Peer Review File

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Response to Reviewers' comments:

1. Introduction

Comment 1:

The description of iCCA incidence does not seem necessary under Introduction. If needed, it should be moved under Discussion.

Reply 1:

Thanks for your suggestion, we have deleted the sentence:" with an incidence of less than 2/100,000 persons".

Changes in the text:

We have deleted the sentence:" with an incidence of less than 2/100,000 persons".

2. Methods

Comment 2:

It is unclear whether resectable iCCA patients were part of the inclusion criteria. If they were part of the inclusion criteria, a description seems necessary for the reason of standby for LT without resection. If iCCA patients were excluded, a description should be included under the exclusion criteria.

Reply 2:

Thanks for your queries. Currently, there is no sufficient criterion for evaluating liver transplantation in patients with iCCA. The aim of this study was to establish a predictive model for the recurrence of iCCA after liver transplantation. This is a retrospective study in which patients were transplanted for hepatocellular carcinoma or decompensated cirrhosis, and cholangiocarcinoma was found pathologically after transplantation. This study only included patients found to have only iCCA at the explant. Patients with mixed iCCA + HCC (in the same or different nodule) were excluded from the current study. If the patient was diagnosed with iCCA before surgery, we would consider two options: resection or transplantation, especially for patients with tumor size less than 2cm. Patients and their families decided which treatment to receive. Many studies have shown that liver transplantation can achieve good prognosis in iCCA patients with tumor size less than 2 cm.

Changes in the text:

We have added “This study only included patients with iCCA at the explant. Patients with mixed iCCA + HCC (in the same or different nodule) were excluded from the study.” to the first paragraph of the methodology section.

Comment 3:

Please describe how many people were excluded due to the exclusion criteria.

Reply 3:

Twenty-seven patients were excluded due to the exclusion criteria.

Changes in the text:

We have added “Twenty-seven patients were excluded due to the exclusion criteria.” to the first paragraph of the methodology section.

Comment 4:

The description regarding the companion status of Cirrhosis as an important variable has been omitted.

Reply 4:

The description regarding the companion status of cirrhosis was shown in Table 1.

Changes in the text:

No

Comment 5:

If the wait for LT exceeded 6 months, some patients received TACE/ablation as a bridge Tx (9 vs. 21 patients, Table 1). Was there a difference in waiting time between the two groups?

Reply 5:

There was no significant difference in waiting time between the two groups. This difference may be related to the number of patients suspected of HCC before transplantation, and different periods of patients in each cohort. The patients in the discovery cohort were from 2008 to 2012, and the patients in the validation cohort were from 2012 to 2017, which may be related to the change of concepts of treatment

in different periods.

Changes in the text:

No

Comment 6:

What were the criteria for selecting 8 potential predictors? Was there an analysis regarding the companion status of Cirrhosis as well as the waiting time until LT following diagnosis? In Ref 10, tumor differentiation (Poorly differentiated) is also a risk factor for tumor recurrence. Why is this information omitted in the manuscript?

Reply 6:

We choose these potential factors mainly based on the published articles, which have a greater impact on the iCCA, and can be detected before transplantation. We mainly hope to develop a simple and useful version model that can predict the postoperative prognosis before transplantation, such as Milan Criteria or Hangzhou Criteria, so we mainly rely on the indicators that can be detected before transplantation to develop the model. However, the degree of cirrhosis and tumor differentiation need to be determined by pathological examination, so it is not suitable for preoperative evaluation of prognosis model. So this information is omitted in the manuscript.

Changes in the text:

No

Comment 7:

What were the criteria or methods to divide Discovery and Validation Cohort?

Reply 7:

Different cohorts of patients came from different periods. The patients in the discovery cohort were from 2008 to 2012, and the patients in the validation cohort were from 2012 to 2017.

Changes in the text:

No

3. Results

Comment 8:

For Table 1, please indicate whether there is a statistical difference in baseline characteristic between Discovery Cohort and Validation Cohort groups. The rate of adjuvant therapy seems to differ between the two groups.

Reply 8:

Yeah, the rate of adjuvant therapy differs between the two groups. This difference may be related to the number of patients suspected of HCC before transplantation, and different periods of patients in each cohort. The patients in the discovery cohort were from 2008 to 2012, and the patients in the validation cohort were from 2012 to 2017, which may be related to the change of concepts of treatment in different periods.

Changes in the text:

No

Comment 9:

For Table 1, the following information needs to be indicated: Total adjuvant therapy received (9(42.9%) vs 21(75%)), total recurrence (6(22.4%) vs 8(28.6%)) and total death rate (12(57.1%) vs 22 (78.6%)).

Reply 9:

Thanks for your suggestion. We have added the information you mentioned to table 1

Changes in the text:

We have added the information you mentioned to table 1.

Comment 10:

For Table 1, please indicate the median waiting time on the waiting list and median follow-up period for both groups.

Reply 10:

Thanks for your suggestion. We have added the median waiting time on the waiting list and median follow-up period to table 1.

Changes in the text:

We have added the median waiting time on the waiting list and median follow-up period to table 1.

Comment 11:

Under Table 2, in the preoperative treatment section, patients who did not receive preoperative treatment seems to be omitted. If these patients were included under the

preoperative treatment section (Yes vs No), did the authors analyze to see if tumor recurrence was predictable? Analysis results regarding tumor differentiation and cirrhosis companion status should also be provided.

Reply 11:

Thanks for your suggestion. Preoperative treatment is indeed an important factor affecting the prognosis, but it is not suitable to be included in the model to predict the postoperative prognosis before transplantation, so we did not adopt it. We mainly hope to develop a simple and useful version of model that can predict the postoperative prognosis before transplantation, such as Milan Criteria or Hangzhou Criteria, so we mainly rely on the indicators that can be detected before transplantation to develop the model. However, the degree of cirrhosis and tumor differentiation need to be determined by pathological examination, so it is not suitable for preoperative evaluation of prognosis model. So this information is omitted in the manuscript.

Changes in the text:

No

4. Discussion

Comment 12:

Page 12 describes intrahepatic cholangiocarcinoma as part of ICC. Please unify this information under iCCA.

Reply 12:

Thanks for your suggestion. We have changed “ICC”to “iCCA”.

Changes in the text:

We have changed “ICC”to “iCCA”.