Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Letter to the Editor

Prognostic value of maximum NEWS-2 scores in addition to ISARIC 4C scores for patients admitted to hospital with COVID-19

Dear Editor

We read with interest the article by Federico and colleagues, which found that secondary bacterial infections play a critical role in adverse outcomes for patients with severe COVID-19.[1] In the United Kingdom (UK), the National Early Warning Score-2 (NEWS-2) score, consisting of an *a priori* weighted composition of the patient's observations, is used routinely to monitor patients in hospital and identify early those who may deteriorate.[2] NEWS-2 was originally developed in a cohort of UK patients who had an underlying diagnosis of bacterial sepsis, but has been shown in previous studies to be sensitive in identifying those at risk of in-hospital cardiac arrest, unanticipated intensive care unit (ICU) admission or death.[3,4] In previous work published in the Journal, we showed that in hospitalised patients with COVID-19, variability in NEWS-2 scores during hospitalization, but not the admission NEWS-2 scores, was related to mortality.[5]

In contrast, the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) 4C Mortality Score (from now on referred to as the ISARIC -NEWS-2 score synergy) was developed specifically to predict risk of death from viral pneumonia in patients with COVID-19.[6] Developed from a large UK cohort, the ISARIC score consists of a statistically weighted composition of age, gender, comorbidities, patient's observations, serum urea and C-reactive protein. Perhaps unsurprisingly, the ISARIC score has been shown to have a higher predictive value for mortality compared to a concomitantly calculated NEWS-2 score, since it takes into account more variables.[6] An ISARIC score on admission is recommended as part of COVID-19 guidance in around half of UK hospitals.[7] However, there is currently no data on whether the highest NEWS-2 scores taken during hospitalization would be of incremental value in predicting mortality taking into account ISARIC scores following admission to hospital.

We therefore set out to investigate this issue by using a cohort of 315 consecutive patients who presented to our Acute Respiratory Unit at the University Hospitals of Leicester NHS Trust, UK between October 2020 and January 2021, during the emergence of the Alpha (B.1.1.7) variant. Data collected as part of a clinical outcome audit are summarised in Table 1. The mean age of the patients was 63 (standard deviation [SD] 15); most were of White ethnicity. Clinical evidence of bacterial infection was low; most had evidence of pneumonia on their chest x-ray. Most participants were given supportive oxygen, antibiotics and steroids during their hospital stay. The mean ISARIC score was 10 (SD 4); mean admission NEWS-2 score was 5 (SD 2) and the mean of the maximum NEWS-2 score recorded for each patient during admission

was 9 (SD 3). Our cohort suffered significant mortality and morbidity: 33% of study participants died; 4% were admitted to ICU and length of stay was close to two weeks (mean: 13 days, SD 11).

Two logistic regression models were used to investigate the incremental value of the maximum NEWS-2 score in addition to other routinely collected clinical variables. A base model was first constructed, using variables that were related to mortality on univariable analysis. The NEWS-2 score was then added onto the base model, in order to find the best model that predicted mortality. The new models' cumulative discrimination compared to the base model was measured using an Area under the Receiver Operating Curve (AUROC). A 2-sided *p* value of ≤ 0.05 was considered statistically significant.
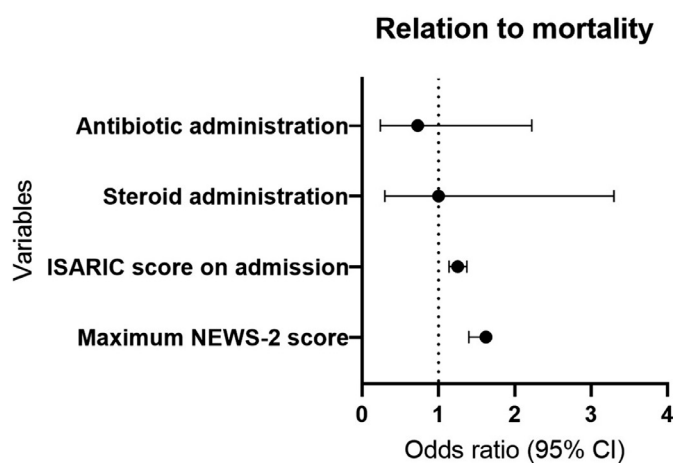
On univariable logistic regression analysis, admission ISARIC score, the maximum NEWS-2 score, treatment with steroids and antibiotics were related to mortality. Consistent with earlier findings, admission NEWS-2 scores was not related to all mortality. In our multivariable model, admission ISARIC score (adjusted odds ratio [aOR: 1.25, 95% confidence intervals [CI]: 1.14–1.36, $p < 0.001$) and the maximum NEWS-2 score (aOR: 1.62, 95% CI: 1.40–1.88, $p < 0.001$) remained independent predictors of mortality (Fig. 1A). Addition of the NEWS-2 score also improved the model's AUROC (from 0.74 to 0.85, Fig. 1B). Note that our study was observational in nature, and therefore our multivariable analysis does not reflect futility of the aforementioned treatment, but rather, strength of the prognostic value of both ISARIC and NEWS-2 scores in our cohort.

In conclusion, our study has found that a combination of an admission ISARIC score, followed by NEWS-2 score monitoring most accurately predicts in-hospital mortality in hospitalized patients with COVID-19. Previous studies have only made head-to-head comparisons of different scoring systems without considering them synergistically.[6,8,9] Whilst the use of NEWS-2 scores alone may have limitations because they do not account for the degree of supplemental oxygen a patient with COVID-19 may require, a high NEWS-2 score during hospitalization continues to have important prognostic value in the prediction of mortality.[10] This could be due to the possibility that NEWS-2 scores are predicting the probability of secondary bacterial sepsis, and/or cardiac arrest. Whilst we acknowledge that evidence of bacterial infection was low in our cohort, e.g. only half of our cohort had sputum/blood cultures done, possibly due to overlap in clinical syndromes between COVID-19 and bacterial infections, as well as the SARS-CoV-2 aerosol-generating concerns around sputum induction. With COVID-19 shifting from a pandemic to an endemic disease, increasing numbers of patients will have pre-existing immunity to SARS-CoV-2, either from previous exposure and/or vaccination. It is therefore reasonable to suggest that the causes of death in patients may shift from acute viral pneumonia (seen mainly in the immune naïve adults experiencing their first COVID-19 infection) to other causes, including superadded bacterial infections or

Table 1

Clinical description of the cohort.

Demographics	Patients
Age (years) – mean (SD)	63 (15)
Gender (male) – number (%)	203 (64%)
Ethnic group – number (%)	
White	192 (61%)
Asian	87 (27%)
Black	9 (3%)
mixed/others	29 (9%)
Clinical characteristics	
ISARIC score – mean (SD)	10 (4)
Admission NEWS-2 score – mean (SD)	5 (2)
Maximum NEWS-2 score recorded during hospitalisation – mean (SD)	9 (3)
Blood/sputum culture done – n (%)	147 (46%)
Pathogen in those with culture	14 (9%)
Coliform	5 (3%)
Staphylococcus aureus	7 (5%)
Pseudomonas	2 (1%)
Stenotrophomonas maltophilia	1 (1%)
Findings of COVID-19 on chest x-ray – n (%)	259 (82%)
Treatment	
O2 – n (%)	296 (93%)
Antibiotics – n (%)	276 (87%)
Dexamethasone – n (%)	276 (87%)
Remdesivir - n (%)	9 (3%)
Tocilizumab – n (%)	14 (4%)
Outcomes	
ITU – n (%)	12 (4%)
Mortality – n (%)	106 (33%)
Length of stay – mean (SD)	13 (11)
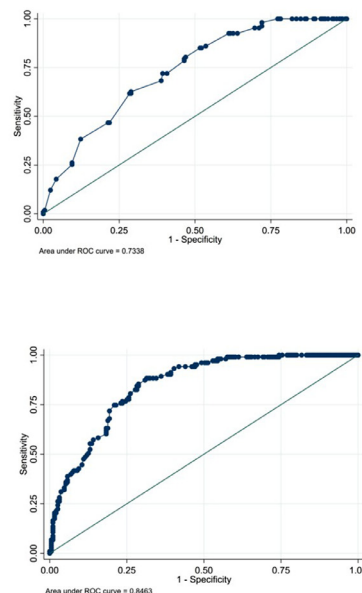
Fig. 1. A. Forest plot showing variables relating to mortality on multivariable logistic regression analysis. **B.** Receiver operating curves for the multivariable logistic regression model. Model A (top): without including the highest NEWS-2 score (variables included: antibiotic administration, steroid administration, ISARIC score). Model B (bottom): including the highest NEWS-2 score (including the same variables as shown in A).

decompensations of any pre-existing chronic medical conditions. In these circumstances, NEWS-2 scores will have an increasing role to play in identifying those who are at most risk of adverse outcomes.

Note that as this study was performed during the emergence of the Alpha (B.1.1.7) variant, in a mostly unvaccinated UK population (UK COVID-19 vaccination started on 8 December 2020), this hybrid ISARIC-NEWS prognostic scoring approach may have different outcomes in the current Omicron (B.1.1.529) surge in a mostly vaccinated population.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Federica M, Maura F, Silvia S, Sabrina O, Cristina GM, Eleonora C, et al. The impact of secondary infections in COVID-19 critically ill patients. *J Infect* 2022. doi:10.1016/j.jinf.2022.03.017.

2. Royal College of Physicians. National early warning score (NEWS 2). Available at https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2. Accessed March 25, 2022, 2017.

3. Prytherch David R, Smith Gary B, Schmidt Paul E, Featherstone Peter I. ViEWS-towards a national early warning score for detecting adult inpatient deterioration. *Resuscitation* 2010;**81**(8):932–7. doi:10.1016/j.resuscitation.2010.04.014.

4. Smith Gary B, Prytherch David R, Meredith P, Schmidt Paul E, Featherstone Peter I. The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. *Resuscitation* 2013;**84**(4):465–70. doi:10.1016/j.resuscitation.2012.12.016.

5. Sze S, Pan D, Williams CML, Wong N, Sahota A, Bell D, et al. Variability, but not admission or trends in NEWS2 score predicts clinical outcome in elderly hospitalised patients with COVID-19. *J Infect* 2021;**82**(1):159–98. doi:10.1016/j.jinf.2020.08.002.

6. Knight Stephen R, Ho A, Pius R, Buchan I, Carson G, Drake Thomas M, et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. *BMJ* 2020;**370**:1–13 September. doi:10.1136/bmj.m3339.

7. Blunsum A.E., Perkins J.S., Arshad A., Bajpai S., Barclay-Eilliott K., Brito-Mutunatagam S., et al. Evaluation of the implementation of the 4C mortality score in United Kingdom hospitals during the second pandemic wave. 2022.

8. Gupta Rishi K, Harrison Ewen M, Ho A, Docherty Annemarie B, Knight Stephen R, van Smeden M, et al. Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: a prospective cohort study. *Lancet Respir Med* 2021;**9**(4):349–59. doi:10.1016/S2213-2600(20)30559-2.

9. Gupta Rishi K, Marks M, Samuels Thomas HA, Luintel A, Rampling T, Chowdhury H, et al. Systematic evaluation and external validation of 22 prognostic models among hospitalised adults with COVID-19: an observational cohort study. *Eur Respir J* 2020;**56**(6). doi:10.1183/13993003.03498-2020.

10. Lim Nicole TY, Pan D, Barker J. NEWS2 system requires modification to identify deteriorating patients with COVID-19. *Clin Med J R Coll Physicians Lond* 2020;**20**(4):E133–4. doi:10.7861/CLINMED.LET.20.4.6.

Syed Akbar[#]
Clinical Decisions Unit, University Hospitals of Leicester NHS Trust, Leicester, UK

Daniel Pan[#]
Infection and HIV Medicine, University Hospitals of Leicester NHS Trust, Leicester, UK
Respiratory Sciences, University of Leicester, Leicester, UK

Abdlrzag Ehdode, Reezwan Islam, Abdulrahman Abouzaid, Kumaran Balasundaram, Mohannad Shihadeh, Krish Patel, Gehad Othman, Onyeka Umerah
Clinical Decisions Unit, University Hospitals of Leicester NHS Trust, Leicester, UK

Shirley Sze
Cardiovascular Sciences, University of Leicester, Leicester, UK

Daniela C Nicoara
Clinical Decisions Unit, University Hospitals of Leicester NHS Trust, Leicester, UK

Gerrit Woltmann
Clinical Decisions Unit, University Hospitals of Leicester NHS Trust, Leicester, UK
Respiratory Sciences, University of Leicester, Leicester, UK

Julian W Tang[*]
Respiratory Sciences, University of Leicester, Leicester, UK
Clinical Microbiology, Leicester Royal Infirmary, Infirmary Square University Hospitals of Leicester NHS Trust, Leicester LE1 5WW, UK

[*]Correspondence author at: Clinical Microbiology, Leicester Royal Infirmary, Infirmary Square University Hospitals of Leicester NHS Trust, Leicester LE1 5WW, UK.
E-mail address: Julian.tang@uhl-tr.nhs.uk (J.W. Tang)
[#] Syed Akbar and Daniel Pan contributed equally to this article.