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ORIGINAL ARTICLE

Comparison of end-to-end anastomosis and interposition graft during pancreatoduodenectomy with portal vein reconstruction for pancreatic ductal adenocarcinoma

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Abstract

Purpose Many studies report that pancreatoduodenectomy (PD) with portal-superior mesenteric vein resection and reconstruction (PVR) is not a contraindication to extended tumor resection for pancreatic ductal adenocarcinoma. However, the clinical benefit of an interposition graft for PVR still remains controversial.

Methods Between January 2001 and December 2017, 199 patients with pancreatic cancer underwent PD either with or without PVR, and their medical records were reviewed retrospectively, paying specific attention to the PVR methods and the long-term outcome.

Results Among the 122 patients with PVR, 97 (79.5%) underwent end-to-end anastomosis and 25 (20.5%) had an interposition graft using the right external iliac vein (REIV). The 2-year and 5-year survival rates of the no-PVR group (54.2% and 30.8%, respectively) were longer than both the end-to-end anastomosis group (24.5% and 13.7%) and the interposition graft group (32% and 10.0%) ($p < 0.001$). However, there was no significant difference in the survival between the end-to-end anastomosis group and the interposition graft group ($p = 0.963$). A multivariate analysis indicated that the level of preoperative serum albumin < 3.5 g/dL (risk ratio (RR) 2.08, 95% confidence interval (CI) 1.26 to 3.43; $p = 0.004$), and postoperative adjuvant chemotherapy (RR 1.82, 95% CI 1.19 to 2.79; $p = 0.006$) were independently associated with overall survival after PVR.

Conclusions An interposition graft using the REIV for PVR following PD is safe and effective. There was no significant prognostic difference between PD with end-to-end anastomosis and with an interposition graft in patients with pancreatic ductal adenocarcinoma.

Keywords Pancreatic cancer · Portal vein resection · Interposition graft

Introduction

Surgery remains the only potential treatment for a cure, though recent advances in therapeutic strategies for pancreatic cancer, such as diagnostic imaging, surgical techniques, intensive care, and chemotherapy, have provided important benefits for a longer survival [1–3]. Several studies reported that PD with PVR for pancreatic cancer is not a contraindication for extended tumor resection and may help to increase R0 resection for pancreatic ductal adenocarcinoma [4–8]. Although many studies have compared PD with PVR to without PVR, there are few studies focused on the surgical methods of vein reconstruction. Several single-center studies and meta-analyses have shown significant predictors of PD with PVR, but the surgical methods are variable [9–11].

Primary end-to-end anastomosis or direct suturing is the most common option for PVR without any interposition grafts. In contrast, longer length of venous resection demands an interposition graft in some cases. A variety of different native vessels and synthetic grafts have been described to bridge the defect. However, there is no consensus on the ideal method of PVR. In addition, there are few studies that reveal the surgical outcome and long-term survival of PD with PVR by comparing end-to-end anastomosis and interposition graft. The aim of this study was to assess the prognostic factors of

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PD with PVR and the difference between end-to-end anastomosis and an interposition graft.

Material and methods

Study patients

Between January 2001 and December 2017, 215 consecutive patients with pancreatic ductal adenocarcinoma (PDAC) underwent PD at our institution. Only patients with a final pathological diagnosis of PDAC were included, and intraductal papillary mucinous neoplasm and neuroendocrine tumors were excluded. Among them, 80 patients received PD without PVR and 135 patients received PD with PVR, and we reviewed the medical records of these cases retrospectively. This study was approved by the Institution Review Board (IRB) at our institution before starting this study.

Surgical procedure

After review by a multidisciplinary board, all the pancreatic cancer cases were assessed for resectability and surgical procedure by hepatobiliary surgeons. Upfront surgery was our institutional policy until 2017 except when the patient preferred chemotherapy. All the procedures, including pylorus-preserving PD or subtotal stomach-preserving PD with regional lymphatic dissection and nerve plexus resection of superior mesenteric artery (SMA), were performed with a curative intent by a well-experienced team. A modified child method was chosen for organ reconstruction in all the cases. PD with PVR was planned and performed in the cases in which we were able to recognize portal vein invasion in the preoperative contrast-enhanced computed tomography (CT). To prevent long time vein reconstructions, *en-bloc* resection of the tumors and portal-mesenteric vein were performed just before PVR in all the cases. We never chose primary closure or a patch for PVR, and thus, either end-to-end anastomosis or an interposition graft was performed. The technique was selected mainly depending on the distance of the removed portal-mesenteric vein, but in some cases with appropriate tension of anastomotic place, we perform end-to-end anastomosis even if resected vein was long. We performed a continuous suture with 6–0 polypropylene for end-to-end anastomosis. For the interposition graft, in all the cases, we harvested the right external iliac vein (REIV) graft extraperitoneally through an upper groin incision, and each stump of the resected REIV was closed with a continuous suture using 4–0 polypropylene. Additionally, we generally do not reconstruct the splenic vein, inferior mesenteric vein, and gastric veins, so the veins were either resected or remained, depending on the tumor location. We defined the reconstruction time as the clamping time of the portal-superior mesenteric vein, which was measured in all the cases. After reconstruction, intraoperative ultrasound was used to check the blood stream. About 20 surgeons participated in the surgery during 17 years and surgeons were randomly chosen. The surgical procedures including approach methods, timing of resection of specimen, the way of organ and portal vein reconstruction have not been changed during study period.

Postoperative anticoagulation

We usually do not use heparin or other anticoagulation during PVR. However, 5000 U of heparin is routinely administrated on post-operative day 0 after all abdominal surgery and 10,000 U/day of heparin is routinely administrated on post-operative day 1–2 for preventing venous thrombosis in our institution. This is not specific medication for PVR and we usually do not add other medications to heparin. We applied a bandage on the right leg tightly to prevent edema right after the surgery.

Histologic evaluation

Handling of the resected specimens was conducted according to the general rules for the study of pancreatic cancer proposed by the Japan Pancreatic Society [12]. During the initial gross examination of the fresh specimens, the anatomic structures and each margin were identified, and the macroscopic margin status was assessed. The specimens were fixed by 10% formalin to preserve these original appearances. After fixation, the PD specimens were sectioned radially at intervals of approximately 5 mm to obtain cross sections of both the common bile duct and main pancreatic duct in one section. R0 status was defined the presence of malignant cells more than 1 mm from the surgical margin.

Variables assessed and follow-up

For the purpose of our study, we reviewed the total operation time, intraoperative blood loss volume, vein reconstruction time, length of the vein graft, histologic findings, and postoperative complications. The patients were followed up for 30 days for any complications and postoperative complications, including mortality, and were graded according to the Clavien-Dindo classification system [13]. After surgery, all the patients were evaluated every 3 months, and the follow-up examinations consisted of measurements of serum CEA and cancer antigen 19–9 levels as well as contrast-enhanced CT and/or ultrasonography. Patency of portal vein was also evaluated every 3 months after surgery. Portal vein stenosis was defined as diameter of anastomotic site less than 30% of that of native site. Other imaging approaches, including MRI and PET, were utilized in selected patients when necessary. Postoperative pancreatic fistula (PoPF) was defined according

to the International Study Group of Pancreatic Fistula (IGSPF) guidelines, and delayed gastric emptying (DGE) was also defined according to the consensus definition proposed by the International Study Group of Pancreatic Surgery (IGSPS) [14]. PoPF, DGE, refractory diarrhea, and refractory ascites (Clavien-Dindo > III) were compared between the end-to-end anastomosis group and the interposition graft group.

Postoperative adjuvant chemotherapy, using gemcitabine hydrochloride or tegafur-gimeracil-oteracil potassium, was administered beginning in 2006.

Statistical analysis

The continuous data are expressed as the median (range) or means ± the standard deviations. The statistical analyses were performed using Student's *t* tests, χ^2 tests, Mann-Whitney *U* test, and Fisher's exact probability tests as appropriate. A univariate analysis was performed using logistic regression. *p*-values less than 0.05 were considered statistically significant. Overall survival was plotted using the Kaplan-Meier method, and the 2 groups were compared using a log-rank test. The variables identified as potentially significant by univariate analysis (*p* value < 0.2) were selected for multivariate analysis with the Cox proportional hazards model to identify independent predictors of survival. All the statistical analyses were performed using IBM SPSS statistics version 23.0® (Tokyo, Japan: IBM Corp).

Results

Study patients

Between January 2001 and December 2017, 80 consecutive patients underwent PD without PVR and 135 consecutive patients underwent PD with PVR and reconstruction for PDAC at our institution. Three cases with R2 resection in PD without PVR and 13 cases with R2 resection in PD with PVR were excluded to compare the survival rates among each surgical procedure. The number of surgeries was gradually increasing in our institution (Fig. 1).

The patients' characteristics of PD without PVR and PD with PVR are shown in Table 1. There was no significant difference in age, sex, body mass index (BMI), American Society of Anesthesiology (ASA) classification, jaundice, albumin level, the ratio of the patients who had a past medical history of diabetes mellitus, and CEA. CA19-9 level and pathological T stage were higher in the group of PD with PVR compared to the group of PD without PVR. There was no significant difference in pathological N stage, though the proportion of the cases with N1 tended to be higher in the group of PD with PVR. The patients' characteristics of PD with PVR are shown in Table 2. In the 122 patients who underwent PD

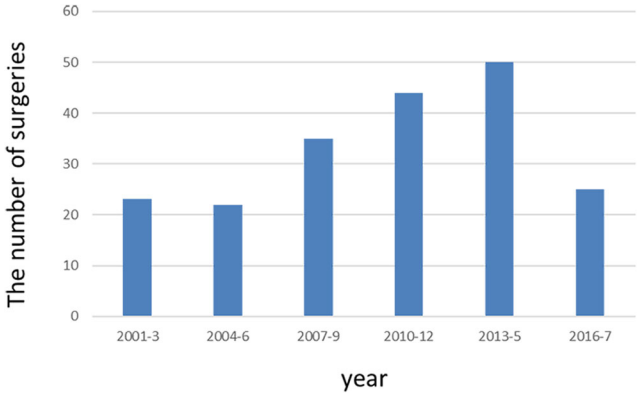

Fig. 1 The number of surgeries

with PVR, we performed end-to-end anastomosis in 97 patients (79.5%) and an interposition graft in 25 patients (20.5%). The male/female sex ratio was 50/47 vs. 12/13 ($p = 0.824$), and the patients ranged in age from 51 to 83 years (mean, 69.5 ± 9.3 years) vs. 50 to 83 years (mean, 65.3 ± 10.0 years) ($p = 0.047$). There were no significant differences between the 2 groups for the BMI, ASA classification, jaundice, albumin level, and the proportion of the cases who had a past medical history of diabetes mellitus. The preoperative blood examination showed the percent of the patients with CEA > 5 ng/mL in end-to-end anastomosis group and interposition graft group, (20 vs. 32%, $p = 0.188$) and CA19-9 > 200 U/mL (44 vs. 64%, $p = 0.115$), was not significantly different. Distribution of TNM stages did not differ between the 2 groups. Four patients in the end-to-end anastomosis group (4%) and 3 patients in the interposition graft group (12%) received neoadjuvant chemotherapy ($p = 0.151$). Forty-one patients (42%) in the end-to-end anastomosis group received adjuvant chemotherapy postoperatively, though only 16% of the interposition graft group received it ($p = 0.019$).

Surgical outcome

There was no significant difference in the operative duration (299 vs. 336 min, $p = 0.019$) and total blood loss (625 vs. 730 mL, $p = 0.390$) between end-to-end anastomosis group and interposition graft group, in spite of the fact that the duration of venous anastomosis was significantly different (11 vs. 24 min, $p < 0.001$). PD with an interposition graft tended to be performed in cases in which the tumor size was larger (30 vs. 40 mm, $p = 0.018$) and when the length of the portal vein resection was longer (30 vs. 45 mm, $p < 0.001$). Common hepatic artery (CHA) resection was performed only in the group of PD with PVR, 6 cases in end-to-end anastomosis group and 1 case in interposition graft group. Pathological results showed no significant difference in positive lymph node metastases, perineural invasion, and lymphovascular invasion. Among our 122 cases, we had expected PV-SMV invasion in 113 cases and not expected in 9 cases before

Table 1 Patient characteristics between the group of PD with and without PVR

	PD without PVR ($n = 77$)	PD with PVR ($n = 122$)	p
Age (year)	68.9 ± 10	68.6 ± 10	0.832
Sex (male/female)	43/34	62/60	0.560
BMI (kg/m^2)	21.8 ± 3.5	21.2 ± 3.0	0.189
ASA classification ≥ 3	8 (10%)	13 (10%)	1.000
Jaundice	39 (51%)	67 (55%)	0.564
Preoperative serum albumin (g/dL)	3.9 ± 0.5	3.9 ± 0.5	0.432
Diabetes mellitus	24 (31%)	41 (34%)	0.758
CEA ≥ 5 (ng/mL)*	17 (23%)	27 (23%)	0.999
CA19-9 ≥ 200 (U/mL)*	26 (35%)	59 (50%)	0.038
Postoperative TNM classification			
T			< 0.001
Tis	2 (3%)	0	
T1	6 (8%)	1 (1%)	
T2	9 (12%)	4 (3%)	
T3	60 (78%)	110 (90%)	
T4	0	7 (6%)	
N			0.053
N0	37 (48%)	41 (34%)	
N1	40 (52%)	81 (66%)	
M			0.998
M0	72 (94%)	114 (93%)	
M1	5 (6%)	8 (7%)	
Preoperative chemotherapy	0 (0%)	7 (6%)	0.044
Postoperative adjuvant chemotherapy	30 (39%)	45 (37%)	0.767

PD, pancreatoduodenectomy

PVR, portal vein resection and reconstruction

BMI, body mass index

ASA, American Society of Anesthesiology

CEA, carcinoembryonic antigen

CA19-9, carbohydrate antigen 19-9

*Missing data ($n = 6$) were not included

surgery. Microscopic portal vein invasion was observed in 42 cases (43%) and 16 cases (64%) of the cases with end-to-end anastomosis and an interposition graft ($p = 0.095$). Among these 58 cases, we expected PV-SMV invasion in 57 cases preoperatively and did not expect it in 1 case. R0 resection was achieved in 90% of the cases with end-to-end anastomosis and in 72% of the cases with an interposition graft ($p = 0.046$). There was no significant difference in the postoperative morbidity (Clavien-Dindo grade ≥ III), though PoPF, DGE, and refractory diarrhea tended to occur more often in the interposition graft group. As regards portal vein stenosis, there was no significant difference between the 2 groups 1 year after surgery (14 vs 16%, $p = 0.529$). Asymptomatic portal vein thrombosis was found in both groups (2 vs 4%, $p = 0.501$). Mortality occurred in 1 case in the end-to-end anastomosis group (Table 3). Deep vein thrombosis (DVT), which was asymptomatic, occurred in 1 out of 25 cases (4%) in the group of interposition graft, whereas it occurred in 2 out of 97 cases (2.1%).

Delayed development of ascites was observed in 6 patients out of 97 patients of end-to-end anastomosis group (6%) and 3 patients out of 25 patients of interposition graft group (12%). Portal hypertension was observed in 1 case of end-to-end anastomosis group and null in interposition graft group.

Long-term outcomes and prognostic factors

The 2-year and 5-year survival rates of the no-PVR group were longer than those of both the end-to-end anastomosis group and the interposition graft group (no-PVR, 54.2% and 30.8%, respectively; end-to-end, 24.5% and 13.7%; graft, 32% and 10.0%, $p < 0.001$). However, there was no significant difference in the survival between the end-to-end anastomosis group and the interposition graft group ($p = 0.963$)

Table 2 Patient characteristics between the group of end-to-end anastomosis and interposition graft

	End-to-end ($n = 97$)	Graft ($n = 25$)	p
Age (year)	69 ± 9	65 ± 10	0.055
Sex (male/female)	50/47	12/13	0.824
BMI (kg/m^2)	21.3 ± 2.8	20.8 ± 3.6	0.537
ASA classification ≥ 3	10 (10%)	3 (12%)	0.728
Jaundice	50 (52%)	17 (68%)	0.178
Preoperative serum albumin (g/dL)	3.9 ± 0.5	4.0 ± 0.6	0.154
Diabetes mellitus	34 (35%)	7 (28%)	0.637
CEA ≥ 5 (ng/mL)*	19 (20%)	8 (32%)	0.188
CA19-9 ≥ 200 (U/mL)*	43 (44%)	16 (64%)	0.115
Postoperative TNM classification			
T			0.666
T1	1 (1%)	0	
T2	4 (4%)	0	
T3	86 (89%)	24 (96%)	
T4	6 (6%)	1 (4%)	
N			0.815
N0	32 (33%)	9 (36%)	
N1	65 (67%)	16 (64%)	
M			0.359
M0	92 (95%)	22 (88%)	
M1	5 (5%)	3 (12%)	
Preoperative chemotherapy	4 (4%)	3 (12%)	0.151
Postoperative adjuvant chemotherapy	41 (42%)	4 (16%)	0.019

BMI, body mass index

ASA, American Society of Anesthesiology

CEA, carcinoembryonic antigen

CA19-9, carbohydrate antigen 19-9

*Missing data ($n = 4$) were not included

(Fig. 2). The median survival time following PD with CHA resection was 11.8 months, respectively, and the corresponding value was 13.3 months following PD without CHA resection ($p = 0.523$). The median survival time following PD with neoadjuvant chemotherapy was 10.8 months, respectively, and the corresponding value was 13.3 months following PD without neoadjuvant chemotherapy ($p = 0.090$).

Multivariate analyses for overall survival without PVR in 77 patients, using an adjusted Cox proportional hazards regression model, showed that the level of preoperative serum albumin < 3.5 g/dL (risk ratio (RR) 2.27, 95% confidence interval (CI) 1.16 to 4.55; $p = 0.018$), lymph node metastases (RR 2.78, 95% CI 1.58 to 4.91; $p < 0.001$), and postoperative adjuvant chemotherapy (RR 2.13, 95% CI 1.16 to 3.79; $p = 0.014$) were independently associated with overall survival (Table 4).

Multivariate analyses for overall survival after PVR in 122 patients, using an adjusted Cox proportional hazards regression model, showed that the level of preoperative serum albumin < 3.5 g/dL (risk ratio (RR) 2.08, 95% confidence interval (CI) 1.26 to 3.43; $p = 0.004$), and postoperative adjuvant chemotherapy (RR 1.82, 95% CI 1.19 to 2.79; $p = 0.006$) were independently associated with overall survival. The PVR method (i.e., end-to-end anastomosis and interposition graft) was not a significant predictor (Table 5).

Discussion

The surgical strategy for pancreatic cancer was developed, and the safety of venous resection combined with PD has been established in past quarter of a century [15–19]. PD with PVR for pancreatic cancer is not a contraindication for extended tumor resection and may help to increase R0 resection for PDAC [4–8]. Few studies have revealed the surgical outcome and long-term survival of PD with PVR by comparing end-to-end anastomosis and an interposition graft. Therefore, the clinical benefit of an interposition graft for PVR still remains controversial.

Table 3 Surgical outcome

	End-to-end (n = 97)	Graft (n = 25)	*p*
Operative duration (min)	299 (143–664)	336 (235–472)	0.019
Duration of venous anastomosis (min)	11 (7–50)	24 (16–44)	< 0.001
Length of portal vein resection (mm)	30 (5–55)	45 (20–70)	< 0.001
Total blood loss (mL)	625 (150–4900)	730 (150–3610)	0.390
Tumor size (mm)	30 (10–70)	40 (24–70)	0.018
Combined arterial resection	4 (4%)	0	1.000
Multivisceral resection	14 (14%)	7 (28%)	0.137
Lymph node metastases	65 (67%)	16 (64%)	0.815
Lymphovascular invasion	93 (96%)	24 (96%)	1.000
Perineural invasion	90 (93%)	22 (88%)	0.361
Microscopic portal vein invasion	42 (43%)	16 (64%)	0.075
Resection margin status			0.046
R0	87 (90%)	18 (72%)	
R1	10 (10%)	7 (28%)	
Morbidity (≥ Clavien-Dindo grade III)	9 (9%)	3 (12%)	0.709
Pancreatic fistula	7 (7%)	3 (12%)	0.426
Delayed gastric emptying	8 (8%)	5 (20%)	0.138
Refractory diarrhea	7 (7%)	5 (20%)	0.069
Refractory ascites	3 (3%)	0	1.000
Portal vein stenosis after PVR			
30 days	1 (1%)	0	0.795
3 months	4 (4%)	1 (4%)	0.729
6 months	6 (6%)	1 (4%)	0.561
1 year	14 (14%)	4 (16%)	0.529
Portal vein thrombosis at 1 year	2 (2%)	1 (4%)	0.501
Mortality	1 (1%)	0	1.000

Expressed as N (%) or median (range)

In our study, PD with PVR yielded a poorer prognosis than PD without PVR, because the patients' backgrounds were a somewhat different and more severe in the PVR group. However, no significant difference in the prognosis was observed between the end-to-end anastomosis and interposition graft groups. This study demonstrated that differences in the surgical methods in PVR did not affect the overall survival regardless of the tumor size, whether the tumor had infiltrated the vein, and the ratio of the R0 resection, which implied that an interposition graft would offer the opportunity to receive a similar prognosis as end-to-end anastomosis.

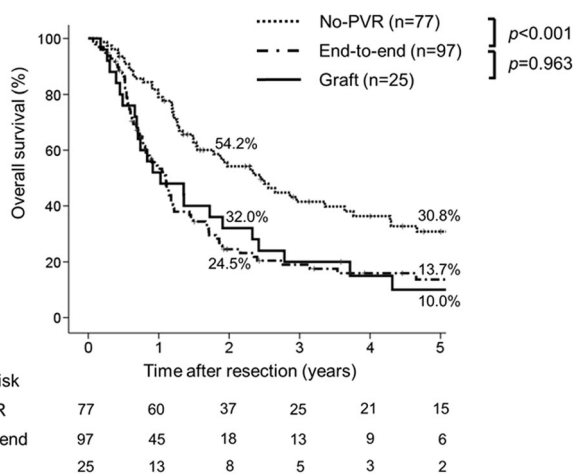

Fig. 2 Survival in relation to the type of surgical method

Many studies have referred to various independent predictors for pancreatic cancer following PD with PVR. Historically, the ratio of the tumor's infiltration to the portal vein and its severity has been one of the arguments in PVR, and surgical indication is still controversial. Takahashi et al. [20] reported that PVR was worth being considered when infiltration was on only one side of the portal vein, and Boggi et al. [21] showed that intimal invasion was one of the poor prognostic factors. Han et al. [22] revealed that tunica intimal invasion was a poor prognostic factor but also showed that microscopic invasion was not observed in 21.1% of the patients and that a better outcome was expected in such patients. Recently, Ravikumar et al. [11] demonstrated that venous tumor infiltration was not associated with a decreased overall survival, including 64 patients in the end-to-end

Table 4 Univariate and multivariate analyses for overall survival after PD without PVR in 77 patients

variable	n	Overall survival		Univariate, *p*	Multivariate	
		2-years (%)	5-years (%)		Risk ratio (95% confidence interval)	*p*
Age (year)				0.355		
< 70	38	50.0	23.7			
≥ 70	39	43.6	15.4			
Sex				0.057		
Male	43	38.2	5.9			
Female	34	53.5	30.2			
BMI (kg/m^2)				0.004		
< 21	32	40.6	0			
≥ 21	45	51.1	33.3			
Preop. serum albumin (g/dL)				0.002		0.018
< 3.5	16	18.8	0		2.27 (1.16–4.55)	
≥ 3.5	61	54.1	24.6		1	
CEA (ng/mL)				0.288		
< 5*	60	44.8	15.5			
≥ 5	17	52.9	29.4			
CA19-9 (U/mL)				0.137		
< 200*	51	51.0	22.4			
≥ 200	26	38.5	11.5			
Tumor size (cm)				0.029		
< 3	46	61.4	25.0			
≥ 3	31	29.0	12.9			
Lymph node metastases				0.003		< 0.001
Absent	37	59.5	32.4		1	
Present	40	35.0	7.5		2.78 (1.58–4.91)	
Resection margin status				0.28		
R0	69	47.8	20.3			
R1	8	37.5	12.5			
Postop. adjuvant chemotherapy				0.066		0.014
Absent	47	38.3	14.9		2.13 (1.16–3.79)	
Present	30	60.0	26.7		1	

PD, pancreatoduodenectomy

PVR, portal vein resection and reconstruction

BMI, body mass index

CEA, carcinoembryonic antigen

CA19-9, carbohydrate antigen 19-9

*Missing data ($n = 2$) were included

anastomosis group and 36 patients in the interposition graft group. In our study, microscopic portal vein invasion was observed more often in the interposition graft group than in the end-to-end anastomosis group (43 vs 64%, respectively, $p = 0.075$), but this event did not have a negative impact on the overall survival between the 2 groups. A previous study reported that lymphovascular invasion and perineural invasion were more frequently observed among patients who received an interposition graft, and the SMV groove was also more likely to be positive in these patients, such that a larger resection was required [11]. This study demonstrated that over 90% of the patients who received PVR had lymphovascular invasion and also that perineural invasion was observed at approximately 90% in each group.

Table 5 Univariate and multivariate analyses for overall survival after portal vein resection in 122 patients

variable	n	Overall survival		Univariate, *p*	Multivariate	
		2-years (%)	5-years (%)		Risk ratio (95% confidence interval)	*p*
Age (year)				0.026		
< 70	60	34.3	17.0			
≥ 70	62	18.4	8.1			
Sex				0.966		
Male	62	25.7	13.5			
Female	60	26.9	12.1			
BMI (kg/m^2)				0.081		0.061
< 21	60	21.1	3.6		1.47 (0.98–2.21)	
≥ 21	62	31.7	20.8		1	
Preop. serum albumin (g/dL)				0.002		0.004
< 3.5	21	10.2	5.1		2.08 (1.26–3.43)	
≥ 3.5	101	29.6	14.3		1	
CEA (ng/mL)				0.350		
< 5*	95	25.0	11.6			
≥ 5	27	31.0	16.5			
CA19-9 (U/mL)				0.101		
< 200*	63	31.7	17.8			
≥ 200	59	20.6	7.4			
Tumor size (cm)				0.137		
< 3	41	36.5	23.5			
≥ 3	81	20.6	5.9			
Lymph node metastases				0.279		
Absent	41	28.5	18.7			
Present	81	25.2	10.0			
Microscopic portal vein invasion				0.120		
Absent	64	28.2	17.6			
Present	58	24.1	6.6			
Resection margin status				0.210		
R0	105	27.8	14.0			
R1	17	17.6	5.9			
Postop. adjuvant chemotherapy				0.004		0.006
Absent	77	19.7	5.5		1.82 (1.19–2.79)	
Present	45	38.2	28.2		1	
Portal vein reconstruction				0.963		
End-to-end	97	24.5	13.7			
Graft	25	32.0	10.0			

BMI, body mass index

CEA, carcinoembryonic antigen

CA19-9, carbohydrate antigen 19-9

*Missing data ($n = 4$) were included

All the surgeries were performed under a curative intent, but we still had R1 resection cases. We achieved R0 resection in 90% of the end-to-end anastomosis group, though the ratio of the R0 resection among the interposition graft group was confined to 72%. Some studies repeatedly report that the R1 status is an independent factor

of a poor prognosis following PD for pancreatic cancer [23–25]. Marchegiani et al. [26] also revealed the prognostic difference between R0 and R1 resection but concluded that tumor size was the most significant predictor for pancreatic cancer in a multivariate analysis. In that study, the survival terms were significantly different between the tumors of 10 to 20 mm, 20 to 30 mm, and 30 to 40 mm sizes (33 vs. 27 vs. 21 months, respectively, $p < 0.01$). Although our study showed that the average tumor size was significantly larger in the patients who received an interposition graft than in the patients who underwent end-to-end anastomosis (39 ± 13 mm vs. 32 ± 10 mm, $p = 0.004$), the overall survival rates were similar, and this was not a significant prognostic factor of PVR in the multivariate analysis. Butturini et al. [27] reported that the resection margin involvement was not a predictor, and adjuvant chemotherapy was a significant factor for survival. Similar to this study, we demonstrated that postoperative adjuvant chemotherapy was one significant predictor of survival in cases with PVR. However, there was a significant difference in the ratio of receiving adjuvant chemotherapy between the 2 groups. Recently, the progression of adjuvant chemotherapy has improved the prognosis of pancreatic cancer and still has the possibility to provide more survival benefits. ESPAC-4 [28] demonstrated that the median overall survival for patients in the gemcitabine plus capecitabine group was 28.0 months compared with 25.5 months in the gemcitabine group (hazard ratio 0.82 [95% CI 0.68–0.98], $p = 0.032$). CONKO-005 [29] was the first study to investigate the combination of chemotherapy and a targeted therapy in the adjuvant treatment of pancreatic cancer, but gemcitabine with erlotinib did not improve the disease-free survival (DFS) or the overall survival over gemcitabine.

Our study demonstrated that the significant predictors with PVR for pancreatic cancer were the level of preoperative serum albumin (< 3.5 g/dL) and postoperative adjuvant chemotherapy. These results implied that patients with an appropriate level of preoperative serum albumin can tolerate severe surgery and are also able to receive benefit from adjuvant chemotherapy. Hendifar et al. [30] showed that low preoperative serum albumin was associated with a worse DFS and overall survival in patients with resected pancreatic cancer, and a lower BMI and serum albumin were associated with a longer postoperative hospital stay. Further investigation on the nutritional status and weight loss is required.

Graft length and selection is still controversial in many reports. Wang et al. [31] reported that graft interposition could be avoided even when the length of the resected vein was up to 4 cm, and Zhang et al. [32] also reported that long PVR (> 5 cm) by end-to-end anastomosis was possible among 8 patients without any complication by using the Cattell-Braasch maneuver. Dua et al. [33] revealed that end-to-end anastomosis had superior patency compared to the alternatives, especially for a short (< 3 cm) reconstruction in PVR. Several studies show the utility of the grafts, including the ovarian vein [34, 35], femoral vein and saphenous vein [36], with polytetrafluoroethylene (PTFE) [37, 38]. In our institution, we always use the REIV for the interposition graft because we consider the REIV graft as a suitable vein graft for PVR in terms of an appropriate diameter, which is the same as the portal vein. Because the REIV is resected more central than the entrance of a communicating branch of an obturator vein to preserve the return flow from the peripheral side, and because we apply a bandage tightly on the right leg after surgery, we usually do not confront the problem of leg edema and have never experienced other symptomatic DVT after surgery [39]. Although the postoperative complication rate was slightly higher in the interposition graft group, this study demonstrated that the interposition graft for PVR was an acceptable procedure in terms of safety and a similar prognosis as end-to-end anastomosis considering that the backgrounds of the patient were slightly worse in several prognostic factors.

We acknowledge several limitations in our study. This was a retrospective study over a long period of time at specialized hepato-pancreato-biliary centers. Therefore, there was institutional and/or publication bias. Additionally, several treatment changes occurred, such as the introduction of perioperative chemotherapy. In this series, patients who underwent preoperative neoadjuvant chemotherapy were limited to a very small number of cases. Although preoperative evaluation of resectability has been refined with advanced diagnostic imaging tools, it is sometimes difficult to evaluate the fibrosis around the SMA. As a result, the R2 resection rate increased in the PVR group in this study. Furthermore, we do not have adequate data to assess the nutritional states and quality of life after PD with PVR. In the future, a multicenter large series study to evaluate the clinical significance of this procedure by a standardized surgical team would greatly improve the limitations of this study.

In conclusion, there was no significant difference in prognosis and graft patency between PD with end-to-end anastomosis and an interposition graft in patients with PDAC. Both techniques are possible and safe and can be utilized based on individual patient circumstances.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent was obtained from all individual participants included in the study.

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