Letter to the Editor

Early allograft dysfunction discovery and prognosis: does the Model for End-stage Liver Disease still prevail?

Yong-Fa Huang[1,2#], Jing-Yi Liu[1,2,3#], Li-Ying Sun[1,2,3], Zhi-Jun Zhu[1,2]

[1]Liver Transplantation Center, National Clinical Research Center for Digestive Diseases, Beijing Friendship Hospital, Capital Medical University, Beijing, China; [2]Clinical Center for Pediatric Liver Transplantation, Capital Medical University, Beijing, China; [3]Department of Critical Liver Diseases, Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China

[#]These authors contributed equally to this work.

Correspondence to: Zhi-Jun Zhu. Liver Transplantation Center, National Clinical Research Center for Digestive Diseases, Beijing Friendship Hospital, Capital Medical University, 95 Yong-An Road, Xicheng District, Beijing 100050, China. Email: zhu-zhijun@outlook.com.

Comment on: Luo T, He SJ, Chen SR, *et al.* Prediction of post-transplant graft survival by different definitions of early allograft dysfunction. Ann Palliat Med 2021;10:8584-95.

Submitted Jun 20, 2022. Accepted for publication Sep 01, 2022.
doi: 10.21037/apm-22-758
View this article at: https://dx.doi.org/10.21037/apm-22-758

We read with great interest in the article by Luo *et al.* about comparison among Olthoff criteria, the Model for End-stage Liver Disease (MELD) score on postoperative day 5 (MELDPOD5), and the Model for Early Allograft Function scoring (MEAF) on their prognostic value for post-transplant graft and patient survival (1). Though all three metrics discriminated the high-risk patients from others effectively, MELDPOD5 displayed quite an advantage over MEAF and Olthoff criteria in predicting 3-month graft survival. Moreover, donor body mass index, donor risk index, intraoperative transfusions, recipient hypertension, and preoperative total bilirubin were identified as predictive factors for MELDPOD5-defined early allograft dysfunction (EAD).

Since EAD is a clinical diagnosis rather than a histopathological term, gold standards including biopsy are not applicable in this situation, and different diagnostic criteria or scoring systems should be naturally calibrated to patients' prognosis. As the first definite system and the most widely accepted one, Olthoff criteria was born from the summation of clinical practice and was then assessed for predicting allograft loss or death (2). MEAF was designed to be a numerical scale for EAD diagnosis: alanine aminotransferase, international normalized ratio, and bilirubin were linearized and then attributed with the same weights in the final formula—the maximum possible values of the three terms were all 3.33 (3). Both Olthoff criteria and MEAF subjectively treat different laboratory findings relatively equally, which might compromise their diagnostic and prognostic performances.

The MELD, on the other hand, was developed initially with Cox proportional-hazards regression for short-term survival of cirrhotic patients after transjugular intrahepatic portosystemic shunt (4). In this way, the hazard ratio from regression served as proper weights for different laboratory findings with an objective, statistical basis. It was quickly extrapolated to various other chronic liver disease settings, and finally accepted as a tool for liver allocation after several amendments regarding the sickest-first priority (5). Though several attempts have been made to explore the long-term prognostic value of pre-transplant MELD before (6), it was not until 2013 that MELD was formally extrapolated to post-transplant population with satisfactory performances (7). Nevertheless, it remains controversial whether the pre-transplant recipient sieving with MELD adds to its post-transplant prognostic strength, and whether the weights of different laboratory findings should be adjusted since post-transplant patients are relieved of "end-stage liver diseases". Moreover, integrating all laboratory tests into one score might lose information, since a recent study reported that EAD patients with merely either aminotransferase elevated had comparable graft and patient survival to those of patients without EAD (8).

Recipient preoperative systemic hypertension was identified as a risk factor for EAD in this article for the first time. The aberrant levels of vasoactive agents and compromised arteriole constriction-relaxation might

contribute to the hazard imposed by systemic hypertension, and further studies should be conducted to confirm this effect. It has been recognized that the donor condition exerted a significant impact on the risk of EAD. Considering the paucity of donated liver, marginal donor has been increasingly adopted to extend life expectancy of those with longer waiting time (9). Since the cohort featured a relatively high proportion of tumor as the indication, we suggest the authors to perform subgroup analysis in order to clarify the effect of donor condition on EAD in tumor patients. This information could be of great help for tumor patients to weigh benefits versus risks of accepting a compromised allograft. With the emerging machine perfusion technology, *ex vivo* repairing of allografts before implantation might serve as an alternative in the near future (10). Clinical trials, including Bridge for HOPE: Hypothermic Oxygenated Perfusion Versus Cold Storage Prior to Liver Transplantation (ClinicalTrials.gov identifier NCT05045794), are under way, and we are looking forward to the new hope for patients and their family.

Acknowledgments

Funding: This work was supported by Capital's Funds for Health Improvement and Research (No. 2020-1-2024).

Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-758/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Luo T, He SJ, Chen SR, et al. Prediction of post-transplant graft survival by different definitions of early allograft dysfunction. Ann Palliat Med 2021;10:8584-95.
2. Olthoff KM, Kulik L, Samstein B, et al. Validation of a current definition of early allograft dysfunction in liver transplant recipients and analysis of risk factors. Liver Transpl 2010;16:943-9.
3. Pareja E, Cortes M, Hervás D, et al. A score model for the continuous grading of early allograft dysfunction severity. Liver Transpl 2015;21:38-46.
4. Kim WR, Mannalithara A, Heimbach JK, et al. MELD 3.0: The Model for End-Stage Liver Disease Updated for the Modern Era. Gastroenterology 2021;161:1887-1895.e4.
5. Ravaioli M, Lai Q, Sessa M, et al. Impact of MELD 30-allocation policy on liver transplant outcomes in Italy. J Hepatol 2022;76:619-27.
6. Yoon JU, Yoo YM, Byeon GJ, et al. The impact of pretransplant hepatic encephalopathy, model for end-stage liver disease (MELD) scale on long-term survival following deceased donor liver transplantation: a retrospective study. Ann Palliat Med 2021;10:5171-80.
7. Wagener G, Raffel B, Young AT, et al. Predicting early allograft failure and mortality after liver transplantation: the role of the postoperative model for end-stage liver disease score. Liver Transpl 2013;19:534-42.
8. Wang K, Lu D, Liu Y, et al. Severity of early allograft dysfunction following donation after circulatory death liver transplantation: a multicentre study. Hepatobiliary Surg Nutr 2021;10:9-19.
9. Villard C, Westman J, Frank J, et al. The potential use of extended criteria donors and eligible recipients in liver transplantation for unresectable colorectal liver metastases in Central Sweden. Hepatobiliary Surg Nutr 2021;10:476-85.
10. Robin F, Jeddou H. Comment on "Hypothermic machine perfusion in liver transplantation-a randomized trial". Hepatobiliary Surg Nutr 2021;10:364-6.

Cite this article as: Huang YF, Liu JY, Sun LY, Zhu ZJ. Early allograft dysfunction discovery and prognosis: does the Model for End-stage Liver Disease still prevail? Ann Palliat Med 2022;11(10):3367-3368. doi: 10.21037/apm-22-758

