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DOI: 10.14744/ejp.2025.04353

Reply to the letter to the editor: 'Non-invasive ventilation outcome (NIVO) score for predicting in-hospital and late mortality of chronic obstructive pulmonary disease (COPD) patients with acute hypercapnia'

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Received: 05-09-2025
Revised: 16-10-2025
Accepted: 27-10-2025
Published: 30-10-2025

Thank you very much for your detailed review and thoughtful comments on our study.[1] The missing data referenced in the manuscript are now provided in Supplementary Tables 1 through 4.

This study aimed to assess the predictive value of the NIVO score[2] for both in-hospital and 90-day mortality (referred to as late mortality in our study) among patients admitted with acute exacerbation of COPD and treated with non-invasive ventilation (NIV). Due to the clinical practices in our hospital and the structure of our national healthcare system, we believe that patients in our cohort had relatively easy access to both home mechanical ventilation (HMV) and NIV. Consequently, NIV may have been initiated not only when acidemia developed during hospitalization but also at the point of hypercapnia detection during exacerbation—even in the absence of acidemia—to prevent progression to respiratory muscle fatigue and subsequent acidosis based on the patient's clinical status.

In this context, the presence of index acidemia may sometimes reflect deterioration due to comorbid conditions such as myocardial infarction, pulmonary embolism, or infection, which may, in turn, influence the predictive accuracy of the NIVO score in this patient population. Among our patients, 145 (58%) presented with acidemia at admission. Of these, 109 had a pH between 7.25 and 7.35. According to the original NIVO scoring, these individuals received a score of 0 for both the "time to acidemia" and "pH < 7.25" components.

How to cite this article: Yavuz Yıldırım S, Akbay MÖ, Kesen Yurtcanlı CH, Ağca M, Ernam D. Reply to the letter to the editor: 'Non-invasive ventilation outcome (NIVO) score for predicting in-hospital and late mortality of chronic obstructive pulmonary disease (COPD) patients with acute hypercapnia'. Eurasian J Pulmonol 2025;27:195-197.

Based on this observation, we hypothesized that the clinical relevance of the "time to acidemia" parameter might differ in our patient population. Therefore, we modified the original definition of this component—without altering the original time window—while maintaining the overall structure of the NIVO score, which is known to be a valid predictor of mortality. We believe that this modification could enhance the score's predictive utility in certain subgroups of patients. Because we did not develop a novel scoring system but instead adapted an existing one, we did not conduct methodological steps such as validation, which would be required in a developmental study. Thus, our study remained cross-sectional.

When analyzing all patients, there was no statistically significant difference between the original and modified NIVO scores in predicting either in-hospital or late mortality ($p = 0.5890$ and $p = 0.1270$, respectively) (Supplementary Tables 5-6, Supplementary Figures 1-2, respectively). Nevertheless, both versions of the score were effective predictors of mortality.

In the acidemic subgroup ($n = 145$), both the original and modified NIVO scores were significant predictors of in-hospital mortality. Although the modified score demonstrated a slightly higher area under the curve (AUC) compared to the original version, the difference was not statistically significant ($p = 0.2299$) (Supplementary Table 7, Supplementary Fig. 3).

A group-wise comparison was performed using SPSS's Split File function to analyze patients with and without home mechanical ventilation (HMV) separately among those presenting with acidemia. Among patients who owned an HMV device, the modified NIVO score demonstrated a statistically significant improvement over the original score in predicting in-hospital mortality ($p = 0.0399$) (Supplementary Table 8, Supplementary Fig. 4).

Detailed subgroup ROC analyses are presented in Supplementary Tables 9 through 14, respectively, and the corresponding ROC curves are provided in Supplementary Figures 5 through 10.

Because the follow-up duration was not recorded during data entry, a Cox regression model could not be applied. Therefore, a limited analysis using logistic regression was conducted instead. After adjusting for age, sex, and duration of COPD, each one-point increase in the NIVO score was associated with a 1.4-fold increase in the odds of in-hospital mortality, whereas the modified score was associated with a 1.7-fold increase among patients presenting with acidemia at admission (Supplementary Table 15).

In the subgroup of patients with acidemia at admission who had access to an HMV device, the odds of in-hospital mortality increased by 2.1 times with each point increase in the original NIVO score and by 3.3 times with the modified score (Supplementary Table 16). Additional regression analyses for the entire cohort and selected subgroups are presented in Supplementary Tables 17 through 20.

When analyzing the entire cohort, both the original and modified NIVO scores were effective predictors of the need for intubation (Supplementary Table 21, Supplementary Fig. 11).

In conclusion, although the overall predictive performance did not differ significantly, the modified NIVO score may offer improved prediction of in-hospital mortality among patients presenting with acidemia and those who own an HMV device. However, the reliability and generalizability of this modification should be further evaluated through prospective study designs and in other populations with similar access to treatment.

We sincerely appreciate your insightful comments and valuable contributions, which have provided meaningful guidance for refining our current work and informing future research.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

Funding

The authors declared that this study received no financial support.

Use of AI for Writing Assistance

No AI technologies utilized.

Author Contributions

Concept – S.Y.Y., M.Ö.A., C.H.K.Y., M.A., D.E.; Design – S.Y.Y., M.Ö.A., C.H.K.Y., M.A., D.E.; Supervision – S.Y.Y., M.Ö.A., C.H.K.Y., M.A., D.E.; Resource – S.Y.Y., M.Ö.A.; Materials – S.Y.Y., M.Ö.A.; Data Collection and/or Processing - S.Y.Y., M.Ö.A., D.E.; Analysis and/or Interpretation - S.Y.Y., C.H.K.Y., D.E.; Literature Review – S.Y.Y., M.Ö.A., D.E.; Writing – S.Y.Y., D.E.; Critical Review – S.Y.Y., M.Ö.A., C.H.K.Y., M.A., D.E.

Peer-review

Externally peer-reviewed.

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