Author’s response to reviews

Title: Predictors of mortality and validation of burn mortality prognostic scores in a Malaysian burns intensive care unit

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Prof Guangde Tu
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Sub: Reply to reviewer comments

Dear Prof Guangde Tu,

We would like to express our deepest appreciation in the time given to reply and comments given to improve this article. We have consulted our statistician and 2 native English reader to proof read our revised manuscript. The response to each comment is as below :-
Reviewer reports:

Federico Franchi, M.D. (Reviewer 1): Tan Chor Lip and colleagues try to identify the predictors of burn mortality in a Malaysian burn intensive care unit. This is a retrospective study involving 525 patients admitted to a Malaysian Hospital. The authors analyzed the predictors of death, the influence of time of burn injury to burn unit admission and the predictivity of burn predictive scores in their population. The topic is relevant but, unfortunately, the study suffers from several methodological limitations. The following are the Major Concerns:

Response: Dear Prof Federico Franchi, on behalf of all the co-authors we would like to express our appreciation and thanks for the time taken to review our manuscript. Our responses are as below:-

Abstract.
The abstract and the objective of the study are not clear. Furthermore, there are too many goals. Unexplained abbreviations make reading even more difficult. The results are also not clear.

Response: We have changed the entire abstract focusing on the objectives of this study. The reviewer has identified the true objectives of this study and we understand that our writing may mislead the target audience. Therefore the 2 main study objectives shall be: “The primary objective was to evaluate and identify risk factors which may predict outcome of in-patient mortality in a Malaysian burn’s population. The secondary objective of this study was to validate the five well known burn mortality prognostic score in predicting mortality in a Malaysian burns intensive care unit.”

This excerpt has been added into the objective section. In accordance to our objective, the entire abstract has been re-written. Abbreviations has been written in full. Entire results have been re-written in accordance to new changes recommended in the following comments.

Introduction.
1. The introduction is too long for the concepts it expresses. It is completely focused on socioeconomic aspects. It can be reduced by 30-40%.

Response: We have shortened the introduction by 40%. We have added in a sentences which bridges the introduction to the study objective.

2. L2-26 Pg 5. Final part of the introduction and Study Objective. This part is unclear and there are too many confusing goals. Please, clarify the objective of the study. In addition, you can explain the population of the study in method section and no in introduction. Finally, all the abbreviations must first be written in full.

Response: The entire study objective has been rewritten for clarity to the target audience; - “The primary objective was to evaluate and identify risk factors which may predict outcome of in-patient mortality in a Malaysian burn’s population.
The secondary objective of this study was to validate the five well known burn mortality prognostic score in predicting mortality in a Malaysian burns intensive care unit.” Patient population is written in the methods section as per comment. All abbreviations have been re-written in full.

Methods.
3. The enrollment period is different from that reported in the abstract. Please reported the correct period of the study.

Response: We apologize for the typing error, the correct period of study is between 1 January 2010 to 31 December 2017. This has been synchronized in both the abstract and methods section.

4. L 7-15 Pg 7 "In this study, we also recorded the time of injury to BICU admission. The purpose of which was to determine if there was an association between duration to admission and mortality. In addition, the estimation of TBSA from the first centre of presentation was recorded and compared to the TBSA estimation in the BICU." All these objectives are confusing to the reader.

Response: Thank you for highlighting this sentence. The meaning of this sentence was to highlight that we recorded the time from injury to burn unit admission. In addition, we also recorded the center of initial treatment prior transfer to BICU. The center of first resuscitation was categorized into the emergency department of our hospital’s burn unit (ED BICU) and other centers outside termed as Periphery Primary and Secondary Health Care Centre (PPSHCC). The reason for highlighting this was to enlighten the target audience that we were evaluating the duration to burn unit admission and the initial center where first treatment was given prior transfer on the outcomes of death. From our study it showed that initial treatment outside of burns unit and duration to transfer into burn unit did not have a statistical significance. This shows that it doesn’t matter of the place where treatment was first administered as most of the tertiary center emergency resuscitative are adapt adequately to handle severely burn patients in Malaysia.

We have deleted the initial sentence and changed it to as below:- “The variables chosen to predict mortality during the hospital stay included gender, age, place of injury, mechanism of injury, TBSA, inhalation injury, mechanical ventilation, tracheotomy, length of time from injury to BICU admission and centre of initial emergency treatment was administered prior transfer/admission to BICU. Center of initial emergency treatment were categorized into the hospital’s emergency department (ED BICU) and outside of the parent emergency department categorized as Periphery Primary and Secondary Health Care Centre (PPSHCC).

5. L 33 Pg 7. This reviewer suggests that you provide a detailed description of each score on the supplementary materials.

Response: Detailed description of each score is done and attached on Supplement 1.doc.
6. Statistical plan described only the analysis of mortality (that probably is the true aim of the study). On the contrary, the calculation of the sample size refers to the comparison between ROC curves. What is the objective of the study? The statistical analysis must be planned for the purpose of the study. In addition, the multivariate analysis conducted must be better described.

Response: The authors agree with the reviewer and after discussion we have decided to delete the sample size calculation part as the primary objective was to identify risk factors for burn mortality and secondary objective was to evaluate the accuracy of the five burn mortality prognostic score at predicting death. The multivariate analysis has been described as follows;-

“All variables with significant p value by univariate analysis were included in the multivariate binary logistic regression using enter method to determine association with mortality.”

Results.
7. Pg 9 L 15. "A total of 525 patients were treated for burn injuries at the BICU of Hospital Sultan Ismail, Malaysia between January 2010 and December 2017, 372 males and 153 females, all of whom fulfilled the inclusion and exclusion criteria." It is not necessary to repeat the recruitment period again.

Response: Recruitment period have been deleted.

8. In the first part of the results, you present the data and comments that are not useful to any of the objectives of the study that you have declared (eg., ethnicity of patients). Please eliminate unnecessary data to make reading easier.

Response: Thank you for the highlighting this, we agree that these data is not in line with objective and has deleted the related socio-demographic data. Deleted portion as follows;

“Distribution of ethnicity reflected the population in the southern region being predominantly Malays (247 patients; 47%) followed by the Chinese (104 patients; 19.8%) and Indians (45 patients; 8%). More than half of the reported burn injuries took place under household and domestic conditions (285 patients; 54.3%), followed by workplace/industrial accident burns (167 patients; 31.8%) and burn injuries as a result from road traffic accidents (28 patients; 5.3%). Thermal injury which includes scalding, flame burns and contact burns were the highest recorded type of burn with 450 patients (85.7%).”

9. In the current form the results are presented in a confused manner. Please reorganize the results in accordance with the objective of the study and with the related sub-analysis, if any.

Response: The entire results portions has been re-organized in accordance to the objective of the study and related sub-analysis with changes made to multivariate analysis from the subsequent related comments.

10. the variables "length of stay and the duration of mechanical ventilation" cannot be considered predictors of mortality. Multivariate analysis should be repeated without introducing these variables into the model.
Response: The variables length of stay and duration of mechanical ventilation has been removed from the statistical analysis and subsequent results/tables. The outcome of the primary objective of this current study showed that among the chosen risk factors that remained after multivariate analysis were older age (p=0.004), wider total body surface area burn (p<0.001) and mechanical ventilation (p<0.001) for burn mortality.

11. What is the ROC of your multivariate model? Is it better than the ROC scores you've tested?

Response: We did not produce roc of our multivariate model. As ROC scores of revised Baux scores already generated very good ROC value at 0.94. and the variables used were the same from our model. Hence, there is no reason to substantiate further needs to create a new model from our dataset as revised baux is has shown good predictive ability of burn mortality.

Discussion.

12. Pg. 11 L50. "Other identified predictors were longer length of stay and the presence of mechanical ventilation [16]." Why reference on your result? Furthermore, the cited manuscript does not report those predictors of mortality.

Response: We apologize for the typing error. The referencing has been deleted.

13. the discussion can be reduced by about 30%. The first part of the discussion (Predictors of burn mortality) must be reviewed in the light of the results obtained by repeating the multivariate analysis.

Response: The discussion part has been reduced by more than 30% and most parts re-written. The first part of discussion was re-written based on the new results of multivariate analysis.

Rosanna Varutti, MD (Reviewer 2): 1) Why do you use heparin in patients with inhalation injury? It would be useful to explain it in the text.

Response: Thank you Prof Rosanna Varutti for your time to review this manuscript. “Nebulised Heparin was given to inhibit pulmonary fibrin clot formation and improve oxygenation for patients with inhalation injury.” – This excerpt is inserted into the main manuscript highlighted in red

2) By age: given the great variability, it would be better to classify patients by age intervals with relative frequency
Response: Patient age has been classified by age intervals as seen in Table 1, highlighted in red.
Thanking you for your time on behalf of all co-authors and hope for a positive reply.

Sincerely and on behalf of all co-authors,

henry

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