



Validation of a risk score to predict patients at risk of critical illness with COVID-19

To the Editor,

Available data suggest that 15% and 5% of patients with COVID-19 develop severe and critical illness, respectively [1]. Early recognition of patients who will develop critical COVID-19 illness is of great importance because it will lead to more aggressive and adapted management which may improve patient's outcome. An example of work along these lines is a recent report in this journal on the predictive value of National Early Warning Score (NEWS) 2 for intensive care unit (ICU) admission of patients with SARS-CoV-2 infection [2]. NEWS includes respiratory rate, oxygen saturation, need for supplemental oxygen, body temperature, blood pressure, heart rate and level of consciousness. When used at hospital admission NEWS was found to be a good predictor for ICU admission. We here report our experience with an alternative approach for risk score prediction of patients at risk for critical illness with COVID-19. The present study was based on a risk score (COVID-GRAM) [3] to predict which patients would develop critical illness (ICU admission, invasive ventilation, death). In their study, Liang et al. [3] constructed the following score data based on 10 variables: X-ray abnormality [OR 3.39; 95% CI 2.14–5.38], age [OR 1.03; 95% CI 1.01–1.05], haemoptysis [OR 4.53; 95% CI 1.36–15.15], dyspnoea [OR 1.88; 95% CI 1.18–3.01], unconsciousness [OR 4.71; 95% CI 1.39–15.98], number of comorbidities [OR 1.60; 95% CI 1.27–2.00], cancer history [OR 4.07; 95% CI 1.23–13.43], neutrophil/lymphocytes ratio (NLR) [OR 1.06; 95% CI 1.02–1.10], lactate dehydrogenase [OR 1.002; 95% CI 1.001–1.004] and direct bilirubin [OR 1.15; 95% CI 1.06–1.24]. According to the score, patients were classified as low risk (0.7%), medium risk (7.3%) and high risk (59.3%). The score has been translated into an online risk calculator that is freely available (<http://118.126.104.170/>). However, the score was only validated in

patients from China and external validation is required. The first objective of our study was to validate the COVID-GRAM. The second objective of the study was to compare predictive value of COVID-GRAM with Neutrophil to lymphocyte ratio (NLR) on admission and on day 3.

We retrospectively calculated this risk score (COVID-GRAM) of 198 patients hospitalized for COVID-19 pneumonia. Baseline demographic and clinical characteristics and outcome are presented in Table 1. The study was approved by our local ethical committee (CEHF 2020/06AVR/201).

Upon 198 patients, 153 patients (77%) and 45 patients (23%) were at medium risk and high risk according to COVID-GRAM score, respectively. There was no patient at low risk. Overall mortality was 15% (29/198) with 52% (15/29) and 48% (14/29) occurring in patients with mild and high risks COVID-GRAM score, respectively. The number of ICU admission was 26 (17%) and 11 (24%) in patients with mild and high risk COVID-GRAM score. The number of intubations was 13 (9.3%) and 5 (12.5%) in patients with mild and high risk COVID-GRAM score.

Univariate and multivariate analysis were performed to evaluate if COVID-GRAM can predict patients who will undergo a poor outcome. Univariate analysis showed that COVID-GRAM score was a significant predictor of mortality (p .001; OR 4.16; IC 95 1.8–9.5) as well as NLR on admission, day 3 and intubation. Multivariate analysis showed that NLR on day 3 (p .035; OR 4.17; IC95 1.11–15.8) and COVID-GRAM (p .011; OR 3.2; IC95 1.31–7.94) remained statistically significant and may predict mortality.

Receiver-operating characteristic (ROC) curves were computed to assess the accuracy of NLR on admission, day 3 and COVID-GRAM in predicting mortality (Figure 1) and showed that the ROC curves are quite similar and there is no difference between the area under the curve (AUC).

Table 1. Clinical and biological characteristics of patients.

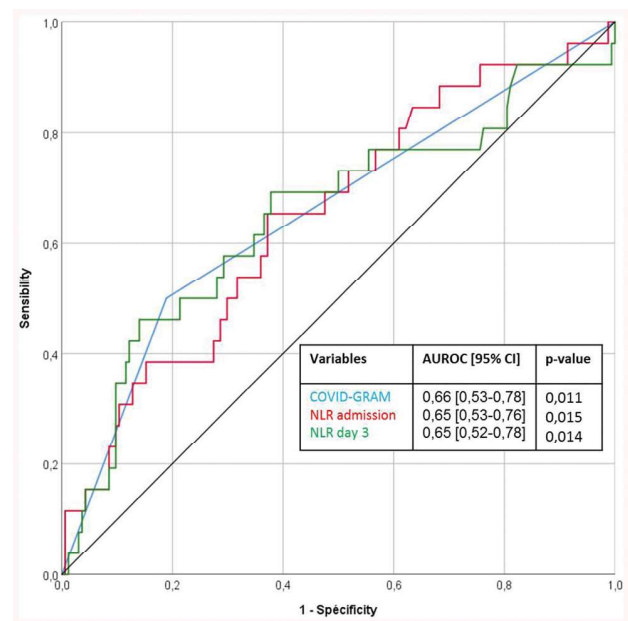
Characteristics	Total effective (%) or mean (SD)
Number of patients	N = 198
Sex (male)	110 (56%)
Mean Age	64 [34–95]
Ethnicity	
Caucasian	118 (59.6%)
Sub-Saharan-African	34 (17.2%)
Mediterranean	41 (20.7%)
Asian	4 (2%)
American	1 (0.5%)
Height	183 (102)
Weight	90 (93)
BMI	29 (23)
Smoking	8 (4%)
Clinical symptoms	
Mean time from onset of symptom to admission	7.2 (3.7)
Fever	156 (79%)
Cough	154 (78%)
Shortness of breath	140 (71%)
Conjunctivitis	2 (1 %)
Sore throat	39 (20%)
Congestion or runny nose	40 (20%)
Headache	55 (28%)
Fatigue	116 (59%)
Muscle aches	70 (35%)
Nausea	36 (18%)
Diarrhea	44 (22%)
Anosmia	9 (4.5%)
Ageusia	13 (7%)
Unconsciousness	1 (0.5%)
Haemoptysis	1 (0.5%)
Mean SpO ₂ (when breathing ambient air)	90%
Number of patients with oxygen therapy	179 (90%)
Mechanical and non-mechanical respiratory support	
HFNC	29 (15%)
Oxygen mask	87 (44%)
CPAP	56 (28%)
Invasive mechanical ventilation	18 (9%)
Co-morbidities	
No-comorbidity	34 (17%)
Cardiovascular disease	107 (54%)
Hypertension	101 (51%)
Chronic pulmonary disease	33 (17%)
Diabetes	49 (25%)
Immunosuppression	24 (12%)
Chronic liver disease	10 (5%)
Chronic kidney disease	36 (18%)
Malignancy	10 (5%)
Biological data	
CRP on admission	103 (82)
CRP on day 3	118 (95)
WBC on admission	6.68 (3.32)
WBC count on day 3	6.43 (3.26)
Absolute neutrophil count on admission	5.13 (2.99)
Absolute neutrophil count on day 3	4.79 (2.91)
Lymphocyte count on admission	0.96 (0.49)
Lymphocyte count on day 3	1.05 (0.58)
NLR on admission	7 (7.4)
NLR on day 3	6.1 (5.5)
Eosinophil count on admission	0.02 (0.04)
LDH	385 (188)
Total bilirubin level	0.53 (0.63)
Ferritin	1196 (1531)
D-Dimer	2633 (4076)
Creatinine	1.37 (1.64)
Troponin T	31.2 (69.13)
X-ray abnormality	190 (95.9%)
Lung CT scan	188 (95%)
Stratification of lung lesions on CT scan	
<10%	15 (7.6%)
10–25%	90 (45.5%)
25–50%	53 (26.8%)
>50%	30 (15.2%)

(continued)

Table 1. Continued.

Characteristics	Total effective (%) or mean (SD)
Outcome	
Mean time from admission to hospital discharge (days)	11.9 (7.7)
Overall death	29 (15%)
Still in hospital	5 (2.5%)
ICU admission	37 (19%)
Death in ICU	11 (6%)
Still in ICU	5 (2.5%)

SD: standard deviation; HFNC: high flow nasal cannula; WBC: white blood cell; NLR: neutrophil to lymphocyte ratio; CPAP: continuous positive airway pressure; CRP: C-reactive protein; ICU: intensive care unit.

**Figure 1.** ROC curves showing accuracy of NLR on admission, NLR on day 3 and COVID-GRAM in predicting mortality

Our study showed that COVID-GRAM is a useful score and may predict patients who will develop critical illness. However, several variables such as D-Dimer, ferritin, creatinine, sex which have been associated with high mortality are not included in COVID-GRAM. Moreover, our study also showed that NLR on admission and day 3 may predict critical illness with a strength similar to that of COVID-GRAM. Liu et al. [4] showed in a retrospective study ($n = 245$) that NLR was an independent risk factor of the in-hospital mortality for COVID-19 patients. Liu et al. [5] showed in a prospective study including 61 patients with COVID-19 that $NLR \geq 3.13$ and age ≥ 50 were predictive factors for patients who are likely to develop severe disease. However, the number of patients was low. COVID-GRAM can be considered as a useful tool to predict patients at moderate to high risk for the development of critical illness; however NLR, a component of this score, is cheap, easily and rapidly calculated biomarkers which may by themselves help to

identify patients at high risk of death in the context of COVID-19. This may be particularly useful in countries with limited resources where chest X-ray, extensive labs analysis are not easily available.

Disclosure statement

All authors confirmed that there are no conflict of interest.

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Received 4 September 2020; revised 9 September 2020;
 accepted 9 September 2020

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