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Early View

Research letter

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Comparison of severity scores for COVID-19 patients with pneumonia: a retrospective study

Running title: severity scores for COVID-19

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Take-Home Message

A-DROP is a reliable tool for risk stratification of death in COVID-19 hospitalised patients on admission.

Abstract

Background Use of existing disease severity scores would greatly contribute to risk stratification and rationally resource allocation in COVID-19 pandemic. However, the performance of these scores in COVID-19 hospitalised patients with pneumonia was still unknown.

Methods In this single center, retrospective study, all hospitalised patients with COVID-19 pneumonia from Wuhan Jin Yin-tan Hospital who had discharged or died as of February 15, 2020 were enrolled. Performance of PSI, CURB-65, A-DROP, CRB-65, SMART-COP, qSOFA and NEWS2 were validated. Net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were also estimated.

Results Among the 654 patients enrolled, 133 patients died and 521 were discharged. Areas of under curves (AUCs) of A-DROP, CURB-65, PSI, SMART-COP, NEWS2, CRB-65 and qSOFA in the prediction of in-hospital death were 0.87, 0.85, 0.85, 0.84, 0.81, 0.80 and 0.73 respectively.

Conclusion ADROP is a reliable tool for risk stratification of death in COVID-19 hospitalised patients on admission.

Keywords: COVID-19 pneumonia, in-hospital death, severity scores, comparison.

The rapidly progressed hypoxemia and acute respiratory distress syndrome were commonly observed in patients with SARS-CoV-2 viral pneumonia.[1] Although several severity scores including Pneumonia Severity Index (PSI),[2] CURB-65,[3] CRB-65.[3] A-DROP[4] and SMART-COP[5] have been developed to identify community acquired pneumonia (CAP) patients with high risk and offer therapeutic advice, the underestimation of death risk of viral pneumonia in these scores has been reported by previous studies.[6, 7] The national early warning score 2 (NEWS2) was developed by National Health Service (NHS) England,[8] along with quick sequential organ failure assessment score (qSOFA), was proposed as candidates for prognostic prediction for severe COVID-19 in the condition of limit medical source.[9] The aim of this study was to compare the accuracy of current score rules in hospitalised patients with COVID-19 pneumonia for predicting the risk of death and evaluate feasibility in improving medical decisions by adopting appropriate score in clinical practice.

Methods

Study patients

Adult inpatients who were diagnosed as COVID-19 according to World Health Organization interim guidance and died/discharged between December 29, 2019 and February 15, 2020 in Jin Yin-tan Hospital, Wuhan city were retrospectively enrolled in this study. After excluding 689 who were still hospitalised as of February 15, 2020, 42 with missing key data which were essential in scoring in their medical records, and 6 deaths within 24 hours after admission, we got 654 cases, including 521 survivors and 133 non-survivors with intact information to complete calculation of all above scores.

The study was approved by the Research Ethics Commission of Jin Yin-tan Hospital (KY-2020-01.01) and the informed consent was waived by the Ethics Commission.

Data collection

Information were obtained from electronic medical records. A standardized data collection form (a modified version of the WHO/International Severe Acute Respiratory and Emerging Infection Consortium case record form for severe acute respiratory infections) was used for data extraction. The score on admission of each patient was noted for 8 severity score rules, including A-DROP, CURB-65, PSI, SMART-COP, NEWS2, CRB-65 and qSOFA. A-DROP was a modified version of the CURB-65 score rules, including the integrated evaluation of age, dehydration, SpO_2 or PaO_2, consciousness and blood pressure.[4] Two researchers were responsible for the accuracy of raw data, and a third party was necessary if doubts existed.

Next-generation sequencing or real-time RT-PCR methods were performed to detect SARS-CoV-2 of respiratory specimens. The PCR re-examination was conducted by throat-swab specimens after clinical remission of symptoms. A patient was allowed to discharge if he achieved clinical improvement and had two throat-swab samples negative for SARS-CoV-2 RNA obtained at least 24 h apart.

Definitions

The illness severity of COVID-19 was defined according to Chinese management guideline for COVID-19 (Version 6.0).[10] The performance of sensitivity, specificity, or area under the curve (AUC) was defined as poor with a value less than 0.5, low with a value between 0.5 and 0.7, moderate with a value between 0.7 and 0.85, and excellent with a value over 0.85.

Statistical analysis

We assessed the predictive performance of A-DROP, CURB-65, PSI, SMART-COP, NEWS2, CRB-65 and qSOFA for in-hospital death by portraying receiver operating characteristic (ROC) curves for each score. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and their 95% confidence intervals (CIs) were calculated. The AUC and 95% CI were estimated to determine the discrimination and net

reclassification improvement (NRI) and integrated discrimination improvement (IDI) were also estimated to assess the improvement of other scores compared with A-DROP score in death prediction.

A two-sided α less than 0.05 was considered statistically significant for all statistical tests. Statistical analyses were performed by the SAS software, version 9.4 (SAS Institute Inc.), unless otherwise indicated.

Results

Score performance and comparison with present scoring systems

Among all 7 scores that were determined by patients' information on admission, A-DROP presented the highest discrimination (AUC, 0.87; 95% CI, 0.84 - 0.90), following by CURB-65 (AUC, 0.85; 95% CI, 0.81 - 0.89), PSI (AUC, 0.85; 95% CI, 0.81 - 0.88), SMART-COP (AUC, 0.84; 95% CI, 0.80 - 0.88), NEWS2 (AUC, 0.81; 95% CI, 0.77 - 0.85), CRB-65 (AUC, 0.80; 95% CI, 0.76 - 0.84), and qSOFA (AUC, 0.73; 95% CI, 0.69 - 0.78) in predicting in-hospital death. Taking A-DROP as reference, the AUC contrast showed an insignificant difference between A-DROP and CURB-65 or A-DROP and PSI, while the discrimination of A-DROP was significantly better than any other score rules. Similar differences were also observed with respect to INR and IDI. The positive differences of INR and IDI indicated the discrimination of A-DROP was improved compared with other scores. (Table 1)

The sensitivity of A-DROP ≥ 2, PSI ≥ 3, SMART-COP ≥ 2, NEWS2 ≥ 5, CRB-65 ≥ 1 and qSOFA ≥ 1 were moderate, whilst that of CURB-65 ≥ 2 was low for identifying patients at risk of death. The specificity of identifying survivors for CURB-65 ≥ 2 was excellent (0.91, 95% CI, 0.89 - 0.93), following by A-DROP ≥ 2, PSI ≥ 3 and SMART-COP ≥ 2, whilst the specificity for the rest scores were low. (Table 1)

Discussion

The accuracy of a variety of severity scores to predict in-hospital death in 654 laboratory confirmed COVID-19 patients admitted to hospital was examined in our study and we found ADROP was a priority clinical tool for predicting the risk of death for patients with COVID-19 pneumonia, compared with other score systems.

A-DROP, a modified version of CURB-65,[4] showed better accuracy of in-hospital death prediction compared to other current widely used CAP-specific tools. According to previous studies, ARDS was common in severe COVID-19 pneumonia.[11, 12] The rapid progression of diffuse bilateral ground-glass opacities CT scan and massive alveolar damage with focal hemorrhage, cellular fibromyxoid exudates and hyaline membrane formation in lung histological examination also suggested a close association between COVID-19 pneumonia and low PaO_2/FiO_2.[13] The modification of more accurate respiratory function evaluation (SpO2 < 90% / PaO2 < 60mmHg in A-DROP vs. respiratory rate ≥ 30/min in CURB-65) could be one reason for improvement in the discrimination of A-DROP. Another reason may be the modification in age (male > 70/female > 75 in A-DROP vs. age > 65 in CURB-65), for the median age of non-survivors with COVID-19 was reported to be 69 years.[14] Besides, the heavier weight on underlying disease instead of respiratory function in PSI may lead to an underestimated severity of COVID-19 pneumonia, compared with A-DROP.

NEWS2 score assesses respiration rate, oxygen saturations, systolic blood pressure, heart rate, temperature and level of consciousness, which were easier for use in emergency department.[8] It was proved as a valid tool for early identifying acutely ill patients with infection. [8] However, without considering the scale of respiratory support therapy, the category of oxygen saturation in NEWS2 score may not reflect the severity of hypoxemia and lung injury accurately. Lacking markers of other organ dysfunction may be also the reason for its unsatisfied performance.

There are some limitations in the study. Firstly, this is a single-center study and the intrinsic defects of retrospective studies were unavoidable, for example, scores at different

time points were unavailable, so we could hardly evaluate disease severity dynamically. Secondly, only patients discharged or died were included in this study and those still being hospitalized were excluded. Thirdly, it is unable to evaluate SOFA's performance for results of arterial blood gas test were absent for most patients in this study.

Conclusion

ADROP is a reliable tool for risk stratification of death in COVID-19 hospitalised patients on admission

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Conflicts of interest

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and no conflicts of interest are reported.

Author Contributions

BC and WJW had the idea for and designed the study and had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. BC, GHF, TC, FZ and ZBL drafted the paper. BC, GHF, FZ, ZBL, YMW, XYG, HL performed the analysis, and all authors critically revised the manuscript for important intellectual content and gave final approval for the version to be published. GHF, FZ, ZBL, JYX, BS, YW, JYX, YZ, SJT and XDW collected the data. All authors agree to be accountable for the all aspects of the work in ensuring that questions related to the accuracy

or integrity of any part of the work are appropriately investigated and resolved. None of the material has been published or is under consideration elsewhere, including the Internet.

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Table 1. The comparison of different clinical prediction rules

Variable	AUC (95% CI)	P	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	NRI	IDI
A-DROP	0.87 (0.84 – 0.90)	Ref	2	0.80 (0.73 - 0.87)	0.86 (0.83 - 0.89)	0.60 (0.52 – 0.67)	0.94 (0.92 – 0.96)	Ref	Ref
CURB-65	0.85 (0.81 - 0.89)	0.2259	2	0.63 (0.55 - 0.71)	0.91 (0.89 - 0.93)	0.65 (0.56 – 0.73)	0.91 (0.88 – 0.93)	0.12	0.06
PSI	0.85 (0.81 - 0.88)	0.1876	3	0.77 (0.70 - 0.84)	0.81 (0.78 - 0.84)	0.50 (0.44– 0.57)	0.93 (0.91 – 0.96)	0.08	0.07
SMART-COP	0.84 (0.80 - 0.88)	0.0405	2	0.83 (0.77 - 0.89)	0.76 (0.72 - 0.80)	0.46 (0.40 – 0.53)	0.94 (0.92 – 0.97)	0.08	0.11
NEWS2	0.81 (0.77 - 0.85)	0.0045	5	0.79 (0.72 - 0.86)	0.69 (0.65 – 0.73)	0.40 (0.34 – 0.46)	0.93 (0.90 – 0.95)	0.17	0.16
CRB-65	0.80 (0.76 - 0.84)	0.0001	1	0.83 (0.77 - 0.89)	0.69 (0.65 – 0.73)	0.40 (0.34 – 0.46)	0.94 (0.92 – 0.96)	0.15	0.15
qSOFA	0.73 (0.69 - 0.78)	<.0001	1	0.82 (0.75 - 0.89)	0.57 (0.53 – 0.61)	0.33 (0.28 – 0.38)	0.93 (0.90 – 0.95)	0.27	0.24

Abbreviations: ROC = Receiver-operating characteristic curve; AUC = area under the curve; CI = confidence interval; qSOFA = quick sequential organ failure assessment; PSI = pneumonia severity index; NEWS2 = national early warning score 2; NPV = negative predictive value; PPV = positive predictive value; IDI = integrated discrimination improvement; NRI = net reclassification improvement.