

Reply to the reviewers' comments

Dear Editor-in-Chief,

We thank you for your decision letter for our manuscript entitled “**Modified binding pancreaticogastrostomy versus modified Blumgart pancreaticojejunostomy after laparoscopic pancreaticoduodenectomy for pancreatic or periampullary tumors**”. We have considered the reviewer's comments and provide below a point-by-point answer to each of them. Changes have been incorporated and highlighted in the revised manuscript. We are grateful to the reviewers for their comments which have helped us improve the manuscript. We hope that you will find this revised version suitable for publication in your esteemed journal.

With kind regards,

Authors

Response to comments

Reviewer 1

1. The manuscript is quiet original, reporting a discrete cohort of patients treated by an old well-known technique, applied to laparoscopy. The findings are very honest, reporting some improved results (reduced POPF) at the price of increased bleedings.

We thank the reviewer for the positive comments

2. Therefore, I would like to suggest to better stress a couple of issues in the discussion. First, laparoscopic technique should not modify the evidence of surgery in order to reduce technical difficulties. Therefore, the ongoing Literature does not recommend pancreaticogastrostomy as a routine.

We agree with the reviewer's comment that surgical techniques should not be modified to reduce the technical difficulties during laparoscopy. Some of the sentences used in the present manuscript that might convey the wrong meaning like “Hence, the two commonly used pancreatic reconstruction techniques in open PD were modified to suit the laparoscopic approach and compared in the present study “, “However, it is technically challenging to replicate the original technique in the laparoscopic approach “were removed in the revised manuscript. Also, we would like to stress that the modified pancreatic reconstruction techniques used in the present series were based on the scientific reasons given in the previous publications. The binding pancreaticogastrostomy (PG) used in the current series was adapted from the

publication by Hong et al. that reported the feasibility of binding PG using a single layer of the full thickness purse-string suture in ten patients undergoing laparoscopic central pancreatectomy^[1]. Modified Blumgart Pancreaticojejunostomy using two transpancreatic sutures was based on the previous reports by Fujii et al. in open pancreaticoduodenectomy and Nagakawa et al., in laparoscopic pancreaticoduodenectomy. Both the studies reported the advantages of using fewer transpancreatic sutures as more stitches placed in the pancreas increase the risk of pancreatic juice leakage. Also, the point suggested by the reviewer that Pancreaticogastrostomy is less commonly used has been added in the discussion. The changes are highlighted in red font in the methods and results section.

References

1. **Hong D**, Liu Y, Peng S, Sun X, Wang Z, Cheng J, Shen G, Zhang Y, Huang D. Binding pancreaticogastrostomy in laparoscopic central pancreatectomy: a novel technique in laparoscopic pancreatic surgery. *Surg Endosc*. 2016; **30**:715-720. [PMID: 26123326;DOI: 10.1007/s00464-015-4265-z]
2. **Fujii T**, Sugimoto H, Yamada S, Kanda M, Suenaga M, Takami H, Hattori M, Inokawa Y, Nomoto S, Fujiwara M, Kodera Y. Modified Blumgart anastomosis for pancreaticojejunostomy: technical improvement in matched historical control study. *J Gastrointest Surg*. 2014; 18:1108-15.[PMID: 24733259; DOI: 10.1007/s11605-014-2523-3]
3. **Nagakawa Y**, Takishita C, Hijikata Y, Osakabe H, Nishino H, Akashi M, Nakajima T, Shiota T, Sahara Y, Hosokawa Y, Ishizaki T, Katsumata K, Tsuchida A. Blumgart method using LAPRA-TY clips facilitates pancreaticojejunostomy in laparoscopic pancreaticoduodenectomy. *Medicine (Baltimore)*. 2020; **99**:e19474. [PMID: 32150110; DOI: 10.1097/MD.00000000000019474]

Reviewer 2

1. When patients were eligible for PG or Blumgart PJ, both had variations of the original technique in order to achieve a pure laparoscopic procedure.

Hence, it is important to address the following: a. The idea of the Blumgart PJ is to lower the shear forces along the cut surface of the pancreas. This is achieved by covering the transection surface with the jejunal wall. This is important as the patients with PJ in this study had only 2 stitches on each side of the pancreatic duct. Although the use of stents mitigated POPF's the clear benefit seems to be obtained from external stents. This has not been specified in the paper. Hence, the variation in the Blumgart technique is a confounder.

We thank the reviewer for highlighting the use of fewer transpancreatic sutures and internal stents as a potential confounder. However, the modification used in the present study was based on the previous reports on Blumgart pancreaticojejunostomy by Fujii et al. in open pancreaticoduodenectomy and Nagakawa et al., in laparoscopic pancreaticoduodenectomy^[1,2]. Both the studies reported the advantages of using fewer transpancreatic sutures as more stitches placed in the pancreas increase the risk of pancreatic juice leakage. The role and type of pancreatic duct stents in reducing postoperative pancreatic fistula is controversial. The internal stent was used in the study by Nagakawa et al., and Mishra et al. ^[1,3]. Fujii et al. used external stents in their series. Hence, we would like to humbly submit that the modifications used in the present series were based on the scientific reasons given in the previous publications. Also, the outcomes of the present study were compared to the results published with the modified technique. The changes are highlighted in red font in the methods and discussion section.

References

1. **Fujii T**, Sugimoto H, Yamada S, Kanda M, Suenaga M, Takami H, Hattori M, Inokawa Y, Nomoto S, Fujiwara M, Kodera Y. Modified Blumgart anastomosis for pancreaticojejunostomy: technical improvement in matched historical control study. *J Gastrointest Surg*. 2014; 18:1108-15.[PMID: 24733259; DOI: 10.1007/s11605-014-2523-3]
2. **Nagakawa Y**, Takishita C, Hijikata Y, Osakabe H, Nishino H, Akashi M, Nakajima T, Shirota T, Sahara Y, Hosokawa Y, Ishizaki T, Katsumata K, Tsuchida A. Blumgart method using LAPRA-TY clips facilitates pancreaticojejunostomy in laparoscopic pancreaticoduodenectomy. *Medicine (Baltimore)*. 2020; **99**:e19474. [PMID: 32150110; DOI: 10.1097/MD.00000000000019474]

3. **Mishra PK, Saluja SS, Gupta M, Rajalingam R, Pattnaik P.** Blumgart's technique of pancreaticojejunostomy: an appraisal. *Dig Surg.* 2011; **28**:281-7. [PMID: 21811074; DOI: 10.1159/000329584]

2. The PG also has a variation but does not seem to have added potential confounders. Accordingly, as reported in the literature, PPH is an important complication in this type of reconstruction.

The binding pancreaticogastrostomy (PG) used in the current series was adapted from the publication by Hong et al. that reported the feasibility of binding PG using a single layer of the full thickness purse-string suture in ten patients undergoing laparoscopic central pancreatectomy^[1]. Hence, as suggested by the reviewer, it is not a potential confounder.

References

1. **Hong D, Liu Y, Peng S, Sun X, Wang Z, Cheng J, Shen G, Zhang Y, Huang D.** Binding pancreaticogastrostomy in laparoscopic central pancreatectomy: a novel technique in laparoscopic pancreatic surgery. *Surg Endosc.* 2016; **30**:715-720. [PMID: 26123326; DOI: 10.1007/s00464-015-4265-z]

3. The authors address that no mortality was recorded. However, was this in-hospital mortality, 30-day or 90-day mortality? In HPB surgery, a 90-d follow-up is a more precise measure to report this outcome.

The reported mortality in the current series is 90-day mortality which has been included in the revised manuscript. The changes are highlighted in red font in the methods section.

4. Regarding definitions, what FRS was used?

Fistula risk score reported by Callery et al. was used in the present series. The reference is included in the methods section of the manuscript (Ref number 17).

Reference

1. Callery MP, Pratt WB, Kent TS, Chaikof EL, Vollmer CM Jr. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. *J Am Coll Surg.* 2013; **216:1-14. [PMID: 23122535; DOI: 10.1016/j.jamcollsurg.2012.09.002]**

5. What was the outcome of the patients with PJ or PG who were not included in the study?

Overall, modified binding PG was performed in 27 patients and modified Blumgart PJ in 29 patients. Both the patients who underwent Binding PG and were not included in the study did not have pancreatic fistula or hemorrhage. Of the four patients who underwent Blumgart pancreaticojejunostomy and were not included in the analysis, one patient developed Grade B pancreatic fistula.

6. When expressing the p-value, it is noteworthy that they are not 0 or 1, they could get close to those values and despite the statistic package, it is better to notate them as >0.999 or <0.0001.

We thank the reviewer for the suggestion, and P values were changed accordingly and the changes are highlighted in red font.

Science editor:

Dear Authors, the main concern of this paper is in the Peer-Reviewer's report (possible confounder)? Please also answer to other comments of Referees.

We have responded point by point to all the queries of the reviewers.

(1). In "Acknowledgment" section before the main text - is the "Nil" stands for "not in list", or is it a typo? Maybe "not applicable" would be an alternative?

Changed acknowledgement to Not applicable

(2). Remove excessive space marks in the main text, examples: "Blumgart PJ between January 2015" (page 2), "total two sutures) to secure" (page 2), "PG was used. Clinical data" (page 5), "surgeon (RK) with sufficient" (page 5), "Blumgart PJ. The present study results" (page 11). Some excessive spaces are also in Table 2. There is also one example when space is not put while it should be: "pancreatic cut surface.In contrast" (page 6).

Errors in spacing has been corrected

(3). For "Informed consent statement" and reference to JIMPER - is there any permanent link or study ID that can be provided in the manuscript?

Study ID has been added in the manuscript

(4). Correct "Transpancreatuc" typo in Figure 2F.

The spelling error has been corrected

Company editor-in-chief:

Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

All the figures are originally generated by the author for this manuscript. The sentence "Copyright ©The Author(s) 2022." added in the powerpoint.

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Table modified as per the instructions

Name of Journal: *World Journal of Clinical Oncology*

Manuscript Type: Original article

Retrospective study

Title: Modified binding pancreaticogastrostomy versus modified Blumgart pancreaticojejunostomy after laparoscopic pancreaticoduodenectomy for pancreatic or periampullary tumors

Running title: Choudhury SR *et al.* Pancreatic reconstruction in laparoscopic pancreaticoduodenectomy

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Author contributions:

Kalayarasan R conceptualized the study and performed the surgical procedures. Choudhury SR and Gnanasekaran S performed the data acquisition and wrote the first draft of the manuscript. Kalayarasan R and Pottakkat B supervised the writing, gave intellectual inputs, and critically revised the manuscript.

Supportive foundations: Not applicable

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Conflict-of-interest statement: All authors have no conflicts of interest to report.

Acknowledgment: Not applicable

Abstract

BACKGROUND: Laparoscopic pancreaticoenteric anastomosis is one of the technically challenging steps of minimally invasive pancreaticoduodenectomy (PD), especially during the learning curve. Despite multiple randomized controlled trials and meta-analyses, the type of pancreatico-enteric anastomosis as a risk factor for post-pancreatectomy complications is debatable. Also, the ideal technique of pancreatic reconstruction during the learning curve of laparoscopic PD has not been well studied.

AIM: The present study compares the short-term outcomes of modified binding pancreaticogastrostomy (PG) and Blumgart pancreaticojejunostomy (PJ) during learning curve of laparoscopic PD.

METHODS: The first 25 patients with resectable pancreatic or periampullary tumors who underwent laparoscopic PD with modified binding PG or modified Blumgart PJ between January 2015 and May 2020 were retrospectively analyzed to compare perioperative outcomes during the same learning curve. A single layer of the full-thickness purse-string suture was placed around the posterior gastrotomy in the modified binding PG. In the modified Blumgart technique, only a single transpancreatic horizontal mattress suture was placed on either side of the pancreatic duct (total two sutures) to secure the pancreatic parenchyma to the jejunum. Also, on the ventral surface, the knot is tied on the jejunal wall without going through the pancreatic parenchyma. Post pancreatectomy complications are graded as per the International Study group for Pancreatic Surgery (ISGPS) criteria.

RESULTS: During the study period, modified binding PG was performed in 27 patients and modified Blumgart PJ in 29 patients. The demographic and clinical parameters of the first 25 patients included in both groups were comparable. Lower

end cholangiocarcinoma and ampullary adenocarcinoma were the primary indications for laparoscopic PD in both groups (32/50, 64%). The median operative time for pancreatic reconstruction was significantly lower in the binding PG group (42 vs. 58 mins, $P=0.01$). The clinically relevant (Grade B/C) postoperative pancreatic fistula (POPF) was significantly more in the modified PJ group (28% vs. 4%, $P=0.04$). In contrast, intraluminal postpancreatectomy hemorrhage (PPH) was more in the binding PG group (32% vs. 4%, $P=0.02$). There was no significant difference in the incidence of delayed gastric emptying between the two groups.

CONCLUSION: During the learning curve of laparoscopic PD, modified binding PG reduces POPF but is associated with increased intraluminal PPH compared to PJ using the modified Blumgart technique.

Keywords:

Pancreaticoduodenectomy; laparoscopy; Pancreatic cancer; Pancreaticojejunostomy; Neoplasms; Tumors

Core tip:

During the learning curve of laparoscopic pancreaticoduodenectomy, modified binding pancreaticogastrostomy reduces the operative time for pancreatic reconstruction. Also, modified binding pancreaticogastrostomy reduces clinically relevant postoperative pancreatic fistula compared to modified Blumgart pancreaticojejunostomy. However, modified binding pancreaticogastrostomy is associated with increased intraluminal postpancreatectomy hemorrhage. The present study results could guide surgeons to tailor the pancreatic reconstruction during the learning curve of laparoscopic pancreaticoduodenectomy.

INTRODUCTION

Laparoscopic pancreaticoduodenectomy (PD) is considered one of the most complex minimal access surgical procedures, requiring proficiency in advanced laparoscopic surgery. With advancements in laparoscopic skills and technology, multiple studies have reported the feasibility, safety, and oncological equivalence of Laparoscopic PD compared to open PD^[1-3]. Despite improved surgical techniques and perioperative management, PD remains a morbid procedure with a 30-50% estimated morbidity rate^[4]. As in open PD, pancreatico-enteric anastomosis remains the Achilles heel in laparoscopic PD, and postoperative pancreatic fistula (POPF) is the critical cause of morbidity in these patients. The type of pancreatico-enteric anastomosis as a risk factor for POPF is still debatable. Multiple retrospective studies, some randomized controlled trials (RCTs), and meta-analyses have reported that pancreaticogastrostomy (PG) is associated with less incidence of POPF compared to pancreatojejunostomy (PJ)^[5,6]. However, other RCTs and meta-analyses did not report any difference between the two anastomotic techniques concerning clinically relevant POPF rates^[7,8].

In laparoscopic PD, in addition to conventional risk factors for POPF, laparoscopic instruments' restricted range of motion poses an additional risk, especially during the learning curve. A review of various techniques of laparoscopic pancreatic reconstruction following laparoscopic PD reported that PJ was more commonly used than PG like open PD^[9]. However, to date, no RCT has compared different techniques of pancreatic reconstruction in laparoscopic PD, precluding a definite conclusion. The ideal method of managing remnant pancreas following laparoscopic PD should be safe and easy to perform, especially during the learning curve. In open PD, binding PG using two layers of purse-string sutures has been described as a safe and technically simpler method of pancreatic reconstruction^[10,11]. Of the many techniques of PJ, the Blumgart method of PJ is a popular one, and its safety has been established in multiple open PD series^[12-14]. However, the outcomes of these techniques of pancreatic reconstruction during the learning curve of Laparoscopic PD have not been previously studied. We used the binding PG and Blumgart

method of PJ that was modified to suit the laparoscopic pancreatic reconstruction^[12,15]. The present study compares the short-term outcomes of modified binding PG and Blumgart technique of PJ for pancreatic reconstruction in laparoscopic PD during the learning curve.

MATERIALS AND METHODS

Patient selection

Laparoscopic PD was started in the institute in January 2015. Till October 2017, modified binding PG was used for pancreatic reconstruction in laparoscopic PD. Subsequently, the modified Blumgart technique was mainly used for pancreatic reconstruction except in patients whose pancreatic duct could not be identified after pancreatic transection, where invagination PJ or binding PG was used. Clinical data of the first 25 patients with resectable pancreatic and periampullary tumors who underwent laparoscopic PD with modified binding PG or modified Blumgart PJ between January 2015 and May 2020 were retrospectively analyzed to evaluate the outcomes during the same learning curve. Pancreatic cancer patients with suspected vascular involvement and those with contraindications for laparoscopic surgery were not considered for laparoscopic PD. Patients who underwent laparoscopic PD with different techniques of pancreatic reconstruction and those who underwent robotic PD were excluded from the analysis. Also, patients who underwent laparoscopic PD for chronic pancreatitis or other nonmalignant etiology were not included in the study. All surgeries were performed by a single surgeon (RK) with sufficient experience in advanced minimally invasive gastrointestinal surgery. The study was approved by the Institute scientific advisory committee (PGRMC 19.04.2021-18) and the Institute ethics committee (JIP/IEC/2021/0194).

Operative technique

The procedure was performed using six laparoscopic ports: One infra umbilical 12 mm port, two 12mm pararectal ports, one left subcostal 12mm port, one right subcostal 5mm port, and one 5mm epigastric port with the patient in French position (supine with leg split). The infraumbilical port is used for laparoscopic camera

except during uncinate dissection when the camera is moved to the right pararectal port. For ligation and division of gastrocolic trunk, division of stomach, lymph node dissection in hepatoduodenal ligament, and bile duct division, the two 12mm ports on the left side are used as primary working ports with the surgeon standing on the left side of the patient. The primary surgeon moves to the patient's right side for the remaining dissection. The two right-sided ports are used as a primary working port for the pancreatic reconstruction using modified binding PG. Two full-thickness stay sutures are taken at the corners of the pancreatic cut surface using 3-0 polypropylene to facilitate pancreatic mobilization and invagination into the stomach (Fig 1). The pancreas is carefully mobilized from the splenic vein and artery after sealing and dividing small vessels for approximately 3-4cm. The left gastric vein that usually drains to the splenic portal vein junction should be identified during pancreatic mobilization to avoid inadvertent injury and troublesome bleeding. Anterior gastrotomy of length approximately 4-5 cm was made proximal to the stapled end of the stomach. A posterior gastrotomy was made at a site where the pancreas can be invaginated without undue tension for a length approximately equivalent to the width of the pancreatic cut surface. In contrast to the original technique of binding PG that used two layers (inner mucosal and outer seromuscular) of purse-string sutures, the modified binding PG technique utilizes only a single layer of a full-thickness purse-string suture^[10,15]. The modified binding PG technique used in the current series was adapted from the publication by Hong et al. that reported the feasibility of binding PG using a single layer of the full thickness purse-string suture in ten patients undergoing laparoscopic central pancreatectomy^[15]. The placement of the purse-string suture using 3-0 polypropylene should start from the superior edge of the posterior gastrotomy to ensure adequate visualization of knots after invagination of the pancreas. The pancreas was lifted using the stay sutures and invaginated into the stomach through posterior gastrotomy. The stay sutures are held with a laparoscopic grasper advanced through anterior gastrotomy. Once the invagination of at least 2cm of the pancreas into the stomach was confirmed, the stay suture is tied to bind the gastric wall to the pancreatic stump. The position of the pancreas inside the stomach was rechecked after completion of the

hepaticojejunostomy to ensure a tension-free anastomosis. An anterior gastrotomy was used for hand sewn gastrojejunostomy.

For PJ using the modified Blumgart technique, the surgeon stands between the patient's legs and uses the infraumbilical and right subcostal ports as working ports. The laparoscopic camera was inserted through the right pararectal port. In the original Blumgart technique, two to three transpancreatic full-thickness U-shaped sutures were placed on either side of the pancreatic duct^[16]. In the modified technique, a single transpancreatic horizontal mattress suture was placed on either side of the pancreatic duct (total two sutures) to secure the pancreatic parenchyma to the jejunum (Fig 2). **The modified Blumgart PJ used in the present series was based on the previous studies in open PD that reported the advantages of using fewer transpancreatic sutures to minimize the risk of pancreatic juice leakage^[12,14].** The 26 mm ½ circle round body needle of 3-0 polypropylene suture was straightened to facilitate the placement of transpancreatic suture. For duct to mucosa anastomosis, six interrupted 4-0 PDS sutures are placed at 4,6,8,10,12 and 2'o clock position. The needle moves in-out direction in the ductal end to ensure accurate placement of pancreatic duct sutures. In-out needle movement was facilitated by taking the initial bite in the pancreatic duct for four, six and 8'o clock sutures. For the remaining sutures, the initial bite was taken in the jejunal end. The pancreatic duct stent was placed after knotting the six and 8'o clock sutures. However, the stent was not fixed with sutures. After knotting the remaining duct to mucosa sutures, the transpancreatic suture needle was used to take a seromuscular bite on the antimesenteric edge of the jejunum. Ligation of these sutures wraps the ventral portion of the pancreatic cut edge with the jejunum. In contrast to the original Blumgart technique, no suture was taken on the anterior surface of the pancreas. A feeding jejunostomy was routinely performed in all patients undergoing laparoscopic PD.

Outcome measures

The patients' demographic and clinical data, including age, gender, body mass index, bilirubin level, preoperative biliary drainage, total operative time, time taken for

pancreatic reconstruction, estimated blood loss, need for blood transfusions, fistula risk score, tumor type was reviewed and compared between two groups^[17]. Postoperative morbidity was graded as per Clavien-Dindo classification^[18]. Delayed gastric emptying [DGE], Postpancreatectomy hemorrhage (PPH) and Postoperative pancreatic fistula [POPF] were graded as per the International Study Group for Pancreatic Surgery [ISGPS] definition^[19-21]. **Postoperative mortality is defined as any death, regardless of cause, occurring within 90 days after surgery in or out of the hospital.**

Statistical analysis

Continuous variables were expressed as median with range. Categorical variables were expressed as proportions. Continuous variables were analyzed using the Mann-Whitney U test. Categorical variables were analyzed using the chi-square test or Fisher's exact test. A P value of less than 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, Version 28.0. (Armonk, NY: IBM Corp)

RESULTS

During the study period, 78 patients underwent minimally invasive PD. Of these, 22 patients [Robotic PD (n=18), nonmalignant etiology (n=2), invagination PJ (n=2)] who did not meet the inclusion criteria were excluded from the analysis. Overall, modified binding PG was performed in 27 patients and modified Blumgart PJ in 29 patients. To evaluate the short-term outcomes during the learning curve of laparoscopic PD first 25 consecutive patients who underwent modified binding PG and modified Blumgart PJ were included in the study.

The demographic and clinical parameters between the two groups were comparable (Table 1). Both groups had lower end cholangiocarcinoma and ampullary adenocarcinoma as the primary indications for laparoscopic PD (32/50, 64%). Hence, most patients had jaundice (43/50, 86%) at presentation. All three patients with Intraductal papillary mucinous neoplasm had the main duct type of tumor. Of the

three patients with neuroendocrine tumor, one patient had an ampullary tumor, and the other two had cancer in the head and uncinate process of the pancreas.

There was no significant difference in the total operative time and estimated blood loss between the two groups (Table 2). However, the median time to perform modified binding PG was significantly less than modified Blumgart PJ. While most patients had intermediate or high fistula risk scores (38/50, 76%), the proportion was not significantly different between the two groups. However, the modified binding PG group had a significantly lesser number of patients with Grade B/C POPF. None of the patients required reoperation for POPF. Overall, nine patients had postpancreatectomy hemorrhage (Grade A- 3, Grade B-5, Grade C-1). The proportion of patients with PPH was significantly more in the modified binding PG group. On the fifth postoperative day, one patient in the binding PG group was reoperated in an emergency due to severe upper gastrointestinal bleeding that manifested as hematemesis. To visualize the pancreatic stump, an anterior gastrotomy was made away from the gastrojejunostomy site. After evacuating the clots in the gastric lumen, an arterial bleeder in the inferior edge of the pancreatic stump was suture ligated. DGE was present in 13 patients (Grade A- 7, Grade B-4, Grade C-2). However, there was no significant difference in the rate of DGE between the two groups. There was no postoperative mortality in both groups.

DISCUSSION

The present study results suggest that during the learning curve of laparoscopic PD, modified binding PG reduces POPF but is associated with increased intraluminal PPH compared to PJ using the modified Blumgart technique. The feasibility, safety, and oncological outcomes of laparoscopic PD have been documented in multiple retrospective series and a few single-center prospective trials^[1-3]. However, the multicentre randomized trial (LEOPARD-2) comparing laparoscopic with open PD was prematurely terminated because of higher complication-related mortality in the laparoscopic group^[22]. As in open PD, pancreatico-enteric anastomosis is the critical cause of morbidity and mortality in patients undergoing laparoscopic PD, especially during the learning curve in low and medium volume centers ^[4,22]. While the

learning curve for laparoscopic PD has not been well studied, a few single-center studies have suggested that operative time and complications stabilize after 30-42 procedures^[23-25]. Hence, in the present study, the perioperative outcomes of the first 25 laparoscopic procedures are compared.

The type of pancreatico-enteric anastomosis as a risk factor for POPF is still controversial. While a few RCTs and meta-analyses have documented the benefits of PG in reducing POPF, others did not find any difference between the two anastomotic techniques^[5-8]. The ideal pancreatic reconstruction technique during the learning curve of laparoscopic PD should be safe and easy to perform. ~~Hence, the two commonly used pancreatic reconstruction techniques in open PD were modified to suit the laparoscopic approach and compared in the present study.~~ The binding technique for pancreatoenteric anastomosis was described by Peng et al. based on the hypothesis that avoiding pancreatic sutures at the level of the anastomosis can minimize POPF^[26]. Initially, he described binding PJ with an excellent postoperative outcome^[26]. However, binding PJ cannot be used when the pancreatic stump is too large to be invaginated into the jejunum. Hence binding PG was developed in which the pancreatic stump was invaginated into the stomach and held in place by two purse-string sutures: an outer seromuscular and inner mucosal purse-string suture^[10]. Despite encouraging outcomes with binding PG in open PD, its safety and feasibility have not been well studied in laparoscopic PD. ~~Hong et al. reported the feasibility of binding PG in ten patients undergoing laparoscopic central pancreatectomy^[27].~~ Wakabayashi et al. reported the feasibility of double purse-string suture PG in robotic PD as a technical report^[27]. In the present study, only a single layer of the full-thickness purse-string suture was used that was adapted from the previous report on the feasibility of binding PG using a single layer of the full thickness purse-string suture in patients undergoing laparoscopic central pancreatectomy^[28]. ~~In the present study, only a single layer of the full-thickness purse-string suture is used to avoid the technical difficulty of placing an inner mucosal purse-string suture by laparoscopic approach.~~ The efficacy of the Blumgart technique in reducing the POPF rate has been documented in multiple open PD series^[29,30]. The transpancreatic, full-thickness, mattress U-sutures used in the

Blumgart technique reduce the tangential tension and shear force at the pancreatic stump. ~~However, it is technically challenging to replicate the original technique in the laparoscopic approach. However~~Also, more sutures on the pancreas increase the POPF risk^[31]. Another potential risk with the original Blumgart technique is excessive compression on the pancreas while tying the transpancreatic sutures. Hence, only two transpancreatic U sutures were used in the present technique. Also, on the ventral surface, only a seromuscular bite was taken on the jejunum without taking any suture on the anterior surface of the pancreas to reduce shear force and excessive compression of the pancreatic parenchyma.

The perioperative outcomes of the modified binding PG and modified Blumgart technique of PJ have not been previously compared in the laparoscopic approach. As documented in the present study, modified binding PG can minimize the pancreatic reconstruction time as it requires only a single layer of the full-thickness purse-string suture. Also, only one patient developed clinically relevant POPF in the binding PG group despite the high fistula risk score of the included patients. In Binding PG, no sutures are taken to fix the pancreas with the stomach, which precludes the risk of suture cut through in the soft pancreas. Also, the portion of the pancreas through which stay sutures are taken is invaginated into the stomach. It ensures that a minor pancreatic leak from the needle entry site enters the gastric lumen rather than the peritoneal cavity. The clinically relevant POPF rate with the modified Blumgart technique was 28% in the present study. The grade B/C POPF rate with the Blumgart technique in open PD ranges from 2.5% to 20.5%^[12-14,29,30]. Nagakawa et al. reported a Grade B/C POPF rate of 20% in their laparoscopic series using the modified Blumgart technique^[31]. The relatively high POPF rate in the present series could be due to the learning curve effect and inclusion of high fistula risk score patients.

In contrast to POPF, modified binding PG is associated with an increased incidence of intraluminal PPH. While most patients had Grade A or B PPH, surgical intervention was required in one patient. Also, seeing blood through the nasogastric gastric tube makes the patient anxious. Raw pancreatic stump lying freely in the

gastric lumen without any compression effect of jejunum may be the reason for an increased incidence of intraluminal PPH. Hong et al. suggested that full-thickness suture closure of pancreatic stump can reduce the incidence of intraluminal PPH with binding PG^[27]. It is recommended to stent the pancreatic duct to avoid including it while taking the hemostatic sutures.

The choice of pancreatic reconstruction in both open and laparoscopic PD is determined by surgeon preference and familiarity with a particular technique. As binding PG is a technically more straightforward procedure, we used it in our initial patients who underwent PD. The increased incidence of intraluminal PPH was the primary reason for changing to modified Blumgart PJ. The present study results suggest that it may be preferable to start with a simpler technique of pancreatic reconstruction to reduce the POPF rate. Modified Binding PG with hemostatic pancreatic sutures on either side of the pancreatic duct may achieve the goal without increasing PPH. Alternatively, tailored pancreatic reconstruction with modified binding PG for patients with a high fistula risk score and modified Blumgart PJ for patients with low fistula risk score may be a reasonable approach during the learning curve of laparoscopic PD. While retrospective study design is the primary limitation of the current series, it is the first study to compare the perioperative outcomes of modified binding PG and modified Blumgart technique of PJ.

CONCLUSION

Modified Binding PG reduces the pancreatic reconstruction time and POPF rate during the learning curve of laparoscopic PD but is associated with increased intraluminal PPH compared to PJ using the modified Blumgart technique.

Article highlights

Research background

Complications related to pancreatico-enteric anastomosis are a significant cause of morbidity, especially during the learning curve in laparoscopic pancreaticoduodenectomy (PD). Despite multiple randomized controlled trials and meta-analyses, the type of pancreatico-enteric anastomosis [pancreaticojejunostomy (PJ) vs. pancreaticogastrostomy (PG)] as a risk factor for post-pancreatectomy complications is debatable.

Research motivation

The ideal technique of pancreatic reconstruction during the learning curve of laparoscopic PD has not been well studied.

Research objectives

To compare the short-term outcomes of modified binding PG and Blumgart technique of PJ for pancreatic reconstruction in laparoscopic PD during the learning curve.

Research methods

The first 25 patients with resectable pancreatic or periampullary tumors who underwent laparoscopic PD and pancreatic reconstruction with modified binding PG or Blumgart PJ between January 2015 and May 2020 were retrospectively analyzed. A single layer of the full-thickness purse-string suture was placed around the posterior gastrotomy in the modified binding PG. In the modified Blumgart technique, a total of two transpancreatic horizontal mattress sutures were placed on either side of the pancreatic duct to secure the pancreatic parenchyma to the jejunum. Also, on the ventral surface, the knot is tied to the jejunal wall without going through the pancreatic parenchyma. Post pancreatectomy complications are graded as per the International Study group for Pancreatic Surgery (ISGPS) criteria and compared to evaluate perioperative outcomes during the same learning curve.

Research results

The demographic and clinical parameters of the patients included in both groups were comparable. The median operative time for pancreatic reconstruction was significantly lower in the binding PG group (42 vs. 58 mins, $P=0.01$). The clinically relevant (Grade B/C) postoperative pancreatic fistula (POPF) was significantly more in the modified PJ group (28% vs. 4%, $P=0.04$). In contrast, intraluminal postpancreatectomy hemorrhage (PPH) was more in the binding PG group (32% vs. 4%, $P=0.02$). There was no significant difference in the incidence of delayed gastric emptying between the two groups.

Research conclusions

Modified binding PG reduces the pancreatic reconstruction time and POPF rate during the learning curve of laparoscopic PD but is associated with increased intraluminal PPH compared to PJ using the modified Blumgart technique.

Research perspectives

Modified Binding PG combined with techniques to reduce PPH like hemostatic pancreatic sutures on either side of the pancreatic duct may reduce POPF without

increasing PPH during the learning curve of laparoscopic PD. A tailored pancreatic reconstruction with modified binding PG for patients with a high fistula risk score and modified Blumgart PJ for patients with low fistula risk score may be a reasonable approach during the learning curve of laparoscopic PD.

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Footnotes

Institutional review board statement: The study was approved by the Institute scientific advisory committee (PGRMC 19.04.2021-18) and the Institute ethics committee (JIP/IEC/2021/0194).

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent. For full disclosure, the details of the study are published on the home page of JIPMER (<http://www.jipmer.edu.in> study ID - JIP/IEC/2021/0194).

Conflict-of-interest statement: We have no financial relationships to disclose.

Data sharing statement: No additional data are available.

Figure Legends

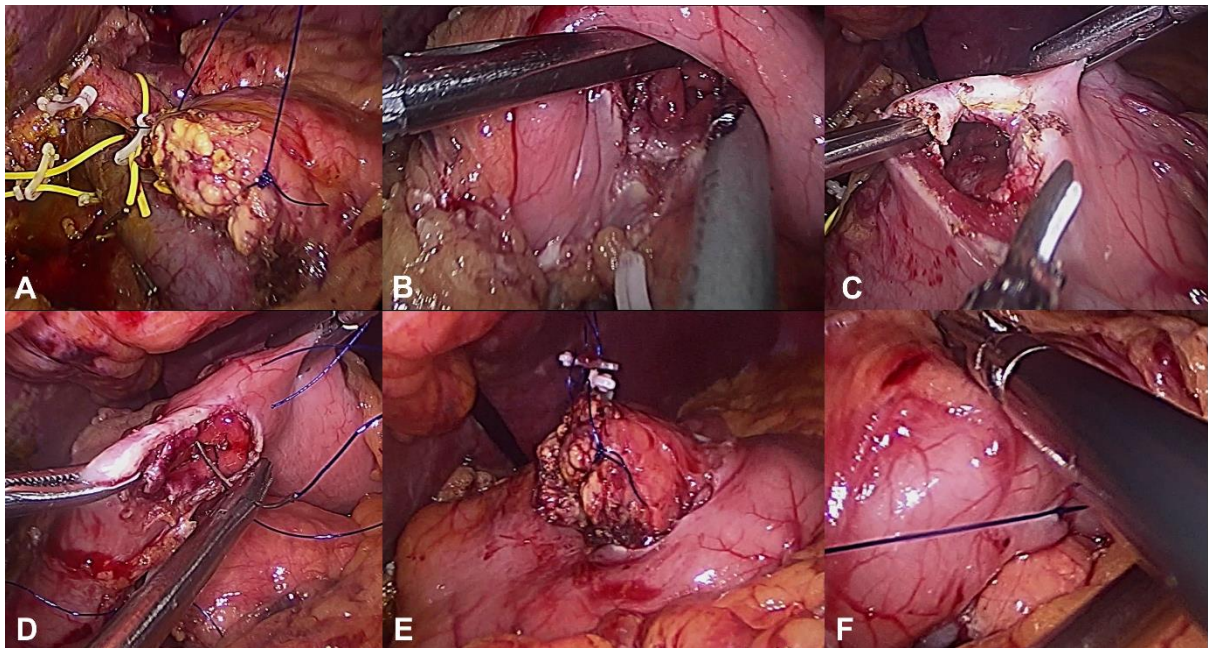


Fig 1 – Steps of modified binding pancreaticogastrostomy. (A) Two full-thickness stay sutures are taken at the corners of the pancreatic cut surface. (B) A posterior gastrotomy is made at a site where the pancreas can be invaginated without undue tension. (C) Anterior gastrotomy of approximately 4-5 cm is made proximal to the stapled end of the stomach. (D) A full-thickness purse-string suture is placed around

the posterior gastrotomy using 2-0 polypropylene. (E). The pancreas lifted using the stay sutures and invaginated into the stomach through posterior gastrotomy. At least 2cm of the pancreas invaginated into the stomach (F). Purse-string suture tied to bind the gastric wall to the pancreatic stump.

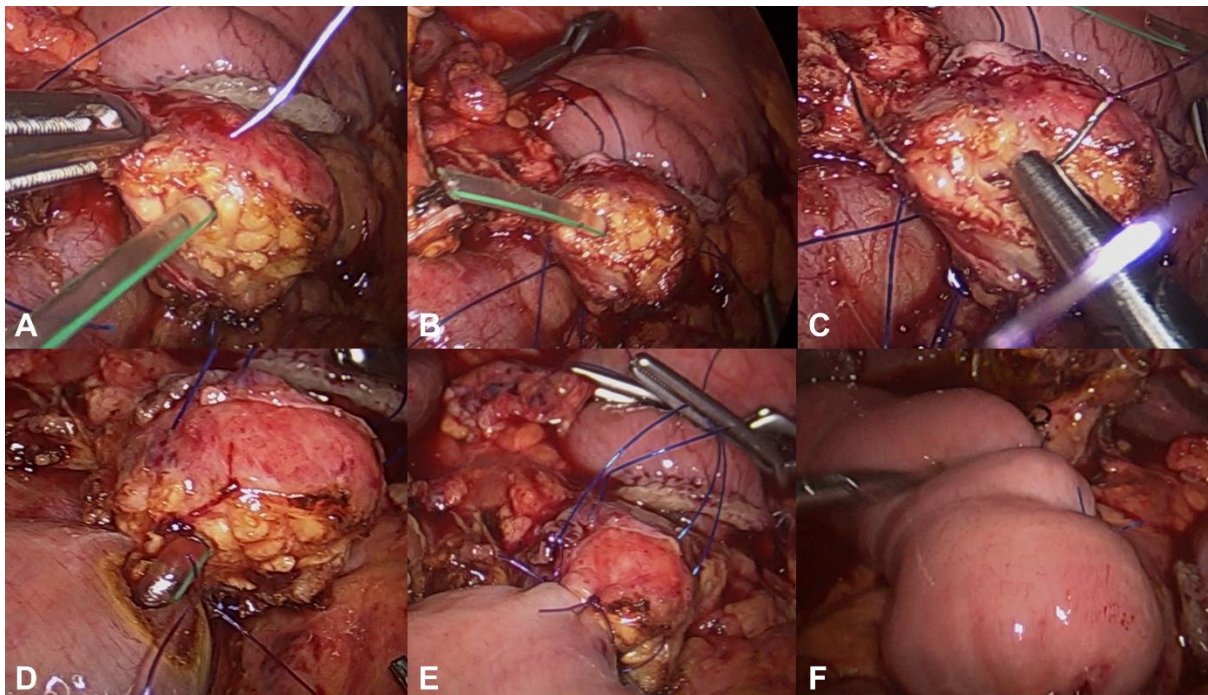


Fig 2 – Steps of modified Blumgart pancreaticojejunostomy. (A) The 26 mm $\frac{1}{2}$ circle round body needle of 3-0 polypropylene suture is straightened to facilitate the placement of transpancreatic suture. (B) One transpancreatic U suture is taken on either side of the pancreatic duct, and the sutures were held with bulldog clamps. (C) 8'o clock duct to mucosa suture taken with the needle moving in-out direction in the ductal end. (D) The pancreatic duct stent is placed after ligating the six and 8'o clock

sutures. (E). Completion of duct to mucosa sutures. (F). **Transpancreatic** U suture is tied to wrap the pancreatic cut edge with the jejunum.

Variable	Binding PG group (n=25)	Modified Blumgart PJ group (n=25)	P value
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Table 1 Comparison of demographic and clinical parameters of patients who underwent laparoscopic pancreatoduodenectomy with binding pancreaticogastrostomy (PG) and modified Blumgart pancreaticojejunostomy (PJ)

Age (years), median (range)	53.7 (37-75)	58.2 (31-79)	0.12
Gender, Male: Female	14:11	15:10	>0.99
BMI (Kg/ m2), median (range)	23.8 (17.6–41.6)	24.6 (18.2–40.0)	0.69
Jaundice, n (%)	22 (88)	21 (84)	>0.99
Cholangitis, n (%)	8 (32)	5 (20)	0.52
Peak total bilirubin levels (mg/ dL), median (range)	12.8 (1.2-28.3)	10.6 (1.1-31.2)	0.59
Preoperative biliary drainage, n (%)	14 (56)	12 (48)	0.78
CA 19-9 (U/ mL), median (range)	55 (1–5,682)	84 (2–3,318)	0.12
Diagnosis, n(%)			
Cholangiocarcinoma	9 (36)	7 (28)	0.76
Pancreatic adenocarcinoma	3 (12)	2 (8)	>0.99
Ampullary adenocarcinoma	7 (28)	9 (36)	0.76
Duodenal Adenocarcinoma	3 (12)	4 (16)	>0.99
Intraductal Papillary	2 (8)	1 (4)	>0.99
Mucinous Neoplasm Pancreas			
Neuroendocrine tumor	1 (4)	2 (8)	>0.99

Table 2 Comparison of perioperative outcomes of patients who underwent laparoscopic pancreatoduodenectomy with binding pancreaticogastrostomy (PG) and modified Blumgart pancreaticojejunostomy (PJ)

Variable	Binding PG group (n=25)	Modified Blumgart PJ group (n=25)	P value
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Total operative time (min), median (range)	445 (390-710)	405 (330-670)	0.06
Operative time for pancreatic reconstruction(min), median (range)	42 (26-65)	58 (44-81)	0.01
Estimated blood loss (ml), median (range)	320 (210-740)	310 (175-950)	0.09
Blood Transfusion, n (%)	6 (24)	7 (28)	>0.99
Gland texture, n (%)			
Soft	17 (68)	19 (76)	0.75
Firm	8 (32)	6 (24)	
Pancreatic duct diameter (mm), median (range)	3 (1-9)	3 (2-10)	>0.99
Fistula risk score, n(%)			
Low	5 (20)	7 (28)	0.74
Intermediate	12 (48)	13 (52)	>0.99
High	8 (32)	5 (20)	0.52
Postoperative morbidity, Clavien–Dindo classification IIIa or more, n(%)	8 (32)	9 (36)	>0.99
Pancreatic fistula (Grade B/C) , n(%)	1 (4)	7 (28)	0.04
Delayed gastric emptying, n(%)	7(28)	6 (24)	>0.99
Post pancreatectomy hemorrhage, n(%)	8 (32)	1 (4)	0.02
Bile leak, n(%)	0	1 (4)	>0.99
Postoperative hospital stay, n(%)	9 (6-38)	8 (5-56)	0.72

Abbreviations

PD - Pancreaticoduodenectomy

PG - Pancreaticogastrostomy

PJ - Pancreaticojejunostomy

ISGPS- International Study group for Pancreatic Surgery

POPF - Postoperative pancreatic fistula

PPH - Postpancreatectomy hemorrhage

RCT - Randomized controlled trial

DGE - Delayed gastric emptying