

In-hospital mortality prediction using frailty scale and severity score in elderly patients with severe COVID-19

Yong Sub Na^{1*}, Jin Hyoung Kim^{2*}, Moon Seong Baek³, Won-Young Kim³, Ae-Rin Baek⁴, Bo young Lee⁵, Gil Myeong Seong⁶, Song-I Lee⁷

¹Department of Pulmonology and Critical Care Medicine, Chosun University Hospital, Gwangju; ²Division of Respiratory and Critical Care Medicine, Department of Internal Medicine, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan; ³Department of Internal Medicine, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul; ⁴Division of Allergy and Pulmonology, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon; ⁵Division of Allergy and Respiratory Diseases, Soonchunhyang University Hospital, Seoul; ⁶Department of Internal Medicine, Jeju National University College of Medicine, Jeju; ⁷Department of Pulmonary and Critical Care Medicine, Chungnam National University Hospital, Daejeon, Korea

Background: Elderly patients with coronavirus disease 2019 (COVID-19) have a high disease severity and mortality. However, the use of the frailty scale and severity score to predict in-hospital mortality in the elderly is not well established. Therefore, in this study, we investigated the use of these scores in COVID-19 cases in the elderly.

Methods: This multicenter retrospective study included severe COVID-19 patients admitted to seven hospitals in Republic of Korea from February 2020 to February 2021. We evaluated patients' Acute Physiology and Chronic Health Evaluation (APACHE) II score; confusion, urea nitrogen, respiratory rate, blood pressure, 65 years of age and older (CURB-65) score; modified early warning score (MEWS); Sequential Organ Failure Assessment (SOFA) score; clinical frailty scale (CFS) score; and Charlson comorbidity index (CCI). We evaluated the predictive value using receiver operating characteristic (ROC) curve analysis.

Results: The study included 318 elderly patients with severe COVID-19 of whom 237 (74.5%) were survivors and 81 (25.5%) were non-survivors. The non-survivor group was older and had more comorbidities than the survivor group. The CFS, CCI, APACHE II, SOFA, CURB-65, and MEWS scores were higher in the non-survivor group than in the survivor group. When analyzed using the ROC curve, SOFA score showed the best performance in predicting the prognosis of elderly patients (area under the curve=0.766, $P<0.001$). CFS and SOFA scores were associated with in-hospital mortality in the multivariate analysis.

Conclusions: The SOFA score is an efficient tool for assessing in-hospital mortality in elderly patients with severe COVID-19.

Key Words: COVID-19; critical care; elderly; mortality

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in Wuhan, China in December, 2019. SARS-CoV-2 causes coronavirus disease 2019 (COVID-19). The World Health Organization declared COVID-19 to be a pandemic in March, 2020 [1]. In the

Original Article

Received: January 3, 2022

Revised: March 24, 2022

Accepted: March 24, 2022

Corresponding author

Song-I Lee

Department of Pulmonary and Critical Care Medicine, Chungnam National University Hospital, 282 Munhwa-ro, Jung-gu, Daejeon 35015, Korea

Tel: +82-42-280-6816

Fax: +82-42-257-5753

E-mail: newcomet01@naver.com

*These authors contributed equally to this study.

Copyright © 2022 The Korean Society of Critical Care Medicine

This is an Open Access article distributed under the terms of Creative Attributions Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Republic of Korea, there have been 551,551 cases diagnosed with COVID-19 and 4,591 deaths from January 3, 2020, to December 17, 2021. As of December 12, 2021, 83,142,509 vaccine doses were administered. Vaccination is currently being implemented worldwide to prevent COVID-19 [2-4]; however, vaccination has not completely prevented COVID-19 [5]. With the recent increase in the number of patients with COVID-19, Korea is suffering from a rapid increase in the number of severely ill patients and a shortage of intensive care unit beds.

Elderly people have a higher COVID-19 severity and mortality than younger people [6-9]. In addition, elderly patients with COVID-19 have more underlying diseases and higher frailty at admission than younger patients [10-14]. High severity score and high frailty score are expected to assist in predicting mortality rate of elderly patients hospitalized with COVID-19 [15-18]. However, it is not well-known whether the best assessment for predicting in-hospital mortality is baseline frailty or the COVID-19 severity score. Therefore, in this study, we aimed to investigate whether the frailty scale and the currently used severity scoring system can predict in-hospital mortality in elderly patients with severe COVID-19.

MATERIALS AND METHODS

This multicenter retrospective study involved seven hospitals treating patients with severe COVID-19 in Republic of Korea from February 2, 2020 to February 28, 2021. We analyzed data collected from all hospitalized severe COVID-19 patients from the seven hospitals. The research was approved by the Ethical Committee of the Promoting Center (No. 2021-04-053) and local ethics committees. The need for written informed consent was waived due to the retrospective nature of the study.

All data were retrieved from electronic medical records. Information about patient characteristics, including gender, age, symptoms, and initial laboratory and radiologic findings, was collected. Moreover, data on the need for invasive treatment (mechanical ventilation, vasopressor treatment, and continuous renal replacement therapy [CRRT]), in-hospital mortality, and duration of hospital stay were extracted. The initial Acute Physiology and Chronic Health Evaluation (APACHE) II; Sequential Organ Failure Assessment (SOFA) score; confusion, urea nitrogen, respiratory rate, blood pressure, 65 years of age and older (CURB-65) score; modified early warning score (MEWS) and Charlson comorbidity index (CCI) score were analyzed to evaluate the patients' condition at the time of admission. The clinical frailty scale (CFS) was used to indicate the

KEY MESSAGES

- The in-hospital mortality of elderly patients with severe coronavirus disease 2019 (COVID-19) was 25.5%.
- The non-survivor group had more underlying diseases, and their initial frailty scale and severity scores tended to be higher than those in the survivor group.
- The Sequential Organ Failure Assessment (SOFA) score demonstrated the best performance in predicting the in-hospital mortality of elderly patients with severe COVID-19.
- Clinical frailty scale and SOFA scores were associated with in-hospital mortality in multivariate analyses, and these may assist in treatment decision-making.

patient's previous functional independence before hospitalization based on the patient's medical status [19]. SARS-CoV-2 infection in hospitalized patients was confirmed via reverse transcriptase-polymerase chain reaction. Severe COVID-19 infection was defined as an oxygen saturation level of 94% or less in room air or a need for oxygen support [20]. These have been confirmed as indicators of COVID-19 severity.

Statistical Analysis

All data are expressed as the percentage for categorical variables and as the median and interquartile range for continuous variables. Pearson's chi-square test or Fisher's exact test was used for categorical data, and Student t-test or Mann-Whitney U-test was used for continuous data. Receiver operating characteristic (ROC) curve analysis was performed to evaluate prediction accuracy. The optimal cutoff value was chosen as the highest product of sensitivity and specificity. Cox regression analysis was performed to identify the predictors of in-hospital mortality. All P-values were two-tailed with statistical significance set at $P < 0.05$. No imputation strategy was conducted because cases of missing data were rare (90/17,718, 0.5%). There were no missing values for frailty scale and severity scores. We used the IBM SPSS ver. 22.0 (IBM Corp., Armonk, NY, USA) to perform all statistical analyses.

RESULTS

Patients' Baseline Characteristics

Of the 1,565 hospitalized COVID-19 patients, 318 patients ≥ 65 years old with severe COVID-19 were included. Of these, 237 patients (74.5%) comprised the survivor group and 81 (25.5%)

comprised the non-survivor group (Figure 1).

Baseline patient characteristics at the time of admission are presented in the Table 1. The median ages of the survivor and non-survivor groups were 76 years (interquartile range [IQR], 69–84) and 80 years (IQR, 75–85), respectively. Chronic obstructive pulmonary disease (COPD; 8.6% vs. 2.1%, $P=0.008$) and diabetes mellitus (DM; 50.6% vs. 31.6%, $P=0.002$) were more common in the non-survivor group than in the survivor group. The non-survivor group had a lower diastolic blood pressure (67 mm Hg [53–79] vs. 72 mm Hg [64–82], $P=0.002$), Glasgow coma scale (15 [12–15] vs. 15 [15–15], $P<0.001$), and higher respiratory rate (RR; 22/min [20–26] vs. 20/min [19–22], $P=0.003$) than the survivor group. The non-survivor group patients had higher initial white blood cell (WBC) counts; neutrophil-to-lymphocyte ratios (NLRs); and blood urea nitrogen (BUN), creatinine, and C-reactive protein levels than survivor group patients. Non-survivor group patients also had lower initial hemoglobin levels, platelet counts, and albumin levels. Normal initial radiographs were fewer in the non-survivor group than in the survivor group (8.6% vs. 18.6%, $P=0.036$).

Treatment and Clinical Outcomes between Survivor and Non-survivor Groups

The treatment and outcomes of patients are presented in Table 2. The use of antibiotics (77.8% vs. 62.4%, $P=0.012$), vasopressors (38.3% vs. 7.2%, $P<0.001$), CRRT (19.8% vs. 1.7%, $P<0.001$), and steroids (90.1% vs. 72.2%, $P=0.001$) was higher in the non-survivor group than in the survivor group. Extracorporeal membrane oxygenation (ECMO; 8.6% vs. 1.3%, $P<0.001$),

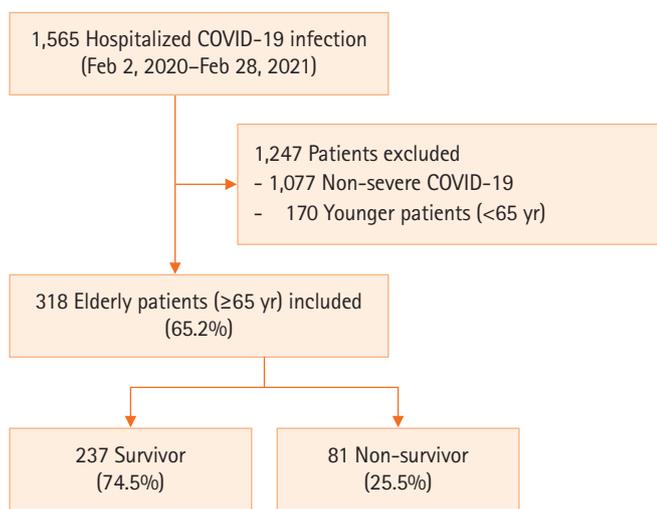


Figure 1. Flowchart of patients. COVID-19: coronavirus disease 2019.

invasive mechanical ventilation (54.3% vs. 15.2%, $P<0.001$), and high-flow nasal cannula (59.3% vs. 26.2%, $P<0.001$) were more commonly used in the non-survivor group. Compared with the survivor group, the non-survivor group had a higher proportion of patients with do-not-resuscitate (DNR) orders (72.8% vs. 7.2%, $P<0.001$).

Frailty Scale and Severity Scores between the Survivor and Non-survivor Groups

Table 3 shows the frailty and severity scores of elderly patients. Compared with the survivor group, the non-survivor group had higher CFS and CCI. In addition, the APACHE II, SOFA, CURB-65 scores, and MEWS were higher in the non-survivor group than in the survivor group.

Prognostic Value of the Frailty Scale and Severity Score

The performance of the CFS, CCI, APACHE II, SOFA, CURB-65, and MEWS in predicting in-hospital mortality was evaluated using ROC curves (Figure 2). The SOFA score demonstrated the best performance in predicting the prognosis of elderly severe COVID-19 patients (area under the curve [AUC], 0.766; $P<0.001$). The CFS (AUC, 0.692; $P<0.001$), CCI (AUC, 0.652; $P<0.001$), APACHE II score (AUC, 0.699; $P<0.001$), CURB-65 (AUC, 0.672; $P<0.001$), and MEWS (AUC, 0.646; $P<0.001$) demonstrated poor performance. The prognostic cut-off value of the SOFA score was 2.50 (sensitivity, 72.8%; specificity, 70.5%).

Predictors of Patients' In-hospital Mortality

Table 4 shows the risk factors associated with in-hospital mortality. In multivariate analysis, age (odds ratio [OR], 1.029; 95% confidence interval [CI], 0.999–1.059; $P=0.054$), high CFS (OR, 1.274; 95% CI, 1.112–1.460; $P<0.001$), high SOFA score (OR, 1.144; 95% CI, 1.082–1.211; $P<0.001$), DM (OR, 1.988; 95% CI, 1.240–3.188; $P=0.001$), COPD (OR, 2.462; 95% CI, 1.093–5.546; $P=0.030$), and high WBC count (OR, 1.051; 95% CI, 1.003–1.101; $P=0.038$) were shown to be factors associated with in-hospital mortality.

DISCUSSION

In this study, the in-hospital mortality rate of elderly patients with severe COVID-19 was 25.5%. Non-survivor group were older, had more underlying comorbidities, frailer, and more severe by severity scores than the survivor group. SOFA score was the best predictor of in-hospital mortality. High CFS, high

Table 1. Baseline characteristics of elderly patients with severe COVID-19 at the time of admission

Variable	All patients (n=318)	Survivor (n=237)	Non-survivor (n=81)	P-value
Age (yr)	78 (71–84)	76 (69–84)	80 (75–85)	0.001
Male	136 (42.8)	96 (40.5)	40 (49.4)	0.163
Smoking	57 (17.9)	44 (18.6)	13 (16.0)	0.610
Symptom at admission	244 (76.7)	181 (76.4)	63 (77.8)	0.796
Symptom to admission (day)	3.0 (1.0–7.0)	4.0 (1.0–8.0)	2.0 (0.8–6.0)	0.451
Body mass index (kg/m ²)	23.1 (20.7–25.9)	23.2 (20.8–25.9)	22.8 (19.8–26.6)	0.519
Resident of a nursing facilities	76 (23.9)	55 (23.2)	21 (25.9)	0.620
Comorbidity				
Hypertension	201 (63.2)	144 (60.8)	57 (70.4)	0.122
DM	116 (36.5)	75 (31.6)	41 (50.6)	0.002
COPD	12 (3.8)	5 (2.1)	7 (8.6)	0.008
Cerebrovascular disease	42 (13.2)	30 (12.7)	12 (14.8)	0.621
Heart failure	16 (5.0)	13 (5.5)	3 (3.7)	0.527
Liver cirrhosis	4 (1.3)	2 (0.8)	2 (2.5)	0.257
Chronic kidney disease	5 (1.6)	4 (1.7)	1 (1.2)	0.777
Malignancy	18 (5.7)	15 (6.3)	3 (3.7)	0.377
Vital sign				
SBP (mm Hg)	121 (108–140)	121 (109–140)	120 (106–134)	0.203
DBP (mm Hg)	71 (61–81)	72 (64–82)	67 (53–79)	0.002
HR (/min)	86 (73–99)	84 (73–97)	90 (71–103)	0.115
RR (/min)	20 (19–24)	20 (19–22)	22 (20–26)	0.003
Body temperature (°C)	36.7 (36.4–37.4)	36.8 (36.4–37.4)	36.6 (36.4–37.2)	0.092
SpO ₂ (%)	95.0 (92.0–98.0)	96.0 (93.0–98.0)	95.0 (90.5–98.0)	0.055
GCS	15 (14–15)	15 (15–15)	15 (12–15)	<0.001
Duration of fever	2.0 (0.0–4.3)	2.0 (0.0–4.0)	2.0 (0.0–6.5)	0.124
Laboratory data				
White blood cell count (1,000/mm ³)	5.91 (4.36–7.98)	5.54 (4.23–7.72)	7.01 (4.95–9.22)	0.007
Neutrophil lymphocyte ratio	4.56 (2.75–9.60)	4.04 (2.52–8.65)	7.62 (4.01–15.60)	0.002
Hemoglobin (g/dl)	12.6 (11.2–13.8)	12.8 (11.5–13.8)	12.2 (10.6–13.5)	0.013
Platelet count (1,000/mm ³)	179 (134–228)	184 (145–234)	154 (116–216)	0.001
Total bilirubin (mg/dl)	0.5 (0.3–0.7)	0.5 (0.3–0.6)	0.5 (0.3–0.7)	0.087
Albumin (g/dl)	3.5 (3.1–3.8)	3.5 (3.2–3.9)	3.2 (2.8–3.6)	<0.001
BUN (mg/dl)	16 (12–24)	16 (11–22)	20 (13–35)	0.001
Creatinine (mg/dl)	0.78 (0.60–1.00)	0.74 (0.58–0.94)	0.82 (0.65–1.29)	0.015
C-reactive protein (mg/dl)	5.70 (2.07–10.58)	4.74 (1.57–9.24)	7.93 (3.80–15.67)	0.002
Chest X-ray				
Normal	51 (16.0)	44 (18.6)	7 (8.6)	0.036
Unilateral	52 (16.4)	39 (16.5)	13 (16.0)	0.932
Bilateral	138 (43.4)	100 (42.2)	38 (46.9)	0.459
Multifocal	77 (24.2)	54 (22.8)	23 (28.4)	0.309

Values are presented as median (interquartile range) or number (%).

COVID-19: coronavirus disease 2019; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; RR: respiratory rate; SpO₂: saturation pulse oxygen; GCS: Glasgow coma scale; BUN: blood urea nitrogen.

SOFA score, age, a concurrent diagnosis of COPD, a concurrent diagnosis of DM, and high WBC count were risk factors for in-hospital mortality in the elderly patients with severe

COVID-19.

Elderly patients commonly have underlying diseases such as DM and COPD. Additionally, the non-survivor group patients

Table 2. Treatment and clinical outcomes of elderly patients with severe COVID-19

Variable	All patients (n=318)	Survivor (n=237)	Non-survivor (n=81)	P-value
Treatment				
Remdesivir	168 (52.8)	119 (50.2)	49 (60.5)	0.109
Antibiotics	211 (66.4)	148 (62.4)	63 (77.8)	0.012
Vasopressor	48 (15.1)	17 (7.2)	31 (38.3)	<0.001
CRRT	20 (6.3)	4 (1.7)	16 (19.8)	<0.001
Steroid	244 (76.7)	171 (72.2)	73 (90.1)	0.001
Oxygen supply device				
Nasal prong	257 (80.8)	209 (88.2)	48 (59.3)	<0.001
HFNC	110 (34.6)	62 (26.2)	48 (59.3)	<0.001
Invasive mechanical ventilation	80 (25.2)	36 (15.2)	44 (54.3)	<0.001
ECMO	10 (3.1)	3 (1.3)	7 (8.6)	0.001
Tracheostomy (%)	27 (8.5)	14 (5.9)	13 (16.0)	0.005
Outcome				
Length of hospital stay (day)	17.0 (12.0–26.0)	17.0 (13.0–25.0)	17.0 (10.0–27.0)	0.748
Secondary infection	103 (32.4)	62 (26.2)	41 (50.6)	<0.001
DNR order	76 (23.9)	17 (7.2)	59 (72.8)	<0.001

Values are presented as number (%) or median (interquartile range).

COVID-19: coronavirus disease 2019; CRRT: continuous renal replacement therapy; HFNC: high-flow nasal cannula; ECMO: extracorporeal membrane oxygenation; DNR: do-not-resuscitate.

Table 3. Frailty scale and severity score of elderly patients with severe COVID-19

Variable	All patients (n=318)	Survivor (n=237)	Non-survivor (n=81)	P-value
Frailty				
Clinical frailty scale	4.0 (3.0–7.0)	3.0 (3.0–6.0)	6.0 (4.0–7.0)	<0.001
Charlson comorbidity index	4.0 (3.0–5.0)	4.0 (3.0–5.0)	5.0 (4.0–6.0)	<0.001
Severity score				
APACHE II score	11.5 (9.0–15.0)	11.0 (8.0–14.0)	14.0 (11.0–19.0)	<0.001
SOFA score	2.0 (1.0–4.0)	1.0 (0.0–3.0)	4.0 (2.0–8.5)	<0.001
CURB-65 score	2.0 (1.0–2.0)	1.0 (1.0–2.0)	2.0 (1.5–3.0)	<0.001
MEWS	1.0 (1.0–2.0)	1.0 (1.0–2.0)	2.0 (1.0–3.0)	<0.001

Values are presented as median (interquartile range).

COVID-19: coronavirus disease 2019; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; CURB-65: confusion, urea nitrogen, respiratory rate, blood pressure, 65 years of age and older; MEWS: modified early warning score.

frequently required treatments such as invasive mechanical ventilation, CRRT, and ECMO. These patients also had DNR orders more frequently. The required treatment and DNR order findings are consistent with those of previous studies [21–26]. In Gao et al.'s study [26], which included older (≥ 65 years) COVID-19 patients, the deceased group had more morbidities including cardiovascular diseases (49% vs. 20%, $P < 0.001$), respiratory diseases (51% vs. 11%, $P < 0.001$), chronic kidney disease (29% vs. 5%, $P < 0.001$) and cerebrovascular disease (20% vs. 3%) than the discharged group. In a study by Vrillon et al. [21], included the very elderly (≥ 85 years) COVID-19 patients, the non-survivor group had more cardioneurovascular diseases

(68.2% vs. 37.0%, $P = 0.013$), more complications like acute respiratory distress syndrome (95.5% vs. 1.9%, $P < 0.001$), and needed more frequent treatment with oxygen (95.5% vs. 46.3%, $P < 0.001$) compared with the survivor group.

In this study, the non-survivor group had higher WBC counts and NLR, BUN, creatinine, and C-reactive protein levels than the survivor group. The non-survivor group also had lower hemoglobin levels, platelet counts, and albumin levels than survivor group. In a study of elderly patients with COVID-19 by Gao et al. [26], the deceased group subjects showed significantly higher levels of C-reactive protein and BUN and significantly lower lymphocyte counts than the discharged group subjects.

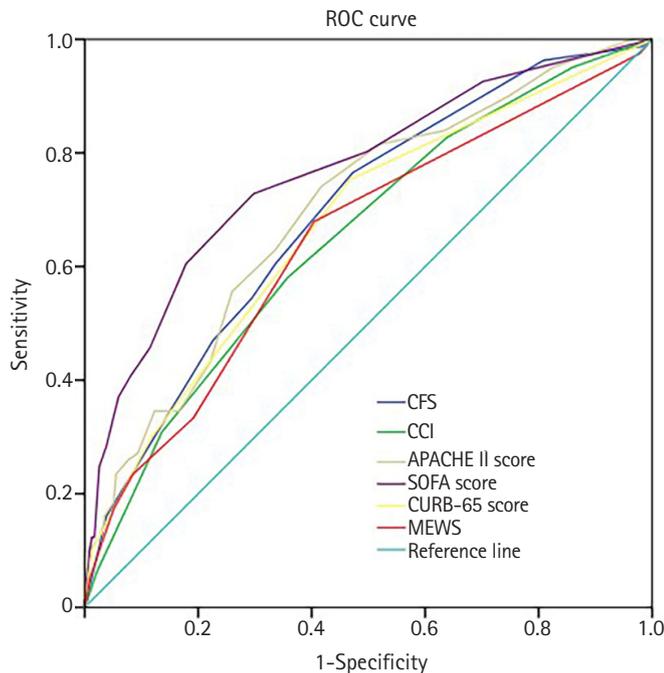


Figure 2. Receiver operating characteristic (ROC) curves of the clinical frailty scale (CFS), Charlson comorbidity index (CCI), Acute Physiology and Chronic Health Evaluation (APACHE) II, Sequential Organ Failure Assessment (SOFA), confusion, urea nitrogen, respiratory rate, blood pressure, 65 years of age and older (CURB-65) scores, and modified early warning score (MEWS) in predicting patients' in-hospital mortality.

Li et al.'s study [27], in the elderly (≥ 60 years) patients with COVID-19, showed that higher WBC and neutrophil counts, creatine kinase-MB levels, D-dimer levels, and procalcitonin levels and lower albumin levels, lower pH values, presence of hypercapnia, and presence of hypoxia were associated with higher mortality. The results of these studies were similar to those of our study that was focused on elderly patients with severe COVID-19.

Elderly patients with severe COVID-19 were frailer and had higher disease severity. Pranata et al. [16] showed that a 12% increase in patient mortality was associated with a one point increase in CFS and that CFS was associated with mortality in a linear fashion. In a study of older patients with COVID-19 by Darren et al. [15], the mortality rate was higher in the patients who had a CFS score of 6 or higher than in the patients with CFS of 1–3. In a study by Tuty Kuswardhani et al. [28], compared to patients with a CCI score of 0, patients with a CCI score of 1–2 and ≥ 3 had higher mortality and poorer outcome. Additionally, the higher the SOFA score, the higher was the mortality rate in patients with severe COVID-19. In this study,

the prognostic cut-off value of the SOFA score for in-hospital mortality was 2.50. In Yang's study [18], the cut-off SOFA score value for predicting severe COVID-19 was 2, and the cut-off value for predicting mortality was 5. In a study of patients with suspected infection admitted to an intensive care unit, an increase in SOFA score of 2 or more was associated with in-hospital mortality [17]. In our study, the SOFA score cut-off of 2.5 seems lower than the SOFA score of critically ill ICU patients in general. This is probably due to the effect of respiratory failure being the main cause of exacerbation in many patients with severe COVID-19. While there have been studies on the usefulness of each score for predicting severity and mortality, no study has analyzed an overall frailty scale and severity score. In this study, scores indicating frailty and patient severity were analyzed, and the SOFA score showed the best predictive power for mortality. However, with the current ICU bed shortage situation, considering several factors when determining ICU admission is preferred [29–31]. Therefore, in actual practice, considering several factors related to mortality, such as CFS, in addition to the SOFA score is necessary in ICU triage.

Age, high CFS, high SOFA score, comorbidities such as DM, COPD, and high WBC count were risk factors of in-hospital mortality in this study. These risk factors have also been shown in other studies. Frailty is related to the prognosis of elderly patients. A multicenter study of elderly COVID-19 patients ≥ 70 years old showed that higher frailty was associated with higher 30-day mortality and a higher rate of treatment limitation [32]. Pranata et al. [16] and Aliberti et al. [33] also showed that higher clinical frailty scores were associated with higher mortality. In other studies, factors associated with mortality include age; Charlson index; presence of diabetes, COPD, CKD, hypertension, or dementia; high d-dimer level; and high neutrophil-lymphocyte ratio [34–36].

This study has several limitations. First, the frailty scale and severity scores were calculated by reviewing medical records and collecting clinical data from an electronic record database. While these scores may differ from actual scores, the difference was judged to be negligible. Second, the hospital participating in the study is a hospital that treats severe COVID-19 patients; patients who have been transferred from the living center and other hospitals may initially show higher severity and poorer laboratory data. However, since most hospitals that treat critically ill patients have many patients from other hospitals, the evaluation and results shown in this study are still useful.

In conclusion, the in-hospital mortality rates of elderly patients with severe COVID-19 was 25.5%. The SOFA score

Table 4. Univariate and multivariate risk factors associated with in hospital mortality (Cox regression model)

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.040 (1.014–1.067)	0.003	1.029 (0.999–1.059)	0.054
Male	1.106 (0.711–1.720)	0.656		
Frailty				
Clinical frailty scale	1.217 (1.094–1.355)	<0.001	1.274 (1.112–1.460)	<0.001
Charlson comorbidity index	1.444 (1.245–1.675)	<0.001	1.103 (0.863–1.411)	0.434
Severity score				
APACHE II score	1.070 (1.035–1.106)	<0.001	1.025 (0.972–1.081)	0.364
SOFA score	1.119 (1.066–1.175)	<0.001	1.144 (1.082–1.211)	<0.001
CURB-65 score	1.608 (1.259–2.053)	<0.001	1.024 (0.727–1.441)	0.894
MEWS	1.144 (1.020–1.283)	0.022	0.916 (0.799–1.050)	0.207
Comorbidity (%)				
DM	1.686 (1.086–2.617)	0.020	1.988 (1.240–3.188)	0.001
COPD	3.717 (1.695–8.154)	0.001	2.462 (1.093–5.546)	0.030
Cerebrovascular disease	1.409 (0.760–2.613)	0.277		
Chronic kidney disease	0.726 (0.101–5.232)	0.751		
Malignancy	0.588 (0.185–1.866)	0.367		
Laboratory data				
White cell count (1,000/mm ³)	1.055 (1.010–1.102)	0.016	1.051 (1.003–1.101)	0.038
Hemoglobin (g/dl)	0.911 (0.824–1.007)	0.068		
Platelet count (1,000/mm ³)	0.996 (0.993–1.000)	0.031	0.998 (0.995–1.002)	0.378
Albumin (g/dl)	0.443 (0.285–0.689)	<0.001	0.875 (0.517–1.481)	0.619
Total bilirubin (mg/dl)	1.549 (1.036–2.316)	0.033	1.373 (0.894–2.108)	0.148
Creatinine (mg/dl)	1.150 (1.016–1.301)	0.027	0.975 (0.821–1.159)	0.778
C-reactive protein (mg/dl)	1.109 (0.994–1.045)	0.142		

OR: odds ratio; CI: confidence interval; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; CURB-65: confusion, urea nitrogen, respiratory rate, blood pressure, 65 years of age and older; MEWS: modified early warning score; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease.

showed the best predictive performance, and the prognostic cut-off value was 2.50. The SOFA score was the most useful tool for predicting critical care and in-hospital mortality in elderly patients with severe COVID-19; and other factors associated with in-hospital mortality were age, CFS, concurrent diagnosis of DM or COPD, and high WBC count.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Yong Sub Na <https://orcid.org/0000-0003-2506-2673>
 Jin Hyoung Kim <https://orcid.org/0000-0002-2229-2388>
 Moon Seong Baek <https://orcid.org/0000-0001-6455-0376>
 Won-Young Kim <https://orcid.org/0000-0002-6038-9818>
 Bo young Lee <https://orcid.org/0000-0001-7399-3822>

Gil Myeong Seong <https://orcid.org/0000-0002-0765-8273>
 Song-I Lee <https://orcid.org/0000-0001-8372-4511>

AUTHOR CONTRIBUTIONS

Conceptualization: YSN, JHK, SIL. Data curation: all authors. Formal analysis: SIL. Methodology: SIL. Visualization: YSN, JHK, SIL. Writing–original draft: all authors. Writing–review & editing: all authors.

REFERENCES

1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Biomed* 2020;91:157-60.
2. Bajema KL, Dahl RM, Evener SL, Prill MM, Rodriguez-Barradas MC, Marconi VC. Comparative effectiveness and antibody responses to moderna and Pfizer-BioNTech COVID-19 vaccines among hospitalized veterans: five veterans affairs medical centers, United States, February 1-September 30, 2021. *MMWR*

- Morb Mortal Wkly Rep 2021;70:1700-5.
3. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021;384:403-16.
 4. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020;383:2603-15.
 5. World Health Organization. COVID-19, Republic of Korea [Internet]. Geneva: World Health Organization; 2021 [cited 2021 Dec 20]. Available from: <https://covid19.who.int/region/wpro/country/kr>.
 6. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
 7. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* 2020;46:846-8.
 8. Zhang L, Hou J, Ma FZ, Li J, Xue S, Xu ZG. The common risk factors for progression and mortality in COVID-19 patients: a meta-analysis. *Arch Virol* 2021;166:2071-87.
 9. Booth A, Reed AB, Ponzo S, Yassaee A, Aral M, Plans D, et al. Population risk factors for severe disease and mortality in COVID-19: a global systematic review and meta-analysis. *PLoS One* 2021;16:e0247461.
 10. Guo T, Shen Q, Guo W, He W, Li J, Zhang Y, et al. Clinical characteristics of elderly patients with COVID-19 in Hunan Province, China: a multicenter, retrospective study. *Gerontology* 2020;66:467-75.
 11. Singhal S, Kumar P, Singh S, Saha S, Dey AB. Clinical features and outcomes of COVID-19 in older adults: a systematic review and meta-analysis. *BMC Geriatr* 2021;21:321.
 12. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: a comparison with young and middle-aged patients. *J Infect* 2020;80:e14-e18.
 13. Pepe M, Maroun-Eid C, Romero R, Arroyo-Espliguero R, Fernández-Rozas I, Aparisi A, et al. Clinical presentation, therapeutic approach, and outcome of young patients admitted for COVID-19, with respect to the elderly counterpart. *Clin Exp Med* 2021;21:249-68.
 14. Owen RK, Conroy SP, Taub N, Jones W, Bryden D, Pareek M, et al. Comparing associations between frailty and mortality in hospitalised older adults with or without COVID-19 infection: a retrospective observational study using electronic health records. *Age Ageing* 2021;50:307-16.
 15. Aw D, Woodrow L, Ogliairi G, Harwood R. Association of frailty with mortality in older inpatients with Covid-19: a cohort study. *Age Ageing* 2020;49:915-22.
 16. Pranata R, Henrina J, Lim MA, Lawrensia S, Yonas E, Vania R, et al. Clinical frailty scale and mortality in COVID-19: a systematic review and dose-response meta-analysis. *Arch Gerontol Geriatr* 2021;93:104324.
 17. Raith EP, Udy AA, Bailey M, McGloughlin S, MacIsaac C, Bello-mo R, et al. Prognostic accuracy of the SOFA score, SIRS criteria, and qSOFA score for in-hospital mortality among adults with suspected infection admitted to the intensive care unit. *JAMA* 2017;317:290-300.
 18. Yang Z, Hu Q, Huang F, Xiong S, Sun Y. The prognostic value of the SOFA score in patients with COVID-19: a retrospective, observational study. *Medicine (Baltimore)* 2021;100:e26900.
 19. Pulok MH, Theou O, van der Valk AM, Rockwood K. The role of illness acuity on the association between frailty and mortality in emergency department patients referred to internal medicine. *Age Ageing* 2020;49:1071-9.
 20. Gandhi RT, Lynch JB, Del Rio C. Mild or moderate Covid-19. *N Engl J Med* 2020;383:1757-66.
 21. Vrillon A, Hourregue C, Azuar J, Grosset L, Boutelier A, Tan S, et al. COVID-19 in older adults: a series of 76 patients aged 85 years and older with COVID-19. *J Am Geriatr Soc* 2020;68:2735-43.
 22. Herrmann ML, Hahn JM, Walter-Frank B, Bollinger DM, Schmauder K, Schnauder G, et al. COVID-19 in persons aged 70+ in an early affected German district: Risk factors, mortality and post-COVID care needs: a retrospective observational study of hospitalized and non-hospitalized patients. *PLoS One* 2021;16:e0253154.
 23. Knopp P, Miles A, Webb TE, Mcloughlin BC, Mannan I, Raja N, et al. Presenting features of COVID-19 in older people: relationships with frailty, inflammation and mortality. *Eur Geriatr Med* 2020;11:1089-94.
 24. Lee JY, Kim HA, Huh K, Hyun M, Rhee JY, Jang S, et al. Risk factors for mortality and respiratory support in elderly patients hospitalized with COVID-19 in Korea. *J Korean Med Sci* 2020;35:e223.
 25. Leung C. Risk factors for predicting mortality in elderly patients with COVID-19: a review of clinical data in China. *Mech Ageing Dev* 2020;188:111255.
 26. Gao S, Jiang F, Jin W, Shi Y, Yang L, Xia Y, et al. Risk factors influencing the prognosis of elderly patients infected with COVID-19: a clinical retrospective study in Wuhan, China. *Ageing (Albany NY)* 2020;12:12504-16.
 27. Li P, Chen L, Liu Z, Pan J, Zhou D, Wang H, et al. Clinical features and short-term outcomes of elderly patients with COVID-19. *Int*

- J Infect Dis* 2020;97:245-50.
28. Tuty Kuswardhani RA, Henrina J, Pranata R, Anthonius Lim M, Lawrensia S, Suastika K. Charlson comorbidity index and a composite of poor outcomes in COVID-19 patients: a systematic review and meta-analysis. *Diabetes Metab Syndr* 2020;14:2103-9.
 29. Joynt GM, Leung AK, Ho CM, So D, Shum HP, Chow FL, et al. Admission triage tool for adult intensive care unit admission in Hong Kong during the COVID-19 outbreak. *Hong Kong Med J* 2022;28:64-72.
 30. Sprung CL, Joynt GM, Christian MD, Truog RD, Rello J, Nates JL. Adult ICU triage during the coronavirus disease 2019 pandemic: who will live and who will die? Recommendations to improve survival. *Crit Care Med* 2020;48:1196-202.
 31. Aziz S, Arabi YM, Alhazzani W, Evans L, Citerio G, Fischkoff K, et al. Managing ICU surge during the COVID-19 crisis: rapid guidelines. *Intensive Care Med* 2020;46:1303-25.
 32. Jung C, Flaatten H, Fjølner J, Bruno RR, Wernly B, Artigas A, et al. The impact of frailty on survival in elderly intensive care patients with COVID-19: the COVIP study. *Crit Care* 2021;25:149.
 33. Aliberti MJ, Szlejf C, Avelino-Silva VI, Suemoto CK, Apolinario D, Dias MB, et al. COVID-19 is not over and age is not enough: using frailty for prognostication in hospitalized patients. *J Am Geriatr Soc* 2021;69:1116-27.
 34. Berenguer J, Borobia AM, Ryan P, Rodríguez-Baño J, Bellón JM, Jarrín I, et al. Development and validation of a prediction model for 30-day mortality in hospitalised patients with COVID-19: the COVID-19 SEIMC score. *Thorax* 2021;76:920-9.
 35. Alves VP, Casemiro FG, Araujo BG, Lima MA, Oliveira RS, Fernandes FT, et al. Factors associated with mortality among elderly people in the COVID-19 pandemic (SARS-CoV-2): a systematic review and meta-analysis. *Int J Environ Res Public Health* 2021;18:8008.
 36. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. *BMC Infect Dis* 2021;21:855.