

## Original Research Article

# A prospective randomized controlled trial comparing laparoscopic versus open Whipple's procedure for periampullary malignancy

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### ABSTRACT

**Background:** Laparoscopic surgery in cases of periampullary region malignancies has been emerging as a preferable alternative to open pancreatoduodenectomy due to their benefits such as early mobilization and shorter duration of hospital stay. We conducted this study to determine whether laparoscopic approach is comparable to open pancreatoduodenectomy in terms of hospital stay, blood loss, complications, pathological radicality with oncological safety and overall postoperative short-term outcomes.

**Methods:** This was a single-center, non-stratified, balanced allocation, open-label, parallel-group randomized control study in which patients who had undergone Whipple's procedure were included. Patients were randomized after confirmation of non-metastatic status into either the laparoscopy (N=15) or open surgery group (N=15). The primary outcome variable was duration of postoperative hospital stays. Secondary outcomes were duration of surgery, blood loss, complication rates (using definitions of the international study group of pancreatic surgery) and pathological radicality of resection.

**Results:** Pain in abdomen was the predominant complaint which was seen in 12 (80%) and 10 (66%) patients each. The other common symptoms were weight loss, vomiting and jaundice. Surgical site infection, mean blood loss and mean operative duration was significantly lower in laparoscopic group ( $P < 0.05$ ). Mean tumor size was more in open group. Mortality was comparable in both the groups.

**Conclusions:** Laparoscopic pancreatoduodenectomy offers significant benefit in terms of hospital stay, surgical site infection, mean blood loss, mean operative duration and mean interval of duration receiving chemo/radiotherapy as compared to open surgery in cases of periampullary region malignancy.

**Keywords:** Complications, Laparoscopic surgery, Outcome, Periampullary region malignancies

### INTRODUCTION

Pancreaticoduodenectomy in pancreatic surgery has been called a "formidable" operation. It is not only a technical challenge to surgeons but also it is also demanding for patients and it exerts a substantial logistical strain on healthcare resources. Halsted, Kausch and Whipple paved the way for modern surgery and the treatment for pancreatic and periampullary cancer as it's known today.<sup>1</sup> Resection of pancreatic head includes the standard pancreatic duodenectomy popularized by Whipple's as

well as its modification such as pylorus preserving pancreatic duodenectomy (PD) and duodenum preserving pancreatic head resection (DPPHR). Periampullary region malignancy is notoriously resistant to non-surgical forms of oncological treatment such as radio-, chemo, and immunotherapy.<sup>2,3</sup>

Surgical resection offers the only chance for cure for Periampullary region malignancy.<sup>4,5</sup> Pancreaticoduodenectomy is also the primary treatment for resectable periampullary tumors.

The pylorus preserving pancreatoduodenectomy is currently the standard procedure in the curative treatment of patients with periampullary cancer. The pylorus preserving pancreatoduodenectomy performed today includes resection of the pancreatic head, duodenum, distal common bile duct and the gallbladder followed by aduodenojejunostomy, hepaticojejunostomy and pancreatoduodenectomy. Until recently, the role of laparoscopy in pancreatic diseases was limited to staging laparoscopy and sometimes a palliative drainage procedure for unresectable malignancies.<sup>6</sup>

Criticism of laparoscopic pancreatic resectional procedures, especially pancreatoduodenectomy, was based on the fact that pancreas-specific complications are leading causes of severe morbidity and mortality, irrespective of approach. Although the benefits of minimally invasive surgery would remain for patients, pancreas-specific complications are not the obvious targets for improvement with these approaches. In addition, factors such as the retroperitoneal location of this organ surrounded by vital structures, and the technically complex approach to pancreatic head tumors, their resection and reconstruction, made the laparoscopic approach more difficult.

Despite these barriers, with technical advances in instrumentation coupled with growing expertise in recent years, several surgeons across the world have acquired the necessary surgical skills to perform this procedure safely with good results, and laparoscopic pancreatoduodenectomy is being performed more frequently for benign and malignant lesions.<sup>7</sup>

Laparoscopic pancreatoduodenectomy, although technically difficult and requiring a high degree of expertise, has shown efficacy equal to that of open pancreatoduodenectomy in terms of complications, oncological safety and overall outcomes, with inherent advantages of minimally invasive surgery such as decreased blood loss, reduced pain, shorter hospital stay and earlier return to work.<sup>8</sup> Although a recent study from a high-volume center reported concerns about greater morbidity for the laparoscopic approach, with a higher pancreatic fistula rate, a meta-analysis including more than 20 000 patients revealed favorable outcomes in well selected patients in centers with a larger volume.<sup>9,10</sup>

The present study was therefore carried out as a Randomized control study to determine whether the laparoscopic approach is comparable to open pancreatoduodenectomy in terms of hospital stay, blood loss, complications, pathological radicality with oncological safety and overall postoperative short-term outcomes.

## **METHODS**

This was a single-center, non-stratified, balanced allocation (1:1) open-label, parallel-group randomized

control trial. After due approval of institutional ethical committee, the study was conducted in the department of surgery at a tertiary care medical college situated in an urban area. All Patients admitted in the department of surgery and who had undergone Whipple's procedure were included in this study on the basis of a predefined inclusion and exclusion criteria. Simple randomization was done using a random number table, with opaque sealed envelopes.

On admission, demographic and anthropometric data were recorded along with a detailed clinical history. All Patients underwent complete physical examination followed by laboratory and radiological investigations. After establishing the diagnosis, tumors were staged according to the TNM classification. Patients with potentially resectable tumors and deemed fit for surgery were considered for staging laparoscopy. Informed consent was obtained from the patient and family regarding participation in the study, the possibility of undergoing either of the mentioned procedures, complications, and expected outcomes.

All patients, irrespective of final operation, had an epidural catheter placed before the procedure; the top-up dose in the postoperative period was decided by an anesthetist, according to individual patient's requirements. Patients were randomized after confirmation of non-metastatic status into either the laparoscopy or open surgery group. The patients were grouped and subsequently analyzed based on the original randomization, in accordance with the intention-to-treat principle, irrespective of their final treatment. All the procedures were performed by either of the two senior surgeons with sufficient experience of open and laparoscopic pancreatoduodenectomy. The surgeries were performed as per institutional protocol.

The primary outcome variable was duration of postoperative hospital stays. Secondary outcomes were duration of surgery, blood loss, complication rate and pathological radicality of resection. For statistical purposes p value less than 0.05 was taken as statistically significant. All statistical tests were done using GraphPad online version software.

## ***Inclusion criteria***

Adult males or females with a diagnosis of resectable on imaging pancreatic head malignancy, malignancy of 2<sup>nd</sup> part duodenum, lower end common bile duct malignancy and ampulla Vater malignancy with:

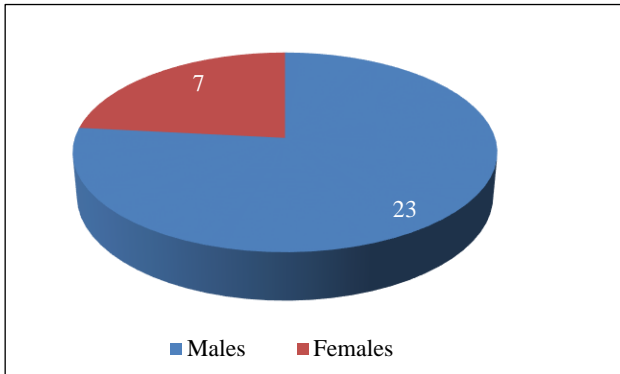
- No evidence of metastasis.
- Radiological Non-involvement of superior mesenteric vein and portal vein.
- Fat plane maintained between celiac axis, hepatic artery and superior mesenteric artery.
- Ready to give consent.

**Exclusion criteria**

- Unresectable tumors at surgery.
- Inoperable tumors receiving palliative chemo-radiation.
- Those who refused consent.
- Lost to follow up.

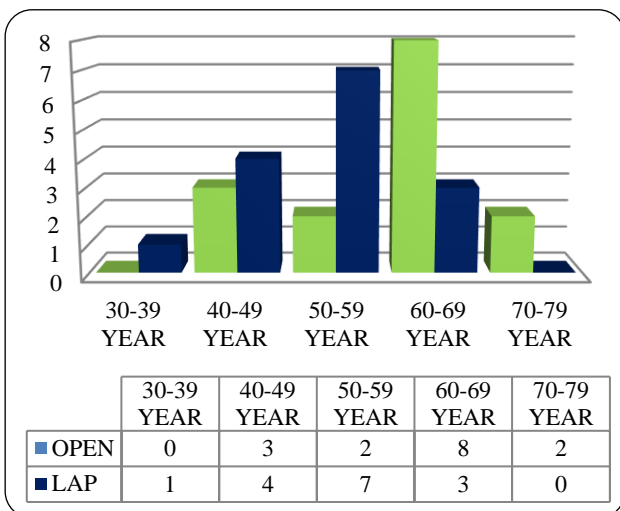
**RESULTS**

Out of 30 studied cases there were 23 males and 7 females with a M:F ratio of 1:0.30 (Figure 1).



**Figure 1: Gender distribution of the affected cases.**

Out of 30 studied cases 15 patients underwent open/conventional Whipple’s procedure (Open Group) and 15 underwent laparoscopic Whipple’s procedure (laparoscopy group). In our study, the maximum number of patients who underwent open surgery were from the age group of 60-69 years. While the maximum number of patients who underwent laparoscopic surgeries were from the age group of 50-59 years (Figure 2).



**Figure 2: Age distribution of the cases.**

Mean BMI in open and laparoscopic group was found to be 23.4kg/m<sup>2</sup> and 25.6kg/m<sup>2</sup> respectively. It was observed in the studied groups, there were 05 smokers in the open

out of 15 and 4 smokers out of 15 in the laparoscopic group. Systemic comorbidities observed in this study were diabetes, systemic hypertension, bronchial asthma, cirrhosis and chronic obstructive pulmonary disease (Table 1).

**Table 1: BMI, smoking and Co-morbidities in both the groups.**

Observed parameters	Open (n=15)	Laparoscopic (n=15)
Mean BMI (kg/m <sup>2</sup> )	23.4	25.6
Mean ASA grade (physical status)		
I	08	09
II	04	06
III	03	00
Smoking	05	04
<b>Comorbidities</b>		
Diabetes	01	02
Systemic hypertension	01	01
Bronchial asthma	01	01
Cirrhosis	01	-
Chronic obstructive pulmonary disease	01	-
Hypothyroidism	01	-

In this study, pain in the abdomen was the chief complaint in both groups. In the open group, 80% patients presented with pain in abdomen whereas in the laparoscopic group, 66% patients presented with pain in abdomen. The other common symptoms observed were yellowish discoloration of eyes (Icterus), weight loss and vomiting (Table 2).

**Table 2: Distribution of signs and symptoms in studied cases.**

Observed parameters	Open (n=15)	Laparoscopic (n=15)	Total
<b>Clinical parameter</b>			
<b>Symptoms</b>			
Pain in abdomen	12(80%)	10(66%)	22
Vomiting	08(53%)	07(46%)	16
History of yellow discoloration of eyes	15(100%)	15(100%)	30
Weight loss	15(100%)	15(100%)	30
Hematemesis/malena	03(20%)	02(13%)	05
Pruritis	08(53%)	06(40%)	14
<b>Signs</b>			
Palpable lump	02(13%)	01(6.6%)	03
Icterus	15(100%)	15(100%)	30
Scratch marks/itching	08(53%)	06(40%)	14

Mean hemoglobin for open group was 10.75mg/dl and laparoscopic group was 10.81mg/dl. Mean albumin was 5.5mg/dl for open group and for laparoscopic group it was 6.8mg/dl. Mean total bilirubin before surgical

intervention was 8.27mg/dl in the open group and 7.02mg/dl in the laparoscopic group (Table 3).

**Table 3: Biochemical parameters in studied cases.**

Biochemical parameter	Open (n=15)	Laparoscopic (n=15)
Haemoglobin (g/dl) (Average)	10.75	10.81
Albumin (mg/dl) (Average)	4.36	5.26
Total Bilirubin (mg/dl) (Average)	8.27	7.02
Preoperative biliary drainage	08(53%)	05(33%)

In this study in the open group, 06 patients out of 15 underwent pylorus preserving Whipple’s procedure and 09 patients underwent classical Whipple’s procedure. Similarly, in the laparoscopic group, 07 patients underwent pylorus preserving Whipple’s procedure and

08 patients underwent classical Whipple’s procedure (Table 4).

**Table 4: Types of pancreaticoduodenectomy in studied cases.**

Observed parameters	Open (n=15)	Laparoscopic (n=15)
Types of pancreaticoduodenectomy	06-PpD 09-CpD	07-PpD 08-CpD
PpD = Pylorus preserving pancreaticoduodenectomy CPD= Classical pancreaticoduodenectomy		

There were significant differences in blood loss which favored Laparoscopic procedure than open procedure. Mean duration of surgery was significantly less in Open group. The difference was found to be statistically significant. The difference in mean blood transfusion, ICU stay, duration of drain tube and Ryle’s tube and starting of oral feeds were not found to be statistically significant in both the groups (Table 5).

**Table 5: Perioperative variables.**

Observed parameters	Open (n=15)	Laparoscopic (n=15)	P Value
Mean blood loss (Milliliters)	347.33	325.28	0.0040* Significant
Mean operative duration (Minutes)	268.2	313.93	0.0052* Significant
Mean blood transfusion	6	3	0.4716 Not Significant
Mean ICU stay (Days)	06	04	0.7306 Not Significant
Mean duration of Drain tube (Days)	12	08	0.2451 Not Significant
Mean duration of Ryle’s Tube (Days)	10	06	0.2723 Not Significant
Oral started from the date of surgery	08	06	0.7152 Not Significant

**Table 6: Observation of postoperative complication.**

Observed parameters	Open	Laparoscopies	P value
Post Pancreatic			
Hemorrhage	3	2	0.419
Grade A	1	1	
Grade B	2	1	
Grade C	0	0	
Pneumonia	03	01	0.6120
Intraabdominal sepsis/collection	02	00	0.2241
Surgical site infection	07	01	0.0352
Delayed gastric emptying	06	03	0.4270
Pancreatic leak	01	03	0.6120
Grade A	0	2	
Grade B	1	1	
Grade C	0	0	
Biliary leak	02	03	0.419
Gastrojejunostomy leak	01	01	1.0000
Re-exploration	01	01	1.0000
Readmission	02	01	1.0000
Mortality	04	02	0.6539

Analysis of the primary outcome showed that the mean duration of hospital stay was 23.06 days in the open group. Mean duration of hospital stay laparoscopic group it was 14.4 days. The mean duration after discharge patient received chemo/radiotherapy in the open group was 15.8 weeks. The mean duration after discharge patient received chemo/radiotherapy was 9.73 weeks in the laparoscopic group. Statistical analysis of both these parameters showed that there was a statistically significant difference in both the groups with respect to primary outcome parameters. The only parameter with statistically significant difference was found to be surgical site infection which was more common in patients who had undergone open procedure. The other parameters were found to be comparable and there was no statistically significant difference in both the groups (Table 6).

On histopathological analysis, distribution of malignancy in the open group there were total 15 patients in which 07 patients of malignancy of the head of pancreas, 05 patients of the ampulla of Vater malignancy, 01 patients of distal CBD malignancy and 02 patients of duodenal carcinoma. In the laparoscopic group, there were total 15

patients out of which 08 patients of malignancy of the head of pancreas, 04 patients of the ampulla of Vater

malignancy, 02 patients of distal CBD malignancy and 01 patients of duodenal carcinoma (Table 7).

**Table 7: Distribution of malignancy with differentiation.**

Distribution and differentiation of malignancy		Open (N=15)	Laparoscopies (N=15)
Distribution of malignancy	Malignancy of Head of the pancreas	7	8
	Ampulla of Vater Malignancy	5	4
	Distal CBD malignancy	1	2
	Duodenal carcinoma	2	1
Differentiation on histopathology analysis.	Well- differentiated	7	6
	Moderately differentiated	5	6
	Poorly differentiated	3	3

**Table 8: Histopathological parameter.**

Histopathological parameter	Open (N=15)	Laparoscopies (N=15)	P value
Mean tumor size (cm)	3.6	3.3	P=0.0001
R0 margin	13	14	0.5977
Mean No. of lymph nodes retrieved	22.7	23.8	0.5530
No. of positive nodes	19	21	P=0.67

The analysis of histopathological parameters of the studied cases showed that R0 margin, Mean number of lymphnodes and number of positive nodes were comparable in both the groups and there was no statistically significant difference in these parameters in both the groups. Mean tumor size was found to be more in open group as compared to laparoscopic group and the difference was found to be statistically significant (Table 8).

**Table 9: TNM staging in the cases.**

TNM stage	Open (n=15)	Laparoscopic (n=15)
IA	04	03
IIA	02	01
IIB	03	04
IIIA	05	05
IIIB	01	02

According to AJCC, NM staging in the open group 04 patients with stage IA, 02 patients with stage IIA, 03 patients in stage IIB, 05 patients with stage IIIA and 01 patients with stage IIIB. According to AJCC, TNM staging in the laparoscopic group, 03 patients with stage IA, 01 patients with stage IIA, 04 patients in stage IIB, 06 patients with stage IIIA and 02 patients with stage IIIB (Table 9).

**DISCUSSION**

This study compared laparoscopic Whipple’s procedure versus open Whipple’s procedure in terms of the aims

and objectives of the study. Our findings were compared with various studies done in the past by various authors. The Whipple’s procedure is only potential cure for periampullary region malignancy. However, the advantages of laparoscopic Whipple’s procedure are still debated over the open procedure. Currently, minimally invasive surgery has rapidly evolved to the pancreatic surgical procedure. Some surveys have shown that laparoscopic pancreaticoduodenectomy is better than open pancreaticoduodenectomy.<sup>11</sup>

Authors such as Asbun and Stauffer have concluded that laparoscopic pancreaticoduodenectomy (LPD) is safe and feasible compared with open pancreaticoduodenectomy (OPD).<sup>12</sup> Similar conclusions were drawn by authors including Palanivelu et al and Croome et al.<sup>13,14</sup> However some other authors such as Dokmak et al reported that LPD is a difficult procedure and has high morbidity hence should not be routinely utilized for resection of periampullary tumors.<sup>15</sup>

In present study, mean age patient for open group was 60.33 and for laparoscopic group was 51.73. Meng et al conducted study and observed mean age of patient for open and lap group was 59.95 and 60.33 respectively.<sup>16</sup> Palanivelu et al stated that mean age of patient open and lap group was 60.33 and 51.73.<sup>13</sup> In our study males were affected predominantly and similar male preponderance has been reported by authors such as Meng et al and Palanivelu et al.<sup>16,13</sup>

In present study patient, 06 patients with comorbidities underwent open Whipple’s procedure. 04 patients with



comorbidities underwent laparoscopic Whipple's procedure. Meng et al, in studied that 22 patients with comorbidities underwent open procedures and 18 patients with comorbidities underwent lap procedure.<sup>16</sup> In present study ASA grade for open group, patients were classified as ASA grade I-08, II-04 and III-03. For laparoscopy group, patients were classified as ASA grade I-09, II-06 and III-00. Comparable ASA grades were reported by Palanivelu et al.<sup>13</sup>

In our study all (100%) patients in both groups presented with the history of jaundice, weight loss vomiting. 03 patients (20%) presented with history of melena/hematemesis in open group. While in laparoscopic group, 02 patients (13%) complained about of malena and hematemesis. Meng et al, study observed that there were 14 patients (24%) in open group and 15 patients (25%) in lap group presented as jaundice with/without pruritis.<sup>16</sup> Asbun et al, Croome et al and Palanivelu et al have baseline characteristics symptoms were similar.<sup>12,14,13</sup>

Average duration of operation in open was 268.2 min. In laparoscopic procedure it was 313.93 min. These results were compared statistically using students t test which showed p-value is 0.0052, stating significant difference between the two groups based on duration of surgery, concludes that open procedure has less operating time. Meng et al, observed that mean operative time was longer in the LPD group vs. OPD group (475 min>335min, P<0.001).<sup>16</sup> Palanivelu et al, concluded that duration of surgery was longer for laparoscopic procedure. (359 vs320, P=0.041).<sup>13</sup>

Average blood loss in open group was more than lap group. (P=0.0040). There was no statistically significant difference in need for transfusion in both the groups. Palanivelu et al and Croome et al in their studies found that blood was less in laparoscopic group than open group.<sup>13,14</sup> Whereas Meng et al, found that there was no significant difference in mean operative blood loss on comparing OPD vs LPD.<sup>16</sup>

The average hospital stay for open group was 23.06 days and 14.4 days for laparoscopic group. The average hospital stay was statistically significantly less in laparoscopic group. Similarly lap group showed shorter time to start oral intake which is not significant (P<0.001). Similar studies conducted by Palanivelu et al, Meng et al and Fischer CP et al and found similar reduction in hospital stay in laparoscopic group as compared to open group.<sup>13,16,17</sup> The other parameters such as duration of ICU stay was found to be comparable in both the groups (P=0.73).

In present study, lap group patients received early chemo/radio therapy than open group (15.8 weeks vs. 9.73 weeks, P=0.0068). Croome et al, reported oncological advantage of laparoscopy over the open approach.<sup>14</sup> The median time to initiate adjuvant therapy

was 48 day in the laparoscopic and 59 day in the open group. The authors also observed that a significant proportion (12%) of the patients in open OPD group had significant delay initiation of adjuvant chemotherapy when compared to the LPD group (5%). The complications such as post pancreatic hemorrhage, pneumonia, delayed gastric emptying, pancreatic leak, biliary leak, gastrojejunostomy leak, need for re-exploration and readmission rates were found to be comparable in both the groups and there was no statistically significant difference in both the groups for these complications. The only significant difference was found to be for the incidence of surgical site infection which was statistically significantly more common in open group as compared to laparoscopic group (P=0.04). Meng et al and Palanivelu et al reported similar complication rates.<sup>16,13</sup> The study conducted by Meng et al, differed in incidence of surgical site infection which was found to be comparable in both the groups (P=0.793).<sup>16</sup> The variables such as tumor size, R0 Margins, number of retrieved and positive lymph nodes were found to be comparable in both the groups. Similar complications were noted in studies conducted by Speicher PJ, Allen PJ et al and HO CK et al.<sup>18-20</sup>

Finally, the analysis of mortality in both the groups showed that 4 deaths occurred in open group and 2 deaths occurred in laparoscopic group. On comparison it was not statically significant (P= 0.65). Similarly, Meng et al and Palanivelu et al, found that there were no significant difference in death rate in open and lap group.<sup>16,13</sup>

## CONCLUSION

This randomized study comparing laparoscopic with open pancreatoduodenectomy in treatment of periampullary region malignancy suggested that laparoscopy offers significant benefit in terms of hospital stay, surgical site infection, mean blood loss, mean operative duration and Mean interval of duration receiving chemo/radiotherapy. Prolonged operating times and technical complexity were found to be the discouraging factors for use of laparoscopic pancreaticoduodenectomy.

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## REFERENCES

1. Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, et al. Six hundred fifty consecutive pancreaticoduodenectomy in the 1990s: pathology, complications, and outcomes. *Ann Surg.* 1997;226:248-57.
2. Bramhall SR, Neoptolemos JP. Adjuvant chemotherapy in pancreatic cancer. *Int J Pancreatol.* 1997;21:59.

3. Buchler M, Friess H, Schultheiss KH, Gebhard C, Kubel R, Muhrer KH, et al. A randomized controlled trial of adjuvant immunotherapy (murine monoclonal antibody 494/32) in resectable pancreatic cancer. *Cancer.* 1991;68:1507.
4. Beger HG, Rau B, Gansauge F, Poch B. Treatment of pancreatic cancer: challenge of the facts. *World J Surg.* 2003;27:1075-84.
5. American Gastroenterological Association. American Gastroenterological Association medical position statement: epidemiology, diagnosis, and treatment of pancreatic ductal adenocarcinoma. *Gastroenterol.* 1999;117:1463-84.
6. Nishimura Y, Hosotani R, Shibamoto Y, Kokubo M, Kanamori S, Sasai K, et al. External and intraoperative radiotherapy for resectable and unresectable pancreatic cancer: Analysis of survival rates and complications. *Int J Radiat Oncol Biol Phys.* 1997;39:9.
7. Jin T, Altaf K, Xiong JJ, Huang W, Javed MA, Mai G, et al. A systematic review and meta-analysis of studies comparing laparoscopic and open distal pancreatectomy. *HPB (Oxford).* 2012;14:711-24.
8. Cho A, Yamamoto H, Nagata M, Takiguchi N, Shimada H, Kainuma O, et al. A totally laparoscopic pylorus-preserving pancreaticoduodenectomy and reconstruction. *Surg Today.* 2009;39:359-62.
9. Wei H, Wei B, Zheng Z, Huang Y, Huang J, Fang J. Comparative study of outcomes after laparoscopic versus open pancreaticoduodenectomy. *Zhonghua Wei Chang Wai Ke Za Zhi.* 2014;17:465-8.
10. Dokmak S, Ftériche FS, Aussilhou B, Bensafta Y, Lévy P, Ruszniewski P, et al. Laparoscopic pancreaticoduodenectomy should not be routine for resection of periampullary tumors. *J Am Coll Surg.* 2015;220:831-8.
11. Kim SC, Song KB, Jung YS, Kim YH, Park DH, Lee SS, et al. Short-term clinical outcomes for 100 consecutive cases of laparoscopic pylorus-preserving pancreatoduodenectomy: improvement with surgical experience. *Surg Endosc.* 2013;27:95-103.
12. Asbun HJ, Stauffer J. Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. *J Am Coll Surg.* 2012;215:810-9.
13. Palanivelu C, Rajan PS, Rangarajan M, Vaithiswaran V, Senthilnathan P, Parthasarathi R, et al. Evolution in techniques of laparoscopic pancreaticoduodenectomy: a decade long experience from a tertiary center. *J Hepatobiliary Pancreat Surg.* 2009;16:731-40.
14. Croome KP, Farnell MB, Que FG, Reid-Lombardo K, Truty MJ, Nagorney DM, et al. Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches? *Ann Surg.* 2014;260:633-8.
15. Dokmak S, Ftériche FS, Aussilhou B, Bensafta Y, Lévy P, Ruszniewski P, et al. Laparoscopic pancreaticoduodenectomy should not be routine for resection of periampullary tumors. *J Am Coll Surg.* 2015;220:831-8.
16. Meng LW, Cai YQ, Li YB, Cai H, Peng B. Comparison of laparoscopic and open pancreaticoduodenectomy for the treatment of nonpancreatic periampullary adenocarcinomas. *Surg Laparosc Endosc Percutan Tech.* 2018;28(1):56-61.
17. Fischer CP, Hong JC. Method of pyloric reconstruction and impact upon delayed gastric emptying and hospital stay after pylorus-preserving pancreaticoduodenectomy. *J Gastrointest Surg.* 2006;10(2):215-9.
18. Speicher PJ, Nussbaum DP, White RR, et al. Defining the learning curve for team-based laparoscopic pancreaticoduodenectomy. *Ann Surg Oncol.* 2014;21:4014-9.
19. Allen PJ, Gönen M, Brennan MF, Bucknor AA, Robinson LM, Pappas MM, et al. Pasireotide for postoperative pancreatic fistula. *N Engl J Med.* 2014;370(21):2014-22.
20. Ho CK, Kleeff J, Friess H, Buchler MW. Complications of pancreatic surgery. *HPB (Oxford).* 2005;7(2):99-108.

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