Author's response to reviews

Title: Should C-reactive protein concentration at ICU discharge be used as a prognostic marker?

Authors:

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Version: 2 Date: 27 August 2010

Author's response to reviews: see over
Dear Prof. Christna Chap,

Thank you very much for your email dated August 19th, 2010. I hereby enclose by email a fresh copy of the manuscript as well as full detailed replies to our reviewers. All the reviewers’ remarks that they have kindly raised were fully addressed “point-by-point” in full details in my accompanying reply. Accordingly you will find that all relevant points were fully incorporated in the new version of the manuscript (in red), while those points that were not applicable were still fully addressed in our replies.

Once more, on behalf of all the authors we would like to express our deepest gratitude for your great help and support.

Best regards
Joana Silvestre

Reviewer Kierzek Gerald

Major Compulsory Revisions:

General criticisms: In our recent paper published in the Intensive Care Medicine (Intensive Care Med. 2009 May; 35(5): 909-13), we included all patients admitted in our intensive care unit with the diagnosis of sepsis during the same period (November 2001–December 2002) and we analyzed CRP levels of the day of ICU admission as a marker of prognosis. In the present study we included all patients that were discharged alive from the ICU (septic and non septic) and the CRP levels of the day of ICU discharge were analyzed as a marker of post ICU prognosis. In this paper we wanted to study whether CRP could be a surrogate marker of unresolved inflammatory processes that could influence post ICU risk of death.

1. Detailed criticisms:
   a. Patients and methods:
      i. First question: This question was already answered above
      ii. Second question: The majority of patients were discharged to ward. This information was added in the new version of the manuscript accordingly.
      iii. Third question: We included all patients discharged alive from ICU. Each patient was included only once and in the event of readmissions only the first admission was considered. This information was changed in the new version manuscript accordingly.
   b. Results:
      i. First, Second and Third: The authors fully agree with reviewer and changes were made accordingly.
      ii. Fourth question: In the subgroup analysis surgical versus medical patients, surgical refers to trauma, obstetric and surgical patients. This was clarified in the new manuscript version.
   c. Discussion:
      i. We fully agree with the reviewer and changes were made accordingly.
2. Minor essential revisions:
   a. Patients and methods:
      i. First question: This question has already addressed
      ii. Second question: CRP is a routinely done in our ICU
      iii. Third question: The discharge criteria were clinical improvement with no further need of intensive care.
   b. Results:
      i. First question We think that the results are clearly presented, and that a flow chart will not bring additional information.
      ii. Second question: Measurements of CRP are presented in mg/dL in all the manuscript. There is no consensus concerning the units; either mg/dl or mg/L are used in different papers in the same journal. As far as we are aware there is no international consensual unit of measurement of CRP.
      iii. Third question: The authors fully agree with reviewer and changes were made accordingly.

Reviewer Mark G Coulthard

The present reviewer presents only two questions:

1. First question: Since we were unable to find any significant differences between the three groups there is no added interest in doing AUC ROC analysis. For sure the AUCROC would be well below 0.75, that is considered the limit to describe the clinical usefulness of a variable. In the table 1, the CRP values between survivors and nonsurvivors are mentioned and here ROC analysis was presented and the ROC curves were added in the new version of the manuscript. The majority of patients were ventilated due to respiratory tract infection (both pneumonia and tracheobronchitis).

2. Second question: The abstract was shortened accordingly. The values in abstract were presented in decreasing order since the authors think that it would be easier to read.

Reviewer Ilja M Hoepelman:

Major Compulsory Revisions:

1. Methods section: The follow-up of this study was until death or hospital discharge. The objective of this study was the analysis of in hospital mortality from patients discharged from Intensive Care Unit. The mean duration of follow-up was 34.8 days with no difference between survivors and nonsurvivors (34.3 ± 26.8 versus 37.6 ± 24.9 days; \( p=0.543 \)). This data was included in the new version of the manuscript.

2. Results: The difference in mortality rate between groups was done using analysis of variance (ANOVA) that is a parametric statistical method indicated to
compare means from three or more samples. The result from ANOVA only tells if a significant difference between samples is present or not; but ANOVA do not tell us where that difference if present is located. Only with post-hoc analysis that is possible. In our study, the difference is not between 15% versus 33%, but between the three groups. We have provided the numbers (N) with the percentages in the new version of the manuscript.

Minor Essential Revisions

1. **Discussion:** This data was added in the manuscript according to the reviewer’s comments.

Discretionary Revisions

1. **Results:** This question has already been addressed before.

2. **Statistical review:** Statisticians reviewed all the statistical analysis that was considered appropriate to our data analysis.