

Reviewer #1:

The authors do a nice job in identifying 2 factors that have increased in carcinogenesis in patients with bile duct cysts, however, they do not explain how this information is useful to clinicians.

1. They should give specific examples of how this new information has changed their practice patterns.

Answer: The currently recommended treatment modality for BDC is operation. For patients with symptoms, surgery is more acceptable. However, the necessity and timing of surgery is a difficult choice in asymptomatic patients. In our hospital, prophylactic operation is recommended to all asymptomatic patients. Some patients choose operation due to the high incidence of bile duct malignancy in BDC. But some of them will want to know if they have risk factors for preoperative carcinogenesis, and that will determine whether they choose surgery or not. Because precise estimates of the risk of preoperative carcinogenesis in BDC are lacking, we performed the present study and found two risk factors. For patients with gallbladder wall thickness >0.3 cm and Todani type IV, surgery should be highly recommended. The above information has been added and discussed in the second paragraph of "INTRODUCTION" section, the second paragraph of "DISCUSSION" section, and "CONCLUSION" section.

2. Furthermore, what do they recommend for patients with Todani IV extensive bilateral intrahepatic cysts? Resection? Transplantation? Just cholecystectomy?

Answer: Complete/radical cyst excision plus Roux-en-Y hepatojejunostomy is the recommended treatment modality for BDC. But, clinically, complete excision is not always achievable, especially in patients with widespread intrahepatic cysts, as is often found with Todani type IVa cysts. For these patients, remove cysts as much as possible and rebuilt proper bile duct flow are recommended. In a previous study, for Type IVa cysts, as long as proper

bile flow was ensured, complete or incomplete excision made no significant difference in terms of late postoperative complications and long-term biliary function (PMID: 30139348 PMID: PMC6107957 DOI: 10.1186/s12876-018-0862-3). Proper bile duct flow, rather than radical excision, is the most critical factor determining treatment outcomes of bile duct cysts. Meanwhile, postoperative carcinogenesis of BDC is primarily caused by recurrent cholangitis, which can also be avoided via proper bile duct flow. The above information has been added and discussed in the first and second paragraphs of "DISCUSSION" section.

3. A flow chart would be extremely helpful to the reader.

Answer: A flow chart has been drawn and added to the manuscript as Fig 1 in the first paragraphs of "RESULT" section.

Reviewer #2:

The authors are to be congratulated on this important single center series describing preoperative risk factors for dysplasia or cancer in patients with congenital bile duct tumors. The writing is clear and succinct. I have only minor comments.

1. In the abstract it should be result not resulte.

Answer: It has been corrected. Thank you for pointing out this terrible mistake.

2. Did the authors compare the presence of anomalous pancreaticobiliary ductal union in the malignant/dysplastic cases versus in those without? Was this a risk factor for malignancy/dysplasia?

Answer: Abnormal pancreatic biliary duct (APBD) was confirmed in 55 patients (50.5%). Fifty-one patients in benign group and 4 in dysplasia/carcinoma group. These information has been presented in the first paragraph of "RESULTS" section, and the difference between groups has

been compared and presented in Table 1. APBD was not a risk factor ($p=0.717$).

3. In the discussion, the authors discussed why their patients had a good prognosis as compared to other series. Another factor may have been that 20 high risk patients were excluded from surgery, which would favor a better overall result for their cohort.

Answer: It is quite possible. This reason has been added to the fifth paragraph of "DISCUSSION" section.

Editors

1. The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Answer: The approved grant application form has been uploaded.

2. The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text;

Answer: The "Article Highlights" section has been added.

3. Please provide the Institutional Review Board Approval Form in Chinese.

Answer: A new Institutional Review Board Approval Form has been provided.