



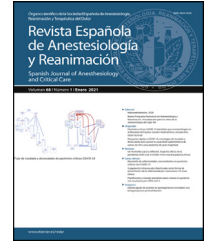
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# Revista Española de Anestesiología y Reanimación

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## LETTER TO THE DIRECTOR

### Response to the letter to the editor: A comment on C-reactive protein and SOFA scale: a simple scale as an early predictor of the need for critical care in patients with COVID-19 pneumonia in Spain<sup>☆</sup>



### Réplica a la carta al director: «Un comentario sobre proteína C reactiva y escala SOFA: una simple escala como factor predictivo temprano de la necesidad de cuidados críticos en los pacientes con neumonía causada por COVID-19 en España»

To the Director:

We would first like to thank the authors of the letter “A commentary on ‘C-Reactive protein and SOFA scale: A simple score as early predictor of critical care requirement in patients with COVID-19 pneumonia in Spain’” for their interest in the results of our study.<sup>1</sup>

We are very pleased to see that the authors of subsequent studies<sup>2–4</sup> have found that the variables included in our multivariate model, which only included patients admitted between March 2020 and June 2020, effectively predict the need for critical care in newly admitted patients, which was the aim of our study.

However, the authors of the letter comment that the C-reactive protein (CRP) values used to discriminate the need for critical care in Smilowitz et al.<sup>2</sup> differ from those used in our analysis. There are many reasons for this discrepancy, including differences in design and objective. One potential limitation of the aforementioned study<sup>2</sup> is that the authors, for the purpose of calculating sample size before recruitment, did not determine the expected difference in CRP values between the group that required critical care and the one that did not, making it impossible to be certain that the sample size was adequate for the purpose of the study. Smilowitz et al., furthermore, do not use measures to find

the best cut-off point (why did they choose 10 mg/dL instead of 9.1 mg/dL, as used in our study?), and the variables used in their multivariate models differ from those used by us in a different population. In addition, the authors do not describe the clinical variables can modify CRP as a marker of the degree of inflammation (time of evolution, previous treatments) nor the distribution among the study groups, making their results unsuitable for comparison with ours. Despite this, Smilowitz et al., like us, found that CRP values are higher in patients that are likely to need critical care.

The same limitations apply to the evaluation of D-dimer data, which, although not the main outcome variable of the study,<sup>2</sup> is analysed in subgroups. This methodology limits the potential validity of the results. Furthermore, the authors<sup>2</sup> do not mention whether the patients identified as candidates for critical care on admission to hospital presented higher D-dimer levels than those not requiring this level of care, or whether or not this presumed difference is due to chance, as was the case in our sample.<sup>1</sup>

Regarding the use of the SOFA scale as a predictor of admission to critical care units, the study mentioned by the authors<sup>3</sup> does not evaluate this aspect in particular, although it does indicate that a SOFA score of 2 or more (similar to that found in our study<sup>1</sup>) is as useful as the NEWS scale for predicting respiratory failure. This suggests that our model may also be useful in these patients.

The other review and meta-analysis mentioned<sup>4</sup> do not include an analysis of variables or clinical scales, which probably explains, at least in part, why their results differ from ours.

Nevertheless, despite all these limitations, we observed that the studies cited show that the variables included in the scale used to predict the need for admission to critical care units in patients presenting in the hospital emergency room with pneumonia described in our study are fit for purpose.

## Funding

The authors declare that they have not received funding for this study.

## References

1. Vaquero-Roncero LM, Sánchez-Barrado E, Escobar-Macias D, Arribas-Pérez P, González de Castro R, González-Porrás JR, et al. Proteína C reactiva y escala SOFA: una simple escala como factor predictivo temprano de la necesidad de cuidados críticos en los

<sup>☆</sup> Please cite this article as: Vaquero Roncero LM, Sánchez Barrado E, Sánchez Hernández MV. Réplica a la carta al director: «Un comentario sobre proteína C reactiva y escala SOFA: una simple escala como factor predictivo temprano de la necesidad de cuidados críticos en los pacientes con neumonía causada por COVID-19 en España». Rev Esp Anestesiología y Reanimación. 2022;69:442–443.

- pacientes con neumonía causada por COVID-19 en España. *Rev Esp Anesthesiol Reanim.* 2021;68(9):513–22.
2. Smilowitz NR, Kunichoff D, Garshick M, Shah B, Pillinger M, Hochman JS, et al. C-reactive protein and clinical outcomes in patients with COVID-19. *Eur Heart J.* 2021;42(23):2270–9.
  3. Lalueza A, Lora-Tamayo J, de la Calle C, Sayas-Catalán J, Arrieta E, Maestro G, et al. Utilidad de las escalas de sepsis para predecir el fallo respiratorio y la muerte en pacientes con COVID-19 fuera de las Unidades de Cuidados Intensivos. *Rev Clin Esp.* 2020. <http://dx.doi.org/10.1016/J.RCE.2020.10.004>.
  4. Kiss S, Gede N, Hegyi P, Németh D, Földi M, Dembrowsky F, et al. Los cambios tempranos en los parámetros de laboratorio son predictores de mortalidad e ingreso en UCI en pacientes con COVID-19: una revisión sistemática y un metanálisis. *Microbiología e Inmunología Médicas.* 2021;210(1):33–47.

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<https://doi.org/10.1016/j.redare.2022.07.003>

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## A commentary on ‘‘C-Reactive protein and SOFA scale: A simple score as early predictor of critical care requirement in patients with COVID-19 pneumonia in Spain’’ (Revista Española de Anestesiología y Reanimación 68 (2021) 513–522)<sup>☆</sup>



### Un comentario sobre «Proteína C reactiva y escala SOFA: una simple escala como factor predictivo temprano de la necesidad de cuidados críticos en los pacientes con neumonía causada por COVID-19 en España» (Revista Española de Anestesiología y Reanimación 68 (2021) 513–522)

To the Editor:

We read with great interest the article published by Vaquero et al.<sup>1</sup> titled ‘‘C-Reactive protein and SOFA scale: A simple score as early predictor of critical care requirement in patients with COVID-19 pneumonia in Spain’’, where the authors identify a SOFA score of  $\geq 2$  combined with CRP  $\geq 9.1$  mg/mL on admission as potential predictors of the need for critical care in patients with pneumonia caused by COVID-19. We thank the authors for such valuable evidence; however, we would like to add a few comments.

In some patients, severe COVID-19 respiratory infection may manifest as a rapidly developing acute respiratory distress syndrome with other serious complications that may eventually be followed by multiple organ failure and death. Studies in patients with COVID-19 have shown that a low lym-

phocyte count, particularly CD8+ cells, and a high leukocyte count together with increased levels of lactate dehydrogenase (LDH), creatine kinase (CK), C-reactive protein (CRP), D-dimer, and high levels of proinflammatory cytokines are associated with more severe inflammation and extensive lung damage, and with higher intensive care unit (ICU) admission and mortality rates.<sup>2</sup>

Smilowitz et al.<sup>3</sup> found that an initial CRP value above the median level (CRP  $\geq 10.8$  mg/dL) was associated with critical illness (47.6% vs. 25.9%; adjusted odds ratio [aOR] 2.83, 95% CI 2.37–3.37) and in-hospital mortality (32.2% vs 17.8%; ORa 2.59, 95% CI 2.11–3.18) compared to an initial CRP value below the median level (CRP < 10.8 mg/dL). They also correlated CRP values with D-dimer values, and concluded that patients with concomitant elevation of CRP and D-dimer (>384 ng/mL) are at greater risk of in-hospital adverse outcomes. Although they also correlate high CRP values with critical illness and mortality, they establish a higher cut-off point than that suggest by Vaquero et al., who do not include D-dimer as a marker of severity. This is important, as other studies have shown the usefulness of D-dimer determination.<sup>1</sup>

Lalueza et al.<sup>4</sup> found the NEWS scale (area under the curve [AUC]): 0.75; 95% CI: 0.69–0.8,  $p < 0.0001$ ) to be the most accurate predictor of respiratory failure in patients with COVID-19 at admission, and the difference between this scale and the SOFA scale approached statistical significance (AUC: 0.73; 95% CI: 0.67–0.79;  $< 0.0001$ ). Regarding mortality, the SOFA score (AUC: 0.77; 95% CI: 0.72–0.83;  $p < 0.0001$ ) was somewhat more accurate than the other scores, and in this regard the NEWS scale approached statistical significance (AUC: 0.72; 95% CI: 0.66–0.78;  $< 0.0001$ ). This indicates that the NEWS scale is the best predictor of respiratory failure, since it obtained the best AUC in this study, while the SOFA scale is the best instrument for predicting mortality. The foregoing reconfirms the usefulness of sepsis scales in the initial clinical evaluation of patients with COVID-19. It also shows the need for studies evaluating the NEWS scale in conjunction with inflammatory markers, because findings suggest that it may more effective than SOFA at predicting the need for early critical care in patients with pneumonia caused by COVID-19.

<sup>☆</sup> Please cite this article as: Vergara Maestre DA, Toro Muñoz MA. Un comentario sobre «Proteína C reactiva y escala SOFA: una simple escala como factor predictivo temprano de la necesidad de cuidados críticos en los pacientes con neumonía causada por COVID-19 en España» (Revista Española de Anestesiología y Reanimación 68 (2021) 513–522). *Rev Esp Anesthesiol Reanim.* 2022;69:443–444.