

Pancreaticoduodenectomy with vascular reconstruction for adenocarcinoma of the pancreas with borderline resectability

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Received: January 27, 2014 Revised: March 13, 2014

Accepted: July 16, 2014

Published online: December 14, 2014

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 outcomes and survivals were compared between the groups. Fifty-five patients with unresectable adenocarcinoma of the pancreas without liver metastasis who received only bypass

operations (group 3) were selected for additional survival comparison.

RESULTS: The median ages of patients were 67 years (range: 37-82 years) in group 1, and 63 years (range: 35-86 years) in group 2. All group 2 patients had resection of the portal vein or the superior mesenteric vein and three patients had resection of the superior mesenteric artery. The pancreatic fistula formation rate was 21.7% (10/46) in group 1 and 15.6% (5/32) 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 one-year, three-year and five-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 one-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 with simultaneous resection were not compromised when compared with that of standard pancreaticoduodenectomy.

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

Core tip: Whipple operation with vascular reconstruction is considered one of the most difficult operations with high morbidity. In this paper, we demonstrate that this complicated surgery can be performed in low-volume centers where a high volume of other complicated liver surgeries, including liver transplant, are performed.

Cheung TT, Poon RTP, Chok KSH, Chan ACY, Tsang SHY, Dai WC, Chan SC, Fan ST, Lo CM. Pancreaticoduodenectomy with vascular reconstruction for adenocarcinoma of the pancreas with borderline resectability. *World J Gastroenterol* 2014; 20(46): 17448-17455 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v20/i46/17448.htm> DOI: <http://dx.doi.org/10.3748/wjg.v20.i46.17448>

INTRODUCTION

Carcinoma of the pancreas is one of the leading causes of death, with 43140 new cases reported in the United States in 2010, which will lead to an estimated 36800 deaths at a five-year survival of 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 improved when compared with 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].

The aim of 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

Study population

From January 2001 to March 2012, 136 patients received pancreaticoduodenectomy at Queen Mary Hospital of the University of Hong Kong, China. Of these, 2.2% (3/136) had adenocarcinoma of the duodenum, 12.5% (17/136) had adenocarcinoma of the common bile duct, 27.9% (38/136) had adenocarcinoma of the ampulla of Vater, and 57.4% (78/136) had adenocarcinoma of the head of the pancreas (Figure 1). None of the patients received neoadjuvant chemotherapy before operation.

The study population included the 78 patients with adenocarcinoma of the pancreas. Forty-six of these patients underwent standard pancreaticoduodenectomy (group 1), and the remaining 32 patients underwent pancreaticoduodenectomy together with vascular resection (group 2). 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 received only bypass surgery (group 3) were selected for additional survival comparison. These were patients who were physically unfit for major pancreaticoduodenectomy or who had long-segment arterial encasement by tumors.

Diagnostic imaging

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 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.

Surgical technique

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 hepato-duodenal ligament were dissected. Dissection of lymph nodes around the celiac and SMA regions was performed in 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 to free the veins 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 resections 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 resections of the PV or the SMV longer than 3 cm, end-to-end anastomosis was performed with the use of a vascular conduit. Conduit selections included autologous vein, cryo-preserved vein and gortex grafts. The anastomosis was constructed continuously in a single layer with 6/0 Prolene suture. One third of the circumference or one diameter 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

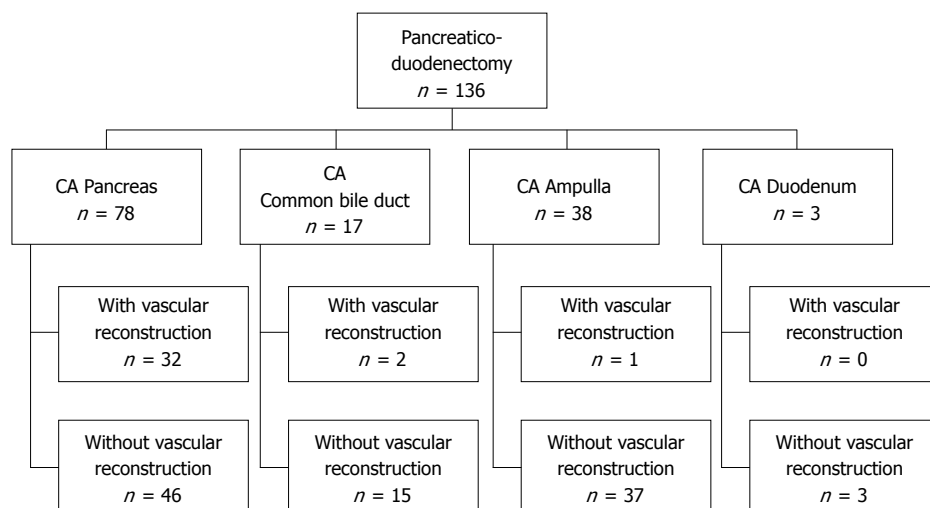


Figure 1 Distribution of pathologies and pancreaticoduodenectomies for the study population.

Table 1 Preoperative clinical parameters

Variables	Group 1 (n = 46)	Group 2 (n = 32)	P value
Age (yr)	67 (37-82)	63 (35-86)	0.452
Male:female, n	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)	1.000
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 (× 10 ⁹ /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 (mmol/L)	102 (5-533)	38 (5-342)	0.020
Albumin (g/L)	39 (27-46)	40.5 (8-47)	0.041

Data are expressed as median (range), or n (%).

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 gastrojeju-

Table 2 Operation details n (%)

Variables	Group 1 (n = 46)	Group 2 (n = 32)	P value
Portal vein resection	-	18 (56.3)	-
Reconstruction method	-	-	-
Primary anastomosis	-	14 (77.8)	-
Cadaveric vein graft	-	3 (16.7)	-
Gortex graft	-	1 (5.6)	-
Superior mesenteric vein resection	-	22 (68.8)	-
Reconstruction method	-	-	-
Primary anastomosis	-	18 (81.8)	-
Cadaveric vein graft	-	3 (13.6)	-
Gortex graft	-	1 (4.5)	-
Superior mesenteric artery resection	-	3 (9.4)	-
Reconstruction method	-	-	-
Primary anastomosis	-	3 (100)	-
Pancreaticojejunostomy construction method	-	-	0.358
Dunking	1 (2.2)	3 (9.4)	-
Duct to mucosa	43 (93.5)	28 (87.5)	-
Double loop	2 (4.3)	1 (3.1)	-
Size of pancreatic duct	-	-	0.239
< 2 mm	1 (2.4)	3 (13.0)	-
2-4 mm	15 (36.6)	8 (34.8)	-
< 4 mm	25 (61.0)	12 (52.2)	-
Pancreatic stent	-	-	0.882
No	32 (69.6)	21 (65.6)	-
Internal	3 (6.5)	3 (9.4)	-
External	11 (23.9)	8 (25.0)	-

nostomy or duodenojejunostomy was then performed, with a nasogastric tube placed in the afferent jejunal limb of the anastomosis. No vagotomy, gastrotomy 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.

Table 3 Short-term outcomes

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)	1.000
Patients with complication	20 (43.5)	10 (31.3)	0.275
Chest infection	3 (6.5)	2 (6.3)	1.000
Pleural effusion	1 (2.2)	1 (3.1)	1.000
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 (0.0)	1.000
Gastrointestinal bleeding	1 (2.2)	1 (3.1)	1.000
Cardiac arrhythmia	4 (8.7)	2 (6.3)	1.000
Acute coronary syndrome	2 (4.3)	1 (3.1)	1.000
Deep vein thrombosis	2 (4.3)	0 (0.0)	0.641
Delayed gastric emptying (> 7 d)	3 (6.5)	5 (15.6)	0.355
Types of pancreatic fistula according to ISGPF			0.662
All types	10 (21.7)	5 (15.6)	
Type A	6 (13.0)	4 (12.5)	
Type B	3 (6.5)	1 (3.13)	
Type C	1 (2.2)	0 (0.0)	

Data are expressed as median (range), or *n* (%). ISGPF: International Study Group on Pancreatic Fistula.

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^[13]. Recurrence was defined as the presence of typical features appearing on CT 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 are expressed as median and range or *n* and percent. 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 Inc., Chicago, IL, United States).

RESULTS

The medians for volume of blood loss (1200 mL *vs* 800 mL; *P* < 0.05) and operation time (715 min *vs* 580 min; *P* < 0.05) were significantly greater in group 2 compared to group 1 (Table 3). Both groups had an intensive care unit

Table 4 Pathologic examination results

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 metastases			0.299
No	21 (45.7)	12 (37.5)	
< 5	22 (47.8)	15 (46.9)	
5-10	2 (4.3)	5 (15.6)	
> 10	1 (2.2)	0 (0.0)	
Pancreaticojejunostomy construction method			0.613
Dunking or other	4 (12.5)	3 (6.5)	
Duct to mucosa	28 (87.5)	43 (93.5)	
R0 resection	35 (75.6)	25 (78.1)	0.793
R1 resection	11 (24.4)	7 (21.9)	
AJCC staging (7 th edition)			0.981
Stage I A	2 (4.3)	2 (6.3)	
Stage I B	4 (8.7)	3 (9.4)	
Stage II A	14 (30.4)	8 (25.0)	
Stage II B	25 (54.3)	18 (56.3)	
Stage III	1 (2.2)	1 (3.1)	
Stage I A/ I B/ II A (no lymph node involvement)	20 (43.5)	13 (40.6)	0.802
Stage II B/ III (advanced)	26 (56.5)	19 (59.4)	

Data are expressed as median (range), or *n* (%). AJCC: American Joint Committee on Cancer.

stay of 2 d and a median hospital stay of 17 d, with no differences observed in postoperative complications.

The median tumor size for both groups was 3 cm, and the majority of patients had fewer than five lymph node metastases (Table 4). There were no differences between the groups regarding the method of pancreaticojejunostomy, type of resection, or disease stage as classified the American Joint Committee on Cancer (AJCC) classification (7th edition)^[14].

The one-, three-, and five-year survival rates in group 1 were 71.1%, 23.6% and 13.5%, respectively (Figure 2A). These were not different from group 2, who showed corresponding rates of 70.6%, 33.3% and 22.2%. The one-, three-, and five-year disease-free survival rates in group 1 were 48.7%, 15.7% and 15.7%, respectively (Figure 2B), which corresponded to 40.3%, 20.2% and 13.4% disease-free survivals in group 2.

The one-year survival of patients in group 3 (stage II B/ III) who had only undergone bypass surgery was 13.8%, which was significantly lower than in group 2 (*P* < 0.05) (Figure 2C). These patients were either considered physically unfit for pancreaticoduodenectomy or found to have an SMA encasement larger than 2 cm during laparotomy. Patients with liver metastasis and distant metastasis were not included in this group.

Patients were classified into early and advanced groups for survival comparison according to the presence of lymph node metastasis. The early group was comprised of patients with stage I A, I B or II A disease. The advanced group was comprised of patients with disease stage II B or III. The median survival durations for group 1 and group 2 patients with early disease were

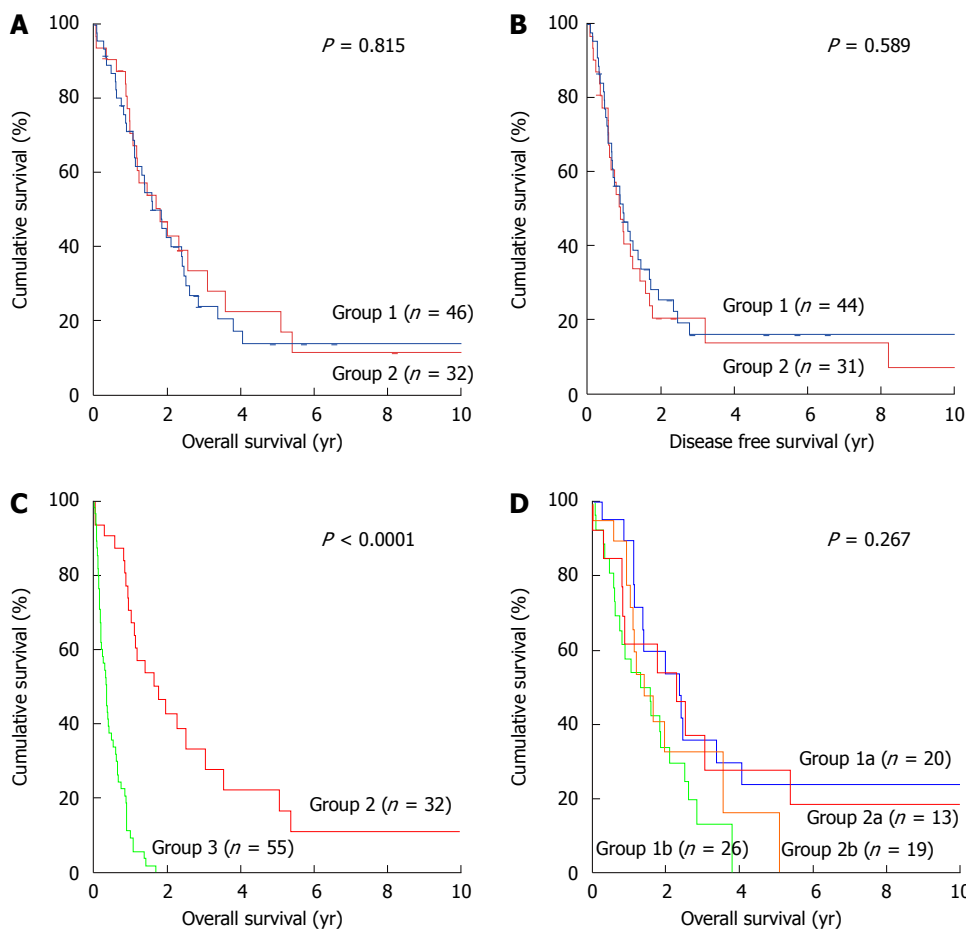


Figure 2 Comparison of survival rates. A: Overall and B: Disease-free survival curves for patients in group 1 and group 2; C: Overall survival curves for patients in group 2 and group 3; D: Stage-specific survival curves for group 1 and group 2 patients; Group 1a and 2A: Stage I and II A disease; Group 1b and 2b: Stage II B and III disease.

similar at 28.8 and 27.5 mo, respectively, and 15.8 and 17.1 mo for advanced disease stages (Figure 2D).

Sixteen factors that might affect patient survival after pancreaticoduodenectomy were identified (Table 5). Multivariate analysis showed that only lymph node metastasis was significant for poorer survival ($P = 0.021$), whereas a univariate analysis identified AJCC disease stage as the only significant factor.

DISCUSSION

Pancreaticoduodenectomy is a technically challenging procedure, and the rate of morbidities (including pancreatic fistula) ranges between 15% and 50%^[15,16]. A gradual decrease in mortality has been observed in recent years, though the patient age and the incidence of comorbid illness have increased. 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 result in poor surgical outcomes. Thus, many centers 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*^[20] described a similar observation in 23 patients whose tumors with a median size of 3 cm led to major vessel involvement.

Due to the retrospective design of this study, we did not present the degree of invasion of the PV or SMV found by histopathologic examinations. Since histologic 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 II A if there is no lymph node metastasis. In accordance with

Table 5 Univariate analyses of factors affecting survival outcomes

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

Data are presented as mean ± SE. AJCC: American Joint Committee on Cancer; ISGPF: International Study Group on Pancreatic Fistula.

this, patients with tumor invasion of the PV or SMV are still considered to have a relatively early-stage cancer. This might be quite contradictory to many clinicians' concepts.

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 these patients 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 chemoradiation have a partial tumor response rate of 56%^[22]. Although it 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.

This study shows that pancreaticoduodenectomy with vascular resection can be performed safely at centers with experience and expertise. The complication and pancreatic fistula rates 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 transplantation. Most of the time, PV or SMV reconstruction is possible without generating tension on the venous anastomosis after a Cattell-Braasch 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 morphologic 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 now be revealed by fine-cut CT scans. 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, as surgical resection provides the best survival outcomes for patients with barely resectable diseases. Pancreatic cancer with arterial invasion is also associated with poor patient survival. In a previous study, patients who had pancreaticoduodenectomy with vascular reconstruction had better survival outcomes than those who had pancreaticoduodenectomy without vascular reconstruction.

coduodenectomy with simultaneous arterial resection had a median overall survival duration of only 15.8 mo^[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, these patients fared far worse than group 2 patients. Approximately 23% of the patients in the study had R1 resection as shown by final pathologic 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 improved. 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 as having a relatively early-stage

cancer.

Terminology

Pancreaticoduodenectomy is also known as the Whipple procedure. It is a major surgical operation that involves resection of the pancreas, duodenum and other organs. It is considered a definitive treatment for malignant tumors at the head of the pancreas or involving the common bile duct, duodenal papilla 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 occurs to the anastomosis.

Peer review

This manuscript is well written and documented. I think that this manuscript is suitable and worth publishing.

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P- Reviewer: Boin IFSF, Chiaro M, Coskun A, ElGeidie AAR

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ISSN 1007-9327

