

Dear Editor and the Reviewers:

We would like to take this opportunity to express our sincere gratitude to the Editor and the Reviewers for their review of our manuscript and the valuable suggestions provided. Please find below our point-by-point responses to these comments raised by the reviewers along with the description of the revisions made in the manuscript. The revisions based on the comments by Reviewer #1 and Science Editor are indicated in red font, whereas those based on the comments by Reviewer #2 are indicated in blue font.

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: For a more detailed analysis, please see attached file WJG ERCPCBDS PS3. First: This studies contributes data to just a few extant data points about safety and efficacy of ERCP for CBDS in some of the "sickest" patients that can be seen. This is all the more important as the number of this subpopulation grows with the aging worldwide population. Second: Study was well designed and executed. Third: Study was completed only in East Asian populations in experienced centers. The results may not prove replicable for non academic centers in Central America, for example. More data is needed worldwide in areas with different levels of expertise and approach (for instance, greater use of General Anesthesia and MAC in the US for ERCP).

As commented by the Reviewer, this was a retrospective study including only experienced centers in Japan. We agree that future multicenter studies including large patient cohorts from institutions with different ERCP experiences are warranted to confirm the findings of our study. We have added this limitation to the revised Discussion section as follows:

“There are several limitations of this study. First, this was a retrospective study that included specialized centers in Japan. Second, although we balanced patients’ characteristics using one-to-one propensity score matching, some unmeasured confounding factors may exist. Therefore, some selection bias may not be excluded. Third, long-term outcomes of ERCP were not examined in this study. Future multicenter studies including large patient cohorts from

institutions with different ERCP experiences are warranted to confirm the safety and efficacy of ERCP for CBDS in patients with a PS score of 3 or 4.

Reviewer #2:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade D (Rejection)

Conclusion: Rejection

Specific Comments to Authors: Dear Editor, Although the article is correctly written and clearly presented, the objective is not clear to me. Indeed, ERCP is a specific therapeutic procedure for which there are clear indications and clear contraindications. If a patient needs ERCP (choledocholithiasis or biliary stricture), there is no adequate, less invasive method that would provide equally good results. Therefore, the decision to perform ERCP or not does not depend on the patient's performance status, but on whether there is an indication for ERCP. Of course, patients who are older and have comorbidities are more likely to have a worse outcome no matter which method we use. Therefore, I think the paper does not add to the knowledge in this area.

We believe that the PS score is an important factor for determining the indications and strategies of ERCP for CBDS in elderly patients in clinical practice. In the present study, the severity of ERCP-related complications was higher in patients with a PS score of 3 or 4 than in those with a PS score of 0–2. In particular, absence of acute cholangitis, including asymptomatic CBDS, was associated with increased risk of ERCP-related complications. Therefore, while patients with acute cholangitis and biliary pancreatitis should be endoscopically treated, conservative treatment or follow-up strategies might be considered as appropriate options in patients without acute cholangitis, especially those with asymptomatic CBDS. We clarified these considerations in relevant places in the Introduction, Discussion, and Research Highlights sections in the revised manuscript.

(1) Science editor:

This is a retrospective cohort study, which examine the safety and efficacy of ERCP for CBDS in patients with PS 3 or 4. However, multi-center, large sample size data analysis

is also needed to prove the conclusions in the manuscript.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade D (Fair)

We agree that our findings are based on a retrospective study including experienced centers in Japan. We also agree that future multicenter studies including large patient cohorts from institutions with different ERCP experiences are warranted to confirm the main study findings. We acknowledge these limitations in the revised Discussion section as follows:

“There are several limitations of this study. First, this was a retrospective study that included specialized centers in Japan. Second, although we balanced patients’ characteristics using one-to-one propensity score matching, some unmeasured confounding factors may exist. Therefore, some selection bias may not be excluded. Third, long-term outcomes of ERCP were not examined in this study. Future multicenter studies including large patient cohorts from institutions with different ERCP experiences are warranted to confirm the safety and efficacy of ERCP for CBDS in patients with a PS score of 3 or 4.”