

Dear Dr. Ma :

Thank you for giving us an opportunity to revise our manuscript. We would also like to thank the reviewers for providing good suggestions. We have revised our manuscript in accordance with the reviewers' suggestions. The point-by-point responses to your comments are provided below.

Reviewer: 1

This manuscript from authors have demonstrated the progress of Pediatric living donor liver transplantation and its good outcomes over one decade in Shanghai. The language of the manuscript is well written. It would be a good addition to the existing literature highlighting progress of PLDLT in Shanghai.

Response:

We appreciate the reviewer's positive comments about our study and agree that the study will be a good summary about the progress of pediatric living donor liver transplantation over one decade in Shanghai and will help to further improve the progress of PLDLT in the future.

Reviewer: 2

This is an overview about the pediatric transplantation and their development in Shanghai. However, there are no new informations how to deal in this subspecialty in transplantation. It is only a description of the program. Not more. I do not recommend the publication in WJG.

Response:

We respectfully but strongly disagree that this study is only a description of the program. In the present study, we not only provided an overview about pediatric transplantation and its development in Shanghai but also analyzed the data. We found that PELD score, operation duration, and ICU length of stay were independent

predictive factors of 1- and 3-year patient survival. The risk factors of survival after pediatric transplantation are still not confirmed. Our study provides important information in this field. We hope that our study will help in improving pediatric survival rate in the future.

Reviewer: 3

The manuscript describes the review of authors' own data of pediatric living donor liver transplantation in high volume center in Shanghai and concluded that PELD score, operation duration, and ICU length of stay were independent predictive factors of 1-year and 3-year patient survival. Since case number and analysis are satisfactory and the results in China is worthwhile, the manuscript deserves publication in World Journal of Gastroenterology. Minor comments: I suggested in the attached file. Especially, use of abbreviation should be reconsidered for the convenience of readers.

Response:

Thank you for your kind feedback. We have revised the manuscript according to your suggestion.

Reviewer: 4

1. Dear authors, thank you for submitting your paper to the World Journal of Gastroenterology, it is certainly an interesting topic that will be valuable to the transplant community. However, there are few comments I like to include in my review and here are they; 1- The title of the paper is very confusing and does not reflect the topic or the contents of the paper, it reads like you are studying the donor population and not the recipients. I think you may consider correcting it to something like this: Pediatric live-donor liver transplant recipients, decade progress in Shanghai: characters and risk factors of mortality.

Response:

Thank you for your suggestion and kind comments. Although we included donor data, we mainly focused on the recipients and not the donors. We have revised the title

according to your suggestion as follows: **Pediatric living donor liver transplantation recipients, a decade's progress in Shanghai: characters and risks factors of mortality.**

2- There are few paragraphs that hard to understand due to the way there were written, that includes the results section, I suggest consulting with an academic secretary with advanced experience with the English language.

Response:

We have revised and rewritten some of the paragraphs. Furthermore, the whole manuscript has been proofread by a professional language editing company (Enago). We hope that the revised manuscript is now acceptable for publication.

3- Do you think that the ICU admission and length of the stay and/or ICU management that led to the poor outcomes? Or simply that the patients who required prolonged ICU care were sicker and/or had complicated intra-operative course that resulted in prolongation of their ICU stay?

4- Can you look at the group that spent more ICU time and compare their pre-operative data and intraoperative data to the group who spent less time in the ICU? I think that will answer this question.

Response:

Many studies have shown that long-stay patients (LSPs) in pediatric ICUs have higher mortality rates than short-stay patients ^[1, 2]. The mortality rates for LSPs and short-stay patients were 17.4% and 7.3%, respectively ^[2]. Furthermore, prolonged ICU length of stay is associated with increased hospital mortality and impaired patient and graft survival after liver transplantation ^[3]. Prolonged ICU length of stay may be due to the medical conditions of the patients, management-related progress between ICU and wards, and different medical care habits of different physicians.-Whatever maybe the reason, our data demonstrated that prolonged ICU length of stay is a

predictive factor of long-term survival of patients. Even if prolongation of ICU stay is because patients are sick or because they have a complicated intraoperative course, ICU length of stay, as a result of multiple factors, predicts the patients' outcome.

We also agree with reviewer that it would be interesting to see whether ICU length of stay *per se* leads to poor outcomes. To address this, we performed propensity score matching adjustment to clarify the role of ICU stay in survival rate. We applied 1:1 nearest neighbor matching without replacement to ensure that conditional bias was minimized. We choose 0.1 as the caliper width. Propensity score, ICU length of stay, length of surgery, and PELD score were included into multivariable Cox regression analysis. After PSM adjustment, we found that ICU length of stay was still a predictive factor of patients' 3-year survival ($P = 0.046$). These results indicate that, even for patients with similar conditions, longer ICU stay is detrimental for long-term survival and that a shorter ICU stay should be pursued for these patients in the future. We have added these points to the Discussion section.

5- How the ICU care have changed over the course of the years that you looked at in your study.

Response:

To the best of our knowledge, ICU management has made the following progress:

1. Tacrolimus/cyclosporine A plus corticosteroids or combined with mycophenolate mofetil are used as immunosuppressive drugs in all children after operation. Compared with cyclosporine A, tacrolimus has a more satisfactory effect in inhibiting rejection and has fewer adverse effects ^[4]. Since 2010, mainly tacrolimus rather than cyclosporine A has been used as an immunosuppressant in Shanghai.
2. Postoperative infection, particularly pulmonary infection, is one of the main reasons for postoperative death in pediatric LDLT ^[5]. Therefore, rational use of antibiotics and immunosuppressants and postoperative laminar flow ICU are important for the reduction of postoperative infections. With increased experience in

ICU management, the postoperative infection rate of children at our center has significantly decreased since 2010, ensuring early postoperative recovery of children. ICU length of stay has shortened significantly since 2010. We have added these points to the Discussion section (page 14, paragraph 3).

REFERENCES

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- 4 Otte JB. Pediatric liver transplantation: Personal perspectives on historical achievements and future challenges. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society* 2016; **22**(9): 1284-1294 [PMID: 27096329 DOI: 10.1002/lt.24470]
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