

Laparoscopic pancreatoduodenectomy combined with portal-superior mesenteric vein resection and reconstruction with interposition graft

Case series

Xin Wang, MD^a, Yunqiang Cai, MD^b, Wei Zhao, MD^c, Pan Gao, MD^b, Yongbin Li, MD^b, Xubao Liu, MD^a, Bing Peng, MD, FACS^{a,b,*}

Abstract

Rationale: With the development of laparoscopic techniques, laparoscopic pancreatoduodenectomy was applied in various indications including pancreatic cancer. Here, we share our experience of venous resection and reconstruction with interposition graft in laparoscopic pancreatoduodenectomy in these patients.

Patient concerns: We reviewed data of laparoscopic pancreatoduodenectomy with venous resection and reconstruction in patients with pancreatic cancer between the dates of October 2010 and November 2017.

Outcomes: Ten patients underwent laparoscopic pancreatoduodenectomy with portal-superior mesenteric vein resection and reconstruction with interposition graft. The mean operative time was 547 min. The mean blood loss was 435 ml. The mean length of venous defect after resection was 5.4 cm. R0 resection was achieved in nine patients (90%). There was one patient who suffered from severe postoperative complication. There was no 30-day mortality in this study. The long-term patency was achieved in all patients.

Conclusion: In this study, we demonstrate the initial experience of laparoscopic pancreaticoduodenectomy with long venous resection and reconstruction. Although applied in small number of patients, it could be another option for well-selected patients with reasonable morbidity and mortality as well as long-term outcomes in experienced minimally invasive surgical team.

Abbreviations: BRPC = borderline resectable pancreatic cancer, CTA = CT angiography, DGE = delayed gastric emptying, EUS = endoscopic ultrasonography, ISGPS = International Study Group of Pancreatic Cancer, LMWH = low-molecular-weight heparin, NCCN = National Comprehensive Cancer Network, PTFE = polytetrafluoroethylene, PV = portal vein, SMA = superior mesenteric artery, SMV = superior mesenteric vein, UICC = Union for International Cancer Control.

Keywords: laparoscopic pancreatoduodenectomy, long-term outcomes, pancreatic cancer, short-term outcomes, vein resection and reconstruction

1. Introduction

Pancreatic cancer is one of the most lethal malignant disease, highlighted by the close parallel between incidence and mortality. The overall 5-year survival of pancreatic cancer remains as low as 8% in the United States.^[1] This dismal prognosis is attributed to

several factors, among which the most important is the late stage at which most patients are diagnosed. According to the Cancer Statistics Review (2002–2008) from the US Surveillance Epidemiology and End Results,^[2] more than 50% patients were diagnosed with metastatic pancreatic cancer that eliminated the possibility of surgery, and only 20% of patients were eligible for curative resection. For the remaining 25% patients, the treatment was difficult and controversy due to tumor involvement of surrounding major vessels. Among them, patients with portal-superior mesenteric vein involvement have been considered as borderline resectable and have similar short-term and long-term outcomes compared with resectable ones.^[3,4] Therefore, both the National Comprehensive Cancer Network (NCCN) and International Study Group of Pancreatic Cancer (ISGPS) recommended synchronous vein resection to achieve R0 margin in patients with suspicious portal-superior mesenteric vein involvement.^[5,6]

With the development of minimally invasive instruments and techniques, an increasing number of publications demonstrate that laparoscopic pancreatoduodenectomy is safe and feasible.^[7–9] For patients with pancreatic cancer, although the technique is both demanding and challenging, several studies have demonstrated that the application of laparoscopic pancreatoduodenectomy could achieve as good the perioperative results and long-term oncological outcomes as the open surgery did.^[10,11] As mentioned before, in order to achieve better long-term outcomes,

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^a Department of Pancreatic Surgery, West China Hospital, Sichuan University, Chengdu, China, ^b Department of Minimal Invasive Surgery, Shangjin Nanfu Hospital, Chengdu, China, ^c Department of Pediatrics, Qingdao Municipal Hospital, Qingdao, China.

* Correspondence: Bing Peng, No. 37, Guoxue Alley, Chengdu, Sichuan, 610041, China (e-mail: hxwangxin2012@hotmail.com).

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patients who are potential candidates for pancreatoduodenectomy in combination with vein resection are being seen with increasing frequency. Venous resection and reconstruction are complex and challenging in laparoscopic pancreatoduodenectomy, a few studies have reported the initial application of laparoscopic venous resection and reconstruction.^[12-14] However, little is known about its technical details, short-term and long-term outcomes, especially for patients with long segmental venous involvement who required an interposition graft reconstruction.

Herein we report the experience of laparoscopic pancreatoduodenectomy combined with portal-superior mesenteric vein resection and reconstruction with interposition graft and provide a review on this topic.

2. Methods

2.1. Patients

This study is conducted in a retrospective manner on three hundred patients who underwent laparoscopic pancreatoduodenectomy between October 2010 and November 2017 at West China Hospital, an academic hospital in China. Over three hundred patients underwent laparoscopic pancreatoduodenectomy in our institutes, including 40 cases that underwent venous resection. Only patients with confirmed pancreatic cancer and those with concomitant portal-superior mesenteric vein resection and reconstruction with interposition graft were included in this study. This study was approved by the Institutional Ethic Committee of West China Hospital, Sichuan University. All the patients have signed the informed consent form for publication. Preoperative tumor assessment was performed with the help of CT, MRI, CT angiography (CTA), and/or endoscopic ultrasonography (EUS). Resectability was determined preoperatively according to the NCCN guideline.^[5] Patients were excluded if they had arterial involvement. Clinical characteristics, perioperative data, pathological information, and follow-up data were collected from all those patients. Patients were analyzed in an intention-to-treat fashion. Postoperative complications were recorded using the Clavien-Dindo classification and ISGPS definition system.^[15-18]

2.2. Surgical techniques

The technique of laparoscopic pancreatoduodenectomy has been described previously. Briefly, patients were placed in a supine position with legs apart. Five trocars were distributed in a semicircular fashion as shown in Figure 1 Surgeon and assistant stand on each side of the patient, whereas the camera holder stand between the two legs of the patient.

The procedure was divided into three major parts:

1. mobilization of ligaments and fascia;
2. specimen resection with venous resection;
3. vein and digestive tract reconstruction.

In the first part, after whole abdominal exploration, the gastrocolic ligament was transected from left to the right to gain an access to the lesser sac. When approaching the right edge of the lesser sac, care should be taken because the gastrocolic ligament was fused with mesocolon. Dissection should follow the avascular plane of the fusion fascia to avoid iatrogenic injury of colic vessels. The hepatic flexure of the right colon was fully taken down, and mobilization of right part of mesocolon was

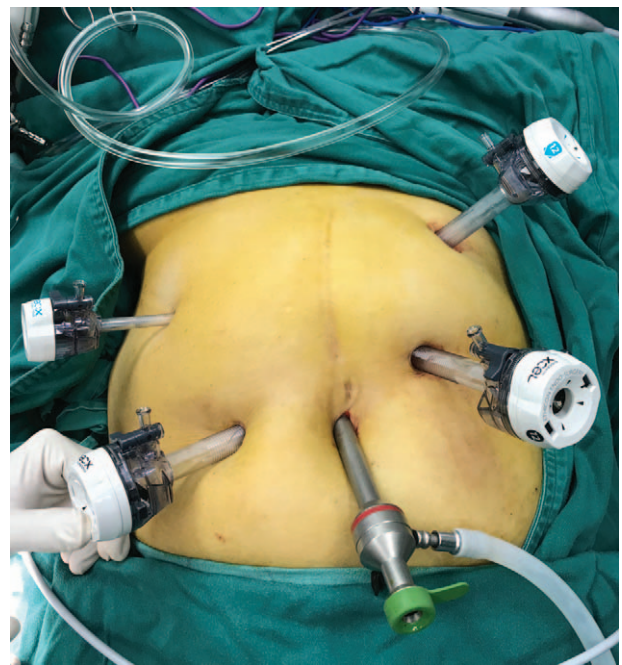


Figure 1. Trocar placement.

performed to expose the third part of duodenum. Then an extended Kocher maneuver, which expose the inferior cava, left renal vein, celiac trunk, aorta, and SMA (superior mesenteric artery), was performed to reconfirm resectability and to mobilize the posterior of pancreatic head. The tunnel between pancreatic neck and SMV (superior mesenteric vein) was not mandatory if the anterior wall of SMV was involved.

In the second part, the distal stomach, proximal jejunum, gallbladder, hepatic duct, and pancreatic neck were dissected, respectively. A standard lymphadenectomy was performed concomitant with the specimen resection. The PV (portal vein) and SMV were mobilized, and two vessel loops were applied for later manipulation. Splenic vein was transected routinely. To minimize the mesoportal clamp time, the remaining of the specimen resection is completed reserving the venous transection as the final step in this procedure. We retracted PV/SMV and the pancreatic head using the vessel loops to expose celiac trunk and SMA. Then the dissection was performed along the SMA and celiac trunk to clear all the tissues on the right side (Fig. 2). Hereto, the uncinated process dissection was completed. Laparoscopic bulldog clamps were applied to temporarily occlude PV and SMV. Finally, an en-bloc resection was completed by transecting the involved vein with sufficient margin.

In the third part, the length of venous defect was measured by a soft ruler, defect of more than 4cm was considered as the indication for artificial interposition graft. Then the portal-superior mesenteric vein reconstruction was performed using an artificial interposition graft (GORE-TEX, W.L. Gore & Associates, Inc). In detail, the reconstruction was performed in a caudal to cephalic manner. The “rotation technique” was applied in the caudal anastomosis, while the “posterior to anterior technique” was applied in the cephalic anastomosis. Specifically, in the “rotation technique,” the assistant rotated the vein and graft simultaneously to complete a 360-degree exposure and the surgeon performed the running suture (Fig. 3). In the

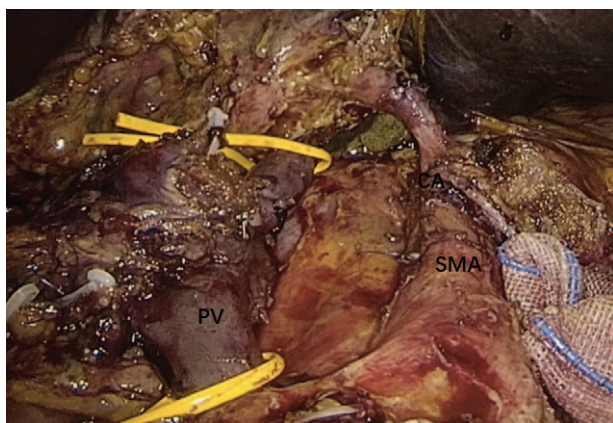


Figure 2. Clear tissue on the right side of SMA. CA=celiac trunk, PV=portal vein, SMA=superior mesenteric vein.

“posterior to anterior technique,” the anastomosis initiated from the posterior wall and then shifted to the anterior wall with running suture (Fig. 4). Then the pancreatojejunostomy was performed in a duct-to-mucosa manner. An internal stent was routinely applied. Followed by the hepatojejunostomy and gastrojejunostomy, after all the reconstruction, specimen was retrieved through the periumbilical incision. Three drainages were placed near the anastomosis.

2.3. After surgery

Low-molecular-weight heparin (LMWH) was applied in all patients for 7 days after surgery. Then the LMWH was replaced by warfarin to maintain an international normalized ratio between 1.5 and 2. Postoperative imaging (CT scan) was routinely performed on the fifth postoperative day and two months after surgery to assess patency of venous reconstruction

and to rule out thrombosis. According to the definition of the Union for International Cancer Control (UICC), R0 margin has no presence of tumor cells at the surface of the resection margin (0mm rule).

3. Results

A total of ten patients underwent laparoscopic pancreatoduodenectomy combined with portal-superior mesenteric vein resection and reconstruction with interposition graft. Patients baseline clinical characteristics were shown in Table 1. There were six males and four females in our study. The mean age was 61 (range from 44 to 70 years). The average BMI was 22.2 kg/m² (range from 17 kg/m² to 25 kg/m²), and the average albumin was 39 g/L (range from 29.5 g/L to 46.8 g/L). As Table 1 shows, total bilirubin was elevated in nine of ten patients with a mean value of 120 μmol/L. Carbohydrate antigen 19-9 was significantly elevated in all of the patients, four of whom had value more than 1000 U/L. In the preoperative image evaluation, the mean tumor size was 4.25 cm (range from 3 cm to 7 cm), and all of them have isolated portal-superior mesenteric vein involvement with different extent. According to NCCN guideline, all the patients were borderline resectable.

The intra-operative and pathological data was shown in Table 2. The mean operative time was 547 min (range from 450 min to 690 min). Mean estimated blood loss was 435 ml (range from 200 ml to 700 ml). The average length of venous defect was 5.4 cm (range from 4 cm to 6 cm). The mean vein clamp time was 44.8 min (range from 28 min to 70 min). There was no transfusion in any patient. Three patients converted to open procedure due to the difficulty confronted in the process of specimen resection. The pathological results were also shown in Table 2. There were 15.8 lymph nodes in average (range from 14 to 19) harvested in surgery. Portal-superior mesenteric vein invasion was confirmed in seven of the ten patients (70%) and R0 resection was achieved nine patients (90%).

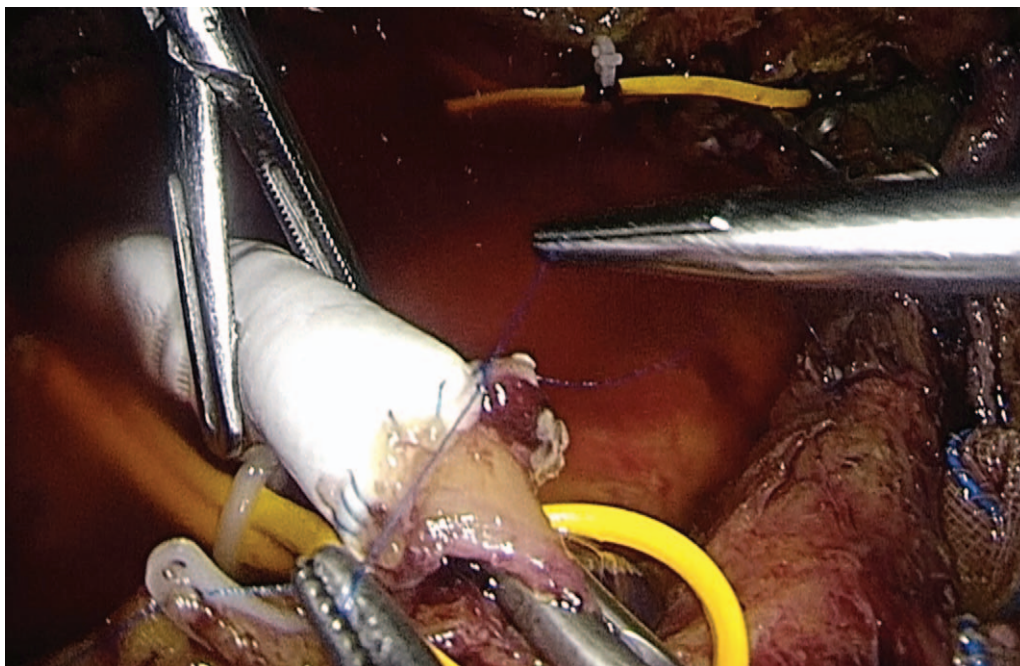


Figure 3. “Rotation technique” in caudal anastomosis.

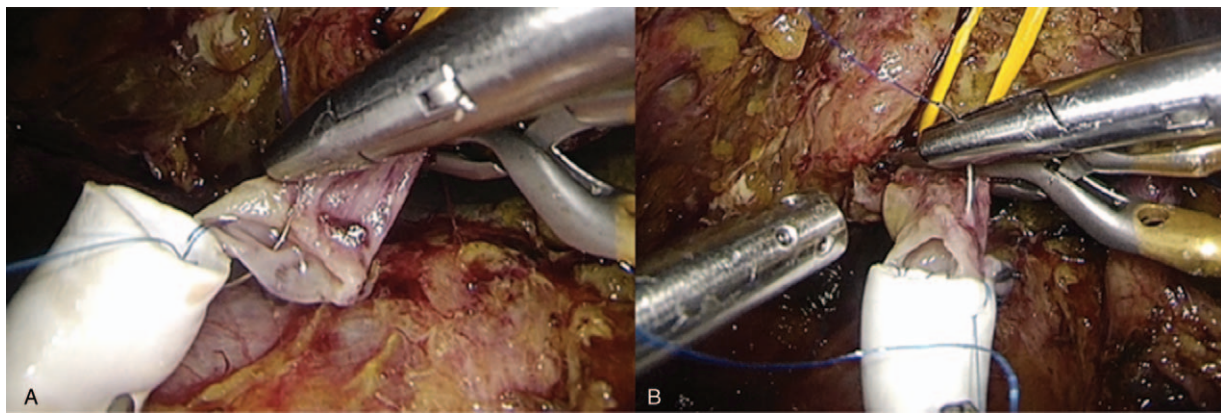


Figure 4. “Posterior to anterior” technique in cephalic anastomosis. Left=posterior wall anastomosis, right=anterior wall anastomosis.

As shown in Table 3, there were three patients who suffered from biochemical pancreatic fistula (Grade A), and there was no patient who suffered from clinical-related pancreatic fistula (Grade B). Early postoperative hemorrhage was occurred in one patient when low-molecular-weight heparin treatment was initiated, and the hemorrhage stopped immediately after low-molecular-weight heparin was terminated. Two patients suffered from venous thrombosis, one patient was asymptomatic and treated with conservative therapy, and the other presented with ascites and treated with thrombolytic therapy. There was no delayed gastric emptying (DGE) in our study. The mean length of hospital stay was 15.5 days (range from 10 days to 22 days). All the patients recovered and discharged uneventfully. There was no 30-day mortality and 90-day readmission in our study. All patients underwent routinely follow-up range from 4 months to 19 months, and the patency of artificial vascular was 100% two months after surgery. Six patients (60%) receive regular chemotherapy after surgery. One patient died 13 months after surgery because of metastasis, and another patient died 9 months after surgery because of heart failure. In the remaining patients, two patients suffered from liver and lung metastasis, and no local recurrence was found in our study.

4. Discussions

As mentioned earlier, pancreatic cancer had a low rate of resectability, which led surgeons to consider more radical surgery. In 1963, Asada reported the first case of successful

pancreatoduodenectomy with portal vein resection.^[19] Then, the term of regional resections, which included combined portal vein and/or arterial resection, was described by Fortner in 1973.^[20] The enthusiasm for this “extended resection” decreased rapidly because of the high morbidity and mortality. Therefore, the rate of resectability for pancreatic cancer had been unchanged for a long time. With the improvement of instruments and operative techniques, the rate of resectability has significantly increased in recent two decades. Therefore, the term “borderline resectable pancreatic cancer” (BRPC) has been evolved to describe cancer, which involved the specific artery and/or vein that might benefit from radical resection. However, based on the current published data, there is no good evidence to demonstrate that arterial resections during pancreatoduodenectomy are of benefit. Such resections may be harmful with increased morbidity and mortality and should not be recommended on a routine basis.^[6,21] On the other hand, current evidence suggested that the morbidity, mortality, and disease-free and overall survival of patients with portal-mesenteric vein resection were no different from those of patients who underwent standard resection and were better than those in patients without surgery because of venous involvement.^[22] ISGPS guideline recommended straightforward resection in the presence of isolated and reconstructable portal-mesenteric vein involvement.^[6] Therefore, in this study, all the patients were diagnosed with isolated portal-superior mesenteric venous involved BRPC preoperatively, and an upfront resection was performed subsequently with synchronous vein resection without neoadjuvant therapy.

Table 1

Baseline clinical characteristics of patients.

Patient no.	Gender	Age	BMI (kg/m ²)	Albumin (g/L)	Total bilirubin (μmol/L)	CA19-9 (U/ml)	Tumor size (cm)	Resectability
1	Female	68	25	45.5	15.6	>1000	7	BRPC
2	Female	59	22	45	160	>1000	5	BRPC
3	Male	67	21	38	120	400	4	BRPC
4	Female	69	23	32.6	100	>1000	3	BRPC
5	Female	48	23	46.8	42.5	91.1	3	BRPC
6	Male	70	21	38	80	250	4	BRPC
7	Male	54	24	39.5	110	592	6	BRPC
8	Male	69	17	29.5	283.5	>1000	3	BRPC
9	Male	44	24	35	239	48.4	4	BRPC
10	Male	61	22	43	50	107	3.5	BRPC

BMI = body mass index, BRPC = borderline resectable pancreatic cancer, CA19-9 = carbohydrate antigen 19-9.

Table 2**Intraoperative and pathological data.**

Patients	Operative time (min)	Estimated blood loss (ml)	Length of venous defect (cm)	Clamp time (min)	Transfusion	Conversion	No. of harvested lymph nodes	Margin status	PV/SMV invasion
1	540	500	6	70	No	No	19	R0	Yes
2	600	300	5	55	No	No	16	R0	Yes
3	510	550	5	38	No	No	16	R1	Yes
4	690	200	6	48	No	No	17	R0	No
5	540	300	6	58	No	No	15	R0	Yes
6	450	200	4	42	No	No	16	R0	No
7	510	600	6	30	No	Yes	15	R0	Yes
8	600	400	5	45	No	No	14	R0	No
9	550	600	6	28	No	Yes	15	R0	Yes
10	480	700	5	34	No	Yes	15	R0	Yes

PV=portal vein, SMV=superior mesenteric vein.

Although there are a lot of studies that demonstrated the feasibility and efficacy of all types of venous resection and reconstruction: primary closure, end-to-end anastomosis, and interposition graft.^[23–25] There are only a few studies that demonstrated the feasibility and technique details of laparoscopic venous resection and reconstruction during Whipple procedure. As early as 2011, Kendrick and colleagues reported the initial experience of major venous resection during total laparoscopic pancreatoduodenectomy, which first demonstrated the feasibility of this technique.^[26] Later on, Panalivelu^[13] reported a case that underwent laparoscopic end-to-end anastomosis, and Dokmak^[14] reported a case that underwent laparoscopic partial venous excision using a patch, respectively. Recently, Khatkov demonstrated the feasibility and safety of laparoscopic pancreatoduodenectomy with venous reconstruction in eight patients.^[27] In addition, Kendrick and colleagues demonstrated that laparoscopic pancreatoduodenectomy with major vascular resection had comparable short-term and long-term outcomes when compared with open technique in a large sample study.^[12] In this study, laparoscopic vascular resection was performed in thirty-one patients, and primary closure was the most commonly used technique in laparoscopic group, followed by end-to-end anastomosis, which consisted of 71% and 23% group patients, respectively. Interposition anastomosis was performed significantly less in laparoscopic group compared with open group (6% vs. 20%, $P < .001$). In some circumstances, an interposition graft anastomosis was mandatory because of long segmental venous involvement. However, the application of laparoscopic venous resection and reconstruction with interposition graft is extremely difficult and technically challenging. Currently, only four patients

who underwent laparoscopic venous interposition anastomosis were reported.^[12,27] Therefore, little is known about the details of this technique.

Here, we shared our initial experience of laparoscopic pancreatoduodenectomy with vein resection and reconstruction by interposition graft in this study. Three patients converted to open procedure due to difficulties confronted during resection, and there was no emergent conversion. The conversion rate (30%) was higher than that of published data.^[12,27,28] It might be because the patients required interposition anastomosis and tend to have larger tumor, longer venous involvement, and more severe adhesion. In our study, splenic vein was compromised to facilitate venous resection and reconstruction. Splenic vein ligation may lead to sinistral portal hypertension. To avoid the development of varices, Ono et al^[29] suggested that it was important to preserve the right colic marginal vein, and reconstruction of the splenic vein should be considered if the right colic marginal vein is divided. After resection of portal-superior mesenteric vein, restoring continuity of the vein is critical. Usually, the choice of reconstruction method should be based on intraoperative judgements of the surgeon. A graft might be required in circumstances that venous was involved more than 3 cm according to current studies.^[30,31] In our study, whether a graft should be used depending on the length of venous defect after resection. In our experience, venous defect more than 4 cm is an indication for graft application. Various interposition grafts have been reported for reconstruction, including autogenic vessels, allogenic vessels, and artificial grafts. Besides, other grafts have also been reported. Dokmak^[32] have reported the application of parietal peritoneum as the vascular graft; however,

Table 3**Postoperative data.**

Patients	Complications	LOS (days)	30-day mortality	90-day readmission
1	Pancreatic fistula (Grade A)	15	No	No
2	No	12	No	No
3	No	16	No	No
4	No	10	No	No
5	Pancreatic Fistula (Grade A), thrombosis, ascites	22	No	No
6	No	16	No	No
7	Thrombosis	12	No	No
8	No	17	No	No
9	Pancreatic fistula (Grade A), hemorrhage	20	No	No
10	No	15	No	No

LOS=length of hospital stay.

the long-term patency for the conduit graft was only 33%. Another study, which used falciform ligament as a graft, also shown low long-term patency rate.^[31] Therefore, the decision to choose vascular grafts depends on the efficacy, conditions, and patient's factors. Here, we applied polytetrafluoroethylene (PTFE) as artificial graft in all the patients. Although two patients suffered from thrombosis after surgery, they were treated successfully and discharged uneventfully, long-term patency was achieved in all patients. The clamp time is another important issue in laparoscopic pancreatoduodenectomy because longer clamp time could lead to digestive tract congestion and other postoperative complications. According to the publication, clamp times varied considerably depending on both anastomosis methods and surgeons' technique.^[12-14] To minimize clamp time, as much as possible, the venous transection as the final step in the resection. In addition, the "rotation technique" and "posterior to anterior technique" were applied in the caudal anastomosis and cephalic anastomosis, respectively. With the help of techniques, the average clamp time was 50 min in seven laparoscopic cases, which is reasonable and acceptable for laparoscopic interposition anastomosis.

Last but not the least, the perioperative and long-term results of these patients are of extreme importance. In terms of perioperative outcomes, a meta-analysis published recently demonstrated that minimally invasive pancreatoduodenectomy was associated with similar postoperative pancreatic fistula, less intra-operative blood loss, less delayed gastric emptying, and shorter hospital stay compared with those of open procedure.^[33] A randomized clinical study suggested laparoscopic pancreatoduodenectomy had a more rapid recovery course without compromising the perioperative outcomes.^[8] Even for patients who underwent concomitant vein resection and reconstruction, there was no significant difference in terms of perioperative data between laparoscopic and open procedures.^[12] In terms of oncological and long-term outcomes, Asbun and colleagues^[10] demonstrated that laparoscopic pancreatoduodenectomy was often characterized by improved lymph nodes harvest and had an impressive 5-year survival rate (32.7% vs. 15.34%) compared with open surgery in patients with pancreatic cancer. In addition, the study conducted by Kendrick and colleagues showed an improved R0 resection rate and similar long-term survival could be achieved by laparoscopic technique in patients with vascular resection. In our study, the intraoperative results were comparable with studies mentioned above. Only one patient suffered from severe postoperative complication (Clavien-Dindo classification \geq III). Postoperative pancreatic fistula occurred in three patients (30%), and all of them are biochemical fistula (Grade A). Further, R0 resection was achieved in nine patients (90%). In a follow-up range from 4 months to nineteen months, three patients (30%) suffered from metastasis, and there was no local recurrence. Beside the invasive biology of pancreatic cancer and the stage of disease, the relative high incidence of metastasis might be partly due to the low acceptance (60%) of adjuvant therapy.

In addition, there are some other factors that could affect the outcomes of patients with pancreatic cancer who underwent laparoscopic pancreatoduodenectomy. The first one is center volume. According to an recently published article, patients treated at high-volume centers had improved perioperative outcomes, short-term mortality, and overall survival.^[34] The other one is the surgical team. It is reported that the replacement of a familiar, experienced surgical assistant was associated with a longer operative time.^[35] In our experience, we initiate laparoscopic pancreatoduodenectomy since 2010. After a period

of learning curve, we performed over 60 laparoscopic pancreatoduodenectomy yearly since 2015, and the figure was increased significantly to 116 cases in 2017, and some challenging cases such as venous resection were performed in the recent two years.^[36] All the surgeries were performed by Dr. Peng's team. Therefore, center-volume and fixed surgical team did have critical impact on complicated laparoscopic procedures such as pancreatoduodenectomy.

5. Conclusions

In this study, we demonstrate the initial experience of laparoscopic pancreaticoduodenectomy with venous resection and reconstruction. Although applied in minority of patients, it could be another option for well-selected patients with reasonable morbidity and mortality as well as long-term outcomes in experienced minimally invasive surgical team. Nonetheless, further studies with larger numbers of patients are needed to clarify the complications and oncological outcomes with adequate statistical power.

Author contributions

Conceptualization: Pan Gao, Yongbin Li, Xubao Liu, Bing Peng.

Data curation: Yunqiang Cai, Pan Gao.

Formal analysis: Xin Wang, Wei Zhao.

Funding acquisition: Xubao Liu, Bing Peng.

Investigation: Xin Wang, Yunqiang Cai, Wei Zhao, Yongbin Li.

Methodology: Xin Wang, Yunqiang Cai, Yongbin Li.

Resources: Xin Wang, Wei Zhao.

Software: Xin Wang.

Supervision: Bing Peng.

Visualization: Xin Wang, Xubao Liu.

Writing – original draft: Xin Wang, Yunqiang Cai, Pan Gao, Bing Peng.

Writing – review & editing: Xin Wang, Wei Zhao, Xubao Liu, Bing Peng.

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