

Answer for peer-review report 1

- 1. What was the incidence of relapsing pancreatitis both before and after ERCP? How many children had single vs multiple attacks?**

The incidence of pancreatitis with pancreaticobiliary maljunction (PBM) is about 20%-26%, of which 80% are recurrent pancreatitis cases (PMID: 31371244, 23183766). In this study, the patients with clinical symptoms of PBM were included, and the clinical manifestations of pancreatitis in children accounted for 62.7%, in some cases accompanied by abnormal liver function or jaundice, and the imaging examination showed bile duct dilatation. We observed recurrent pancreatitis after ERCP interventions in 8 children (10.6%).

- 2. Please be upfront in the M and M section about the number of patients with choledochal cysts at time of ERCP and the total number who required subsequent surgery. Define radical surgery in the text and abstract.**

The number of children with choledochal cysts was 16 (16/75, 12%), which has been mentioned in the manuscript. Of these, 6 received subsequent surgery. Also, radical surgery has been defined in the text and abstract.

- 3. Please define who was excluded in this series. You state that those patient “with symptomatic PBM and those with PBM who underwent endoscopic therapy in one of these three centers...were included in the study.” As an endoscopist who has done pediatric ERCP for 3 decades, I am cognizant that in individuals with large choledochal cysts and APBU on MRCP, there is no indication to do ERCP.**

The experience at our endoscopy center suggests that ERCP can be used for patients with large choledochal cysts and APBU for improving drainage and resolving complications, and it is an appropriate and less invasive method for symptom relief, such as biliary pancreatitis or obstructive jaundice.

- 4. In an intention to treat analyses, one should exclude (censor) analyses of patients lost to follow-up.**

I have excluded the patients lost to follow-up in the intention to treat analyses according to your suggestion.

5. Was the gallbladder removed in one or the other subtype of PBM? Should it have been?

A total of 11 children with PBM were followed up and subsequently underwent surgical resection (prophylactic excision of the extrahepatic bile duct and hepaticojejunostomy), including gall bladder removal.

6. Table 2 Tables should stand alone. Define A, B, C, D types of PBM.

I have changed the column titles of the table to TypeA, Type B, Type C, Type D respectively.

7. Please define the difference between a dilated bile duct and a choledochal cyst.

Usually, the normal common bile duct diameter in children is 4 ~ 6 mm, and ducts with diameter larger than this range are considered as dilated bile ducts. Choledochal cyst refers to the part of choledochal that shows a cystic shape or fusiform dilated structure.

8. Figures 1B and 1C are suboptimal. Please submit better images.

I have replaced the figures 1B and 1C.

Answer for peer-review report 2

- 1. Please add the efficacy rate after ERCP, and surgery rate and the period until surgery for each type of PBM.**

In the discussion section, I have defined the efficacy rate as the percentage of patients remaining asymptomatic for long periods, it was as high as 82.4% (56/68). Additionally, there were 11 patients (11/68, 16.2%) who underwent surgical resection after ERCP. However, the data for the period until surgery for each type of PBM were not included in this follow-up.

Answer for peer-review report 3

- 1. The ERCP is an aggressive therapeutic procedure, but in your report there is not information about the real indication of ERCP. There is no information about the diagnosis of each patient before the ERCP procedure (Table 1), but we really need to know the diagnosis that justify the ERCP procedure performance. Abdominal pain, fever with the diagnosis before ERCP and the final type of PBM found.**

Because this is a retrospective study, we have only introduced the inclusion criteria of this study. Generally, the standard use of ERCP operation is mainly PBM with complications such as biliary pancreatitis, obstructive jaundice, cholangitis, meanwhile, MRCP or ultrasonography suggested choledochal dilatation, bile duct calculi or pancreatic protein plugs, which was the indications for ERCP intervention. (I have added this information in the revised manuscript)

- 2. “the endoscopists performed EST”, that stands for...?**

EST stands for endoscopic sphincterotomy, which is an operations of ERCP.

- 3. Do endoscopic retrograde pancreatic drainage (ERCP), and endoscopic retrograde biliary drainage (ERBD) mean placement of a pancreatic or biliary stent??**

Endoscopic retrograde biliary drainage (ERBD) means placement of a biliary stent; endoscopic retrograde pancreatic drainage (ERPD) means placement of a pancreatic stent.

- 4. Do you perform MRCP cholangiography before the ERCP in all the patients? However. You have not included any information about their diagnosis in the results sections, please do it and tell us if ERCP confirmed it.**

All 75 patients underwent MRCP or B-scan ultrasonography before ERCP surgery. Only 25 (33.4%) of these were diagnosed with PBM. I have added this information to the results section.

- 5. The most important concern when we look through (examine) this paper is the accuracy**

of your diagnosis of PBM, and this is something the writers should make more efforts to convince us and clarify. For instances, the images that you enclosed are not good enough to demonstrate PBM, like figures B and C. If these images were the best to choose to show the diagnosis of PBM, the readers could have doubt about the precision of your diagnosis of PBM, following the ERCP images, or measuring pancreatic enzymes during the ERCP procedure?? Can you comment something about it?

I have replaced the figures B and C for more representative pictures. About precision of the diagnosis of PBM, firstly, we conducted an endoscopic angiography of the bile duct during the ERCP procedure. When the biliary and pancreatic duct morphology indicated PBM, followed by extracted bile from the bile duct and conducted amylase and lipase measurements. A very high pancreatic enzyme value in the bile, which may be due to pancreatic fluid regurgitation into the bile duct, further confirmed the diagnosis of PBM.

6. Do you perform acute post ERCP pancreatitis prophylaxis with pancreatic stent?

A pancreatic stent was not routinely placed for preventing acute post ERCP pancreatitis, except for in cases of pancreatic duct stenosis or pancreatic duct stones. Because we believe that stents placed in a pancreatic duct without morphological changes may be more likely to induce postoperative pancreatitis

7. The authors a 16% of post ERCP complications, but the authors did not show anything about their severity graduation in the result section; was there any severe complication?

All adverse events were included in the 16% post ERCP complications, no severe complication were observed. I have mentioned the information in the results and in the discussion sections. i.e., “All the 12 patients recovered after conservative treatment, severe complications, such as periangillary perforation, were not observed.” “Post-ERCP pancreatitis (PEP) was the most common complication. In this study, procedure-related PEP was observed in 9 cases (12%). The severity of the conditions was mild to moderate, and all patients recovered after conventional conservative treatment.”

- 8. Could the authors explain a little more about any possible relationship between post ERCP pancreatitis or recurrent pancreatitis and any special type of PBM? It could be added more information about it.**

In fact, in our previous study we analyzed the relationship between the prevalence and risk factors of post ERCP pancreatitis (PEP) in children by gender, age, disease spectrum, operations and contrast agent dose. The results suggested that there was no statistically significant difference in the occurrence of PEP in the disease spectrum. In addition, only 9 children in this study had PEP, and the statistical analysis bias was relatively large, hence, no further analysis was conducted.

- 9. Eight patients (10.6%) suffered from recurrent pancreatitis” any special type of PBM present? While 5 of them (6.7%) underwent additional ERCP therapy (which type...). It seems a high percentages of surgical intervention in this group of patients: “Eleven patients (14.7%) received radical enventally, Why? And what does it mean radical surgery??**

Eight patients (10.6%) experienced recurrent pancreatitis; 3 were type A, 2 type B, 1 type C, and 2 type D PBM patients.

Eleven patients (14.7%) received radical surgery enventally. The following were the reasons for 5 of these patients experiencing recurrent pancreatitis after repeated ERCP operations, 2 patients experienced recurrent fever after operations, and 4 patients requested the surgery due to personal concerns, and were concerned about the risk of developing cancer at a later time.

The radical surgery is prophylactic excision of the extrahepatic bile duct and hepaticojejunostomy.