Author's response to reviews

Title: Utility of Procalcitonin (PCT) and Mid regional pro-Adrenomedullin (MR-proADM) in risk stratification of critically ill febrile patients in Emergency Department (ED). A comparison with APACHE II score.

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Author’s response to reviews:

Dear Editor,

we revised the manuscript “Utility of Procalcitonin (PCT) and Mid regional pro-Adrenomedullin (MR-proADM) in risk stratification of critically ill febrile patients in Emergency Department (ED). A comparison with APACHE II score” according to the suggestions of the referees.

In this cover letter we gave a point-by-point response to the concerns.

Thank you for the opportunity you gave us.

Best regards,

Dr. Francesco Travaglino, MD

Referee 1: Geetika Sood

Major revisions:

1. Yes, the suspicion of infection was based on a clinical hypothesis, made by the emergency physician

2. The prognostic weight of the two biomarkers was supported by the correlation between them and the APACHE II score, being the latter a prognostic score routinely performed.

3. We corrected the assumptions in the paper, following your suggestions. It is correct to affirm that a direct independently correlation between mortality and the
two biomarkers cannot be demonstrated. Our study is based on the correlation
between the to molecules and the APACHE II score. This one is recognized as a
prognostic score, predicting mortality.

4. We modified the paragraph in object.

5. It is correct that our study doesn’t analyze the effectiveness of PCT in reducing
the antibiotic consumption in ED, however our statement is deduced by current
medical literature (see included references). We revised the paragraph
explaining it in a clearer way.

6. The query is correct. However it is known that for both MR-proADM and PCT
the levels present in bloodstream are infinitesimal and also their international unit
of measure are very small (nmol/L and ng/ml, respectively). This leads to the fact
that if you measure also minimal differences of these biomarkers between
patients and controls, these differences result statistically significant. The
controls were all healthy subjects.

Minor revisions:
All the suggestions have been considered and we modified the paper. In
particular, at suggestion n°7, the term “bactericide” activity has been changed in
the correct form “bactericidal” activity.

Referee 2: Raffaele Altara

Major Revisions:
1. The control group has been now well defined in the “material and methods”
section

2. The number of patients hospitalized is 99: it has been added in the
manuscript.

3. a. The beneficial role on the patient depends on the fact that a more accurate
stratification and an identification of a more severe patient leads to a more
aggressive and prompt treatment, improving in this way the prognosis.

b. It is correct to assume that our study does not evaluate the cost-benefit
analysis. Our conclusion was only an hypothesis, but we deleted the relative
phrase, as we agree with the referee.

4. key messages 3,4 and 5 can be explained by what specified at point 3

Minor Revisions
1. The figures have been checked

2. The febrile patient definition according to the body temperature has been
changed

3. Table 2 has been modified as suggested

Corrections have been made to written English.