Reviewer's report

Title: Enhancement of CURB65 score with proadrenomedullin (CURB65-A) for outcome prediction in lower respiratory tract infections: Derivation of a clinical algorithm

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Reviewer: ALBERTO CAPELASTEGUI

Reviewer's report:

General comments:
This is an interesting analysis aimed at assessing whether the prognostic information provided by ProADM improved the prediction of risk by the CURB65 score with regards to both adverse events and mortality in CAP and non-CAP-LRTI patients.

The study’s objective is clinically relevant, especially for its potential effects on triage decisions. The limitations of risk assessment tools (CURB65, PSI) on this question are evident. The combination of ProADM and the CURB65 score may provide for physicians an added level of confidence for treating low-risk cases (CURB65 0-1) as outpatients, and also help identify those patients with high risk based on CURB65 score who show however, a good prognostic (Figure 6 is very interesting in this regard).

The way it is written the study raises several questions and some points that should be addressed.

Major comments:

1- The study’s main problem is to have included cases of pneumonia together with cases with uncompensated COPD and also cases of bronchitis. The differences between these three diseases is very important conceptually, in addition they differ in their baseline characteristics, process-of-care and outcomes (Table 2).

On the other hand, the number of non-CAP cases included is very low (379), with only 10 deaths found among them (thus their statistical impact is limited). This is enhanced by the fact that uncompensated COPD is not the same as bronchitis.

The authors should concentrate their study on CAP and comment with lots of caution the results related to the non-CAP-LRTI group.

2- In the authors’ section for “any disease specific complications” the “adverse events” must be defined with greater precision. In particular, they need to show detailed information about the type and the number of those “specific complications”. They should also take into account that they are grouping under “adverse events” death, ICU admission and emphysema, among others.

Including variables as different as death and for instance emphysema, in a
composite end point is a limitation that should be noted. This limitation would imply that all comments related to results surrounding “adverse events” should be stated with extreme caution.

3- Discussion, page 12, paragraph 3. The authors should discuss in more detail the apparent differences between their results and those found in reference 12. The differences are probably not so deep: Figure 5, B, CURB65 0-1 and ProADM categories, mortality rates 1.2%-0.5%-1.8%. Are there differences? What’s the p trend? It would also be useful to know the p trend for CURB65 2 and 3-5 categories.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.