

Assessing Influences of Perioperative Transfusion on Early- and Late-Term Outcomes after Living Donor Liver Transplantation: Methodological Issues

Fu-Shan Xue, Ming Tian

Department of Anesthesiology, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China

To the Editor: In a retrospective study by Zheng *et al.*^[1] assessing the influences of perioperative single-donor platelet apheresis and red blood cell transfusion on 90-day and overall survival in 126 recipients who underwent their first adult-to-adult living donor liver transplantation (LDLT), multivariate regression analysis showed that platelet transfusion was only associated with postoperative early-term mortality, but had no significant impact on postoperative overall long-term mortality. Furthermore, units of red blood cell transfusion were independent predictors of postoperative long-term outcomes. Given that perioperative blood transfusion has been associated with postoperative outcomes of LDLT patients, their findings have potential implications. However, this is a retrospective study, which can introduce a number of potential confounders. Although they have done a valuable job, some methodological issues seem important to avoid any optimistic interpretation or misinterpretation of their results.

First, we noted that compared to the recipients without platelet transfusion, the recipients with platelet transfusion had the higher preoperative end-stage liver disease score, Child–Pugh classification, international normalized ratio, and total bilirubin level and lower preoperative hemoglobin level and platelet counts. All of those suggest that patients with platelet transfusion have more serious preoperative conditions, which can adversely affect postoperative outcomes of LDLT patients.^[2] In our opinion, no matter how refined the adjustment is for differences in preoperative conditions, it is never possible to ensure a complete adjustment for differences between patients with and without platelet transfusion. Furthermore, multivariate regression analysis cannot differentiate whether platelet transfusion is a true determinant of postoperative early-term mortality or simply a synthetic manifestation of worsened preoperative conditions that can significantly increase postoperative early-term mortality. Although platelet transfusion in this study is associated with increased postoperative early-term mortality, the leap from association to causation is impossible with the retrospective design. Considering that the positive impact of platelets has been recently implicated in patients undergoing LDLT and postoperative low platelet counts after LDLT has been shown as a predictor of early-term adverse outcomes,^[3] we argue that the large-scale randomized controlled clinical trials are still needed to

determine whether there is a causal relationship between platelet transfusion and postoperative early-term mortality in patients undergoing LDLT.

Second, compared to the recipients without platelet transfusion, the recipients with platelet transfusion had a larger intraoperative blood loss and transfusion volume. However, the readers were not provided with intraoperative hemodynamic management. In fact, intraoperative fluctuation of mean blood pressure has been shown as an independent predictor of early-term mortality following LDLT.^[4] Most importantly, postoperative complications were not provided. In available literature, early postoperative hypoalbuminemia has been significantly associated with the overall mortality after LDLT. Furthermore, acute kidney injury is a frequent complication of LDLT patients and is a significant risk factor of increased early- and late-term mortality.^[5] In addition, postoperative allograft dysfunction, postreperfusion syndrome, intra-abdominal or gastrointestinal bleeding, pulmonary or infectious complications, sepsis, biliary tract complications including biliary stenosis or leakage, major vascular complications including isolated or combined hepatic artery, portal vein and hepatic vein thrombosis or stenosis, and multiple-organ failure, are the independent risk factors of increased early- and late-term mortality after LDLT. In a retrospective study, multivariate regression analysis is indeed useful for adjusting potential confounders and controlling selection biases. However, an important limitation of this statistical method is the assumption of a particular mathematical relation between intervention and measured outcome. To obtain the true inferences of multivariate regression analysis for adjusted hazard ratio of measured outcome, all of known risk factors affecting measured outcome must be taken into the model as much as possible. If an important risk factor is missed, multivariate adjustment for hazard

Address for correspondence: Prof. Fu-Shan Xue,
Department of Anesthesiology, Beijing Friendship Hospital,
Capital Medical University, No. 95 Yong-An Road, Xi-Cheng District,
Beijing 100050, China
E-Mail: xuefushan@aliyun.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

© 2018 Chinese Medical Journal | Produced by Wolters Kluwer - Medknow

Received: 09-03-2018 **Edited by:** Qiang Shi

How to cite this article: Xue FS, Tian M. Assessing Influences of Perioperative Transfusion on Early- and Late-Term Outcomes after Living Donor Liver Transplantation: Methodological Issues. *Chin Med J* 2018;131:1259-60.

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.4103/0366-6999.231526

ratio of measured outcome can be biased and even a spurious association between intervention and outcome of interest may be obtained. We are concerned that no inclusion of intraoperative hemodynamic variables and postoperative complications into the model would have tampered with the inferences of multiple regression analysis when assessing association between platelet transfusion and postoperative mortality.

Finally, the endpoints of this study included the early-term outcome assessed by 90-day cumulative survival rate and the late-term outcomes assessed by 1-, 3-, and 5-year cumulative survival rates. It must be emphasized that there are significant differences in mortality risk factors between early and late periods after LDLT. The early-term mortality is most likely related to the surgery and perioperative managements, whereas the late-term mortality is significantly attributable to the appearance of late surgical complications, recurrence of diseases, or complications of long-term immunosuppression, such as infection, malignancy, and renal failure.^[2] Thus, use of the same perioperative variables and statistical methods to assess influences of perioperative platelet and red blood cell transfusions on early- and late-term adverse outcomes after LDLT is inappropriate. Perhaps, this is a possible reason for finding of this study that platelet transfusion has different effects on postoperative early- and late-term mortality.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Zheng W, Zhao KM, Luo LH, Yu Y, Zhu SM. Perioperative single-donor platelet apheresis and red blood cell transfusion impact on 90-day and overall survival in living donor liver transplantation. *Chin Med J* 2018;131:426-34. doi: 10.4103/0366-6999.225049.
2. Jadowiec CC, Taner T. Liver transplantation: Current status and challenges. *World J Gastroenterol* 2016;22:4438-45. doi: 10.3748/wjg.v22.i18.4438.
3. Li L, Wang H, Yang J, Jiang L, Yang J, Wang W, *et al.* Immediate postoperative low platelet counts after living donor liver transplantation predict early allograft dysfunction. *Medicine (Baltimore)* 2015;94:e1373. doi: 10.1097/MD.0000000000001373.
4. Chung HS, Jung DH, Park CS. Intraoperative predictors of short-term mortality in living donor liver transplantation due to acute liver failure. *Transplant Proc* 2013;45:236-40. doi: 10.1016/j.transproceed.2012.06.077.
5. Park MH, Shim HS, Kim WH, Kim HJ, Kim DJ, Lee SH, *et al.* Clinical risk scoring models for prediction of acute kidney injury after living donor liver transplantation: A retrospective observational study. *PLoS One* 2015;10:e0136230. doi: 10.1371/journal.pone.0136230.