# Answering Reviewers

Dear Editor,

We feel appreciated for your letter and the comments about our paper (Manuscript NO.: 75624). We have carefully checked the manuscript and revised it in line with the comments of reviewers and editorial office. We submit here the revised manuscript together with a list of changes. If you have any question about this manuscript, please don't hesitate to let me know.

**Response to reviewer # 1:**

Thank you for your recognition of our research. Our answers to your comments are as follows:

**1.How do authors define end stage AE?**

The end-stage hepatic AE described in this study bases on the "Stage-specific criteria to alveolar echinococcosis" of Expert Consensus WHO-Informal Working Group on Echinococcosis [1]. Although some end-stage hepatic AE can be treated with hepatectomy surgery, but it is difficult to perform radical hepatectomy in vivo when AE lesion invades the hepatocaval confluence. Fortunately, ex-vivo liver resection and auto-transplantation (ELRA) can better realize the radical resection of end-stage hepatic AE with severely compromised outflow tract, and the reconstruction of the affected vessels.

The ELRA indication that we are following is: extensive AE lesions

with hepato-caval confluence and involvement of three hepatic veins, involvement of up to tertiary portal and arterial branches requiring critical reconstruction, patients with graft volume ≥40% of estimated standard liver volume (ESLV); patients with total bilirubin level higher than twice the upper limit of normal value (≤60 lmol/L) [2].

## 2. How did the authors calculated the degree of involvement like 120 degree, was it on pre op assessment or in the OR?

The evaluation of RHIVC involvement and lumen defect contained preoperative assessment and intraoperative reevaluate. Firstly, all subjects received abdominal computed tomography angiography (CTA) and three-dimensional reconstruction (3DR) before surgery, aiming to assess the extent of vessels involvement. For patients whose CTA results suggested RHIVC severe stenosis or occlusion, IVC digital subtraction angiography (DSA) was also performed. During the operation, we will further confirm the degree of vascular defect under direct vision after radical resection of AE lesion. Finally, the surgical team makes the final decision after consultation.

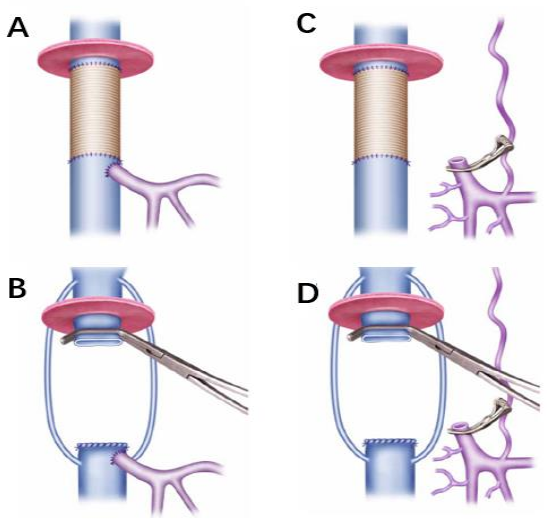
## 3.Is there any role of using albendazole therapy before surgery, as in this study only 27 patients were given albendazole before surgery?

Currently, there is no clear consensus on whether albendazole therapy

before surgery is effective. However, as most of the patients come from northwest areas with underdeveloped medical services, patients do not have access to advanced medical advice in time. In addition, all of the 27 patients were receiving albendazole therapy before presenting to our center. Based on the latest clinical guidelines, our center recommends 2 years of albendazole therapy after surgery.

## 4. Was any venous bypass used in the patients? Its surprising to see that there were no bowel congestion after average of 4-6 hours of anhepatic phase?

In our center, whether a venous bypass is necessary depends on the intraoperative evaluation. The rules we follow are presented as follows [2]: (A) For those with unstable hemodynamic situation, poor intestine condition and inadequate collateral circulation, both of caval reconstruction and porto-systemic shunt were required. (B) For those with stable hemodynamic situation and good intestine condition but with inadequate collateral circulation, caval reconstruction alone was performed. (C) For those with poor intestinal condition but with adequate collateral circulation, porto-systemic shunt alone was mandated. (D) Regarding patients with stable hemodynamics and rich collateral circulation without intestinal congestion, neither porto-systemic shunt nor caval reconstruction was performed.




## 5. what was incidence of bile duct strictures after surgery in this population?

Based on our previous data from 114 patients, the incidence of bile duct strictures was 4.39% (5/114). In addition, Zeng et al. [3] reported a 5.45% incidence of bile duct strictures in 55 patients with hepatic AE who received ELRA, closing to our results.

## 6. Were there any recurrences in the patients?

The current recommendations for alveolar echinococcosis management consider the cancer-like nature of the disease, and thus employ the model of cancer care management, with interdisciplinary team consultations for therapeutic decisions, the combination of surgical and drug treatments, a long-term follow-up as well as health education of patients [4]. Since the Ex vivo liver resection and auto-transplantation (ELRA) were first reported by our team for end-stage hepatic AE patient in 2011[5], no postoperative recurrence has been reported so far.

# References

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[2] Aji T, Dong J H, Shao Y M, Zhao J M, Li T, Tuxun T E H J, Shalayiadang P, Ran B, Jiang T M, Zhang R Q, He Y B, Huang J F, Wen H. Ex vivo liver resection and autotransplantation as alternative to allotransplantation for end-stage hepatic alveolar echinococcosis. J Hepatol. 2018: 1037 [PMID: 447267500009 DOI:10.1016/j.jhep.2018.07.006].

[3] Xintao Zeng, Xianwei Yang, Pei Yang, Hua Luo, Wentao Wang ,Lunan Yan. Individualized biliary reconstruction techniques in autotransplantation for end-stage hepatic alveolar echinococcosis. HPB, 2020, 22, 578–587. DOI:10.1016/j.hpb.2019.08.003.

[4] Wen H, Vuitton L, Tuxun T, Li J, Vuitton D A, Zhang W B, McManus D P. Echinococcosis: Advances in the 21st Century. Clin Microbiol Rev. 2019: [PMID: 466308200007 DOI: 10.1128/CMR.00075-18].

[5] Wen H, Dong J H, Zhang J H, Zhao J M, Shao Y M, Duan W D, Liang Y R, Ji X W, Tai Q W, Aji T, Li T. Ex vivo liver resection followed by autotransplantation for end-stage hepatic alveolar echinococcosis. Chin Med J (Engl). 2011: 2813 [PMID: 22040485].

**Response to reviewer # 2:**

Many thanks for your comments on our letter, we have revised the manuscript according to your comments:

1. We revised the ABSTRACT and INTRODUCTION section according to your suggestions (marked in red).

2. The variables、groups evaluate and postoperative follow-up were described in MATERIALS AND METHODS section according to STROBE guidelines (marked in red).

3. The p-values of differences among groups were added to the tables and manuscript according to your advice (marked in red).

4. We have restructured the DISCUSSION section accordingly based on your comments.

**Response to editorial office's comments:**

Thank you for your great support for our work. After carefully studying your advice, we have made corresponding changes to the manuscript:

1. We commissioned Meiwen Education to further language polishing for revised manuscript, and a new language editorial certificate have given.

2. We have reformatted the figures as required, and organize them into a single PowerPoint file.

3. We made a standard three-line table for all of the tables in our article.

4. We declare that all figures in this article are original picture. We added the copyright information to the PowerPoint file.

Best regards.

——Hao Wen