

Peer Review File

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Reviewer comments

1. Comment: The English language of the paper is very poor, which needs substantial editing after extensive editing.

Response: Many thanks for your comment. We have revised the content according to the comments. We have adjusted the problems of the English language and polished the article, hoping to make it more fluent, concise, and understandable.

2. Comment: The title is very long and difficult to understand. Please consider to write it in a brief and clear way.

Response: Thank you very much for the comments. We have revised the title according to the comments (see page 1, line 2-4). The revised title is "Differences of Intraoperative Outcomes and Postoperative Complications between Intrahepatic Cholangiocarcinoma and Colorectal Liver Metastasis in Different Surgical Methods". This study aimed to explore the difference in intraoperative outcomes and postoperative complications between intrahepatic cholangiocarcinoma (IHCC) and colorectal liver metastasis (CRLM) in different surgical methods according to major liver resection and minor liver resection.

3. Comment: Abstract. In the part of methods, please describe the study design and measures of intraoperative outcomes and postoperative complications. The part of results is unnecessarily long. I suggest the authors to report main findings only. The conclusion should be made with cautions because of the small sample sizes after PSM matching.

Response: Many thanks for your comment. We have adjusted the content of the Abstract. (1) We have added these in the part of methods (see page 3, line 57-61). The intraoperative variables included intraoperative blood transfusion, duration of operation, and intraoperative blood loss. The postoperative complications were measured

according to the Clavien-Dindo classification. Grade III to V complications were defined as major complications.

(2) We have made appropriate cuts to the results section, keeping only the necessary results (see page 3-4, line 62-72). This study revealed major hepatectomy for IHCC led to significantly higher morbidity of postoperative complications than CRLM patients. For minor hepatectomy, there was no difference in postoperative complications between IHCC and CRLM. The small sample sizes after PSM may be a limitation of this study. In future studies, we will expand the sample size to better solve this problem. However, after the matching of patients undergoing primary resection, the number of HCC and CRLM patients was 46, and the results obtained from this sample size have a certain degree of credibility. Our results were similar to previous studies. The total number of patients undergoing minor resection was relatively small, resulting in a small sample size after PSM, which led to deviations in the results. But before PSM, there was no significant difference between the intraoperative outcomes and postoperative complications between IHCC and CRLM patients. And we got the same results after PSM. Therefore, we believe that although our research sample size is not large enough, the results still have a certain reference value.

4. Comment: Background. First, it remains unclear why the authors compared intraoperative outcomes and postoperative complications between IHCC and CRLM patients receiving different surgical procedures. Please provide more insights on the clinical significance of this research topic. Second, the authors should have a brief review on known surgical outcomes between IHCC and CRLM patients and factors associated with them, in particular surgical methods. Third, the author mentioned PSM here. The authors should describe the strengths of this approach, which may address the limitations of previous studies.

Response: Special thanks for your comment. We have modified our content as advised.

(1) We have modified our text as advised (see page 6-7, line 113-136). Hepatectomy stands as the cornerstone for the curative management of liver malignancies. Advances in perioperative management have translated into reduced mortality and morbidity over time. Whereas a better understanding of such differences might help to improve

perioperative management and outcomes, no comprehensive comparative study is currently available in the literature. This observation motivated the current study. Preoperative management and short-term outcomes after MH for IHCC or CRLM were first compared. This study firstly conducted a propensity score matching (PSM) study to explore the difference of intraoperative outcomes and postoperative complications between IHCC and CRLM in different surgical methods.

(2) We have added a brief review of previous related studies (see page 6, line 118-130). Zhang XF et al. found that major hepatectomy for IHCC was not associated with an overall survival benefit, yet was associated with increased perioperative morbidity. For CRLM, more and more researches promote parenchyma-sparing liver resection. Because it has substantially decreased intraoperative blood loss and postoperative liver failure. Doussot A et al. suggested that IHCC patients were inherently more at risk after major hepatectomy as compared to CRLM patients, but portal lymphadenectomy was significantly more performed for IHCC. Not surprisingly, vascular and biliary injury during portal lymphadenectomy may lead to specific complications such as bleeding, biliary ischemia, or lymphatic leak. Different preoperative planning and surgical management may be the reason for different intraoperative outcomes and postoperative complications.

(3) The propensity score matching (PSM) method was used to balance the imbalanced clinicopathological characteristics between IHCC and CRLM patients. In a previous study, portal lymphadenectomy was significantly more performed for IHCC. Not surprisingly, vascular and biliary injury during portal lymphadenectomy may lead to specific complications such as bleeding, biliary ischemia, or lymphatic leak. In our study, based on the significant distribution difference of pre-operative treatment and lymphadenectomy between those patients, the combination of the pre-operative treatment and lymphadenectomy (PTL) on these two factors was constructed to eliminate the influence of these two factors on the outcomes and ensure the feasibility of PSM.

5. Comment: Methodology. Please clearly indicate the clinical research design of this study at the beginning. Second, the authors should have a detailed descriptions on the

assessment of intraoperative outcomes and postoperative complications, as well as other clinical covariates. Third, because I do not think PSM is suitable for the data because the sample sizes of this study are small. Findings from PSM analysis are at high risk for selection bias.

Response: Thank you very much for the comments. We have revised this part according to the comments.

(1) We have modified our text as advised (see page 7-8, line 148-158). This was a retrospective study based on the CRLM and HICC datasets. Clinical variables included age, gender, ASA score, BMI, and preoperative test markers. Tumor-related variables included tumor size and number. Eligible patients were divided into two groups according to major hepatectomy and minor hepatectomy. Then, patients with IHCC and CRLM were compared between the two groups to find if there were differences in clinical covariates. In each group, propensity score matching (PSM) was performed based on the results. The primary outcomes included intraoperative variables and postoperative complications. The secondary objective was to identify independent predictors of postoperative mortality and morbidity in patients undergoing hepatectomy whether for IHCC or CRLM.

(2) We have added relevant content in the part of methods following the comments (see page 8, line 167-171). Intraoperative variables, including intraoperative blood transfusion, duration of operation, and intraoperative blood loss, were used to evaluate the patient's intraoperative condition. The postoperative complications were measured according to the Clavien-Dindo classification. Grade III to V complications were defined as major complications. If patients experienced multiple postoperative complications, the highest grade was used.

(3) Thank you again for your comments. This problem may be a limitation of this study. In future studies, we will expand the sample size to better solve this problem. We think PSM analysis is still necessary. The PSM was used to eliminate the significant differences of clinicopathological characteristics between HICC and CRLM groups, the aim of which was to reduce clinicopathological characteristics bias in the comparison of intraoperative outcome and post-operative complications between two groups.

6. Comment: Statistics. This part is poorly written. First please indicate Mann-Whitney U test and other tests were used to compare between which groups. Second, I suggest the authors not to use PSM. The authors may consider surgical methods and type of cancer (IHCC vs. CRLM) as two important predictors in the multiple analysis when regressing on intraoperative outcomes and postoperative complications. Third, please indicate $P < 0.05$ is two-sided or not.

Response: Thank you for underlining these deficiencies. This section has been revised and modified according to the suggestions by the reviewers.

(1) We have revised the part of statistics according to the comments (see page 8, line 176-177). The Mann-Whitney U test was performed to analyze continuous variables, including operation time and intraoperative blood loss, et al.

(2) The small sample size after matching is indeed a limitation of our research, which may lead to biased results. Your suggestions will be the direction of our follow-up research. However, the purpose of this study is to compare the differences in the intraoperative and postoperative outcomes between IHCC and CRLM patients. A better understanding of such differences might help to improve perioperative management and outcomes, and better perioperative and operative management can translate into reducing mortality and morbidity. This study found differences in baseline data of IHCC and CRLM patients who underwent the same liver resection method. If PSM is not used, these differences may cause bias in the results. We were unable to determine whether the difference in intraoperative outcomes and postoperative complications of two liver malignant tumors after the same liver resection was due to differences in the patient and the disease itself, or due to surgical operations or preoperative treatment. Compared with CRLM patients, IHCC patients received significantly more frequent lymphadenectomy (76.3% vs 0.0%, $P < 0.001$) and less preoperative treatment (7.6% vs 67.7%, $P < 0.001$). Based on the significant distribution difference of preoperative treatment and lymphadenectomy between those patients, the combination of the preoperative treatment and lymphadenectomy (PTL) on these two factors was constructed to eliminate the influence of these two factors on the outcomes and ensure the feasibility of PSM. We obtained two groups of patients with the same baseline

through PSM, which was conducive to the subsequent analysis.

(3) We have modified the relevant content in the part of Statistical analysis (see page 9, line 188). A two-tailed P value of less than 0.05 was considered significant.