Dear Editor-in-Chief of WJCC

Thank you for helpful comments on the manuscript titled 'Significance of dysplasia in the bile duct resection margin of patients with extrahepatic cholangiocarcinoma: A retrospective analysis' (NO: 71394). We have revised our manuscript as suggested by the reviewers and agree to the points the reviewers have indicated. They are as follows:

[Reviewer's Comments]

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This manuscript is of good quality. It retrospectively analyzes the prognostic significance of extrahepatic cholangiocarcinoma patients with resection margin dysplasia, and proposes that LGD positive resection margin is not an important indicator of the survival of EHCC patients. It is a very meaningful retrospective analysis. The paper will be great addition to existing literature. Some questions were asked to the author:

1: It is recommended to add relevant data of patients with preoperative drainage.

→ Thank you for helpful comment. We added the data on preoperative drainage in the result section and Table 1.

After: Preoperative bile drainage was performed in 95.7% of enrolled patients. In 78% of cases, endoscopic bile drainage was used, and in 22%, percutaneous transhepatic biliary drainage was used.

After:

Preoperative drainage	
None	5
Endoscopic bile drainage	87
PTBD	24

2: I would like the authors to read the STROBE Statement and prepare the manuscript according to the STROBE Statement.

→ Thank you for helpful comment. I read the STROBE Statement thoroughly and tried to write a manuscript according to the checklist as much as possible. The shortcomings of this study will be taken into account in the next study in mind. Thank you again.

3: The author did not provide an approved funding application form. Please upload the grant application form or related approval documents.

→ I will upload the funding application form written in Korean.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: In this retrospective study, the authors evaluated the prognostic significance of dysplasia-positive margins in patients with extrahepatic cholangiocarcinoma (EHCC). They concluded that HGD/CIS margin in resected EHCC was associated with poor survival but LGD-positive resection margin was not a significant indicator for the survival of patients with EHCC. This is a well-written article but has some issues to be addressed.

Minor comments:

1) The authors mentioned that LGD positive resection margin in elderly patients could be reasonable to judge it as negative resection margin considering old age and HGD/CIS were independent factors associated with poor survival for patients with EHCC. However, the authors should provide more suggestions about how to manage the postoperative patients with EHCC based on the resection margin status. For example, do the authors think that the adjuvant chemotherapy and/or radiation should be given to the patients with HGD/CIS margins?

→ Thank you for helpful comment.

→ As mentioned in the manuscript, since the clinical prognosis in the LGD group is good enough

compared to that of negative margin group, it can be suggested that that no additional treatment is required in the LGD group.

→ However, in the patient group with HGD/CIS margin, the results of this study clearly showed higher recurrence rate and poorer survival rate compared to other LGD margin and negative margin group. In order to confirm the benefits of additional surgery or adjuvant chemotherapy/radiation therapy for the HGD/CIS group, a randomized control study should be conducted with a sufficient patient group.

→ In this study, no additional surgery was performed in all patients. And adjuvant therapy was not performed according to a comprehensive indication, but according to the patient's condition and the doctor's arbitrary judgment. Furthermore, the number of patients is insufficient to conduct a study to confirm the effect of adjuvant therapy through subgroup analysis within the HGD/CIS group. Therefore, a comparative study with a large number of HGD/CIS patients is needed in the future.

→ The following paragraph was added in the discussions section to describe our view about the management of the postoperative patients with EHCC according to resection margin

After: In contrast, the HGD/CIS margin group clearly showed higher recurrence rate and poorer survival rate compared to other LGD margin and negative margin group. Various attempts can be made to improve the prognosis in patients with HGD/CIS margin, but it is difficult in our study to establish a consensus on the benefits of adjuvant chemotherapy and/or radiation treatment for the HGD/CIS patient group. It is because postoperative adjuvant therapy were performed according to the clinician's decision and the patient's condition. Furthermore, the duration of chemotherapy applied to the patient, the dose of chemotherapy, and the chemotherapy regimen were varied without a certain criterion. Therefore, a comparative study with a large number of HGD/CIS patients to confirm the benefits of adjuvant therapy is needed in the future.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: In this manuscript, the authors reported their experience and their data in the field of resected cholangiocarcinoma. The title is informative and so is the abstract and the keywords. The text is written in a clear way. I have some concerns about the reproducibility of data and the limitation of the study.

1. Were the margins examined by the same anatomopathologist? What was done in case of doubts?

→ Thank you for helpful comment. The following paragraph was added in the method section.

After: In most cases, histological examination of resection margin was performed by a pathologist specializing in gastrointestinal pathology. For ambiguous histologic findings, the final results were reported after discussion with other specialists in the pathology department.

2. Additionally the post-surgery strategy was different (chemo, radio and there is no information about the length of post-surgery treatment) this aspect should be considered in the statistical analysis or at least considered as a limitation of the study. This article has some credit, however, the limitation of this study should be more complete.

→ Thank you for helpful comment. As you pointed out, that will be a limitation of this study

→ Postoperative adjuvant chemotherapy and/or radiation therapy were performed according to the clinician's decision and the patient's condition. Furthermore, the duration of chemotherapy applied to the patient, the dose of chemotherapy, and the chemotherapy regimen were varied without a certain criterion. As a retrospective study, this point is regarded as a limitation and will be mentioned in the discussion section.

After: In contrast, the HGD/CIS margin group clearly showed higher recurrence rate and poorer survival rate compared to other LGD margin and negative margin group. Various attempts can be made to improve the prognosis in patients with HGD/CIS margin, but it is difficult in our study to establish a consensus on the benefits of adjuvant chemotherapy and/or radiation treatment for the HGD/CIS patient group. It is because postoperative adjuvant therapy were performed according to the clinician's decision and the patient's condition. Furthermore, the duration of chemotherapy applied to the patient, the dose of chemotherapy, and the chemotherapy regimen were varied without a certain criterion. Therefore, a comparative study with a large number of HGD/CIS patients to confirm the benefits of adjuvant therapy is needed in the future.

We agree with the reviewers in all points and the corrections in an annotated version are the points the reviewers have indicated. Thank you for the reviewers again to consider our manuscript to be published in WJCC. We look forward to receiving your answer soon.

Sincerely,

Hyo Jung Kim, M.D., Ph.D.