

Peer Review File

Article information: <https://dx.doi.org/10.21037/apm-21-1012>

Comment 1: I am not sure why the authors submitted this manuscript to Annals of “Palliative Medicine”. I recommend the authors to submit this study for more transplant-specific journals.

Reply 1: Thank you for your kind recommendation. *Annals of “Palliative Medicine”* covers multiple disciplines, including oncology, psychology, surgery, nursing, public health, education, and so on, focusing on the frontier development of preclinical research to clinical research, and has gained a certain reputation internationally. Since 2018, *Annals of Palliative Medicine* has published more than 10 high-quality articles in the field of organ transplantation. It is a great encouragement and honor for us to be recognized by the editorial Office and published in this journal. Therefore, we submitted this manuscript to *Annals of “Palliative Medicine”*.

Comment 2: Methods: Please describe the reason why the recipients diagnosed with vascular thrombosis during the first 7 days after OLT were excluded.

Reply 2: Thank you for your suggestion. The point you mentioned is the key to our repeated consideration in the preparatory phase of the research. We read a lot of papers and found that similar studies have excluded patients with vascular embolism within 7 days after surgery, (ref 17 and 18 in the manuscript). EAD reflects the early graft dysfunction after transplantation and the poor recovery of liver function in the early stage after transplantation, which is directly reflected in the increase of laboratory indexes. However, vascular thrombosis within the first 7 days after transplantation is regarded as non-hepatogenic trigger leading to the increase of liver enzyme indexes, which interferes with the statistical results of prognosis. Therefore, when we sought accurate and rigorous statistical design, we should eliminate this interference factor.

Changes in the text: we added some reasons about regarding it as one of the exclusion criteria (see Page 5, line 108-110).

Comment 3: Table 2: Statistical method to compare AUROCs should be explained.

Reply 3: Thank you for your suggestion. We used the MedCalc software and DeLong's test reported by DeLong et al (1988) to judge the statistical difference

between AUROCs.

Changes in the text: We added the statistical method for comparing AUROCs in Method section (see Page 7, line 149-150).

Comment 4: Table 3: The authors need to evaluate the ABO compatibility instead of donor/recipient blood type.

Reply 4: Thank you for your suggestion. ABO incompatibility can cause rejection and impair liver function after OLT. We added this information in the revised manuscript according to your suggestion.

Changes in the text: Table 3.

Comment 5: Please compare postoperative requirement of dialysis in the high- and low- MELDPOD5 groups.

Reply 5: Thank you for your suggestion. As suggested, we have collected data about the postoperative requirement of dialysis in our database. We found a higher proportion of postoperative requirement of dialysis in patients with EAD and the difference was statistically significant ($P < 0.001$). More details have been added in the manuscript.

Changes in the text: we have modified our text and Table 3 as advised (see Page 11, line 229-231 and Page 13, line 291-293).

Comment 6: Please add captions for Fig. S4 (A)-(F). Are those Kaplan-Meier Curves represent patient survivals of graft survivals.

Reply 6: Thank you for your suggestion. As suggested, we added captions and some expressions in the figure legend of Fig.S4.

Changes in the text: Fig. S4 and its figure legend.

Comment 7: As compared to the Olthoff EAD criteria and the MEAF score, the MELDPOD5 showed preferable predictive power for graft/patient survival, however, the Olthoff EAD criteria and the MEAF score remained to have definite predictive abilities (Fig. 2, 3, S2, S3). What will be expected in clinical liver transplantation when the MELDPOD5 will be used instead of the Olthoff EAD criteria and the MEAF score?

Reply 7: Thank you for your comments. It is of great clinical relevance to find an early transplant outcome that would be related to graft or patient survival. EAD is one

of the most important outcomes serving for this aim. However, recently there are studies showing that the most frequently used Olthoff EAD criteria is not a good predictor for graft survival (ref 24 in the manuscript). Particularly, it is under hot debates whether the Olthoff EAD criteria is a good end-point in the trials related to liver machine perfusion. Therefore, the researchers in the field have been trying to find a better EAD criteria. MELDPOD5 is a linear parameter easily calculated by the online calculator. In our study, the results showed that MELDPOD5 can better predict patient or graft survival than the Olthoff EAD criteria and MEAF score. Therefore, MELDPOD5 might be a better EAD criteria for assessing post-transplant patient outcomes and serving as a better end-point in clinical trials.

Changes in the text: Page 14, Line 296-298.

Comment 8: Discussion: Authors described that "EAD indeed has predictive value for both short-term and long-term prognosis in our center. " The one-year postoperative monitoring was not long enough to evaluate long-term outcome. Did the MELDPOD5-defined EAD correlate with early postoperative outcomes such as Clavien-Dindo morbidity classification, length of hospital/ICU stay?

Reply 8: Thank you for your suggestions. Just as you emphasized in the question whether the long-term survival rate can be better reflected in our article, we reviewed the manuscript and believed that the 12-month survival rate and the long-term survival rate should not be equated here. Therefore, in the revision, we have revised our conclusions about EAD for long-term prognosis.

As you mentioned, Clavien-Dindo morbidity classification is a compelling tool for evaluating patient prognosis and surgical quality after surgery. However, in our transplant center, the classification is not routinely used. Therefore, the clinical data about it has not been fully collected, and retrospective analysis of these data would result in apparent errors. The lack of Clavien-Dindo morbidity classification is a limitation of our research. In the future, we intend to construct a Clavien-Dindo morbidity classification database during follow-up, and explore its clinical value in our center.

As you suggested, we re-evaluated the patient's postoperative conditions including ICU and hospital stay. We found that the ICU stay ($P < 0.001$) and hospitalization ($P = 0.003$) of the EAD (defined by MELDPOD5) group increased significantly, compared with the Non-EAD group.

Changes in the text: we modified our text as advised (see Table 3, Page 11, line 231-232, Page 13, line 290-295 and page 14, line 303-306).

Comment 9: Authors described that "though MELDPOD5 has shown extraordinary predictive power in Chinese and European single-center research, this cannot be generalizable to most transplant centers in different continents. The differences in people from different ethnic and regions call for a global large-scale multi-center study to reach a consensus." I do agree with those suggestions.

Reply 9: Thank you for your comment.

Comment 10: Please correct multiple typos (page 2, line 75, showed>shown; page 5, line 188, decease>deceased; etc.).

Reply 10: Thank you for pointing out our mistakes, which improves the quality of our manuscript.

Changes in the text: we revised our text as advised (see Page 12, line 264 and Page 14, line 301).