Reviewer’s report

Title: Mortality in patients with COPD exacerbations attending emergency departments

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Reviewer: Nicholas Hart

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General Comments
In this large prospective multi-centre observational cohort study (16 hospitals recruiting at 1.4 patients per month for 27 months), the authors have reported, based on predictive modelling, 5 factors (age, use of accessory muscle/paradoxical breathing, MRC dyspnoea score, altered GCS and use of LTOT or home NIV) that can be used to predict early mortality in patients attending the emergency department (ED) with acute exacerbations of COPD. Overall, the methodology is sound and the authors have developed a severity score to predict the mortality risk in one half of the patient cohort and then subsequently validated the score in the other second half of the cohort.

Major Comments
1. The development of a scoring system combining these five variables is novel. However, age, baseline dyspnoea, use of LTOT, NIV use and altered level of consciousness have all been reported previously as predictors of poor outcome. In this reviewer’s opinion, (a) the extent to which these data add to our current understanding of acute exacerbations of COPD, in particular, in terms of poor outcome needs to be clarified (b) the reason for excluding the ‘frequent exacerbators’ is counterintuitive and this approach needs explanation and (c) it needs to be highlighted that none of the five variables reported are modifiable, so the rationale for potential clinical strategies to be developed to reduce early mortality is limited.

2. The scoring system is potentially useful but this reviewer considers it needs modification for the clinical reader. Indeed the clinician wishes to have a ‘quick and easy’ method to risk stratify the patient into risk of ICU/RICU admission and mortality risk with risks reported for these two categories. Reviewing of Figure 1, a ‘cut off’ value of #7 >7 for ICU/RICU admission and #11 >11 for mortality. The current scoring system does not facilitate risk prediction for admission (50-89% across the 4 categories) or IMV (1-5% across the 4 categories) as the prevalence is very high and very low, respectively. Hence, for the clinician a focus on ICU/RICU admission and mortality risk would be useful clinically.

3. Although information was collected during hospital admission or ED attendance, there were no data reported regarding the trajectory of physiological or symptomatic change between admission to hospital and discharge, although this information has presumably been routinely collected (e.g. oxygen
saturations, respiratory rate, heart rate, breathlessness scores). In-hospital mortality or death soon after discharge may be an indicator of poor underlying health status and lung function, however, it may also suggest failure of inpatient and post discharge treatment, which would be demonstrated by limited change in physiological parameters, including early warning and breathlessness scores. Finally, outcome is related to delivery of care and this reviewer would appreciate data detailing mortality between the sites.

4. The relevance of re-admission data cannot be underestimated. It would be of interest to review the readmission data, or data on acute healthcare utilisation after discharge from the index event, to assess the utility of the AECOPD severity score in predicting readmissions within, for example, 28 days and 3 months. The positive and negative predictive values for early mortality and readmission are wholly important to the clinician.

5. Although we acknowledge that there has been no previous studies reporting mortality prediction models in COPD patients attending the ED, there has been previous studies that have reported predictors of re-admission and mortality in hospitalised COPD patients. Indeed, Steer et al (Thorax 2012) identified baseline dyspnoea and a composite score (the DECAF score) as a predictor of poor outcome. Comparison of the DeCOPD score and DECAF score would be interesting for the reader.

6. The authors stratified the inclusion criteria to exclude those with (1) other major pathologies and co-morbidities (2) COPD not confirmed on spirometry (3) ‘frequent exacerbator’ phenotype attending ED on >1 occasion. With the 145 incomplete datasets, of the 3267 patients screened 24% of patients were not included. Was there a mortality difference between the multiple ED attenders (14% re-attendance rate) and the single ED attenders? Did co-morbidity confer a poor outcome as the authors hypothesised during the study design? What was the final diagnosis of the 56 patients without spirometric evidence of COPD?

7. Missing MRC data was treated the same as MRC Grade 5. This needs further discussion as this attracts the highest score of 5 points out of 18 points. Should this not be treated as part of the missing datasets? How was baseline MRC dyspnoea score measured? Was this from the patient on admission or from their notes?

8. GCS is a multiple component assessment test (E4/4, V5/5, M6/6). How altered was the GCS? Was the main changes in a specific domain e.g. Verbal – confusion. These points need clarification.

9. The mild, moderate, severe and very severe risk classification needs clarification in terms of risk of within hospital death, death within 1-week of discharge and death within 1-month of discharge

10. Did length of use of LTOT or NIV influence the findings?

11. How was accessory muscle activity confirmed and quantified?

12. Why did ABG not add value to the scoring system? Was it because the pH values were all in the normal physiological range as a number of patients were excluded i.e. those who attended ED more than once. This needs further
discussion.

13. The authors comment on ‘generalizability’ in the discussion, in particular, in the context of gender. This reviewer is concerned that 390 patients were excluded as they attended the ED on more than one occasion.

Minor Comments
1. Introduction needs more detail including a number of key references in this area.
2. The English needs attention in places
3. ‘Extensive bronchiectasis’ was an exclusion criteria. How was this defined?
4. ‘IRCU’ needs to be replaced with ‘RICU’ – Respiratory Intensive Care Unit
5. Statistics section could be shortened or placed in the on line supplement
6. By paradoxical movement, do the authors mean ‘Hoover’s’ sign i.e. in-drawing of the lower rib-cage during inspiration

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: I have no declarations of interest relating to this manuscript.