

Reviewer #1: Thanks for the opportunity to review the paper entitled "Liver transplantation for combined hepatocellular carcinoma and cholangiocarcinoma: A multicenter study". The authors compared the differences in survival and recurrence between HCC and cHCC-CC. The following comments need to be addressed before acceptance.

1. The topic is not very purposeful.
 - ➔ The aim of this study was to compare outcomes between living donor liver transplantation (LDLT) patients with HCC and LT patients with cHCC-CC and to identify risk factors for tumor recurrence and death after LT in cHCC-CC patients.
2. Patients who were diagnosed with cHCC-CC and who underwent LT at nine medical centers between January 2000 and December 2018 were selected as the research Group. Patients who received LDLT for HCC at Samsung Medical Center from January 2013 to March 2017 were selected as the control group. Why were the two groups of patients enrolled in different study periods? Why were data from only one center selected for the control group? This can lead to bias in the results.
 - ➔ I agreed with your opinion, and I also knew our data had a bias. The study period of cHCC-CC patients was from 2000 to 2018, but most cases recently received liver transplants. The study period of HCC patients from 2013 to 2017 as a control group was investigated considering a similar follow-up period. It would be best to collect LDLT patients from nine institutions, but it was very difficult to receive all data from nine institutions. Therefore, we compared cHCC-CC patients and HCC patients from one institution as the control group.
3. The authors declared: After propensity score matching, the median age of donors in the HCC group was significantly younger than in the cHCC-CC group. However, this conclusion was not consistent with that of Table 1.
 - ➔ It is correct that the donor age of the HCC group is younger than that of the cHCC-CC group in Table 1 and the result section after propensity score matching. The median donor age in the HCC group and the cHCC-CC group was 27 years (range; 16-63 years) and 33 years (range, 11-58 years) after propensity score matching, respectively. Before propensity score matching, the median donor age of the HCC group was not different compared with that of the cHCC-CC group.

4. The median follow-up duration was 44.5 months (range: 1.4-72.5 months) in the HCC group and 39.6 months (range: 0.1-212.5 months) in the cHCC-CC group. 0.1 month means 3 days, is this right?

➔ It is correct that 0.1 month is 3 days.

5. The authors declared they used generalized estimating equations for predicting factors for tumor recurrence and survival. generalized estimating equations is generally used for the evaluation of repeated measurement design data. Is it valid to use generalized estimating equations in this study?

➔ Predicting tumor recurrence and survival in the dataset after propensity score matching are analyzed through GEE. This part was consulted by the statistics team.

6. Table 5 provides the results of the post-PSM. but it is necessary to supplement the results of the pre-PSM.

➔ We performed a further analysis in the pre-PSM set based on your comments. We summarized the results and added them to Supplementary Table 1.

Reviewer #2: Combined with practical clinical problems, this study proposed that the prognosis after cHCC-CC liver transplantation was relatively poor, and analyzed the related influencing factors. The conclusion was finally reached: Poor prognosis of patients diagnosed with cHCC-CC after LT can be predicted based on explant liver. Frequent regular surveillance for cHCC-CC patients should be required for early detection of tumor recurrence. It has certain guiding significance for clinical

practice. But I have some comments as follows:

1. For the treatment of liver cancer, local regional treatment is an important means, such as ablative therapy, TACE, radiotherapy, etc., which is commonly used in clinic. In some research centers, needle biopsy of the tumor will be performed at the same time during the ablation to clarify the pathological diagnosis and guide the subsequent treatment. The authors of the study mentioned in lines 100 and 111 that "... diagnosed with cHCC-CC in their postoperative pathology reports..." , no reference was made to whether a needle biopsy was performed at the time of local regional treatment, but was it appropriate to conclude, in lines 274 and 275, that "Thus, a liver biopsy prior to LT might not reveal the exact diagnosis?"

➔ Korean liver cancer guidelines diagnose HCC radiologically, thus liver biopsies are not routinely performed during local treatment. Almost all of our patient cases were diagnosed and treated as HCC, therefore no liver biopsy was performed prior to liver transplantation.

Reference) KLCA and NCC Korea. 2022 KLCA-NCC Korea practice guidelines for the management of hepatocellular carcinoma. Clin Mol Hepatol 2022(4)583-705

2. This study mentioned that "frequency of locoregional therapies >3" was the factor that influenced tumor recurrence. In the article, lines 123 and 124 mentioned "... history of locoregional therapy, including frequency of locoregional therapy, transarterial chemoembolization (TACE), LR, radiofrequency ablation (RFA), or radiation..." . May I ask: Was the same treatment regimen used for the three local treatments or was it sequential with other treatments? We know that a patient may not have the same clinical effect with three TACE treatments in a row as with two TACE plus one ablation. Please check it. Thank you.

➔ The total number of sequential treatments with local regional treatments, such as liver resection, RFA, TACE, or radiation therapy, was included. Hepatectomy was not considered separately.

3. PSM was used as a statistical method. The author mentioned in lines 153 and 154 that "Therefore, propensity score matching was conducted prior to comparisons of OS and DFS between the HCC and the cHCC-CC propensity score matched groups ", and the statistical

results of PSM were available in Table1,2,3. However, it was not clearly stated when the statistical results of PSM need to be referred to in the description of results. For example: In line 210, it was mentioned that "but encapsulation, tumor necrosis, microvascular invasion, BDTT, intrahepatic metastasis, and multicentric occurrence did not differ between the two groups ", while $P < 0.05$ for the microvascular invasion in the statistical results of PSM in Table 3.

- ➔ After propensity score matching, the proportion of LDLT and ABO-incompatibility in the HCC group was significantly higher than in the cHCC-CC group. The median microsteatosis in the HCC group was significantly higher than in the cHCC-CC group, but median GRWR, warm ischemic time, operation time in the HCC group were significantly smaller and shorter than in the cHCC-CC group. The presence of tumor necrosis in the HCC group was significantly lower than in the cHCC-CC group, but the presence of microvascular invasion in the HCC group was significantly higher than in the cHCC group. There were no statistically significant differences in tumor size, tumor number, the numbers of beyond Milan criteria, tumor grade 3 or 4, encapsulation, PVTT, BDTT, intrahepatic metastasis, multicentric occurrence, and lymph node metastasis between the two groups.

4. The meanings of (C) and (D) are not expressed in FIG. 1-3.

- ➔ We added the explanation in the result section and figure legends.