

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8141-review.doc).

Title: Application of air insufflation test in preventing clinical pancreatic fistula after pancreaticoduodenectomy

Author: Hui Yang, Xiao-Fei Lu, Yun-Fei Xu, Hong-Da Liu, Sen Guo, Yi Liu, Yu-Xin Chen

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11469

The manuscript has been improved according to the suggestions of reviewers:

Revision has been made according to the suggestions of the reviewer point to point.

Reviewer 1.

Question 1: There are some minor problems with the language used and some polishing of the grammar is necessary.

Answer: Thank you for your advice. We have seek to make use of a copyediting service provided by professional English language editing company as the editor suggested and a corresponding recommendation letter was got from this company.

Question 2: I would also suggest that use of the term air insufflation would be preferable to inflatable.

Answer: Thank you for this advice. We have used the term of air insufflation instead of inflatable in the updated article.

Question 3: In the discussion, the technique is described again. This is superfluous as it is adequately described in the methods

Answer: Thanks for your comment. According to the recommendation, we have deleted the superfluous discussion which has been described in the methods.

Reviewer 2

Question 1-A: what is the risk factors for development of POPF

Answer: Thank you for your advice. It is our fault that the manuscript did not summarize the risk factors for development of POPF, we have revised our manuscript, and added the risk factors for POPF in our new manuscript.

Question1-B: Many strategies have been reported to prevent PF, but none of these strategies aims to detect pancreatic leakage during operation, and their efficacy in preventing PF also remains controversial in different literatures: What are these strategies?

Answer: Thank you for this comment. The strategies which have been reported to prevent pancreatic fistula were detailed introduced in the discussion part of this article, and we have moved them to the introduction part in the new article as advised. Thanks.

Question 1-C: Please rewrite the aim of work?

Answer: According to your recommendation, we have rewritten the aim of work. Thank you for this advice.

Question 2- A: How u can choice the patients for inflatable test?

Answer: Thank you. The air insufflation test was firstly carried out in April 2012 at our institution, and the patients included in the air insufflation test group were those treated from April 2012 to August 2013. Statistical analysis revealed that the patients in the air insufflation test group were similar with the patients in the non-air insufflation test group in terms of clinical characteristics, operative factors, pancreatic factors and pathological diagnoses (Table 1 and 2).

Question 2-B: what is the meaning of this paragraph please rewrite

Answer: Thank you for this advice. We have rewritten this paragraph, which aims to introduce the the way to get the patients' clinical information and the indications to perform preoperative biliary drainage, which was analyzed in the univariate analysis as a factor for PF.

Question 2-C: how y choice type of PJ (duct to mucosa and invaginated PJ)

Answer: Thank you for this comment. Nowadays, although many arguments have been proposed for the method to anastomosis the pancreatic stump with the gastrointestinal tract, the best method for dealing with the pancreatic stump after pancreaticoduodenectomy remains in question. An individual surgeon's mastery of a specific anastomotic technique, in conjunction with a large personal experience, play essential roles in performing pancreaticojejunostomy. In present study, the choice of type of pancreaticojejunostomy was made mainly based on the the characteristics of the patients and the individual experience of the surgeons. In general, for the patients with soft pancreatic texture and small pancreatic duct, the invagination pancreaticojejunostomy was carried out, and for other patients, the duct to mucosa anastomosis was performed. Statistical analysis showed that the air insufflation test group was similar with the non-air insufflation test group in terms of type of pancreaticojejunostomy (Table 2).

Question 2-D: As regards the inflatable test what is the median amount of fluid and air needed in each cases what is the pressure needed? how u can asses the pressure what are the factors that affect the the test (pancreatic duct diameter, texture of pancreas, type of PJ anastomosis) what is the effect of this pressure on the integrity of anastomosis Then , the anastomosis was investigated again until no bubble was found. If the leakage could not be resolved in this way, then, re-anastomosis was performed.is re-anastomosis even for the sound part? how u do re-anastomosis)

Answer: Thank you for these professional advice. Actually, in clinical practice, we monitor the pressure in the jejunal stump during the whole process of performing air insufflation test and we regard the pressure moderate when the tension of the jejunal wall is the same as normal liver tissue or oral lip. The pressure can not be too high, or the integrity of anastomosis can be damaged and acute pancreatitis can be caused. The fluid is regarded as moderate when it swallows the pancrraticojejunal anastomosis. The amount of air and fluid needed in each case are not quantitatively calculated. The most important procedure in the process is to monitor the pressure in the jejunal stump, others factors, such as the pancreatic duct diameter, texture of pancreas and

type of pancreaticojejunostomy are not quite essential to the test. When repair is needed, interrupted suture was carried out only on the area where the bubbles generated. If the leakage could not be resolved in this way, then, re-anastomosis, including the sound part, was performed. If the leakage could not be resolved after twice re-anastomosis, duct to mucosa anastomosis was usually changed to invagination anastomosis. In other cases, the re-anastomosis was performed as the original type of pancreaticojejunostomy. Thanks.

Question 3-A: Inflatable test was successfully carried out for all the 46 patients in the inflatable test group. Pancreatic leakage was found in 10 patients during the test, and immediate repair or re-anastomosis was performed. what is the pancreatic texture in these 10 patients what is the median diameter of PD in these 10 patients what is their postoperative course (incidence of POPF) Incidence of POPF in the rest 36 patients in inflatable group)

Answer: Thank you these comments. The pancreatic texture and pancreatic duct diameter of the 10 patients who were performed immediate repair or re-anastomosis during operations were similar with the other 36 patients in the air insufflation test group and the 65 patients in the non-air insufflation test group (data are shown in the following table). Besides, the overall POPF rate, non-clinical POPF rate and clinical POPF rate of these 10 patients were 20% (n=2), 20% (n=2) and 0% (n=0), respectively. The overall POPF rate, non-clinical POPF rate and clinical POPF rate of the rest 36 patients in the air insufflation test group were 19.4% (n=7), 11.1% (n=4) and 8.3% (n=3), respectively. Interestingly, statistical analysis revealed that the overall POPF rate, non-clinical POPF rate and clinical POPF rate of the 36 patients were similar with the 65 patients in the non-air insufflation test group ($P>0.05$), supporting the contribution of the repair or re-anastomosis after the air insufflation test to the significant reduction of clinical PF in the AIT group.

Table Comparison of the pancreatic texture and pancreatic duct diameter

	air insufflation test group (n=46)		P^a	non-air insufflation test group (n=65)	P^b	P^c
	10 patients ¹	36 patients ²				
Pancreatic texture			1.000		0.850	0.691
Soft	7	27		51		
Hard	3	9		14		
Pancreatic duct diameter			1.000		1.000	0.836
≤ 3 mm	7	24		42		
> 3 mm	3	12		23		

1. the 10 patients who were performed repair or re-anastomosis after air insufflation test during operation; 2. the rest 36 patients in the air insufflation test group.

a. comparison between the 10 patients who were performed repair or re-anastomosis after air insufflation test during operation and the rest 36 patients in the air insufflation test group; b. comparison between the the 10 patients who were performed repair or re-anastomosis after air insufflation test during operation and the 65 patients in the non-air insufflation test group; c. comparison between the the rest 36 patients in the air insufflation test group and the 65 patients in the non-air insufflation test group.

Question 3-B: please clarify the groups in the results. No significant differences were found in mortality rate (2.2% versus 1.5%, $P=1.00$) and overall complication rate (43.5% versus 52.3%,

P=0.36)between the two groups.(Table 3) PF was the most frequent complication after PD. ThePF rate (19.6% versus 30.8%, P=0.19)and the grade A PF rate (13.0% versus 7.7%, P=0.54)were comparable between the two groups.

Answer: Thanks for this advice. The groups have been clarified in the updated manuscript.

Question 4-A and B: this study is a retrospective study and carry multiple biases. add limitation of the study

Answer: Thanks for this comment. We have add limitations of the study to the updated manuscript.

Question 4-C: discussion is redundant please shorten this paragraph

Answer: We have revised and shortened this paragraph in the updated article. Thank you for this instruction.

Question 4-D: why duct to mucosa is usually changed to invaginated Pj?

Answer: Thanks for this professional comment. Duct to mucosa anastomosis is usually changed to invagination anastomosis for the following reasons: Firstly, leakage after twice re-anastomosis suggest that the duct to mucosa anastomosis may be not suitable for this patient because of the texture of the pancreas or the diameter of the pancreatic duct. Secondly, the invagination anastomosis is easier to be performed than the duct to mucosa anastomosis, and there is no need to anastomosis the pancreatic duct again.

Sincerely yours,

Prof. Yu-Xin Chen



Hepatobiliary Surgery Department of Qilu Hospital, Shandong University, NO.44 WenhuaXi Road, Jinan, Shandong Province, China.

Phone nubmer: +86-8764033628

Email: yxs20081020@gmail.com; yh793067@126.com