Response to Reviewers' Comments

We would like to thank the reviewers for the helpful review of our manuscript. Their comments and suggestions have significantly improved the manuscript. We have addressed all the comments and reworked our manuscript accordingly.

Reviewer #1

Major comments:

1. ***In the Abstract, clarify the source of the validation data set and the distribution of the derivation and validation cohorts.***

Response:

Thank you for the comment. The whole study cohort is comprised of adult heart transplant recipients between 2000 and 2015 extracted from the UNOS registry. The dataset was randomly split into a derivation set (80%) and a validation set (20%). As per reviewer's suggestion, we have reworked the "Abstract" section and the revised texts were highlighted in yellow color.

2. ***How were the patients divided into the derivation and validation cohorts? Randomly allocated?***

Response:

The whole dataset was randomly split into a derivation set (80%) and a validation set (20%). To eliminate selection bias, the distribution of each variable in the two sets was compared using statistical tests. The results shown in Table 1 can verify that there is no significant difference between the derivation and validation sets. To further clarify this, we have provided more explanations in the "Abstract" and the "Statistical analysis" Section. The texts were highlighted in yellow color.

3. ***What is the point of including drugs that are no longer used (OKT3 and daclizumab) in the analysis? If OKT3 and daclizumab were omitted from the analysis, I wonder if ATGAM or basiliximab would emerge as risk factors, which would be a more clinically-relevant result…***

Response:

Thank you for the comment. We have conducted extra analysis by excluding the induction drugs of OKT3 and daclizumab. After deleting the two drugs, ATGAM and basiliximab were not shown up to be significant. A new section "*Prediction of cSCC without OKT3 and daclizumab*" was added to the manuscript to present the new results. The new section was highlighted in yellow color.

4. ***The presence of coronary artery disease and CHD are likely surrogates for patient age.***

Response:

Thank you for the comment. We have tested the correlation between patient age and coronary artery disease as well as CHD using ANOVA. There is a strong correlation (p-value <0.05) between patient age and the two diseases. We have added a statement in the second graph in the "DISCUSSION" section to clarify this.

5. ***In Table 5, should the high-risk group be compared to the low- and very-low risk groups?***

Response:

Thank you for the comment. We have compared the high-risk group to the low- and very-low risk group in the "Risk Stratification" section and in Table 5. Please see the texts highlighted in yellow color.

6. ***An important limitation is the use of a single data source for the derivation and the validation cohorts and it should be explicitly stated that these findings will need to be replicated in a separate patient population and ideally prospectively.***

Response:

Thank you for the comment. We have explicitly stated this limitation in the "Limits of the study" section. The revised texts were highlighted in the manuscript.

7. ***In the title, I would specify that adult cardiac allograft recipients were studied.***

Response:

Per the suggestion of the reviewer, we have specified that adult cardiac allograft recipients were studied in the title.

Reviewer #2

Major comments:

1. ***Just add the limitation of a retrospective design of the paper.***

Response:

Thank you for the comments. We have added this limitation in the Section of “Limits of the study”. The texts were highlighted in yellow color.