Author’s response to reviews

Title: Endoscopic balloon dilatation for benign hepaticojejunostomy anastomotic stricture using short double-balloon enteroscopy in patients with a prior Whipple's procedure: a retrospective study

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Version: 1 Date: 30 Sep 2017

Author’s response to reviews:

Oct 01, 2017

Tovah Aronin
Editor-in-Chief
BMC Gastroenterology

RE: Submission of revised Manuscript ID BMGE-D-17-00386
Dear Editor:

Thank you for your email dated 04-Sep-2017 in which you provided us with the reviewers’ comments.

We carefully reviewed the comments and revised the manuscript accordingly. Our responses are given in a point-by-point manner below.

We hope the revised manuscript is now suitable for publication in your esteemed journal and look forward to hearing from you.

Sincerely,

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Response to Reviewer: 1
Thank you for your helpful comments, which allowed us to significantly improve our manuscript.

Comment 1. How did you judge strictures as benign? Please describe if there are cases that biopsy etc. was performed.

Response: We thank the reviewer for this insightful comment. The strictures were determined to be benign by characteristics seen on endoscopy and cholangiography during the procedure. In addition, the clinical course; laboratory values; and findings on imaging with CT, MRI, cholangioscopy, and cholangiography before surgery in addition to pathological findings of the resected specimen were sometimes useful for making the determination. If finding suspicious for malignancy (e.g., irregular papillogranular surface or nodular tumor seen on endoscopy or irregular filling defect seen on cholangiography) were seen, a biopsy was performed. For clarification, we added the following text to the Methods section:

We defined benign HJAS as a pinpoint orifice or cicatricial mucosa without irregular papillogranular surface, nodular tumor, or irregular filling defect by cholangiography. (Page 8, lines 102-104)

It should be noted that since the study some strictures were found to be malignant on biopsy; however, these cases were not included in this study. The patients in this study were followed for a median of 3.5 (range, 1.9–5.0) years after balloon dilatation and no malignancies or recurrences of cancer were observed.

Comment 2. If there are articles referring to the balloon inflation method, please cite them.

Response: We thank the reviewer for this helpful comment. The balloon inflation method was referred to in the following articles:


The reference numbers were added to the text as suggested. (Page 10, line 132)

Response to Reviewer: 2

Thank you for your helpful comments, which allowed us to significantly improve our manuscript.

Minor revisions

Comment 1. Author's median times of scope insertion and biliary cannulation rate, that is, short term results, are very excellent in present article. Balloon dilation under double balloon endoscopy is first choice for treatment of HJAS? If stent deployment is better, which cases is correct for stent deployment?

Response: We thank the reviewer for this insightful comment. Balloon dilation under double-balloon endoscopy is the treatment of first choice for benign HJAS in our hospital. However, in this study, 6 patients were excluded because they were treated with balloon dilatation and stent deployment during the first procedure as described in Figure 1.

Regarding these 6 patients, 3 (50%) were cases of incomplete stone removal of concomitant hepatolithiasis; therefore, we placed the stents to prevent cholangitis due to the remaining stones. The other 3 patients (50%) were cases in which the anastomosis stricture formed a membranous obstruction resulting in severe cholangitis; therefore, we placed the stents to maintain patency and control infection.
As described in the Discussion section (Page 20-21, lines 274-289), in our previous report on endoscopic treatment for HJAS after living-donor liver transplantation (LT), the period of bile duct patency was significantly longer in the balloon dilatation + biliary stent group (n = 7) than in the balloon dilatation alone group (n = 7) during a median follow-up of 22 months (P = 0.017) (Reference 13, Surg Endosc. 2016; 30: 5338–44.). In addition, the most common therapy for benign biliary strictures with duct-to-duct reconstruction after LT involves endoscopic balloon dilatation and placement of multiple plastic stents followed by periodic replacement of the stents for approximately one year to allow for expansion and remodeling of the strictures. Although the anastomotic strictures after LT, which result from ischemia, fibrotic healing, and surgical technique, may be different from HJAS after pancreatoduodenectomy (PD) or pylorus-preserving pancreatoduodenectomy (PPPD), balloon dilatation combined with stent deployment might be recommended for definite resolution and maintenance of biliary flow in patients who have previously undergone PD and PPPD. Further study is needed to determine the usefulness of these combined therapies, especially considering their drawbacks, such as the need for repeat ERCPs for stent exchange and the risk of cholangitis resulting from stent occlusion.

Additionally, we could not determine the risk factors for recurrent HJAS after balloon dilatation in this study. When the risk factors are known, patients at risk would probably benefit from treatments such as stent placement.

Comment 2. Author's success rate of inserting double balloon endoscopy to HJ anastomosis is 100%, very high and inserting time is median 13 minutes, short. Difficulty of inserting double balloon endoscopy is similar among enrolled cases in this present article?

Response: We thank the Reviewer for this insightful comment. In fact, it is not difficult to insert the scope in HJAS patients with a prior history of Whipple’s disease because it makes identification of the route for successful scope insertion easier as described in our previous article (reference 7, Surg Endosc. 2015 Jul;29(7):1944-51). But, we occasionally face difficult cases due to the excessive length of the afferent limb or severe adhesion of the afferent limb. In this study, such cases are also included.

Comment 3. Are these results similar compared with those of other stricture, for example, Roux-en-Y anastomosis?

Response: We thank the reviewer for this helpful comment. Between November 2008 and November 2014, 30 patients with suspected benign HJAS with Roux-en-Y anastomosis
underwent DB-ERC at our hospital. The technical success rates were 60% (18/30) and adverse events occurred in 13% (4/30; cholangitis, bleeding, jejunal laceration, and ischemia). In addition, of 22 patients (73%) followed-up for >1 year, 8 (36%) had recurrent HJAS, and the cumulative anastomotic patency rate of patients with a history of Whipple’s disease compared to Roux-en-Y patients was not significantly different by log-rank test. Therefore, the technical success rate was lower and the adverse event rate was higher compared those of this study.

The causes of technical failure in Roux-en-Y patients were unsuccessful scope insertion (n=9) and unsuccessful treatment (n=3). In particular, scope insertion for HJAS is difficult in patients with a Roux-en-Y anastomosis without gastrectomy (Tomoda K, Tsutsumi K, et al. Dig Endosc. 2015 Nov;27:775). In contrast, it is not difficult to insert the scope in patients with a history of Whipple’s disease like the patients described in this study. Therefore, we believe that endoscopic treatment using balloon enteroscopy is the treatment of choice in Whipple’s patient.

Comment 4. Author's long-term HJA patency at one, two, and three year were 73%, 55%, and 49%, respectively. What do authors think about these long term outcomes comparison of percutaneous transhepatic treatment?

Response: We thank the reviewer for this important comment. Based on previous reports, long-term outcome with endoscopic balloon dilatation alone is inferior to that if percutaneous transhepatic treatment. Also, percutaneous transhepatic dilatation for HJAS requires long-term indwelling stents to obtain acceptable results. Therefore, balloon dilatation combined with stent deployment might be effective for definite resolution and maintenance of biliary flow in patients who have previously undergone PD and PPPD. Further study is needed to determine the usefulness of these combined therapies, especially considering their drawbacks, such as the need for repeat ERCPs for stent exchange and the risk of cholangitis resulting from stent occlusion.

Comment 5. On respect of long term outcomes, stent deployment is considered as better treatment than balloon dilation only?

Response: We thank the reviewer for this insightful comment.
The advantage of endoscopic balloon dilatation alone is that it is a single treatment with high technical and clinical success and low adverse events. As shown in this study, initial balloon dilatation alone can be effective for 3 years in approximately 50% of patients. On the other hand, stent deployment requires repeat ERCPs for stent exchange and increases the risk of cholangitis due to stent occlusion. Therefore, we believe that balloon dilatation alone may be considered the first-line treatment for HJAS in patients who have previously undergone PD or PPPD as described in Discussion section. (Page 21-22, lines 291-295)

Also, we could not determine the risk factors for recurrent HJAS after balloon dilatation in this study. When the risk factors are known, patients at risk would probably benefit from treatments such as stent placement.