Development and Validation of a Novel Risk Score for Predicting Clinical Deterioration in COVID-19 Patients: The ABCD Risk Score

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Abstract

Introduction

For the appropriate allocation of medical resources to at-risk COVID-19 patients, a simple risk scoring model for the risk stratification of clinical deterioration in the early stage of symptom onset would be invaluable. Here, we report the development and validation of such a model for clinical deterioration in COVID-19.

Methods

This multicenter retrospective cohort study conducted in Japan included adult patients (≧18 years old) with confirmed COVID-19 according to molecular diagnostic methods and hospitalized in two hospitals. Patients who did not undergo laboratory tests within 10 days of initial symptom onset and those who were treated with oxygen therapy before hospitalization were excluded. Patients were divided into derivation (n=446) and temporal validation (n=305) datasets based on hospitalization period. The primary outcome was need for oxygen therapy within 14 days of hospitalization.

Results

A novel ABCD Risk Score (range, 0–12) comprising age, body mass index, C-reactive protein, and lactate dehydrogenase levels at admission was developed in the derivation dataset. This risk score showed good discrimination for clinical deterioration (concordance statistics, 0.86; 95% confidence interval [CI]: 0.72–0.90) with good calibration (intercept, 0.01; slope, 0.99) in the temporal validation dataset. Three risk groups were defined: low risk (≤3 points), intermediate risk (4–6 points), and high risk (≥7 points). In the validation dataset, the clinical deterioration rates for these three groups were 7.1% (95% CI: 3.1%–13.6%), 32.9% (95% CI: 22.3%–44.9%), and 73.3% (95% CI: 64.5%–81.0%), respectively. The risk score showed better discrimination and calibration performance than four previously reported risk scoring models.

Conclusion

Our novel ABCD Risk Score can be used for the risk stratification of clinical deterioration in COVID-19 patients at an early stage of symptom onset.

Introduction

Novel coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an ongoing global pandemic (1). The scientific community is actively exploring biomarker and prognostic models of COVID-19 deterioration and mortality to allow for the appropriate allocation of medical resources to patients who are at increased risk of disease progression. A crucial issue in clinical practice is identifying people who are at risk of clinical deterioration from those without symptoms as well as from patients with mild/moderate symptoms who do not require hospitalization and those with severe/critical symptoms who need oxygen therapy, systemic glucocorticoids (2), and anti-viral therapy (3).

Several biomarkers of clinical deterioration in COVID-19 have been identified, such as complete blood count (lymphocyte count (4) and neutrophil-to-lymphocyte ratio [NLR] (5)), biochemical tests (blood urea nitrogen [BUN] (6, 7) and lactate dehydrogenase [LDH] (8)), blood inflammatory markers (C-reactive protein [CRP], interleukin-6 [IL-6] (9, 10), and ferritin (11)), and blood coagulation tests (D-dimer (12)). Scoring models for risk stratification have been developed using biomarkers, clinical signs, and imaging findings (13–28). However, most reported prediction models are considered to have a high risk of bias and overestimation of their reported performance due to deficient temporal and external validation (29). Also, most prediction models were derived and validated in the Chinese population alone (13, 14, 16, 18–24) and need additional time-consuming laboratory tests (19), two points of observation (14), and CT imaging findings (17, 18, 21, 23, 24). It would be beneficial in clinical practice to be able identify patients with early-stage disease who are at high risk of clinical deterioration by using simpler and more reliable criteria that have been developed based on clinical characteristics and routine laboratory tests.

To this end, we conducted a multicenter retrospective cohort study enrolling 751 hospitalized patients with COVID-19 in Japan to develop and validate a new simple and accurate model for predicting the deterioration of COVID-19 patients at the early stage

(within 10 days) of symptom onset.

Materials And Methods

Study design and patients

The study design is shown in Fig. 1. We conducted a retrospective, multicenter cohort study at Saitama Medical University Hospital and Self-Defense Forces Central Hospital in Japan, which are designated medical institutions for infectious diseases under the Infectious Disease Control Law, Japan. We enrolled adult patients (≥ 18 years old) with confirmed COVID-19 by molecular diagnostic methods (quantitative reverse transcription polymerase chain reaction [RT-qPCR] or loop-mediated isothermal amplification [LAMP]) and hospitalized for isolation and treatment under the Infectious Disease Control Law. Patients who did not undergo routine blood examinations (complete blood count, serum biochemical tests, and coagulation tests) within 10 days of initial symptom onset were excluded from this study. We also excluded patients who were treated with oxygen therapy before hospitalization.

First, patients who were hospitalized from February to October 2020 were enrolled for a derivation dataset. Then, patients who were hospitalized from November 2020 to March 2021 were enrolled for a temporal validation dataset. In Japan, four waves of COVID-19 have occurred from February 2020 to May 2021. The patients admitted in the first and second waves and in the third and fourth waves were included in the derivation and temporal validation datasets, respectively (**Appendix 1**). A comparison dataset for comparing risk scoring models included all patients admitted during the study period. Clinical information was retrospectively collected from the hospital electrical medical records and included clinical records and laboratory findings. The primary outcome was in-hospital clinical deterioration within 14 days of hospitalization.

Definitions

Clinical characteristics and laboratory findings at admission were used to derive and validate the risk scoring model. Clinical deterioration was defined as administration of oxygen therapy with SpO_2 < 93% on room air during the hospitalization. The observation period was defined as the period from patient's admission to patient's discharge or 14 days after the admission, whichever came first. The day of initial symptom onset was defined as the day of symptom appearance according to the patients or their family members. For asymptomatic patients, initial symptom onset was determined as the day of hospitalization. Disease severity was classified by a clinician with 8 years' experience in infectious disease physician (KI) according to the 8-category ordinal scale recommended by the World Health Organization (30).

Statistical analysis

Continuous variables are expressed as the mean and standard deviation or median and interquartile range (IQR) and were compared using a *t*-test or Wilcoxon rank-sum test for parametric or non-parametric data, respectively. Categorical variables are presented as frequency and percentage (%) and were compared using a chi-square test or Fisher's exact test, as appropriate. A two-sided p value < 0.05 was considered statistically significant. All statistical analyses were conducted using R (v 4.0.2; R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org/).

Candidate predictor selection and model development

Based on the literature, 12 candidate predictor variables were selected from clinical characteristics and potential biomarkers associated with clinical deterioration. Self-reported clinical symptoms were excluded for better objectivity. Values unavailable for at least 25% of the patients in the derivation dataset were also excluded. Finally, 9 candidate predictor variables—age, sex at birth, body mass index [BMI], comorbidities of diabetes mellitus and hypertension, NLR, BUN, LDH, and CRP—were selected for analysis by consensus at a team meeting during the derivation phase. There were no missing values for these 9 candidate predictor variables in the derivation dataset (**Appendix 2**).

The model building process for developing the risk score was conducted according to the method reported by Knight et al. (31) with minor modifications. In the first step, generalized additive model (GAM) fit to a Cox regression models were built by incorporating continuous variables with P-spline smoothers in combination with categorical variables as linear components. A criterion-based approach to variable selection was applied based on the deviance explained and restricted maximum likelihood.

Second, optimal cutoff values for continuous variables were selected from visually inspected plots of component continuous variables with P-spline smoothers. Third, final models using categorized variables were specified with least absolute shrinkage and selection operator (LASSO) Cox regression. L1-penalized coefficients were derived using 10-fold cross-validation to select the value of lambda (minimized cross-validated sum of squared residuals) in the derivation dataset. Shrunk coefficients were converted to a point with appropriate scaling to create the risk scoring model.

Discrimination of the developed risk scoring model—named the **A**ge, **B**MI, **C**RP, L**D**H [**ABCD**] Risk Score—was evaluated using the area under the receiver operating characteristic (ROC) curve and concordance statistics (C-statistics) in the derivation dataset. The 95% confidence interval (95% CI) of the C-statistics was calculated by bootstrapped resampling (2000 samples). Calibration of the ABCD Risk Score was assessed by using a calibration plot and Brier score.

Model validation

A temporal validation dataset of patients was used for validation of the ABCD Risk Score obtained in the derivation phase. The same clinical and laboratory data were available for analysis in both cohorts. There were no missing values for the ABCD Risk Score in the temporal validation dataset. Discrimination and calibration were evaluated in a validation dataset. The cutoff values of the ABCD Risk Score for three risk groups—low, intermediate, and high—were determined by consensus at a team meeting. Kaplan–Meier survival curves for the patients in each risk group were generated to illustrate the partitioning of the risk of disease deterioration, and differences in clinical deterioration between risk groups were assessed by log-rank test.

Comparison with other risk scoring models of clinical deterioration in COVID-19

The ABCD Risk Score was compared within the comparison dataset with previously reported risk scoring models. Sixteen risk scoring models for clinical deterioration were extracted from the literature; 12 were excluded due to a lack of clinical symptoms, CT findings, or ultrasound findings in the comparison dataset (13–15, 17–19, 21–24, 27, 28). Finally, four risk scoring models were selected for evaluation in this study (16, 20, 25, 26). Discrimination, calibration, and decision curve analysis of each risk scoring model was evaluated in the comparison dataset (Fig. 1). Because the rate of missing values was 20% for D-dimer in the comparison of the risk scoring models, the missing values were imputed by a random forest imputation method.

Results

Patients’ characteristics in the derivation cohort

Between February and October 2020, 636 patients with laboratory-confirmed COVID-19 were hospitalized at Saitama Medical University Hospital and Self-Defense Forces Central Hospital in Japan. A total of 190 people were excluded according to the exclusion criteria of the study, leaving 446 participants for the final analysis (Fig. 1). The median patient age was 48 years (IQR, 35–67), and 265 (59.4%) were male at birth (Table 1). The median period from initial symptom onset to serum collection was 4 days (IQR, 3–6). At the end of the observation period, 90 patients (20.2%) were confirmed to have had clinical deterioration (Table 1). Of these 90 patients, 20 (22.2%) were supplied oxygen by high-flow nasal cannula (HFNC) and noninvasive positive pressure ventilation (NPPV), 8 (8.9%) were incubated and treated with invasive mechanical ventilation (IMV), and 7 (7.8%) died. A statistical comparison of the nonclinical deterioration and deterioration groups confirmed that the 9 selected factors were associated with clinical deterioration (Table 1).

Table 1
Baseline clinical characteristics of the derivation and temporal validation datasets

	Derivation dataset				Temporal validation dataset			
	Total (n = 446)	Nonclinical deterioration (n = 356)	Clinical deterioration (n = 90)	p value	Total (n = 305)	Nonclinical deterioration (n = 185)	Clinical deterioration (n = 120)	p value
Demographic characteristic								
Age, years	48 (35–67)	44 (33–59)	69 (56–78)	< 0.001	65 (47–79)	53 (36–72)	75 (63–82)	< 0.001
Sex at birth								
Male	265 (59.4%)	199 (55.9%)	66 (73.3%)	0.003	183 (60.0%)	105 (56.8%)	78 (65.0%)	0.19
Female	181 (40.6%)	157 (44.1%)	24 (26.7%)		122 (40.0%)	80 (43.2%)	42 (35.0%)	< 0.001
Body mass index, kg/m^2	23 (20–25)	22 (20–25)	24 (22–27)	< 0.001	23 (21–26)	23 (21–26)	23 (21–26)	0.001
Comorbidity								
Hypertension	91 (20.4%)	57 (16.0%)	34 (37.8%)	< 0.001	105 (34.4%)	46 (24.9%)	59 (49.2%)	
Diabetes mellitus	42 (9.4%)	22 (6.2%)	20 (22.2%)	< 0.001	47 (15.4%)	18 (9.7%)	29 (24.2%)	
Laboratory finding								
White blood cell count, 10^9 cells per L	4.5 (3.4–5.8)	4.4 (3.6–5.6)	5.0 (3.9–6.8)	0.002	5.2 (4.1–6.5)	5.0 (4.1–6.2)	6.4 (4.3–7.2)	0.006
Neutrophil count, 10^9 cells per L	2.8 (2.1–3.8)	2.7 (2.0–3.6)	3.6 (2.6–5.4)	< 0.001	3.4 (2.6–4.6)	2.7 (2.0–3.6)	3.6 (2.6–5.4)	< 0.001
Lymphocyte count, 10^9 cells per L	1.2 (0.9–1.5)	1.3 (1.0–1.6)	0.8 (0.6–1.1)	< 0.001	1.2 (0.8–1.5)	1.3 (1.0–1.6)	1.0 (0.7–1.3)	< 0.001
Neutrophil-to-lymphocyte ratio	2.4 (1.5–3.6)	2.2 (1.5–3.1)	4.0 (2.9–7.1)	< 0.001	2.9 (2.0–4.8)	2.3 (1.8–3.6)	4.4 (2.6–7.4)	< 0.001
Lactate dehydrogenase, IU/L	198 (168–252)	185 (160–222)	299 (236–373)	< 0.001	221 (187–289)	201 (175–235)	267 (225–360)	< 0.001
Urea nitrogen, mg/dL	13 (10–16)	12 (10–15)	16 (13–20)	< 0.001	14 (11–21)	13 (11–17)	18 (13–25)	< 0.001
Creatinine, mg/dL	0.8 (0.7–0.9)	0.8 (0.7–0.9)	0.9 (0.8–1.1)	< 0.001	0.8 (0.6–1.0)	0.8 (0.6–0.9)	0.9 (0.7–1.0)	0.010

Data are median (IQR) or n/N (%) unless otherwise stated. Categorical variables were analyzed using a chi-square test. Continuous variables were analyzed using a Wilcoxon signed-rank test. In-hospital outcome indicates the highest score of the 8-category ordinal scale occurring during the observation period. HFNC, high-flow nasal cannula; NPPV, noninvasive positive pressure ventilation; IMV, invasive mechanical ventilation; and ECMO, extracorporeal membrane oxygenation.

	Derivation dataset				Temporal validation dataset			
Aspartate aminotransferase, IU/L	34 (20–35)	24 (19–31)	38 (29–57)	< 0.001	28 (22–36)	25 (20–31)	33 (25–46)	< 0.001
Alanine aminotransferase, IU/L	24 (15–38)	23 (15–34)	32 (18–45)	< 0.001	29 (16–40)	22 (15–34)	23 (16–35)	0.450
C-reactive protein, mg/dL	0.6 (0.1–2.6)	0.3 (0.1–1.3)	5.3 (2.4–9.7)	< 0.001	1.6 (0.3–4.5)	0.6 (0.1–2.0)	4.3 (2.2–9.4)	< 0.001
In-hospital outcome (8-category ordinal scale)								
1–3 (hospitalized, no oxygen therapy)	356 (79.8%)	356 (100.0%)	-	-	185 (60.7%)	185 (100.0%)	-	-
4 (oxygen therapy by mask or nasal prongs)	55 (12.3%)	-	55 (61.1%)	-	86 (28.2%)	-	86 (71.7%)	-
5 (oxygen therapy by HFNC and NPPV)	18 (4.0%)	-	20 (22.2%)	-	17 (5.6%)	-	17 (14.2%)	-
6 (oxygen therapy by IMV)	8 (1.8%)	-	8 (8.9%)	-	7 (2.3%)	-	7 (5.8%)	-
7 (oxygen therapy by ECMO)	0 (0%)	-	-	-	1 (0.3%)	-	1 (0.8%)	-
8 (death)	7 (1.6%)	-	7 (7.8%)	-	9 (3.0%)	-	9 (7.5%)	-

Data are median (IQR) or n/N (%) unless otherwise stated. Categorical variables were analyzed using a chi-square test. Continuous variables were analyzed using a Wilcoxon signed-rank test. In-hospital outcome indicates the highest score of the 8-category ordinal scale occurring during the observation period. HFNC, high-flow nasal cannula; NPPV, noninvasive positive pressure ventilation; IMV, invasive mechanical ventilation; and ECMO, extracorporeal membrane oxygenation.

Model for predicting development

Of the 9 candidate predictor variables selected for model creation, 4 important predictors of clinical deterioration were identified by using the GAM fit to a Cox regression models: age, BMI, CRP, and LDH (**Appendix 3**). Five candidates—sex at birth, comorbidities of diabetes mellitus and hypertension, NLR, and BUN—were excluded at this step. The appropriate cutoff values were selected as continuous variables to develop a simple risk scoring model (**Appendix 4**). All variables remained in the final model after a LASSO Cox regression model, and we converted the penalized regression coefficients into a risk index—the ABCD Risk Score—by using the appropriate scaling (Table 2 **and Appendix 5**). The ABCD Risk Score showed good discrimination for clinical deterioration in the derivation dataset (C-statistics, 0.93; 95% CI: 0.90–0.96, **Appendix 6**). A calibration plot of the ABCD Risk Score showed an intercept of 0.01 and slope of 0.98 (Brier score, 0.078), suggesting good calibration (**Appendix 6**).

Table 2
ABCD Risk Score for clinical deterioration in COVID-19

Variable	Penalized coefficient	Penalized coefficient (×2 scaling)	ABCD Risk Score
Age, years			
<50	-	-	-
50–69	0.63	1.26	+ 1
≥70	1.37	2.74	+ 3
Body mass index, kg/m^2			
<25	-		-
≥25	0.60	1.20	+ 1
C-reactive protein, mg/L			
<2.0	-	-	-
2.0–4.9	1.27	2.54	+ 3
≥5.0	1.99	3.98	+ 4
Lactate dehydrogenase, IU/L			
<200	-	-	-
200–299	1.00	1.99	+ 2
≥300	1.95	3.89	+ 4
Total score	**-**	**-**	**+ 12**

The penalized coefficient was derived from a least absolute shrinkage and selection operator (LASSO) Cox regression model.

Model validation

The validation dataset included 305 patients referred to the study hospitals from November 2020 to March 2021 (Fig. 1**)**. The median age of the patients in the cohort was 65 years (IQR, 47–79) and 183 (60.0%) were male at birth (Table 1). The median period from initial symptom onset to serum collection was 5 days (IQR, 3–8). The overall disease deterioration rate was 39.3% (120 patients). The ABCD Risk Score showed good discrimination performance in the validation dataset (C-statistics, 0.86; 95% CI: 0.82–0.90; Fig. 2). The discrimination of the ABCD Risk Score was better than that of the single predictors: age (0.78, 0.69–0.80), BMI (0.51, 0.44–0.57), CRP (0.81, 0.76–0.85), and LDH (0.78, 0.72–0.83) (Fig. 2). A calibration plot of the ABCD Risk Score showed an intercept of 0.01 and slope of 0.99 (Brier score, 0.147), suggesting good calibration (Fig. 2). Finally, three groups with significantly different clinical deterioration rates were defined: a low-risk group (ABCD Risk Score, ≤ 3 points), an intermediate-risk group (4–6 points), and a high-risk group (≥ 7 points). In-hospital disease deterioration rates were 7.1% (3.1–13.6%) for the low-risk group, 32.9% (22.3–44.9%) for the intermediate-risk group, and 73.3% (64.5–81.0%) for the high-risk group (log-rank test, $p < 0.001$; Table 3 **and** Fig. 3).

Table 3
Risk of clinical deterioration in the validation dataset according to the ABCD Risk Score

	Validation dataset (n = 305)			
Risk group	Classified		Clinical deterioration	
	No. of patients	%	No. of patients	% (95% CI)
Low (≤ 3 points)	112	36.7	8	7.1% (3.1–13.6%)
Intermediate (4–6 points)	73	23.9	24	32.9% (22.3–44.9%)
High (≥ 7 points)	120	39.3	88	73.3% (64.5–81.0%)

Comparison of the ABCD Risk Score with other risk scoring models

The ABCD Risk Score was compared with four previously reported risk scoring models—CALL score (16), N/L*CRP*D-dimer score (20), EWAS score (25), and HNC-LL score (26)—in the comparison dataset (Fig. 1). The overall disease deterioration rate was 28.0% (**Appendix 7**). The ABCD Risk Score exhibited higher discrimination for clinical deterioration (C-statistics, 0.91; 95% CI: 0.88–0.93) than the other risk scores: CALL score (0.82, 0.79–0.85); N/L*CRP*D-dimer score (0.87, 0.84–0.90); EWAS score (0.86, 0.84–0.89); and HNC-LL score (0.86, 0.83–0.89) (Table 4 **and Appendix 8**). In addition, the calibration plot of the ABCD Risk Score showed good calibration, with the lowest Brier score of the risk scoring models (Table 4 **and Appendix 8**). Decision curve analysis indicated that the ABCD Risk Score had better clinical utility across a wide range of threshold risks than the other risk scores (Fig. 4).

Table 4
Comparison of the discrimination of the risk scores for clinical deterioration in patients with COVID-19

	Comparison dataset (n = 761)			
	C-Statistics	95% CI	Brier score	Reference
ABCD Risk Score	0.91	0.88–0.93	0.108	-
CALL score	0.82	0.79–0.85	0.153	Dong et al. (16)
N/L*CRP*D-dimer score	0.87	0.84–0.90	0.148	Ying et al. (20)
EWAS score	0.86	0.84–0.89	0.126	Yabing et al. (25)
HNC-LL score	0.86	0.83–0.89	0.124	Xiao et al. (26)

Discussion

The results of this retrospective multicenter cohort study revealed that our simple ABCD Risk Score has good performance for the risk stratification of clinical deterioration in COVID-19 patients at an early stage of symptom onset (≤ 10 days).

In clinical practice, risk stratification of the clinical deterioration of COVID-19 patients is paramount because the need for oxygen therapy in patients is strongly associated with decision-making regarding hospitalization and systemic treatment with dexamethasone (2) and remdesivir (3) to decrease mortality. Therefore, all risk scoring models for the risk stratification of clinical deterioration should be simple and based on rapid tests that can be performed in both in-hospital and outpatient clinic settings. The ABCD Risk Score uses only clinical characteristics and routine laboratory tests that can be collected rapidly and that have been implicated in previous studies as potential risk factors for the clinical deterioration and mortality of COVID-19. Older age has been included in many models for predicting COVID-19 and pneumonia mortality (6–8, 31, 32). A higher BMI has been strongly associated with the clinical deterioration and mortality of COVID-19 (33, 34). CRP is widely used as a marker of inflammation in the clinical setting. CRP is secreted into the circulation by the liver in response to circulatory inflammatory mediators such as IL-6, and elevated serum CRP levels reflect the clinical activity of pneumonia (9, 10) and cytokine storm of COVID-19 (35). Elevated

serum LDH levels are associated with lung tissue damage (36), and serum LDH is considered a marker of disease activity and progression in COVID-19-related pneumonia (37). Risk scoring models with the same prediction variables and weight as the ABCD Risk Score have not been reported. The ABCD Risk Score showed higher discrimination and calibration performance than other risk scoring models that used clinical characteristics and routine laboratory tests (16, 20, 25, 26). In addition, decision curve analysis determined that the ABCD Risk Score had better clinical utility than the other risk scores. Because of its simplicity and performance, the ABCD Risk Score can be a broadly applicable tool in both in-hospital and outpatient clinics, even in regions with limited medical resources.

A previous large-scale multicenter registry study that enrolled inpatients at health care facilities from January to July 2020 in Japan with a median age of 52 years (IQR, 34–68) determined a clinical deterioration rate of 27.8% (1443 of 5194 patients) (38). The derivation dataset seems to be representative of the target population. However, the clinical deterioration rate and age distribution were higher in our temporal validation datasets than in the above registry study and in our derivation dataset (Table 1). The difference in clinical characteristics between the temporal validation and derivation datasets may be due to sampling bias. Local governments are responsible for the assignment of all patients with COVID-19 to health care facilities. A higher number of patients with COVID-19 per day was evident during the time period of the temporal validation dataset than during that of the derivation dataset (**Appendix 1**). So, it is possible that the local government preferentially assigned patients at risk of clinical deterioration, such as elderly patients, to hospitals during the period of the temporal validation dataset rather than during that of the derivation dataset. The ABCD Risk Score showed good discrimination and calibration performance in both datasets, and therefore it may have the potential to cover people with a wide range of clinical deterioration rates.

This study has several limitations. The head-to-head comparison between the ABCD Risk Score and existing risk scoring models used clinical signs and CT imaging that were not included in this study because of missing values from datasets. In addition, the vaccination strategy for COVID-19 has been started worldwide and several studies have shown that vaccination can reduce the severity and mortality of COVID-19 (39, 40). The ABCD Risk Score does not consider the effects of vaccination because COVID-19 vaccination was not available during our study period in Japan. Finally, the ABCD Risk Score was developed and validated in a dataset including patients from a single country. Although the clinical utility of the ABCD Risk Score will need to be assessed in an externally validated implementation study prior to multicountry adoption in routine practice, the ABCD Risk Score has the potential to individualize patients with COVID-19 through optimal risk stratification of clinical deterioration.

Conclusion

Our novel and simple ABCD Risk Score can be used for risk stratification of clinical deterioration in COVID-19 patients at an early stage of symptom onset (≤ 10 days).

Abbreviations

BMI, body mass index; BUN, blood urea nitrogen; C-statistics, concordance statistics; COVID-19, novel coronavirus disease 2019; CRP, C-reactive protein; GAM, generalized additive model; HFNC, high-flow nasal cannula; IL-6, interleukin-6; IMV, invasive mechanical ventilation; IQR, interquartile range; LAMP, loop-mediated isothermal amplification; LASSO, least absolute shrinkage and selection operator; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio; NPPV, noninvasive positive pressure ventilation; ROC, receiver operating characteristic; RT-qPCR, quantitative reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the Institutional Review Boards of the National Institute of Health Sciences (approval number 333), Saitama Medical University Hospital (approval number 20123.01), and Self-Defense Forces Central Hospital (approval number 02-046). Informed consent was obtained in the form of opt-out on the website.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors report no conflicts of interest relevant to the published work.

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Authors' contributions

KI and TM conceived and designed the study; YK, ST, MM, MNI and AI collected clinical data and performed data analysis; KI performed statistical analysis; KI and TM drafted and edited the manuscript; KM, NT, and YS revised the manuscript. All authors have read and approved the final manuscript.

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Figures

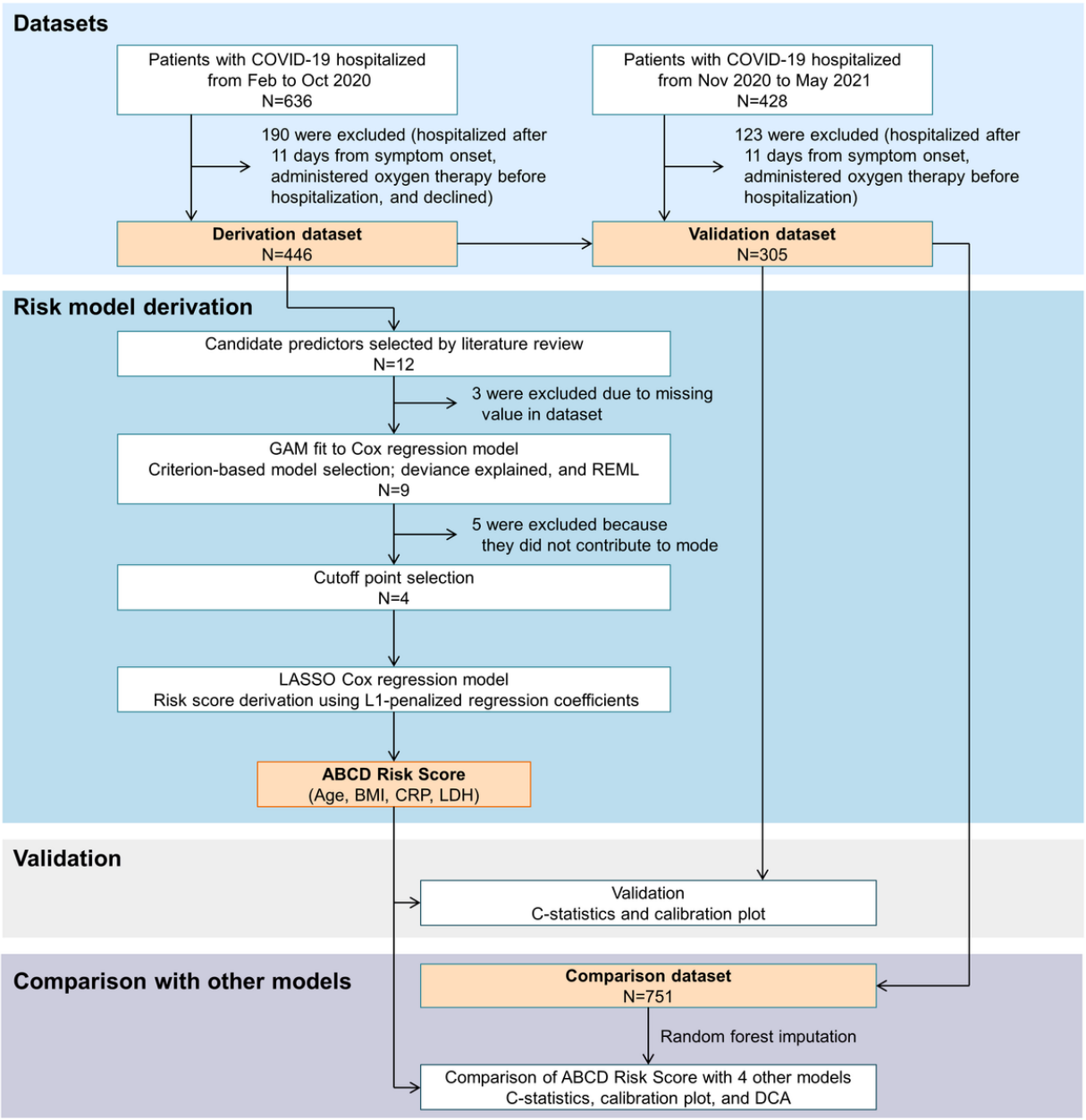

Figure 1

Flowchart for ABCD Risk Score derivation and validation. GAM, generalized additive model; REML, restricted maximum likelihood; LASSO, least absolute shrinkage and selection operator; BMI, body mass index; CRP, C-reactive protein; LDH, lactate dehydrogenase; and DCA, decision curve analysis.

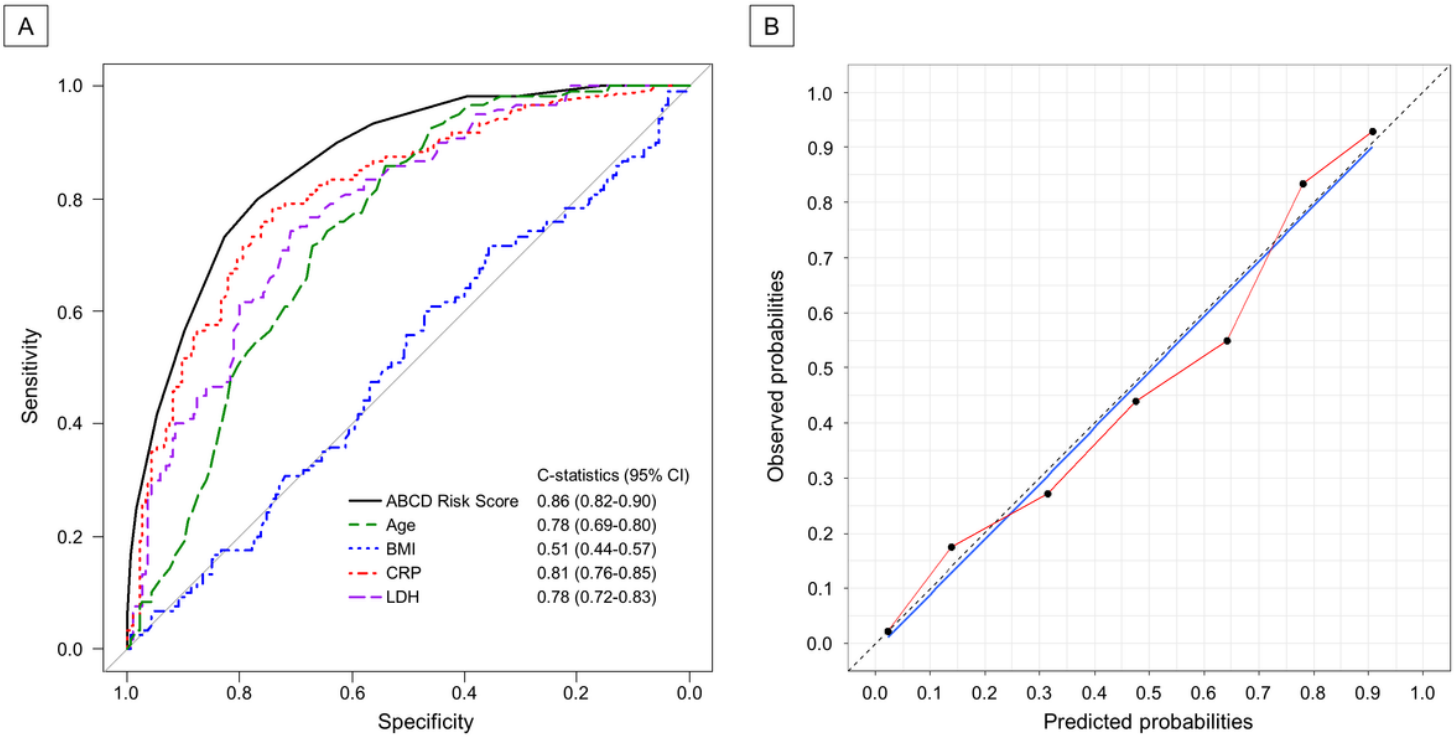

Figure 2

Discrimination and calibration of the ABCD Risk Score in the temporal validation dataset. Concordance statistics (C-statistics) were calculated by receiver operating characteristic curve (ROC) analysis (A). The 95% confidence interval of the C-statistics was calculated by bootstrapped resampling (2000 samples). Predicted versus observed probability of clinical deterioration with the ABCD Risk Score is shown as a calibration plot (B). Each point of the ABCD Risk Score is shown as a black dot. The fitted curve is shown as a blue line. BMI, body mass index; CRP, C-reactive protein; and LDH, lactate dehydrogenase.

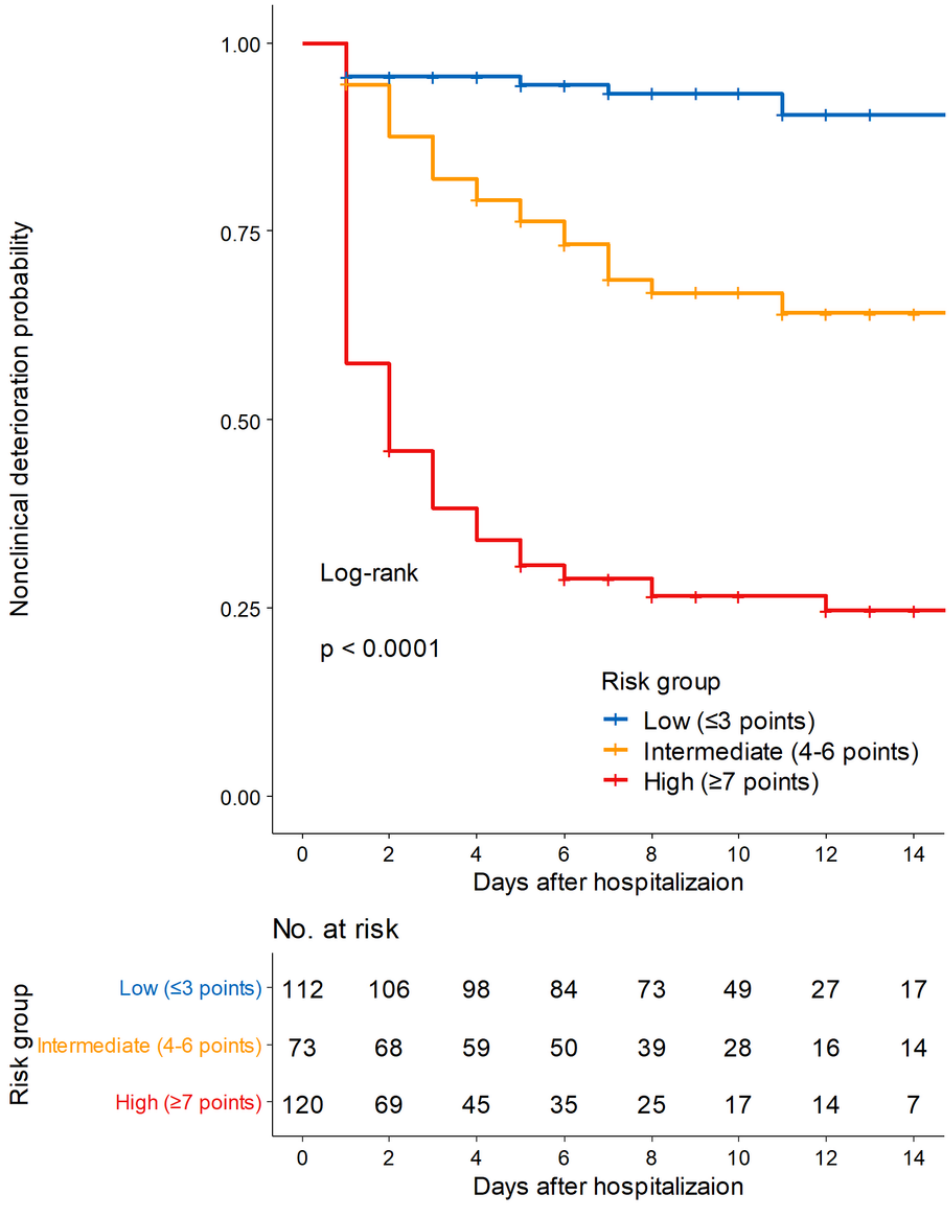

Figure 3

Kaplan–Meier curves for in-hospital clinical deterioration. Kaplan–Meier curves for clinical deterioration in the temporal validation dataset. Risk groups were determined based on the ABCD Risk Score. Low-risk group, ≤3 points; intermediate-risk group, 4–6 points; and high-risk group, ≥7 points.

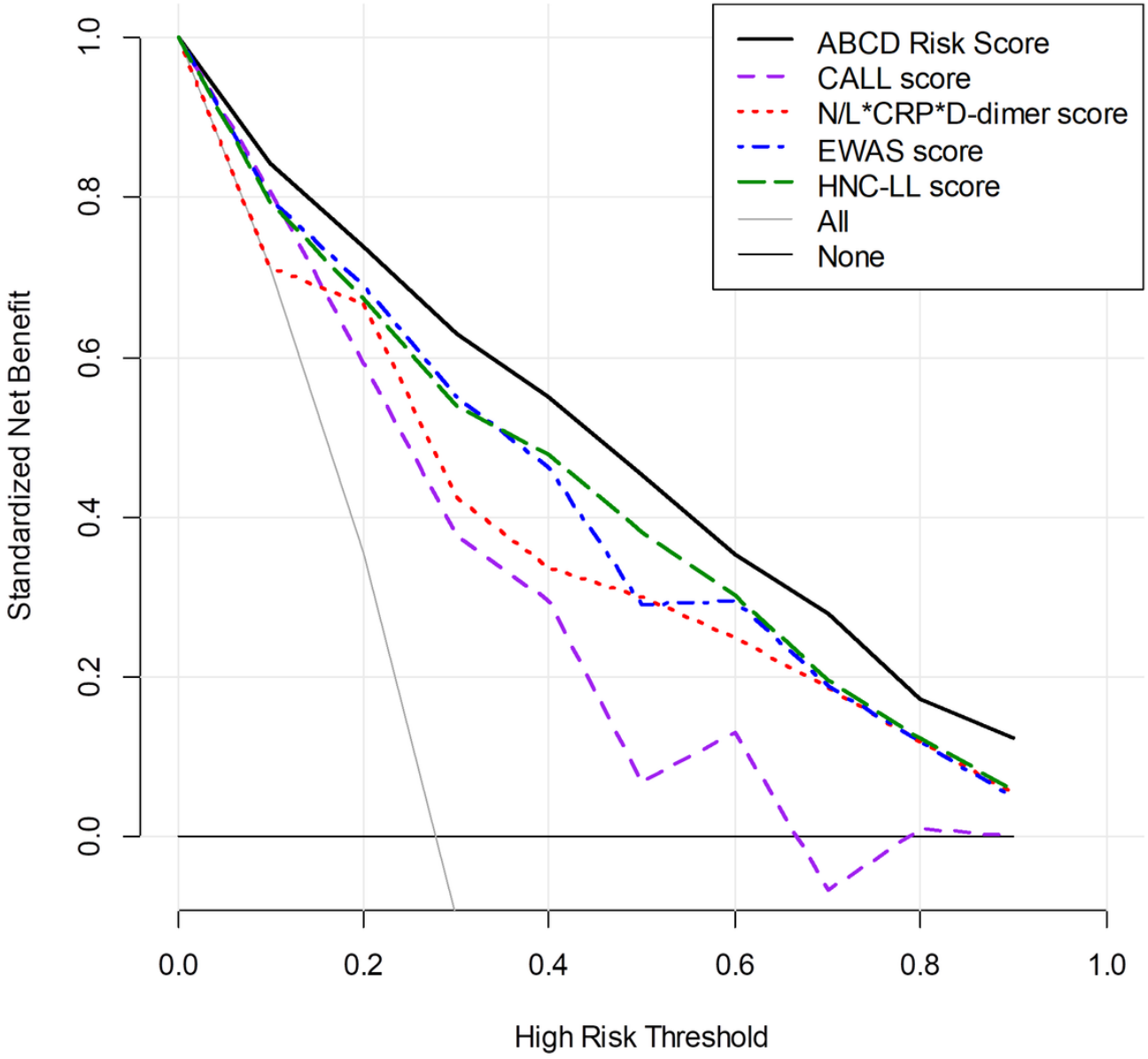

Figure 4

Decision curve analysis for comparing the ABCD Risk Score and other risk models. Lines are shown for the standardized net benefit curve of the ABCD Risk Score and the other four risk scoring models for treating all patients and treating no patients.

Supplementary Files

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