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**Pancreaticoduodenectomy with vascular reconstruction for adenocarcinoma of the pancreas with borderline respectability**

Cheung TT *et al*. Pancreaticoduodenectomy with vascular reconstruction for adenocarcinoma

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**Abstract**

**AIM:** To analyze whether pancreaticoduodenectomy with simultaneous resection of tumor-involved vessels is a safe approach with acceptable patient survival.

**METHODS:** Between January 2001 and March 2012, 136 patients received pancreaticoduodenectomy for adenocarcinoma at our hospital. Seventy-eight patients diagnosed with pancreatic head carcinoma were included in this study. Among them, 46 patients received standard pancreaticoduodenectomy (group 1) and 32 patients received pancreaticoduodenectomy with simultaneous resection of the portal vein or the superior mesenteric vein or artery (group 2) followed by reconstruction. The immediate surgical outcome and survival were compared between groups. Fifty-five patients with unresectable adenocarcinoma of the pancreas without liver metastasis who had only bypass operation performed (group 3) were selected for additional survival comparison.

**RESULTS:** In group 1 (*n* = 46), the median patient age was 67 years (range: 37-82 years). In group 2 (*n* = 32), it was 63 years (range: 35-86 years). All patients in group 2 had resection of the portal vein or the superior mesenteric vein and 3 patients had resection of the superior mesenteric artery. The pancreatic fistula formation rate was 21.7% in group 1 and 15.6% in group 2 (*P* = 0.662). Two hospital deaths (4.3%) occurred in group 1 and one hospital death (3.1%) occurred in group 2 (*P* = 0.641). The 1-year, 3-year and 5-year overall survival rates in group 1 were 71.1%, 23.6% and 13.5% respectively. The corresponding rates in group 2 were 70.6%, 33.3% and 22.2% (*P* = 0.815). The 1-year survival rate in group 3 was 13.8%. Pancreaticoduodenectomy with simultaneous vascular resection was safe for pancreatic head adenocarcinoma.

**CONCLUSION:** The short-term and survival outcomes were not compromised when compared with that of standard pancreaticoduodenectomy.

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**Key words:** Head of pancreas; Whipple operation; Portal vein resection; Survival analysis; Morbidity; Mortality; Adjuvant therapy; Liver transplant

**Core tip:** Whipple operation with vascular reconstruction is considered one of the most difficult operation with high morbidity. In this paper, we demonstrated that this complicated surgery can be performed in low volume center where there is a high volume of other complicated liver surgery including liver transplant is performed.

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**INTRODUCTION**

Carcinoma of the pancreas is one of the leading causes of death. According to cancer statistics reported in the United States, there were 43140 new cases in 2010, which would lead to 36800 estimated deaths. The 5-year survival for this disease is only around 6%[1]. Amongst different treatment options, surgical resection offers the best survival outcome to patients with carcinoma of the head of the pancreas[2]. With the advancement in technology and experience sharing, the hospital mortality and morbidity for pancreaticoduodenectomy, also known as the Whipple operation, have been improving when compared with those in the first report in 1935[3]. However, the surgery remains a challenging operation, with hospital mortality rates ranging from 1% to 6% even at experienced centers[4,5]. The issue is even more complicated if the tumor involves major vessels around the pancreatic region. The definition of borderline resectability is controversial. Although many centers have advocated resection of the tumor together with the superior mesenteric vein (SMV) or the portal vein (PV), many other centers simply do not consider operation for this group of patients after balancing the risk of surgery and predicted survival outcomes[6,7].

This study was to compare standard pancreaticoduodenectomy and pancreaticoduodenectomy with simultaneous vascular resection with or without vascular reconstruction in terms of survival outcomes in patients who had adenocarcinoma of the pancreas with borderline resectability.

**MATERIALS AND METHODS**

From January 2001 to March 2012, 136 patients received pancreaticoduodenectomy at Queen Mary Hospital, the University of Hong Kong, Hong Kong, China. Seventy-eight (40.8%) of them had adenocarcinoma of the head of the pancreas, 17 (8.9%) had adenocarcinoma of the common bile duct, 38 (19.8%) had adenocarcinoma of the ampulla of Vater, and 3 (1.5%) had adenocarcinoma of the duodenum. Thirty-two patients (91.4%) who required tumor resection together with vascular resection had adenocarcinoma of the pancreas. The details are listed in Figure 1. Patients who had adenocarcinoma of the pancreas were included in this study. None of the patients received neoadjuvant chemotherapy before operation.

Forty-six patients (25 male and 21 female) underwent standard pancreaticoduodenectomy (group 1). They were 37-82 years old with a median age of 67. Twenty-five patients (54.3%) had a preoperative history of chronic disease (cardiovascular disease, pulmonary disease, renal impairment or diabetes mellitus). Thirty-two patients (20 male and 12 female) underwent pancreaticoduodenectomy together with vascular resection (group 2). They were 35-86 years old with a median age of 63. Sixteen patients (50%) had a preoperative history of chronic disease (cardiovascular disease, pulmonary disease, renal impairment or diabetes mellitus). The patients’ preoperative data including their clinical presentations are listed in Table 1.

Fifty-five patients with unresectable adenocarcinoma of the pancreas without liver metastasis who had only bypass surgery performed (group 3) were selected for additional survival comparison. These were patients who were physically unfit for major pancreaticoduodenectomy or patients who had long-segment arterial encasement by tumors.

***Surgical technique***

Contrast computed tomography (CT) of the abdomen was performed for all the patients. A tumor was considered unresectable if the contrast CT scan showed obvious extrapancreatic metastasis. Pancreaticoduodenectomy was offered to patients with a patent SMV-PV confluence despite suspected tumor involvement of the PV or SMV. Operation was also offered to selected patients with suspected tumor involvement of the short segment of the superior mesenteric artery (SMA). Tumors involving the celiac artery were considered not suitable for surgical resection.

All operations were performed by a team of surgeons specialized in hepatobiliary and pancreatic surgery. Conventional or pylorus-preserving pancreaticoduodenectomy was performed according to the decision of the responsible surgeon. Lymph nodes around the head of the pancreas, the common hepatic artery and the hepatoduodenal ligament were dissected. Dissection of lymph nodes around the celiac and SMA regions was performed in selected patients who showed evidence of lymph node enlargement. Wedge or segmental resection of the PV or SMV was performed if a pancreatic head mass was inseparable from the vein. The pancreas was dissected from the splenic vein to the left of the mesenteric–portal junction and then transected at this level. All tissue around the PV and SMV was circumferentially cleared so that the PV and SMV were completely freed up to the bifurcation of the PV and down to the branches of the SMV. The PV was then sectioned between the vascular clamp, and the surgical specimen was removed. For segmental resection of the PV or the SMV shorter than 3 cm, end-to-end anastomosis without the use of a graft was possible in all patients in group 2 after adequate mobilization of the SMV and the PV[8] . For segmental resection of the PV or the SMV longer than 3 cm, end-to-end anastomosis with the use of a vascular conduit was made. Conduit selections included autologous vein graft, cryo-preserved vein graft and gortex graft. The anastomosis was constructed with 6/0 Prolene suture continuously in a single layer. One third of the circumference or one diameter of growth factor of the PV was allowed in the final knotting in order to avoid narrowing of the anastomosis[9]. For resection of the SMA or hepatic artery, the anastomosis was performed with the microvascular technique with 9/0 nylon suture[10].

Pancreaticoduodenectomy anastomosis was performed by an end-to-side, duct-to-mucosa, two-layer anastomosis using interrupted fine Prolene sutures. The diameter of the pancreatic duct was measured in every case. If the pancreatic duct was thinner than 2 mm or if the pancreas was considered soft in consistency by the operating surgeon, the dunking method without duct-to-mucosa anastomosis or the double loop technique was employed[11].

Pancreatic stenting was employed if the pancreatic duct was small. For external drainage, depending on the size of the pancreatic duct, an Fr 3-8 polyvinyl catheter with multiple side holes was inserted into the pancreatic duct. A stent with the largest size that could be put into the pancreatic duct was used. Catheter migration was prevented by an anchoring stitch that secured the catheter onto the mucosa of the jejunal side of the pancreaticoduodenectomy anastomosis with a single absorbable suture. For internal drainage, an internal drain was put across the pancreaticoduodenectomy anastomosis, with the tip of the catheter distal to the anastomosis[12].

After performing the anastomosis, an end-to-side, single-layer, interrupted hepaticojejunostomy without stenting was performed using the same jejunal loop. A single-layer, continuous, hand-sewn antecolic gastrojejunostomy or duodenojejunostomy was then performed, with a nasogastric tube placed in the afferent jejunal limb of the anastomosis. No vagotomy, gastrostomy or feeding jejunostomy was performed. A drain was placed anterior to the pancreaticoduodenectomy anastomosis, and another drain was placed posterior to the anastomosis. The vascular reconstruction technique and methods of pancreaticoduodenectomy anastomosis are shown in Table 2.

All patients were followed up monthly in the first year and then quarterly if no recurrence was detected. CT was performed one month after the operation, quarterly in the first year, and half-yearly subsequently. Pancreatic fistula was classified into type A, B and C according to the International Study Group of Pancreatic Fistula (ISGPF) definition[13]. Recurrence was defined as the presence of typical features appearing on CT scans or magnetic resonance imaging scans on follow up. If necessary, recurrence was confirmed by cytology. Patients were referred to medical oncologists for consideration for adjuvant chemotherapy after the surgery.

***Statistical analysis***

The baseline characteristics of patients were expressed as medians and ranges. The Mann-Whitney *U* test was used to compare continuous variables, and Pearson’s *χ*2 test was used to compare discrete variables. Survival analysis was performed on the time of disease-free survival *vs* tumor recurrence or death. Survival curves were computed with the Kaplan-Meier method and compared between groups by the log-rank test. Significance was defined as *P* < 0.05. All statistical calculations were made with the computer software SPSS/PC+ (SPSS, Chicago, IL, United States).

**RESULTS**

The median volume of blood loss was 800 mL (range: 250-1600 mL) in group 1 and 1200 mL (range: 100-5000 mL) in group 2 (*P* = 0.007). The median operation time was 580 min (range: 378-855 min) in group 1 and 715 min (range: 487-992 min) in group 2 (*P* < 0.0001). Both groups had an intensive care unit stay of 2 d and a median hospital stay of 17 d. Two hospital deaths (4.3%) occurred in group 1 and one hospital death (3.1%) occurred in group 2. Twenty patients (43.5%) in group 1 developed postoperative complications and 10 patients (31.3%) in group 2 developed surgical complications (*P* = 0.275). In group 1, 10 patients (21.8%) had pancreatic fistula, of whom 6 (13%) had type-A pancreatic fistula, 3 (6.5%) had type-B pancreatic fistula, and 1 (2.2%) had type-C pancreatic fistula. In group 2, 5 patients (15.6%) had pancreatic fistula. Four (12.5%) of them had type-A pancreatic fistula, 1 (3.13%) had type-B pancreatic fistula, and none had type-C pancreatic fistula (*P* = 0.662). The details of postoperative outcomes are listed in Table 3.

In group 1, the median tumor size was 3 cm (range: 1-8 cm). In group 2, it was also 3 cm (range: 1.6-6 cm) (*P* = 0.315). In group 1, 21 patients (45.7%) did not have any lymph node metastasis, 22 patients (47.8%) had 1-4 lymph node metastases, 2 patients (4.3%) had 5-10 lymph node metastases, and 1 patient (2.2%) had more than 10 lymph node metastases. In group 2, 12 patients (37.5%) had no lymph node metastasis, 15 patients (49.6%) had 1-4 lymph node metastases, and 5 patients (15.6%) had 5-10 lymph node metastases (*P* = 0.299). The percentages of patients with disease of stage IA, IB, IIA, IIB and III according to the American Joint Committee on Cancer (AJCC) classification (7th edition)[14] were 4.3%, 8.7%, 30.4%, 54.3% and 2.2% respectively in group 1, *vs* 6.3%, 6.3%, 28.1%, 56.3% and 3.1% respectively in group 2 (*P* = 0.981).

The 1-year, 3-year and 5-year survival rates in group 1 were 71.1%, 23.6% and 13.5% respectively. The corresponding rates in group 2 were 70.6%, 33.3% and 22.2%. The survival curves are shown in Figure 2A.

The 1-year, 3-year and 5-year disease-free survival rates in group 1 were 48.7%, 15.7% and 15.7% respectively. The corresponding rates in group 2 were 40.3%, 20.2% and 13.4% (*P* = 0.589). The survival curves are shown in Figure 2B.

The 1-year survival of patients in group 3 (stage IIB/III) who had only undergone bypass surgery was 13.8%. Group 3 consisted of patients who had disease of stage IIB or III. They were either considered physically unfit for pancreaticoduodenectomy or found to have an SMA encasement bigger than 2 cm during laparotomy. Patients with liver metastasis and distant metastasis were not included in this group. Patient survival in group 3 *vs* group 2 is presented in Figure 2C.

Patients were classified into early and advanced groups for survival comparison according to the presence of lymph node metastasis. The early group comprised of patients with disease of stage IA, IB or IIA. The advanced group comprised of patients with disease of stage IIB or III.

The median survival duration for group-1 patients with early disease was 28.8 mo, *vs* 27.5 mo in group 2 (*P* = 0.685). The median survival duration for group-1 patients with advanced disease was 15.8 mo, *vs* 17.1 mo in group 2 (*P* = 0.391). The survival curves are shown in Figure 2D.

Sixteen factors that might affect patient survival after pancreaticoduodenectomy were identified. Multivariate analysis showed that only lymph node metastasis was significant for poorer survival (*P* = 0.021).

**DISCUSSION**

Pancreaticoduodenectomy is a technically challenging procedure. It was first described in 1935[3]. The rate of morbidities (including pancreatic fistula) has been in the range of 15%-50%[15,16]. A gradual decrease in mortality has been observed in recent years, although the patient age and the incidence of comorbid illness have been rising. It is generally agreed that a hospital mortality rate of 3%-5% is acceptable for pancreaticoduodenectomy without vascular resection at high-volume centers[4]. However, it is believed that the risk of this operation is high if simultaneous vascular resection with reconstruction is required. Many surgeons have taken a more conservative approach when the tumor is considered barely resectable[17,18].

Tumor invasion of the PV or SMV is considered a sign of advanced disease, which is likely to entail poor surgical outcomes. Many centers, hence, adopt more conservative approaches for patients with vascular invasion[19]. In this study, we found that tumor invasion or dense adhesion to the PV or SMV did not correlate with the stage of disease. The median tumor size was 3 cm in both groups, but tumors as small as 1.6 cm could have invaded the PV or SMV, necessitating vascular resection. It is tumor location rather than tumor size that affects surgical planning. Fuhrman et al. have described a similar observation in 23 patients, whose tumors, with a median size of 3 cm, had led to major vessel involvement[20].

Due to the retrospective design of this study, we did not present the degree of invasion of the PV or SMV found by histopathological examinations. Since histological information can only be obtained after surgery, an operating surgeon has to judge during laparotomy whether there is genuine vascular invasion and whether simultaneous vascular resection is required. At centers experienced in vascular reconstruction, simultaneous resection for suspected venous invasion should be performed. The AJCC has not considered tumor invasion of the PV or SMV a factor affecting tumor staging, and therefore a tumor with PV or SMV involvement is classified stage IIA if there is no lymph node metastasis. In accordance with this, patients with tumor invasion of the PV or SMV can still be considered having a relatively early-stage cancer. This might be quite contradictory to many clinicians’ concept.

The definition of borderline resectability for pancreatic cancer remains controversial. Varadhachary *et al*[21] proposed three categories of patients with tumors with borderline resectability: types A, B and C. Type-A patients have tumors with one or more of the following three findings on CT images: (1) tumor abutment (≤ 180° of the circumference of the vessel) of the SMA or celiac axis; (2) tumor abutment or encasement (> 180° of the circumference of the vessel) of a short segment of the hepatic artery, typically at the origin of the gastroduodenal artery; and (3) tumor-related occlusion of a short segment of the SMV, PV, or SMV-PV confluence that is amenable to vascular resection and reconstruction because of a patent SMV and PV below and above the area of occlusion. Type-B patients have tumors with extrapancreatic metastasis. Type-C patients are patients who have marginal physical fitness for major operations.

In fact, many patients with adenocarcinoma of the pancreas can have a relatively early cancer stage even if they are classified as a type-A patient. The decision on treatment strategy for them depends on the risk and benefit of surgery and whether or not there is a good alternative treatment. Neoadjuvant chemotherapy has been suggested to increase the resection rate. Chemotherapy or chemoirradiation has been shown to have a partial tumor response rate of 56%[22]. Although neoadjuvant therapy might be effective for some patients, subjecting every patient with SMV or PV involvement to neoadjuvant therapy without considering upfront surgery would allow progression of cancer in 40% of patients, who would not respond well to neoadjuvant treatment.

This study showed that pancreaticoduodenectomy with vascular resection can be performed safely at centers with experience and expertise. The complication rate and the pancreatic fistula rate in group 2 were not inferior to those in group 1. No SMV or PV thrombosis was found in the study. The experience and techniques in vessel reconstruction we have learned from our liver transplant program can be transferred to many complicated hepatobiliary and pancreatic surgeries[10,23,24]. Techniques used in reconstruction of the PV, SMV or SMA are identical to those used in liver implantation. Most of the time, PV or SMV reconstruction is possible without generating tension on the venous anastomosis after a Cattel Brash maneuver[25]. When simultaneous resection of a PV longer than 5 cm is required during pancreaticoduodenectomy, cadaveric vein grafts available from the liver transplant program give extra flexibility for the vascular reconstruction.

Contrast CT is one of the most sensitive ways for preoperative staging of pancreatic cancer[26,27]. It has been suggested that the morphological features of portal vein invasion could predict the survival outcomes of patients. Patients with extensive tumor involvement of the vessel would have poorer survival[27,28]. Likewise, possible regional lymph node metastases can be revealed by fine-cut CT scan nowadays. Regional lymph node metastases are associated with poor patient survival. However, these so-called poor prognostic indicators should only be regarded as a prognostic suggestion before surgery, and should not become an absolute contraindication to surgery because after all surgical resection provides the best survival outcomes for patients with barely resectable diseases. Pancreatic cancer with arterial invasion is also known to be associated with poor patient survival. In a study, patients who had pancreaticoduodenectomy with simultaneous arterial resection had a median overall survival duration of 15.8 mo only[29]. In our present study, patients having only bypass surgery with palliative intention (group 3) were included for comparison. Many of these patients were not subjected to pancreaticoduodenectomy because they were not physically fit for major surgery. In terms of survival, group-3 patients fared far worse than group-2 patients. Around 23% of the patients in the study had R1 resection as shown by final pathological examination. Many of these patients had posterior margin involvement. No difference in the distribution of margin involvement was found between group 1 and group 2. As there is no association between SMV or PV invasion and R1 resection, and the degree of posterior margin involvement cannot be known before laparotomy, patients should not be denied pancreaticoduodenectomy on the basis of CT images of vascular invasion.

Adenocarcinoma of the pancreas is a cancer with poor patient survival. Surgical resection provides the best chance of cure. Pancreaticoduodenectomy with simultaneous vascular resection is a safe and effective treatment option. The postoperative morbidity and pancreatic fistula rates are not inferior at centers with expertise. In patients who suffer from adenocarcinoma of the pancreas with portal venous invasion, survival after this complicated procedure is not compromised when compared with that after standard pancreaticoduodenectomy.

**COMMENTS**

***Background***

Carcinoma of the pancreas is one of the leading causes of death. With advancement in technology and experience-sharing, the hospital mortality and morbidity for pancreaticoduodenectomy have been improving. However, pancreaticoduodenectomy remains a challenging operation with possible hospital mortality. The issue becomes even more complicated if the major vessels around the pancreatic region are involved. Although many centers advocate en bloc resection of the tumor and the portal vein or superior mesenteric vein, many others do not consider operation for this group of patients after balancing predicted survival outcomes against the risk of surgery.

***Research frontiers***

Pancreaticoduodenectomy with vascular resection is considered a high-risk operation. It also requires experience in vascular reconstruction. This study shows that it can achieve excellent survival outcomes for patients with pancreatic adenocarcinoma at centers with expertise.

***Innovations and breakthroughs***

This study shows that skills honed in complicated hepatobiliary operations can be transferred to pancreatic surgery. Approximately 300 partial hepatectomies and 100 liver transplants are conducted at Queen Mary Hospital every year, but there are only about 30 pancreaticoduodenectomies a year. This is partly because pancreaticoduodenectomy is not a centralized operation in Hong Kong; many other hospitals also perform this operation. However, this study shows that with expertise, pancreaticoduodenectomy with vascular resection can achieve good patient survival with low morbidity.

***Applications***

At centers with experience in vascular reconstruction, en bloc resection of tumor and vessels with suspected invasion should be performed. The American Joint Committee on Cancer does not consider tumor invasion of the portal or superior mesenteric vein a factor affecting staging, and thus a tumor involving the portal or superior mesenteric vein without any lymph node metastasis is classified as stage IIA. Patients who have tumor invasion of the portal or superior mesenteric vein can still be considered having a relatively early-stage cancer.

***Terminology***

Pancreaticoduodenectomy is also known as the Whipple procedure. It is a major [surgical operation](http://en.wikipedia.org/wiki/Surgery) that involves resection of the [pancreas](http://en.wikipedia.org/wiki/Pancreas), [duodenum](http://en.wikipedia.org/wiki/Duodenum) and other organs. It is considered a definitive treatment for malignant tumor at the head of the pancreas or involving the [common bile duct](http://en.wikipedia.org/wiki/Common_bile_duct), [duodenal papilla](http://en.wikipedia.org/w/index.php?title=Duodenal_papilla&action=edit&redlink=1) or duodenum near the pancreas. The portal vein and the superior mesenteric vein are major vessels that connect the bowel to the liver. Reconstruction of these vessels is a crucial step if they are also resected in the Whipple procedure. Catastrophic consequences could arise if leakage or stricture happens to the anastomosis.

***Peer review***

This manuscript is well written and documented. I think that this manuscript is suitable and worth to be published.

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**Figure Legends**

**Figure 1 Pancreaticoduodenectomy performed for different kinds of pathology during the study period.** CA: Carbohydrate antigen.



P=0.815

Group 2 (n=32)

Group 1 (n=46)

Figure 2A



P=0.589

Group 1 (n=44)

Group 2 (n=31)

Figure 2B



P<0.0001

Group 2 (n=32)

Group 3 (n=55)

Figure 2C



Group 1: stage I and stage IIA disease (n=20)

Group 2: stage I and stage IIA disease (n=13)

Group 2: stage IIB and stage III disease (n=19)

Group 1: stage IIB and stage III disease (n=26)

P=0.267

Figure 2D

**Figure 2 Comparison of overall survival.** A: Comparison of overall survival between group 1 and group 2; B: Comparison of disease-free survival between group 1 and group 2; C: Comparison of overall survival between group 2 and group 3; D: Comparison of stage-specific survival in group 1 and group 2.

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Group 1****(*n* = 46)** | **Group 2****(*n* = 32)** | ***P*-value** |
| Age (yr) | 67 (37-82) | 63 (35-86) | 0.452 |
| Male:Female | 25:21 | 20:12 | 0.473 |
| Presence of comorbid illness | 25 (54.3) | 16 (50.0) | 0.705 |
| * Cardiovascular disease
 | 15 (32.6) | 9 (28.1) | 0.673 |
| Pulmonary disease | 5 (10.9) | 1 (3.1) | 0.406 |
| Renal disease | 2 (4.3) | 1 (3.1) | 1 |
| Diabetes Mellitus | 9 (19.6) | 11 (34.4) | 0.141 |
| Hemoglobin (g/dL) | 12.5 (9.0-15.6) | 12.7 (9.5-15.6) | 0.614 |
| White blood cell count (×109/L) | 6.9 (3.6-21.2) | 6.7 (3.9-13.1) | 0.763 |
| Prothrombin time (s) | 11.4 (9.8-40.8) | 11.3 (9.0-14.4) | 0.421 |
| International normalized ratio  | 1.0 (0.8-3.6) | 1.0 (0.8-1.2) | 0.938 |
| Serum creatinine (mmol/L) | 75 (52-212) | 84 (47-143) | 0.607 |
| Serum bilirubin (umol/L) | 102 (5-533) | 38 (5-342) | 0.02 |
| Albumin (g/L) | 39 (27-46) | 40.5 (8-47) | 0.041 |

**Table 1 Preoperative clinical parameters for group 1 and group 2 *n* (%)**

**Table 2 Operation details of group 1 and group 2 *n* (%)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Group 1****(*n* = 46)** | **Group 2****(*n* = 32)** | ***P*-value** |
| Portal vein resection | - | 18 (56.3) | - |
| Reconstruction methodPrimary anastomosisCadaveric vein graftGortex graft  | - | 14 (77.8)3 (16.7)1 (5.6) | - |
| Superior mesenteric vein resection | - | 22 (68.8) | - |
| Reconstruction methodPrimary anastomosisCadaveric vein graftGortex graft  | - | 18 (81.8)3 (13.6)1 (4.5) | - |
| Superior mesenteric artery resection | - | 3 (9.4) | - |
| Reconstruction methodPrimary anastomosis | - | 3 (100) | - |
| Pancreaticojejunostomy construction methodDunkingDuct to mucosaDouble loop | 1 (2.2)43 (93.5)2 (4.3) | 3 (9.4)28 (87.5)1 (3.1) | 0.358 |
| Size of pancreatic duct< 2 mm2-4 mm< 4 mm | 1 (2.4)15 (36.6)25 (61.0) | 3 (13.0)8 (34.8)12 (52.2) | 0.239 |
| Pancreatic stentNoInternalExternal | 32 (69.6)3 (6.5)11 (23.9) | 21 (65.6)3 (9.4)8 (25.0) | 0.882 |

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Group 1****(*n* = 46)** | **Group 2****(*n* = 32)** | ***P*-value** |
| Blood loss (mL) | 800 (250-1600) | 1200 (100-5000) | 0.007 |
| Operation time (min) | 580 (378-855) | 715 (487-992) | < 0.0001 |
| Hospital stay (d) | 17 (9-120) | 17 (11-89) | 0.316 |
| Intensive care unit stay (d) | 2 (1-10) | 2 (0-24) | 0.847 |
| Hospital death | 2 (4.3) | 1 (3.1) | 1 |
| Patients with complication | 20 (43.5) | 10 (31.3) | 0.275 |
| Chest infection | 3 (6.5) | 2 (6.3) | 1 |
| Pleural effusion | 1 (2.2) | 1 (3.1) | 1 |
| Wound infection | 7 (15.2) | 1 (3.1) | 0.176 |
| Subphrenic abscess or collection | 5 (10.9) | 1 (3.1) | 0.406 |
| Intra-abdominal bleeding | 1 (2.2) | 0 (0) | 1 |
| Gastrointestinal bleeding | 1 (2.2) | 1 (3.1) | 1 |
| Cardiac arrhythmia | 4 (8.7) | 2 (6.3) | 1 |
| Acute coronary syndrome | 2 (4.3) | 1 (3.1) | 1 |
| Deep vein thrombosis  | 2 (4.3) | 0 (0) | 0.641 |
| Delayed gastric emptying (> 7 d) | 3 (6.5) | 5 (15.6) | 0.355 |
| Types of pancreatic fistula according to ISGPFAll typesType AType BType C | 10 (21.7)6 (13)3 (6.5)1 (2.2) | 5 (15.6)4 (12.5)1 (3.13)0 (0) | 0.662 |

**Table 3 Short-term outcomes in group 1 and group 2 *n* (%)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Group 1****(*n* = 46)** | **Group 2****(*n* = 32)** | ***P*-value** |
| Tumor size (cm) | 3 (1.0-8.0) | 3 (1.6-6.0) | 0.315 |
| Lymph node metastasesNo< 55-10> 10 | 21 (45.7)22 (47.8)2 (4.3)1 (2.2) | 12 (37.5)15 (46.9)5 (15.6)0 (0) | 0.299 |
| Pancreaticojejunostomy construction methodDunking or otherDuct to mucosa | 4 (12.5)28 (87.5) | 3 (6.5)43 (93.5) | 0.613 |
| R0 resectionR1 resection | 35 (75.6)11 (24.4) | 25(78.1)7(21.9) | 0.793 |
| AJCC staging (7th edition)Stage IAStage IBStage IIAStage IIBStage III | 2 (4.3)4 (8.7)14 (30.4)25 (54.3)1 (2.2) | 2 (6.3)3 (9.4)8 (25.0)18 (56.3)1 (3.1) | 0.981 |
| Stage IA/IB/IIA (no lymph node involvement)Stage IIB/III (advanced) | 20 (43.5)26 (56.5) | 13 (40.6)19 (59.4) | 0.802 |

**Table 4 Pathological examination results in group 1 and group 2**

**Table 5 Univariate analysis of factors affecting survival outcomes**

|  |  |  |
| --- | --- | --- |
|  | **Median survival1 (mo)** | ***P*-value** |
| Median age (yr)≤ 64 (*n* = 40)> 64 (*n* = 38) | 22.35 (3.73)15.84 (4.40) | 0.634 |
| SexMale (*n* = 45)Female (*n* = 33) | 22.35 (6.32)19.26 (3.74) | 0.445 |
| ComorbidityNo (*n* = 37)Yes (*n* = 41) | 20.05 (4.08)21.36 (4.34) | 0.890 |
| Preoperative cholangitisNo (*n* = 76)Yes (*n* = 2) | 19.26 (3.54)21.36 (-) | 0.487 |
| Postoperative complicationNo (*n* = 48) Yes (*n* = 30) | 23.79 (5.26)16.76 (4.18) | 0.204 |
| International normalized ratio ≤ 1 (*n* = 55)> 1 (*n* = 15) | 21.36 (2.79)27.51 (14.53) | 0.924 |
| Creatinine level (mmol/L) ≤ 79 (*n* = 37)> 79 (*n* = 36) | 23.79 (4.42)13.90 (2.98) | 0.652 |
| Total bilirubin level (umol/L) ≤ 72 (*n* = 39)> 72 (*n* = 38) | 22.35 (3.16)16.66 (5.01) | 0.581 |
| Serum albumin level (g/L) ≤ 40 (*n* = 44)> 40 (*n* = 29) | 28.79 (8.12)19.09 (3.77) | 0.419 |
| Blood loss (mL) ≤ 850 (*n* = 36)> 850 (*n* = 33) | 28.79 (5.84)21.36 (4.89) | 0.284 |
| Tumor Size (cm) ≤ 3 (*n* = 43)> 3 (*n* = 28) | 16.76 (3.22)19.09 (7.97) | 0.630 |
| R1 resectionNo (*n* = 59)Yes (*n* = 18) | 25.34 (5.32)13.44 (3.87) | 0.055 |
| Lymph node metastasesNo (*n* = 33) < 5 (*n* = 37)5-10 (*n* = 7)> 10 (*n* = 1) | 28.79 (3.82)17.12 (3.05)11.40 (5.68)22.18 (-) | 0.113 |
| Disease stage (AJCC staging, 7th edition)Early (IA + IB + IC) (*n* = 33)Advanced (IIB + III + IV) (*n* = 45) | 28.79 (5.00)17.12 (3.41) | 0.036 |
| Simultaneous vascular resectionYes (*n* = 32)No (*n* = 46) | 21.36 (5.93)19.26 (3.58) | 0.815 |
| Pancreatic fistula type (according to ISGPF)No fistula + type A (*n* = 73)Type B + type C (*n* = 5) | 20.05 (3.43)13.90 (6.61) | 0.488 |

1In square brackets: standard error. AJCC: American Joint Committee on Cancer; ISGPF: International Study Group on Pancreatic Fistula.