Correspondence on 'Preliminary predictive criteria for COVID-19 cytokine storm'

We read with great interest the recent article by Caricchio *et al* reporting preliminary predictive criteria for COVID-19 cytokine storm (COVID-CS).[1] Early risk stratification for disease course and mortality is important especially in critically ill patients with severe COVID-19 to guide physicians in their evaluation to define patients at risk not surviving COVID-19 who may benefit from specific interventions.[2] To develop a predictive model, the authors used univariate logistic regressions to identify variables and clusters associated with COVID-CS, resulting in defined optimal cut-off values.[1] The model identified patients at risk for COVID-CS, associated with longer hospitalisation and increased mortality. While ferritin and C-reactive protein (CRP) did not add predictive power, these parameters were included in the final criteria per expert preference for clinical reassurance of ongoing systemic inflammation. Therefore, we here describe the performance of the COVID-CS predictive model for the requirement of intensive care unit (ICU) supportive care and mortality in a single-centre cohort of 20 critically ill patients with confirmed SARS-CoV-2 infection. In addition, we analysed the impact of including ferritin and CRP measurements for the usability of the COVID-CS model to predict disease severity and mortality in severe COVID-19.

Assessed at ICU admission, 7 of 20 (35%) patients fulfilled the criteria of the COVID-CS predictive model including ferritin and CRP. Risk classification using the COVID-CS predictive model assessed at ICU admission was associated with prolonged ICU length of stay before patients could be relocated to a non-ICU medical ward (HR 3.3, 95% CI 1.0–10.4; p=0.0428; figure 1A). In the group of patients who met the COVID-CS criteria, we observed 3 of 7 (42.9%) patients not surviving COVID-19 as compared with the group not fulfilling the COVID-CS criteria at ICU admission with 2 of 13 (15.4%) patients (HR 2.3, 95% CI 0.38–13.7; p=0.3698; figure 1B,C). Interestingly, excluding ferritin and C-reactive protein (CRP) measurements further improved the prediction of ICU stay of length (HR 4.0, 95% CI 1.3–12.2; p=0.0163) and mortality (HR 9.1, 95% CI 1.6–53.2; p=0.0141; figure 1D–F). In summary, we here confirm the accuracy of the model established by Caricchio *et al* to predict mortality in a single-centre cohort of severe COVID-19 patients requiring ICU supportive care. Additionally, the COVID-CS predictive model for disease severity and mortality assessed at ICU admission is superior when levels of ferritin and CRP are excluded.

The final model reported by Caricchio *et al* classified patients at risk for COVID-CS based on (1) documented COVID-19, (2) ferritin >250 ng/mL and CRP >4.6 mg/dL and (3) one feature from each cluster: cluster I (low albumin, low lymphocytes, high neutrophils), cluster II (elevated alanine aminotransferase, aspartate aminotransferase, D-dimers, lactate dehydrogenase, troponin I) and cluster 3 (low anion gap, high chloride, high potassium, high blood urea nitrogen:creatinine ratio).[1] We here confirm that risk classification for mortality using the COVID-CS predictive model assessed at ICU admission also identifies patients at risk not surviving severe COVID-19 requiring ICU supportive care. Furthermore, the COVID-CS predictive model for disease severity and mortality when assessed at ICU admission is superior by exclusion levels of ferritin and CRP. This is in line with the study by Caricchio *et al* reporting that ferritin and CRP did not add predictive power.[1] In conclusion, we here confirm that risk stratification for COVID-CS is also predictive in an independent cohort of critically ill patients with severe COVID-19, highlighting the relevance of hyperinflammation and tissue damage associated with disease severity and COVID-19 mortality as reported previously.[3–6]

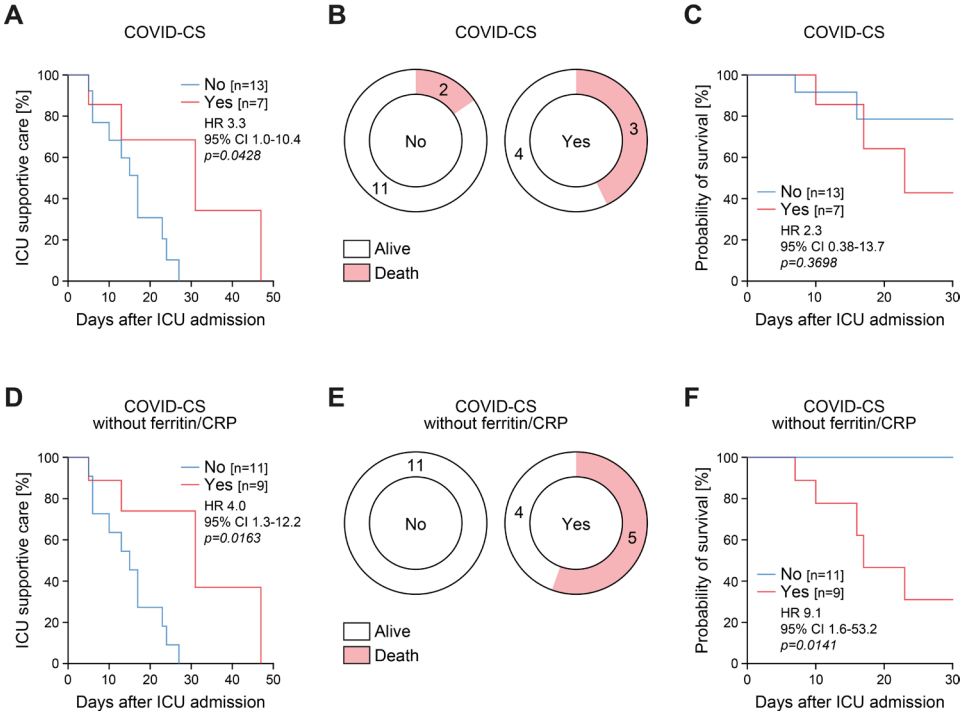

Figure 1 (A) ICU stay of length in patients with severe COVID-19 grouped for COVID-CS. (B,C) Mortality and probability of survival analysis grouped for COVID-CS. (D) ICU stay of length in patients with severe COVID-19 grouped for COVID-CS without ferritin and CRP measurements. (E,F) Mortality and probability of survival analysis grouped for COVID-CS without ferritin and CRP measurements. COVID-CS, COVID-19 cytokine storm; CRP, C-reactive protein; ICU, intensive care unit.

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