 2005;31:1345-55.
9. Probst L, Schalk E, Liebregts T, Zeremski V, Tzalavras A, von Bergwelt-Baildon M, et al. Prognostic accuracy of SOFA, qSOFA and SIRS SIRS criteria in hematological cancer patients: A retrospective multicenter study. J Intensive Care 2019;7:1-10.
10. Jahn M, Rekowski J, Gerken G, Kribben A, Canbay A, Katsounas A. The predictive performance of SAPS 2 and SAPS 3 in an intermediate care unit for internal medicine at a German university transplant center; A retrospective analysis. PLoS One 2019;14:1-16.
11. Bouch D, Thompson JP. Severity scoring systems in the critically ill. Continuing education in anaesthesia, critical care & pain 2008;8:181-5.
12. World Health Organization. Global surveillance for COVID-19 caused by human infection with COVID-19 virus: Interim Guidance. 2020 Mar 20. 4 p.
13. World Health Organization. Case record form instructions severe acute respiratory infection clinical characterisation data tools. 2016 Jan 7. 14 p.
14. Institut national d'études démographiques. The contribution of demography to the COVID-19 pandemics. 2020 Mar 27. 2 p.
15. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA 2020;323: 1775-6.
16. Liu S, Yao N, Qiu Y, He C. Predictive performance of SOFA and qSOFA for in-hospital mortality in severe novel coronavirus disease. Am J Emerg Med 2020;38:2074-80.
17. Tang X, Du R-H, Wang R, Cao T-Z, Guan L-L, Yang C-Q, et al. Comparison of Hospitalized Patients With ARDS Caused by COVID-19 and H1N1. Chest 2020;158:195-205.
18. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395: 1054-62.
19. Innocenti F, Tozzi C, Donnini C, De Villa E, Conti A, Zanobetti M, et al. SOFA score in septic patients: incremental prognostic value over age, comorbidities, and parameters of sepsis severity. Intern Emerg Med 2018;13:405-12.
20. Agbuduwe C, Basu S. Hematolological Manifestations of COVID-19: From Cytopenia to Coagulopathy. Eur J Haematol 2020;105:540-6.
21. Marik PE, Taeb AM. SIRS, qSOFA and new sepsis definition. J Thorac Dis 2017;9:943-5.
22. Vasilevskis EE, Pandharipande PP, Graves AJ, Shintani A, Tsuruta R, Ely EW, et al. Validity of a Modified Sequential Organ Failure Assessment Score Using the Richmond Agitation-Sedation Scale. Crit Care Med 2016;44:138-46.