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Original Article

Discriminant Ability of In-Hospital Mortality Based on Prognostic Scores of Elderly Patients with COVID-19: A Taiwan Medical Center Study

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SUMMARY

Introduction: The coronavirus disease 2019 (COVID-19) has brought excessive patients in emergency departments. Several COVID-19 prediction scores have been developed to aid in the patient disposition of emergency physicians. This study aimed to validate different COVID-19 prediction scores.
Method: "DynaMed" was used to retrieve high-quality COVID-19 prediction scores for the evaluation of in-hospital mortality rate. SEIMC score, 4C-Mortality score, SOARS score, and Veterans Health Administration COVID-19 (VACO) Index were selected. A retrospective, single-center study was done on elderly patients hospitalized for COVID-19 from May 2021 to July 2021 in MacKay Memorial Hospital. Patients who were (I) negative for COVID-19 examination, (II) aged < 65 years old, (III) previously infected with COVID-19 and de-isolated (IV) hospital-acquired COVID-19 infection, (V) not admitted for hospitalization, and (VI) with missing of demographic characteristics were excluded. The area under the receiver operating characteristic curves (AUC) was computed to predict the in-hospital mortality rate.
Result: Of 66,090 patients who underwent COVID-19 examination in MacKay Memorial Hospital, 133 patients were included in this study, with 26 deceased patients (19.5%). Among included patients, the median age was 74.38 years and 53% patients were male. Of the selected COVID-19 prediction scores, 4C-Mortality Score (AUC = 0.8), SEIMC score (AUC = 0.75), and SOARS score (AUC = 0.72) contained a good prognostic value, with an AUC > 0.70. VACO index demonstrated less predictive value (AUC = 0.61).
Conclusion: COVID-19 prediction scores were validated, and it was found that 4C-Mortality Score, SEIMC score, and SOARS score performed well in predicting the in-hospital mortality rate of elderly patients with COVID-19, and 4C-Mortality score is best appreciated.

1. Introduction

The coronavirus disease 2019 (COVID-19) has become a global pandemic since March 2020.[1] As of December 2021, 264 million patients suffered from COVID-19, including over 5.2 million deceased patients. Taiwan encountered an unfortunate outbreak struck Taiwan on May 2021. Over 14 thousand people were infected with COVID-19, and 778 patients expired. During the outbreak, healthcare facilities endured an excessive influx of patients. To distinguish COVID-19-confirmed patients from home treatment to hospitalization is of crucial importance. Multiple prediction scores were utilized at that time; however, their applicability may vary based on country, race, and healthcare facility.

MacKay memorial hospital is a medical center in the crowded Taipei. Well-established measurements of screen unit and quarantine wards were formally reported.[2–4] During the pandemic, the hospital was transformed into a COVID-19-designated hospital and provided medical treatment for patients with COVID-19.

This study aimed to examine the discriminant ability of existing COVID-19 scores to predict the in-hospital mortality rate of elderly patients in a COVID-19-designated hospital in Taiwan.

2. Materials and methods

2.1. Study design and setting

This is a retrospective study conducted in the ED of a COVID-19-designated tertiary medical center in Taiwan. This study was reported based on the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidelines.[5]

2.2. Study population

A flow chart of the included patient population is shown in Figure 1. Reverse transcriptase-polymerase chain reaction (PCR) for COVID-19 was done on respiratory samples of patients from May

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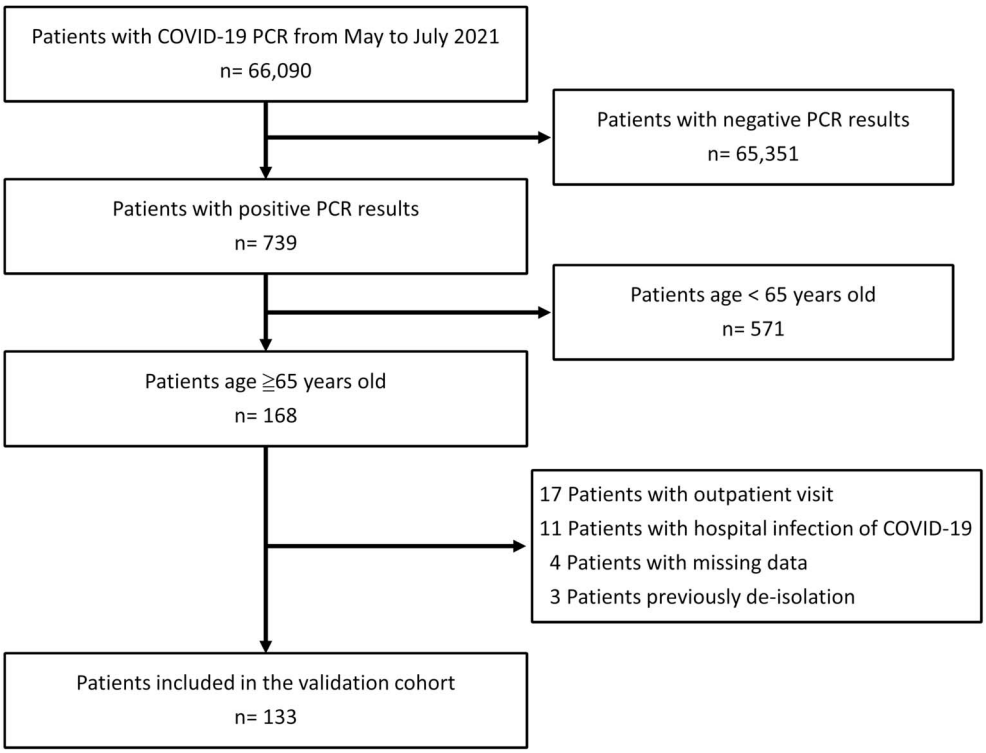


Figure 1. Flow chart of selected patients. PCR, polymerase chain reaction.

1, 2021 to July 31, 2021. Patients who were (I) negative for COVID-19 examination, (II) aged < 65 years old, (III) previously infected with COVID-19 and de-isolated, (IV) hospital-acquired COVID-19 infection, (V) not admitted for hospitalization, and (VI) with missing of demographic characteristics were excluded.

2.3. Ethics statement

The design and execution of this retrospective study were approved by the Institutional Review Board of MacKay Memorial Hospital (21MMHIS377e).

2.4. Selection of published COVID-19 prediction scores

The selection of high-quality evidence-based COVID-19 prediction scores utilized the database "DynaMed," which combined evidence-based methodology and literature surveillance to both complement and clarify the information. The selected COVID-19 prediction scores were ranked as reliable evidence after being appraised by experts. They included 4C-Mortality Score,[6] SEIMC score,[7] SOARS score,[8] and Veterans Health Administration COVID-19 (VACO) Index.[9] The last search in "DynaMed: COVID-19 (Novel Coronavirus) – Prognosis" was performed on December 1, 2021.[10] The detailed characteristics of the selected COVID-19 prediction scores are shown in Table 1.

2.5. Variables

The variables collected in this study included age, gender, past medical history, symptoms, vital signs at the initial presentation in

Table 1
Detailed characteristics of selected COVID-19 prediction scores.

Prediction score	Demographic	Medical history	Vitals signs	Symptoms	Laboratory data
4C-Mortality	Age, sex	Chronic cardiac disease, chronic respiratory disease (excluding asthma), chronic renal disease (estimated glomerular filtration rate ≤ 30), mild to severe liver disease, dementia, chronic neurological conditions, connective tissue disease, diabetes mellitus (diet, tablet, or insulin controlled), HIV or AIDS, and malignancy	GCS, RR, SpO2 on room air		BUN, CRP
SEIMC	Age, sex			Dyspnea	eGFR, NLR
SOARS	Age	Cerebrovascular disease	RR, SpO2 on room air, BMI		
VACO Index	Age, sex	Myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, hemiplegia or paraplegia, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, diabetes without chronic complications, diabetes with chronic complications, renal disease, malignancy, metastatic solid tumor, mild liver disease, moderate or severe liver disease, and AIDS/HIV			

Abbreviation: AIDS/HIV: Acquired Immunodeficiency Syndrome/human immunodeficiency virus; BUN: blood urea nitrogen; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; GCS: Glasgow Coma Scale; NLR: neutrophil-tolymphocyte ratio; RR: respiratory rate; SpO2: peripheral capillary oxygen saturation.

ED, laboratory examinations within 24 h, and radiographic imaging. Their comorbidities were accessed according to Charlson comorbidity index.[11]

2.6. Outcome

The primary outcome was the in-hospital mortality of elderly patients with COVID-19.

2.7. Statistical analysis

All continuous data were analyzed with independent sample t test to determine the difference between the groups. Nominal variables were compared using Pearson chi-square test or Fisher's exact test, depending on the sample size.

The variables for each patient were filled in and calculated using the selected COVID-19 prediction scores. A receiver operating characteristic (ROC) curve was utilized to determine the overall performance of each COVID-19 prediction score for the discriminant ability of in-hospital mortality rate. To compare the ROC curves, an area under the curve (AUC) was made according to DeLong method.[12,13] Sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio were also calculated.

All tests were two-sided, and a p value < 0.05 was considered significant. Analyses were performed using the software SPSS (version 26.0; SPSS Inc., Armonk, NY, USA).

3. Result

A total of 66,090 patients were eligible for this study. After the exclusion of patients who were negative for COVID-19 PCR examination (n = 65,351), with age < 65 years old (n = 571), only outpatient visits (n = 17), hospital-acquired COVID-19 infection (n = 11), previously infected by COVID-19 and was de-isolated (n = 3), and with missing demographic characteristics (n = 4), 133 patients remained. A detailed flow chart is presented in Figure 1.

The demographics of the 133 patients included in the study are shown in Table 2. Their mean age was 74.38 ± 6.56 years, and 53% of the patients were male. Twenty-six patients (19.5% of all patients) encountered an in-hospital mortality after COVID-19 infection. A statistical comparison between patients who survived and deceased patients revealed no significant difference in their mean age, gender, and percentage of nursing home resident. There was also no difference in the past medical history of hypertension, diabetes mellitus, coronary artery disease, cerebrovascular disease, and neoplasm. Compared with the survival group, there was higher prevalence of chronic kidney disease and heart failure in the death group.

Upon ED presentation, there were no statistical differences in body temperature and mean arterial pressure. However, the in-hospital mortality group was associated with an increased heart rate and respiratory rate. A decreased Glasgow coma scale was also found in the in-hospital mortality group. The laboratory data related to in-hospital mortality were higher blood urea nitrogen, creatinine, and C-reactive protein levels.

All selected COVID-19 prediction scores had a good predictive value of in-hospital mortality rate. Among them, 4C-mortality score manifested the highest AUC (AUC = 0.8; cut-off value: 9.5), followed by SEIMC (AUC = 0.75; cut-off value: 19.5), SOARS (AUC = 0.72; cut-off value: 3.5), and VACO index (AUC = 0.61; cut-off value: 0.14). VACO index was the only COVID-19 prediction score that did not

Table 2
Basic characteristics of patients included in the study.

	All patients (N = 133)	Survival (N = 107)	Death (N = 26)	p value
Demographic data				
Age, mean ± SD	74.4 ± 6.5	74.2 ± 6.6	75.3 ± 6.6	0.446
Male	53.7%	51%	58%	0.568
Nursing Home	4.4%	5%	4%	0.850
Medical history				
HTN	51.5%	47.7%	65.0%	0.107
DM	30.6%	27.1%	42.3%	0.131
CAD	6.0%	4.7%	12.0%	0.189
HF	4.5%	1.9%	15.6%	0.003*
CKD	12.7%	7.5%	35.5%	0.000*
CVA	5.2%	3.7%	12.0%	0.112
Neoplasm	8.2%	8.4%	8.0%	0.906
Vital signs (mean ± SD)				
GCS	14.1 ± 2.6	14.3 ± 2.2	13.2 ± 3.9	0.046*
BT	37.5 ± 1.0	37.5 ± 0.9	37.7 ± 1.2	0.318
HR	92.00 ± 22.6	90.6 ± 18.6	100.7 ± 31.8	0.035*
RR	20.6 ± 9.2	19.4 ± 2.9	21.9 ± 7.2	0.006*
MAP	91.7 ± 17.9	92.0 ± 15.1	92.3 ± 26.6	0.935
Laboratory data (mean ± SD)				
Hb (g/dL)	13.1 ± 2.1	13.1 ± 1.9	13.1 ± 3.0	0.913
PLT (10^3/uL)	194.5 ± 85.3	191.1 ± 81.3	195.8 ± 92.8	0.798
WBC (10^3/uL)	9.7 ± 14.4	9.5 ± 15.9	9.7 ± 3.9	0.968
GOT (IU/L)	48.2 ± 31.7	45.9 ± 29.7	59.2 ± 38.7	0.057
BUN (mg/dL)	29.5 ± 31.7	24.6 ± 27.2	47.3 ± 38.5	0.001*
Cre (mg/dL)	2.1 ± 3.8	1.5 ± 1.7	3.1 ± 3.5	0.001*
Na (mEq/L)	135.3 ± 6.0	135.2 ± 6.1	135.6 ± 6.1	0.781
K (mEq/L)	4.7 ± 7.3	4.58 ± 7.8	4.4 ± 1.1	0.885
TnI (ng/mL)	0.2 ± 1.1	0.3 ± 1.2	0.3 ± 0.1	0.978
CRP (mg/dL)	8.4 ± 7.8	7.1 ± 6.7	14.7 ± 9.4	0.000*

Abbreviation: BT: body temperature; BUN: blood urea nitrogen; CAD: coronary artery disease; CKD: chronic kidney disease; Cre: creatinine; CRP: C-reactive protein; CVA: cerebrovascular accident; DM: diabetes mellitus; GCS: Glasgow Coma Scale; GOT: glutamic oxaloacetic transaminase; Hb: hemoglobin; HF: heart failure; HR: heart rate; HTN: hypertension; K: potassium; MAP: mean arterial pressure; Na: sodium; PLT: platelet; RR: respiratory rate; SD: standard deviation; TnI: troponin-I; WBC: white blood cell.

achieve a statistical significance (p = 0.72). The ROC curves of the selected COVID-19 prediction scores are shown in Figure 2.

4. Discussion

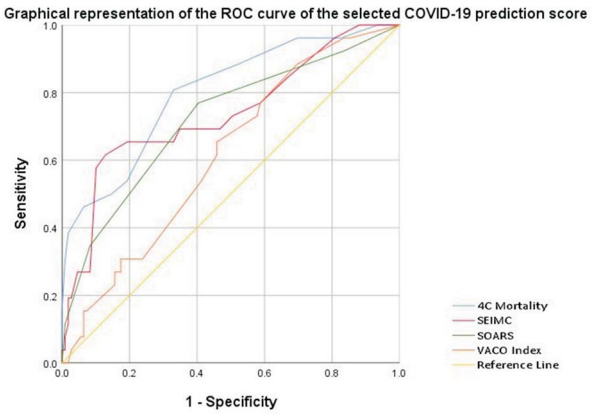
Our major findings supported the 4C-mortality has the highest discriminant ability for in-hospital mortality rate of elderly patients with COVID-19. This result can assist ED physician in disposition of COVID-19 infected elderly patient.

In this study, 4C-Mortality score, SEIMC score, and SOARS score demonstrated good discriminant power in predicting the in-hospital mortality rate (AUC > 0.70).[12–14] The VACO index was less accurate. The high accuracy of 4C-Mortality score was previously reported in studies from different countries.[15–17] One large cohort study in Paris that included 14,343 patients showed a decreased accuracy of SEIMC score in elderly patients (age > 65 years old).[16] This phenomenon could result from the age factor of SEIMC score. If the patient's age is above 75 years old, the age factor value of SEIMC score will exceed 9 points, which will be classified into a very high-risk mortality group. In this study, the average age of in-hospital mortality patients was above 75 years old, while that of the surviving group was not. The SOARS score, validated using the 4C-mortality cohort with an AUC of 0.74, was first published in July 2021.[8,18] Our study obtained a similar AUC of 0.72.

In this study, the VACO index showed a relatively unfavorable predictive value compared to other COVID-19 prediction scores. This result could be attributed to two main factors. First, the original VACO index was developed in a veteran cohort, which was mainly composed of a male population.[9] A former external validation study that performed the VACO index on 1,307 US academic medical center inpatients and 427,224 US Medicare patients also found that the AUC of the VACO index in elderly patients decreased from AUC = 0.82 and AUC = 0.80 to AUC = 0.69 and AUC = 0.67, respectively.[19] This study demonstrated the aforementioned results, with AUC = 0.61 in elderly patients. Second, the study population contained a much lower Charlson comorbidity index than the original study.[9] This could also affect the predictive value since the Charlson comorbidity index is multiplied with a larger coefficient in VACO index.

This study has some limitations. First, this was a retrospective study, so missing data cannot be avoided. Second, the COVID-19 prediction scores were validated in small sample size. Further multicenter studies should be performed in Taiwan to achieve a better insight on the different COVID-19 prediction scores.

In conclusion, the COVID-19 prediction scores of 4C-mortality score, SEIMC score, SOARS score, and VACO index for elderly patients with COVID-19 were examined. The results support the use of 4C-Mortality score to guide in ED disposition and provide a favorable health care for elderly patients with COVID-19.



Prediction Score	AUC	Sensitivity (%)	Specificity (%)	PLR	NLR	Cut-off Value
4C-Mortality	0.80	81	61	2.45	0.28	9.5
SEIMC	0.75	62	87	4.77	0.44	19.5
SOARS	0.72	77	59	1.88	0.39	3.5
VACO index	0.61	65	54	1.41	0.65	0.14

Figure 2. Graphical representation of the ROC curve of the selected covid-19 prediction score. Abbreviations: AUC: area under the curve; NLR: negative likelihood ratio; PLR: positive likelihood ratio.

Conflict of interest

There are no conflicts of interest to declare.

Funding

This research received no external funding.

Data availability statement

The data are not publicly available due to restrictions regarding the Ethical Committee Institution.

Ethics approval the design and execution of this retrospective study was approved by the Institutional Review Board of MacKay Memorial Hospital (21MMHIS377e).

Consent to participate informed consent was waived because of the retrospective nature of the study and the analysis used anonymous clinical data.

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