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Reevaluation of the Indications for Radical Pancreatectomy to Treat Pancreatic Carcinoma: Is Portal Vein Infiltration a Contraindication?

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Abstract

Purpose. Portal vein resection (PVR) has become more widely performed owing to improvements in the perioperative mortality rate. The present study was performed to determine whether portal vein infiltration is a contraindication against radical pancreatectomy for patients with pancreatic carcinoma.

Methods. Between 1990 and 1997, a total of 66 patients with invasive ductal carcinoma of the pancreas underwent surgical resection at the Department of Surgery II, Hokkaido University Hospital. After the exclusion of those who underwent distal pancreatectomy, the remaining 43 patients were divided into a PVR(+) group (n = 28) and a PVR(−) group (n = 15). The clinicopathological characteristics, morbidity, and mortality were statistically compared between the two groups.

Results. The overall survival rate of the patients who required PVR was not significantly different from that of those who underwent pancreatic resection without PVR.

Conclusion. These findings suggest that combined PVR should not be a contraindication to radical pancreatectomy for pancreatic carcinoma with positive vascular invasion.

Key words Pancreatic carcinoma · Portal vein infiltration · Portal vein resection · Survival

Introduction

Pancreatic cancer is often already in an advanced stage at the time of diagnosis, invading surrounding structures or having metastasized to distant organs such as the liver. In the past, surgical resection was not feasible when the tumor had infiltrated the retroperitoneum and the portal vein. However, since Fortner introduced combined resection and reconstruction of the portal vein for locally advanced carcinoma of the pancreas with portal vein infiltration,[1] focusing on improvements in resectability and curability, many surgeons have started to perform portal vein resection (PVR).

In recent years, the surgical procedure for pancreatic cancer has become more advanced and many surgeons have reported improvements in mortality as well as morbidity.[2–4] In this study, we examined the clinical significance of PVR in terms of the surgical procedure, its safety, and improvements in mortality.

Patients and Methods

Between 1990 and 1997, a total of 66 patients with invasive ductal carcinoma of the pancreas underwent surgical resection with curative intent at the Second Department of Surgery, Hokkaido University Hospital. After the exclusion of those who underwent distal pancreatectomy, 43 patients were the subjects of this study. They were subsequently divided into two groups depending on whether or not PVR was performed. The PVR(+) group consisted of 28 patients (65%) who underwent PVR while the PVR(−) group consisted of 15 patients (35%) who did not. PVR was performed for patients who did not appear to have distant metastasis or peritoneal dissemination, and when no tumor infiltration in the portal vein and superior mesenteric vein was detected by preoperative examination and intraoperative findings. In addition, the regional lymph nodes and retroperitoneal tissues, including the neural plexuses around the superior mesenteric artery and common hepatic artery, were dissected. In the PVR(+) group, a primary end-to-end anastomosis was done using a monofilament suture in 24 patients. Interposition grafts

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(in the form of autosplenic vein grafts) were used in only two patients, and two others underwent lateral venorrhaphy of the portal vein for tumor clearance. Antithrombogenic bypass catheters[5] were used to prevent portal congestion in 13 patients (46%).

Various factors were statistically compared between the two groups. For demographics, intraoperative factors, tumor characteristics, and survival rates, the mean values of these data were analyzed and evaluated. The survival rates of individuals were analyzed by the Kaplan-Meier method and the data obtained were compared using the generalized Wilcoxon test. The Fisher's exact probability test, the Mann-Whitney *U*-test, and the chi-squared test were also used for analysis. *P* values of less than 0.05 were considered statistically significant.

Results

The clinicopathological characteristics of the patients in the PVR(+) and the PVR(−) groups are shown in Table 1. The median age of patients in the PVR(+) group was 60.9 years (range 31–78 years) which was not significantly different from that in the PVR(−) group of 65.0 years (range 31–78 years). The male/female ratios were also similar in the two groups, at 17:11 in the PVR(+) group *vs* 10:5 in the PVR(−) group. The operative procedures performed were: total pancreatectomy in 5 patients (all from the PVR(+) group); pancreaticoduodenectomy in 33 patients (20 from the PVR(+) group and 13 from the PVR(−) group); and pylorus-preserving pancreaticoduodenectomy in 5 patients (3 from the PVR(+) group and 2 from the PVR(−) group).

The total operative time in the PVR(+) group was significantly longer than that in the PVR(−) group at 551 min (range 340–955 min) *vs* 414 min (range 278–583 min). The estimated intraoperative blood loss did not differ significantly between the two groups, being 3083 ml (range 420–14280 ml) in the PVR(+) group compared with 2095 ml (range 980–5840 ml) in the PVR(−) group. The median tumor size in the PVR(+) group at 4.7 cm (range 2.0–9.0 cm) was not significantly different from that in the PVR(−) group at 4.5 cm (range 2.0–10.0 cm), respectively. The microscopic surgical margins were found to be histologically positive in 18 (64%) patients from the PVR(+) group compared with 6 (40%) from the PVR(−) group, this difference not being significant. Metastatic lymph node involvement was identified pathologically in 24 (88%) and 13 (73%) patients from the PVR(+) and PVR(−) groups, respectively, which was not a significant difference. Tumor grade was not significantly different between the two groups. The postoperative hospital stay was also similar in length between the two groups, at 68.8 days from the PVR(+) group and 59.6 days for the PVR(−) group.

Postoperative complications developed in 13 of the PVR(+) group patients (46%) and in 9 of the PVR(−) group patients (60%). There was no significant difference in the number or type of complications (Table 2).

There was no significant difference in survival between the two groups, with one postoperative death in the PVR(+) group (4%) and one in the PVR(−) group (7%). The other nonsurvivors in the two groups all died of pancreatic cancer (Fig. 1).

Portal vein infiltration was histologically detected in 21 of the 28 patients who underwent PVR (75%). A

Table 1. Clinicopathological characteristics of the 43 patients who underwent resection of pancreatic cancers

	PVR(+) (n = 28)	PVR(−) (n = 15)	P value
Age (years)	60.9 (31–78)	65.0 (38–78)	NS
Sex (male/female)	17/11	10/5	NS
Operative factors			
Procedure (TP/PD/PpPD)	5/20/3	0/13/2	NS
Estimated blood loss (ml)	3083 (720–14280)	2095 (980–5840)	NS
Operative time (min)	551 (340–955)	414 (278–583)	<0.05
Tumor characteristics			
Tumor size (cm)	4.7 (2.0–9.0)	4.5 (2.0–10.0)	NS
Positive resection margin	18 (64%)	6 (40%)	NS
Positive lymph node metastasis	24 (86%)	13 (87%)	NS
Differentiation (well/poor)	8/20	4/11	NS
Outcome			
Postoperative hospital stay (days)	68.8	59.6	NS
Postoperative complications	13 (46%)	9 (60%)	NS
Perioperative death	1 (4%)	1 (7%)	NS

PVR, portal vein resection; TP, total pancreatectomy; PD, pancreaticoduodenectomy; PpPD, pylorus-preserving pancreaticoduodenectomy; well, well-differentiated type; Poor, poorly differentiated type; NS, not significant

Table 2. Perioperative complications

Complication	PVR(+) (n = 28)	PVR(−) (n = 15)
Intra-abdominal collection	8	4
Arterial bleeding	2	2
Cholangitis	1	1
Penumonia	1	1
Others[a]	1	1
Total	13 (46%)	9 (60%)

PVR, portal vein resection
There was no significant difference in the number or kind of complications between the two groups
[a] Colonic necrosis (PVR(+)) and renal failure (PVR(−))

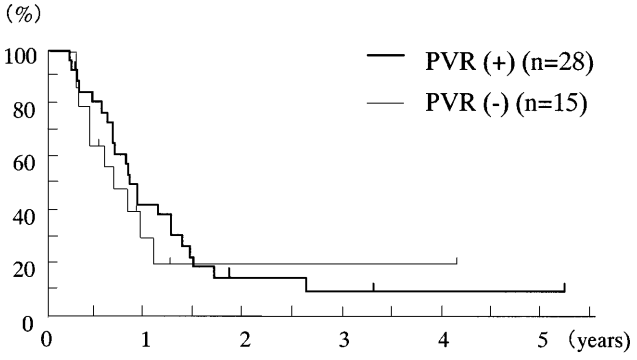

Fig. 1. Comulative survival rates of the 43 consecutive patients who underwent pancreatectomy with portal vein resection (*PVR*) or without. There was no significant difference in survival between the two groups

comparison of the survival rates according to whether or not histological portal vein infiltration was present did not reveal any significant difference (Fig. 2).

Discussion

Regional pancreatectomy with vascular resection for pancreatic tumors was initially described in 1973 by Fortner,[1] and while many surgeons adopted his procedure, the associated mortality and morbidity rates were high, and the rate of achieving complete resection was low.[6,7] Thus, until recently, PVR was thought not to prolong the survival of patients undergoing pancreatectomy. However, advances in surgical procedures to resect pancreatic tumors, and in postoperative care, have increased the survival rate and lowered the morbidity rate,[2–4] which has encouraged many surgeons to use the PVR procedure. Klempnauer et al. reviewed 54 cases of patients who underwent complicated resection of the mesentericoportal vein, the common hepatic artery, or the superior mesenteric artery, and reported that vascular resection and reconstruction did not increase the

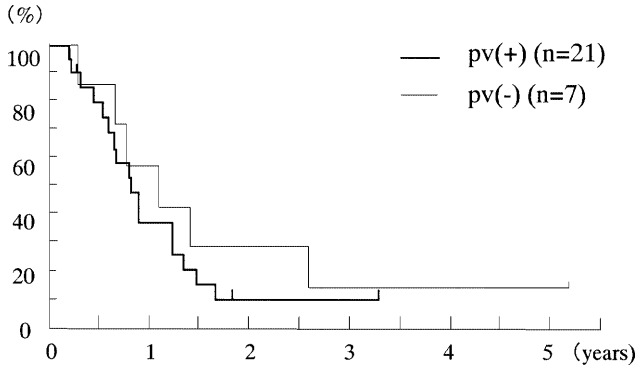

Fig. 2. Cumulative survival rates of the 28 consecutive patients who underwent PVR according to histological invasion of the portal vein in the PVR(+) group. There was no significant difference in survival between the two groups. *pv*(+), histologically positive invasion; *pv*(−), histologically negative invasion

rate of complications or mortality.[8] This report coincides with those of other surgeons who also found no differences in morbidity and mortality rates between patients who underwent PVR and those who did not.[9–11]

In our study, there were no significant differences between the PVR(+) and PVR(−) groups in intraoperative blood loss, morbidity, mortality, or postoperative hospital stay, indicating that portal vein resection and reconstruction can be safely achieved.

Furthermore, the results of our study which showed no significant difference in long-term prognosis between 28 patients who underwent portal vein resection and 15 patients who did not, were supportive of those of past reports. To explain why there was no difference in survival, Harrison and colleagues suggested that true vascular invasion is difficult to differentiate from inflammatory adhesions.[11]

The assessment of tumor infiltration to the portal vein is currently reliant on preoperative portography or macroscopic findings during the operation, which are very limited, although some surgeons suggest that preoperative portography can give some indication of the appropriate extent of surgery.[12,13] Detecting the precise site of tumor infiltration is only possible by histopathological analysis. In our study, although all the PVR operations were conducted with a macroscopically negative margin, tumor infiltration was found microscopically in 21 of the 28 patients who underwent PVR (75%), while 7 had inflammatory adhesions without cancer invasion (25%). A comparison of the mortality rates according to the histological grade of the tumor did not significantly differ between the two groups. Histological tumor invasion to PV/SMV was not a prognostic factor. Harrison and colleagues emphasized that the need for PVR was not a predictor of aggressive tumor

biology, but rather a reflection of tumor size and location.[11] Many surgeons have been investigating the various prognostic factors.[14–17]

In addition to portal vein invasion, we investigated tumor size, lymph node metastasis, surgical margin, and histological grade, and found no differences between the two groups. We also carried out a multivariate analysis of 158 pancreatic tumors resected during the period between 1980 and 1994, which indicated that histological differentiation of the tumor was the key factor affecting the survival rate.[18]

These results showed that we should not discourage PVR for locally advanced pancreatic carcinoma involving the portal vein, since it has been shown to be technically successful and there are more factors influencing prognosis than portal vein invasion.

When treating patients with pancreatic cancer, we should clarify the clinical features of patients who would benefit by undergoing tumor resection. Koshiba et al. detected matrix metalloproteinase-2 in all of the pancreatic cancers they analyzed and their metastatic tissue.[19] Similarly, we should also investigate the important biological factors of tumors affecting the survival, even at the molecular level, and make accurate preoperative diagnoses using techniques such as pancreatoscopic biopsy for histopathological and genomic analyses.

In conclusion, combined PVR should not be a contraindication of radical pancreatectomy for pancreatic carcinoma with positive vascular invasion.

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