

Peer Review File

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Reviewer Comments

This is a novel study to develop a nomogram to determine post LT survival in patients with HBV-ACLF. There is value to this paper, but several comments would need to be addressed

1. The primary concern is the nomogram is imprecise. This is particularly the case regarding the white blood cell count, where the picture is in increments of five. Therefore, if a white count is 7.7, how is the clinician supposed to determine the number of points? The alt/ast ratio is also imprecise in increments of 2. The authors treated this as a continuous variable but did not indicate that this variable is rounded to increments of 2. Therefore, this could lead to further imprecision

For this paper and nomogram to be of real value, the authors should create an online calculator, where specific inputs are entered to determine the number of points and prognosis estimation. The majority of publications which create a scoring system are not creating an online calculator. Otherwise, it is difficult to justify using this nomogram in clinical practice. The digital version should be retested and compared to other scores (clifc acf, etc)

Reply: Thanks for the nice advice. We have created an online calculator of the nomogram (<https://hbv-aclf-nomogram.shinyapps.io/dynnomapp/>) and added the description in our results (see Page 13, line 18-21; Page 14, line 1). In this online calculator, clinicians can enter corresponding patients' data included in the nomogram to get instant prognostic estimation.

2. The authors have demonstrated number of organ failures as an important variable. However, not all organ failures are equal. I would like to see univariable analysis regarding the type of organ failure. If there is a difference between organ failure type affecting post LT mortality, then each specific organ failure (lung, circulatory etc) should be used in the multivariable analysis.

Reply: Thanks for the good suggestion. We have performed univariable analysis regarding each type of organ failure in order to compare contribution of different organ failure type. We found that each type of organ failure is significant in univariable analysis. However, when these variables are entered into multivariable analysis with other significant variables, type of organ failure is not significant (Table 2). This could be explained by the confounding effect of number of organ failure. Thus, we did not make change to the nomogram based on current combination. To further compare the role of different type of organ failure, we compare the survival statistics and performed survival curves among subgroups divided by type of organ failure (see Page 10, line 20-21; Page 11, line 1, line 12-15; Supplemental Figure 2, Supplemental Table 3). Patient with cardiovascular, brain and lung failure had a higher 1-year mortality rate than other types of organ failure. These results highlight a careful decision for transplantation on patients present with certain organ failures. (see Page 17, line 8-12)

3. A few references should be added. I would add Artzner et al, *ajt* 2020 and the authors should comment if they compared the nomogram to the TAM score. If they were unable to do so, they should also state. In addition, the authors should comment on how the nomogram does not account for improvement in organ failure prior to LT (cite Sundaram et al, *J Hep* 2019).

Reply: Thanks for the nice advice. The TAM score model consists of arterial lactate level, mechanical ventilation, age and leukocyte counts (*Am J Transplant.* 2020;20(9):2437-48). Since the data of arterial lactate level was not available in our hospital information system, we were unable to collect this data to compare our nomogram to TAM score. (see Page 18, line 18-21; Page 19, line 1)

Sundaram et al. found that patients who recovered from ACLF-3 at registration to ACLF 0-2 at transplantation, had a significantly higher one-year survival after transplantation (*J Hepatol.* 2020;72(3):481-8). Despite ACLF grade alteration from registration to transplantation, final ACLF grade at LT had a more decisive role in predicting survival, which may provide some hints for clinician in evaluation patients for liver transplantation. Also, longer time of final ACLF grade which patient developed before transplantation may indicate poorer post-LT survival, though relevant data is not statistically significant. Our nomogram derived from clinical features within 1 week before transplantation and did not include data at registration for waitlist, which is restricted by the availability of registry data. Thus, the predictive ability of the nomogram is more reflective of final ACLF grade before liver transplantation. If patients of ACLF-3 grade at registration downgrade to ACLF 0-2 grades before LT, nomogram points will be smaller due to decreased number of organ failures. These downgraded patients will have a better survival probability based on our nomogram. (see Page 17, line 17-21; Page 18, line 1-8)

Minor points:

1. do not abbreviate alt/ast ratio. This should be written out as it is not a commonly used abbreviation

Reply: Thanks for the good suggestion. Abbreviation of alt/ast ratio used in the article has been written out in an appropriate way.

2. For limitations, the authors need to state that their findings are specific to hbv and may not apply to other etiologies

Reply: Thanks for the good advice. Since the nomogram is derived from HBV-ACLF patients, it may not be applied to other etiologies. We had added this statement in Discussion (see Page 19, line 10-12)