Dear Editor-in-Chief and Reviewers,
We are thankful to you and the reviewers for the insightful critic and comments. We also thank you for giving us the opportunity for resubmission after revision to the manuscript. This is a revised submission of our manuscript. We have enhanced the manuscript accordingly and enclosed below is the point-to-point response with the changes made highlighted in yellow as per the journal's requirements.

Yours sincerely,
Corresponding author

Reviewer #1:

Cons. 1.The study number included in this study is relatively small, and all studies are from Asian country.

Response:

Thank you for highlighting this. We fully agree that the number of included studies based on our inclusion criteria is small and all derived from Asian countries. We also understand that this may limit generalisability of our findings in cohorts that have not been represented in our analysis. As for the scarcity of articles included, we explained our reason for the scope of our review and analysis, which led to our strict inclusion criteria and subsequently the inclusion of a relatively small number of studies. We also explained the intended aims of our analysis and how we wish it will be used to guide surgeons in their decision-making process.

We have added in the following:
"The number of studies included in this meta-analysis is relatively small. This was a result of our strict inclusion criteria of studies comparing post-hepatectomy outcomes of ICC in HCV+ and HCV- subgroups. A previous meta-analysis by Wang et al. had concluded that HCV infection was associated with worse survival outcomes in ICC patients irregardless of treatment modality prescribed. Thus, we aim to provide more targeted insight on the subgroup of patients indicated for curative resection. With the inclusion of newer studies, we present an updated meta-analysis on these outcomes and hope to provide guidance for clinical decision-making in ICC patients indicated for hepatectomy with HCV+ status."

Regarding the included studies being from Asian countries, we recognize that this may potentially be a source of bias in representing the Asian cohorts as compared to the Western or European cohorts. We also acknowledge in our discussion that while global incidence of cholangiocarcinoma is highest in Asia, its incidence in Western countries have been on the rise over the past decade. We also commented on the prevalence of HCV infection globally, highlighting regions such as the Eastern Mediterranean and European regions suffering the highest disease burden. Another aim of this study is to appeal for the conception of future studies in these regions to represent these populations.

2.All study included in this study is retrospective study

Response:

Thank you for highlighting this point as well. We agree that this is a limitation in our study. Ideally, we would have liked to include studies with higher-quality evidence, such as RCTs and prospective studies, in our study. However, there was no RCTs and prospective studies that meet our inclusion criteria. We hope that our study encourages the conception of future studies that employ these methods.

We have included the following in our limitations:
"All the included studies were retrospective observational studies which has inherent selection bias. The absence of high-quality evidence from RCTs and prospective studies may limit interpretation of the outcomes from our analysis. Subsequent studies should employ methods such as PSM and RCTs to reduce bias for more conclusive results."

3. The relationship between the HCV infection and the stage of cholangiocarcinoma has not been clarified. 4. The relationship between the HCV infection and the metastasis of cholangiocarcinoma has not been reported

Response:

Thank you for your kind suggestion. We agree that tumor stage and presence of metastasis are important predictors of post-resection survival in ICC. As such, an analysis and discussion regarding a possible relation between advanced stage tumors, metastatic disease and HCV infection will provide valuable insight. We did perform meta-analysis to compare the impact of HCV+ status on stage of disease and lymph node metastases: there was no significant difference between HCV+ and incidence of stage 4 disease (n=145 patients, OR 0.64, 95% CI: 0.32, 1.28, p=0.21) and lymph node metastases (n=349 patients, OR 0.85, 95% CI: 0.53, 1.37, p=0.51). As you rightly pointed out, this relationship should be discussed.

We have included this in our discussion:
"Advanced tumor stage and metastatic disease are poor prognostic factors in cholangiocarcinoma [53]. In advanced staged tumors, several factors contribute to more aggressive tumor behavior. Notably, presence of vascular invasion increases the risk of haematogenous spread of tumor cells, and tumor multiplicity provide additional nidus for tumor to grow and spread from [54-56]. Unexpectedly as well, nodal disease has been shown to be associated with worse survival (22.9 months vs 30.1 months, p=0.03) [57]. The question lies on whether HCV+ increases the risk of more advanced disease or nodal metastases, since HCV infection results in EMT as described above. This question remains to be unanswered based on our findings, but may be due to the low sample size of the included studies."

5. This research has limited novelty. It just verify a previous conclusion, and do not provide a new point of view

Response:

Thank you for this important comment. We agree that our hypothesis draws inspiration from a previous meta-analysis by Wang et al. which concluded that long-term outcomes of cholangiocarcinoma in HCV-infected patients are significantly worse than HCV-naive patients. However, Wang et al. did not perform subgroup analysis for patients who underwent hepatectomy. No previous reviews or meta-

analyses studies this subgroup as well. As such, we felt that there was a gap in this aspect of the literature and aim for our study to provide insight on the topic.

This was already included in our discussion previously:
"A previous meta-analysis by Wang et al. explored the impact of HCV infection on survival outcomes in patients with ICC, regardless of treatment modality, and showed poorer prognosis in HCV+ patients. However, we wish to understand the implications of HCV on long-term outcomes following curative LR in ICC."

Company Editor-in-Chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Virology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response:

Thank you. We have also provided the original .pptx files with the changes made.