

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Establishment of a prediction model for prehospital return of spontaneous circulation in out-of-hospital patients with cardiac arrest"(ID:87075). Those comments are all valuable and very helpful for revising and improving our paper as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. We highlighted the revised/added contents with yellow color in the revised manuscript. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: I read with interest the article "An Analysis on Factors Influencing the Pre-hospital Return of Spontaneous Circulation in Out-of-hospital Patients with Cardiac Arrest and the Establishment of a Nomogram Prediction Model". It is a complex statistical analysis of clinical data with the purpose of developing a nomogram prediction model for the outcome of patients with out-of-hospital arrest. The authors singled out several important clinical variables related to the outcome of these severe patients; age, bystander CPR, initial rhythm, CPR duration, ventilation mode and pathogeny. I find the article valuable and I have no substantial objections. Before potential publication, I advise making minor changes; Pathogenesis means comorbidity? It is necessary to state the full name of a medical term with the abbreviation in parentheses at each first appearance in the text. Is there a cut-off value (values) in this model that indicate a significant chance of establishing spontaneous circulation vs. fatal outcome? Relatively small number of cited articles related to the topic - I advise to increase the number. Literary references Edit the article according to the WJC propositions

Dear Reviewer #1:

We thank the reviewer for reading our paper carefully and giving the above positive comments. Based on your review comments, I further seriously considered the flaws and shortcomings of the article and made some modifications. The following is the specific response for your great comments.

1. "Pathogenesis means comorbidity?"

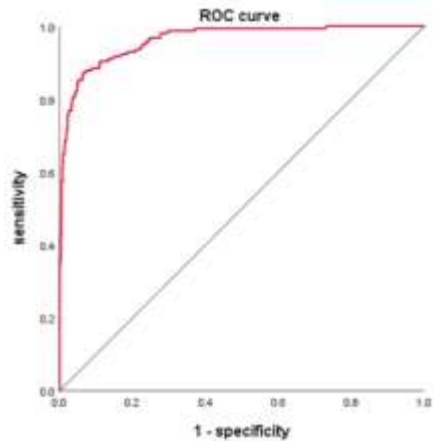
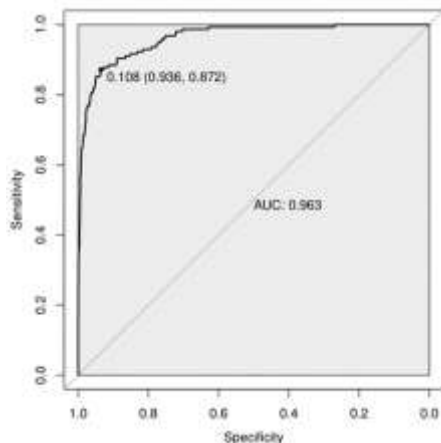
Thank you for this very insightful comment, I have to admit the existing and troubling problem in this article, owing to the fact that the collection of diagnostic information only includes the first item of diagnosis in EMR systems. Thus, in some patients, it cannot be ruled out whether the pathogenesis is a comorbidity in the disease development

2. "It is necessary to state the full name of a medical term with the abbreviation in parentheses at each first appearance in the text."

Thanks for pointing out this error, we have corrected this error in this revision.

3. "Is there a cut-off value (values) in this model that indicate a significant chance of establishing spontaneous circulation vs. fatal outcome?"

Thank you for making this valuable suggestion. Sorry for the lack of clarity, we add the description of the cut-off value in the part of discussion. In our article, the CPR duration is divided into two groups at 30 min according to the optimal cut-off value of CPR duration (27.5min). The supplementary code is as follows. In addition, we have replaced the image of ROC, with the cut-off value of the model labelled.



```
library(pROC)
library(maxstat)
library(survminer)
library(survival)
library(readxl)

# dichotomize function
dichotomize <- function (x, cutoff) {
  x_new <- ifelse(x>cutoff,1,0)
  x_new
}
# optimal cut-off for binary outcome

roc_Duration_of_CPR_nocut <-
roc(data$P_ROSC,data$Duration_of_CPR_nocut)
```

```
plot(roc_Duration_of_CPR_nocut)

cutoff_binary <-
coords(roc_Duration_of_CPR_nocut,
"best",best.method = "youden",transpose = FALSE)

data$Duration_of_CPR_nocut_dich_optimal_binary <-
dichotomize(data$Duration_of_CPR_nocut,cutoff=cutoff_binary$threshold[1]) # add [1] in case of multiple optimal cut-offs

cutoff_binary
cutoff_binary
threshold specificity sensitivity
1 27.5 0.9501779 0.8397436
```

The R code image of ROC

```
plot(roc.final,print.auc = TRUE, auc.polygon = F,lwd=2,max.auc.polygon= TRUE, print.thres = TRUE)
```

4. “Relatively small number of cited articles related to the topic - I advise to increase the number.”

Yes, the comparison experiment is important. After further reviewing the relevant literature, we added some content, highlighted the contents with yellow color in the revised manuscript, in the part of discussion, and updated the citations.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is a good, well thought study with robust statistical analysis.

However authors need to address the points below Authors should note that 1. Many abbreviations are used in this article. All abbreviations in the Text, Abstract and Figure/Legend should be preceded by their spelling in full on a prior occasion. 2. The Abstract and Text are considered separately, so in both areas this rule has to be followed independently. 3. Many abbreviations are used in the text which makes reading difficult (especially when they are not preceded by their full spelling). To make for easier reading, authors should include a list of all abbreviations and their full spelling at the beginning of the Text, before the Introduction 4. Legend for the Figure must explain fully what the figure shows, so that the Figure can be understood without looking at the Text. All abbreviations in Legend must be explained with full spelling eg ROC receiver operating characteristic, mod=? 5. There are 2 Figure 1s: ""Figure 1 Factor selection of P-ROSC via LASSO regression; Figure 1 A nomogram prediction model of P-ROSC"" 6. There is no explanation about the nomogram in the text. Furthermore in the Legend, "the corresponding value of the total score was the predicted probability of P-ROSC" needs to be phrased more clearly. Does this mean 0.9 is 90% probability? 7. There are 3 lines in the graph of Fig 3, but only one is labelled in the graph.

Dear Reviewer #2:

We greatly appreciate your positive assessment for "Accept" of our work and insightful comments. As detailed below, all the comments have been carefully considered and properly implemented in the revised manuscript.

1. "Many abbreviations are used in this article. All abbreviations in the Text, Abstract and Figure/Legend should be preceded by their spelling in full on a prior occasion."

Thanks for pointing out this error, we have corrected this error in this revision.

2. "The Abstract and Text are considered separately, so in both areas this rule has to be followed independently."

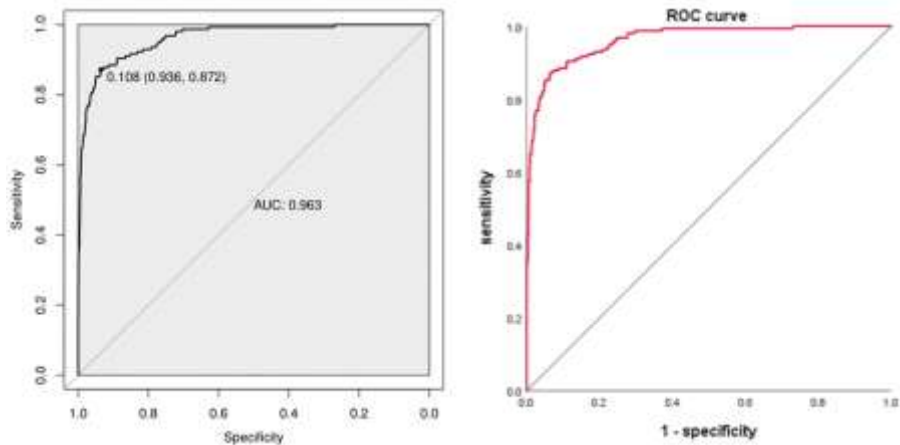
Thanks for pointing out this error. As you suggested, we have revised the abbreviations in both abstract and text

3. "Many abbreviations are used in the text which makes reading difficult (especially when they are not preceded by their full spelling). To make for easier reading, authors should include a list of all abbreviations and their full spelling at the beginning of the Text, before the Introduction"

Thanks for pointing out our error, we apologize for this negligence, and add a list of all abbreviations and their full spelling at the beginning.

4. "Legend for the Figure must explain fully what the figure shows, so that the Figure can be understood without looking at the Text. All abbreviations in Legend must be explained with full spelling eg ROC receiver operating characteristic, mod=?"

Thank you for making this valuable suggestion, we have replaced the image of ROC, with the cut-off value of the model labelled to better convey the information.



The R code image of ROC

```
plot(roc.final, print.auc = TRUE, auc.polygon = F, lwd=2, max.auc.polygon= TRUE, print.thres = TRUE)
```

5. “There are 2 Figure 1s: ”Figure 1 Factor selection of P-ROSC via LASSO regression; Figure 1 A nomogram prediction model of P-ROSC”

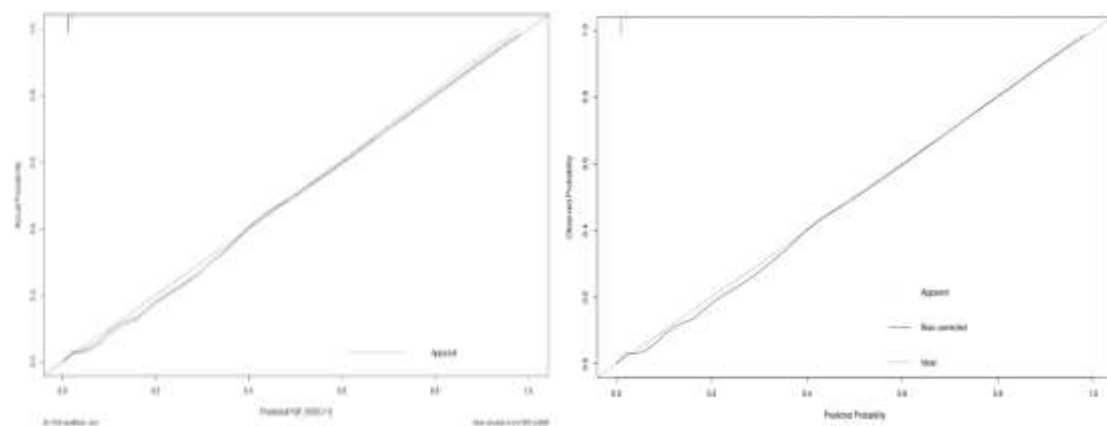
Thanks for pointing out our error, we apologize for this negligence, and have made correct changes to the annotations and references to the images

6. There is no explanation about the nomogram in the text. Furthermore in the Legend, "the corresponding value of the total score was the predicted probability of P-ROSC" needs to be phrased more clearly. Does this mean 0.9 is 90% probability?

Sorry for the lack of clarity, we have changed and re-described annotations of the images more explicitly. The revised contents are highlighted with yellow color in the revised manuscript

7. There are 3 lines in the graph of Fig 3, but only one is labelled in the graph.

Thanks for pointing out our error. Yes, there was a mistake with R software causing lack of label in the graph, we change the R code to produce a new complete without missing graph.



```
cal <- calibrate(lrm.final, method="boot", B=1000)
```

```
plot(cal,
      xlim = c(0,1),
      ylim = c(0,1),
      xlab = "Predicted Probability",
```

```
ylab = "Observed Probability",  
subtitles = FALSE)
```