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Original Article

Safety and Feasibility of Pancreaticoduodenectomy with Venous Reconstruction: Maharaj Nakorn Chiang Mai Hospital's Experience

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Abstract

Background: **Pancreaticoduodenectomy (PD) with venous reconstruction is becoming a more common practice in locally advanced pancreatic adenocarcinoma in which tumors adhere or invade portal vein (PV) or superior mesenteric vein (SMV). Our objective was to compare short-term outcomes of PD with venous reconstruction (VR group) to a standard PD (non-VR group) in our center.**

Materials and Methods: **This retrospective study recruited 43 patients who underwent PD by a single surgeon from July 2010- June 2013. Seventeen patients underwent PD with VR and 26 were in non-VR group. All charts were reviewed, including demographic data, operative details, and complications. Disease-free survival (DFS) and overall survival were evaluated.**

Results: **Of 43 patients, there were significant differences in operative time and amount of blood loss between both groups. However, length of stay of both groups had no difference. Pathological PV/SMV invasion in VR group was 41.7%. Mortality rate was not different in both groups. Overall survival and DFS in the VR group were 9 months and 6.5 months respectively.**

Conclusion: **PD with venous reconstruction is safe and effective in selected cases. Short-term outcomes are similar to those in non-vascular reconstruction group. Mortality rate in both groups are high. PD with VR should remain the standard of care for locally advanced peri-ampullary cancer.**

Keywords: **Pancreaticoduodenectomy, whipple operation, venous reconstruction, pancreatic cancer**

Introduction

Pancreatic adenocarcinoma is the fourth leading cause of cancer death in men, after lung, prostate, and colorectal cancer, and the fifth leading cause of cancer death in women, following lung, breast, colorectal, and ovarian cancer[1]. In 2000, 217,000 new cases were reported globally, with 213,000 resultant deaths[2]. Pancreatic resection is known as one of the most complicated and technically challenging surgical procedures known to general and hepatobiliary-pancreatic (HBP) surgeons. It is not only technically challenge, but also substantial logistical strain on health

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care resources. For tumors that are located in the peripancreatic head area, pancreaticodudenectomy (PD) is recognized as the optimal definite treatment. In 1973, Fortner[3] showed that a more radical resection should improve survival by better tumor clearance. When tumor adhered to portal vein (PV) or superior mesenteric vein (SMV), often regarded as unresectability, en bloc resection of the involved vessels should be attempted. As surgical expertise has improved over the past few decades, and the quality of high-volume centers especially for technically demanding surgeries, such as pancreatic resection has been proven, thus, it is not surprising that perioperative morbidity and mortality rates reported for pancreatic resections with or without PV or SMV resection are identical[4,5,6,7,8]. Moreover, the long-term survival of patients who have had pancreatic resection in combination with PV resection is far superior compared with those in whom only palliative surgical management was performed. Based on these facts, we would like to report the results from 46 patients that underwent PD and PD with venous reconstruction (VR) to compare perioperative outcome. One-year survival in VR group was also examined.

Patient Selection and Methods

Data of patients who underwent PD by the first author (S.J.) at the Division of Hepatobiliary-pancreatic Surgery, Department of Surgery, Maharaj Nakorn Chiang Mai Hospital, Faculty of Medicine, Chiang Mai University between July 2010 and June 2013 were reviewed. Tri-phase computed tomography (CT) scan of the abdomen and pelvis or magnetic resonance imaging (MRI) of the abdomen and pelvis were used to assess resectability. Endoscopy and biopsy were performed in patients who were suspected of carcinoma of the ampulla of Vater and carcinoma of the duodenum. Patients who had clinical cholangitis, malnutrition or needed to wait for a long time before surgery received placement of preoperative biliary drainage by Percutaneous Transhepatic Biliary Drainage (PTBD) or Endoscopic Retrograde Cholangio-Pancreatography (ERCP) with plastic stent. The decision to perform endoscopic biliary drainage depended on clinical situation and opinion of the gastroenterologists or surgeons. We waited until this group of patients regained near normal liver function tests and good nutritional status before their operation was performed. Operative details, including patient factors (gender, age, weight, type of tumor and tumor size), operative time, blood loss, complications and one year survival were recorded. The neoadjuvant treatment protocol was not established during time of study period. All works were performed after the approval of Institutional Review Board.

Operative details

Majority of cases underwent standard pylorus-preserving PD (PPPD). Classical PD was performed in cases of inadequate surgical margins. Pancreatic-biliary-enteric continuity was performed by using a retrocolic jejunal limb with end-to-side pancreaticojejunostomy (duct to mucosa), end-to-side hepaticojejunostomy, and end-to-side duodenojejunostomy in PPPD. The author preferred a small feeding tube number 5 or 8 French for stenting pancreaticojejunostomy anastomosis when encountered with small pancreatic duct. The external pancreatic stent was never used. When evidence of direct extension to the PV or SMV was encountered, en bloc vascular resection was performed with vascular reconstruction accomplished by either primary end-to-end anastomosis or by placing an interposition graft. We ligated the splenic vein and performed proximal and distal control at PV-SMV. The vein was divided and the remaining tissue was dissected at the retroperitoneal margin. In our early experience, we routinely used a shunt between the PV and SMV to reduce visceral congestion and liver ischemia. More recently, a shunt is used just in complex case as an interposition graft. For reducing the gap between vascular anastomosis, falciform and triangular ligaments were divided to mobilize right and left lobes of liver. In some cases, we clamped the superior mesenteric artery (SMA) to reduce congestion of small bowel.

Clamping time, operative time and blood loss were recorded in operative note. Liver function test was examined when patient returned to ward. Patency of vascular anastomosis was checked by Doppler ultrasound on the first post-operative day. Amylase levels in serum and drain fluid were examined on the third post-operative day. When patients had a pancreatic fistula according to the International Study Group of Pancreatic Fistula (ISGPF) criteria[9], the drain was retained until volume and level of amylase declined to

normal. If all laboratory values were in normal range and patients resumed oral food, they were discharged. All patients were scheduled to meet the attending staff in the Division of HBP Surgery at two weeks, one month and then every three months until one year. Pathology reports including type and grading of tumor, lymph node status, margin, venous invasion status were reported by a specialized HBP pathologist. The use of adjuvant chemotherapy in each patient was determined by clinical performance of patient and agreement between oncologist and surgeon.

Statistical analysis

Data were analyzed by STATA version 11.0. Continuous data from both groups were compared by student's t test to report p-value, if data had a normal distribution. When data had distribution that was not normal, the p-value was reported by a rank sum test (Mann-Whitney U test). Categorical data were compared by Chi-square test/Fisher's exact test. Median survival time and one year survival were analyzed.

Results

During the study period, records from 43 patients who underwent PD were evaluated. The baseline characteristics of the patients are shown in Tables 1 and 2.

There were 21 female and 22 male patients. The primary diseases treated were pancreatic adenocarcinoma (n=13), cholangiocarcinoma (n=7), carcinoma of ampulla of Vater (n=17), benign disease (n=3), pancreatic neuroendocrine tumor (n=2) and duodenal carcinoma (n=1). Overall morbidity and 30-day mortality rates were 18.6% and 9.3 % respectively. The pancreatic fistula rate in overall patients was 11.6 %.

In the VR group, the mean patient age was 56.7 years. Patients receiving treatment included pancreatic adenocarcinoma (n=10), cholangiocarcinoma (n=4), ampulla of Vater carcinoma (n=1) and nonfunctioning pancreatic neuroendocrine tumor (n=2) as shown in Figure 1. Two patients underwent concomitant arterial reconstruction because their replaced right hepatic artery came from the superior mesenteric artery and passed through the tumor. A colectomy was performed due to invasion of the colic vessel and colonic serosa. Proportion of vascular reconstruction technique was shown in Figure 2. Venous reconstruction was performed by end to end anastomosis in nine patients (Figure 3). In seven patients an autogenous vein graft was used for the left renal vein in four cases (Figure 4), and for the inferior mesenteric vein in three cases (Figure 5). Polytetrafluoroethylene (PTFE) graft was used in one case due to lack of autogenous vein graft. The median operative blood loss in this group was 1,217.6 mL. (300 - 3,000 mL) and the mean vascular gap was around 3 cm. (1.8- 5 cm). The vascular anastomosis was evaluated for all patients by intraoperative and postoperative Doppler ultrasound. None of these patients had occlusion of their reconstructed vessel. There was a positive margin in 4 patients (23.5%) and lymph node metastasis was found in 11 patients (64.7 %). In this series, pathology of the excised pancreas was confirmed with PV or SMV invasion in 41.7% of cases.

Two patients (11.7%) died in the postoperative period from septic shock at 8 and 14 days after surgery. The median hospital stay was 16 days (9 - 60). One

Table 1 Demographics, tumor histology, operative detail and post-operative data of all 43 patients that underwent PD from July 2010 to June 2013.

Variable	
Age; year	59.2 ± 10.8
Weight; kg	55.9 ± 11.0
Pre-op albumin	3.01 ± 0.8
Carbohydrate antigen 19-9 (range)	566.6 (0.7- 2182)
Primary (%)	
Pancreatic adenocarcinoma	13 (30.2)
Cholangiocarcinoma	7 (16.3)
Ampulla of vater carcinoma	17 (39.5)
Duodenal carcinoma	1 (2.3)
Pancreatic neuroendocrine tumor	2 (4.6)
Benign disease	3 (7)
Operation (%)	
Non Vascular reconstruction	26 (60.5)
Vascular reconstruction	17 (39.5)
Mean operative time; min (range)	487.4 ± 126.2 (215- 840)
Mean Blood loss; ml (range)	774.1 ± 686.6 (50 - 3000)
Mean Hospital stay; day (range)	19.03 ± 23.6 (7- 125)
30 day mortality	4 (9.3%)
Morbidity (%)	8 (18.6)
Sepsis	3 (7)
Pancreatic fistula	5 (11.6)
Intraabdominal fluid collection	1 (7)
Acute renal failure	1 (2.3)
Bleeding	2 (4.6)
Re-operation	2 (4.6)

Table 2 Comparative demographic and operative data between non venous reconstruction (non VR) and venous reconstruction (VR) group

Variable	non VR	VR	*p*-value
Number (%)	26 (60.47)	17 (39.53)	-
Age in years	61 ± 12.3	56.7 _ 10.4	0.216
Weight; kg	55.9 ± 10.8	55.9 _ 11.7	0.990
Mean blood loss; ml (range)	373.1 ± 276.1 (50-1200)	1217.6 ± 741.8 (300-3000)	<0.001
Mean operative time; min (range)	390.4 ± 79.39 (300-530)	564.1 ± 119.7 (440-840)	<0.001
Mean hospital stay; day (range)	18.4 ± 24.16 (7-125)	16.17 ± 12.62 (9-60)	0.726
Tumor size; cm	3.3 ± 5.02	3.9 ± 1.57	0.639
Positive margin (%)	2/26 (7.7)	4/17 (23.5)	0.539
Node positive (%)	7/26 (26.9)	11/17 (64.7)	0.026
Pancreatic fistula (%)	3/26 (11.5)	2/17 (11.8)	1.000
30 days mortality (%)	2/26 (11.5)	2/17 (11.8)	1.000
Re-operation	1/26 (3.8)	1/17 (5.9)	1.000

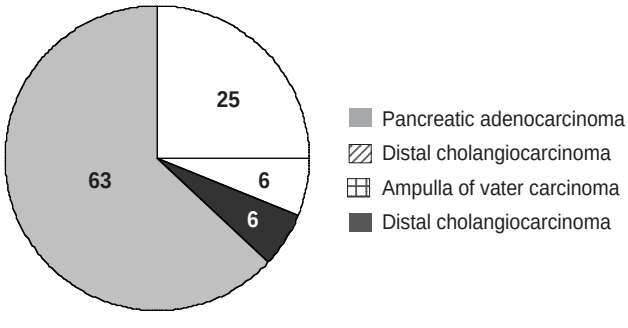

Figure 1 Proportion of primary tumors in VR group.

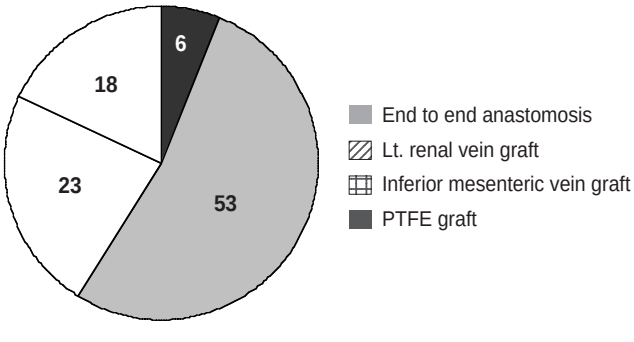

Figure 2 Proportion of vascular reconstruction technique in VR group

Table 3 Operative characteristics and perioperative complications in 17 patients in venous reconstruction group

Variables	
Primary disease	
Pancreatic adenocarcinoma	10 (58.8)
Cholangiocarcinoma	4 (23.5)
Ampulla of vater carcinoma	1 (5.9)
Pancreatic neuroendocrine tumor	2 (11.8)
Mean mesoportal clamping time; min (range)	31.8 ± 6.2 (23-42)
Mean vascular gap; cm(range)	3 ± 1.2 (1.8-5)
Mean post-operative ALT	182.7 ± 395
30 days mortality (%)	2 (11.7)
Pathological SMV invasion	7 (41.7)
Major perioperative complication*	
Reoperation	1 (5.9)
Bleeding	1 (5.9)
Pancreatic fistula (%)	2 (11.7)
Intra-abdominal fluid collection (%)	1 (5.9)
Pulmonary complications	1 (5.9)
Sepsis syndrome (%)	2 (11.7)
Acute renal failure (%)	3 (17.6)

patient in this group had pancreatic fistula and multiple intra-abdominal fluid collections that required a 60-day hospital stay. Another patient sustained acute renal failure from the sacrificed left renal vein for venous graft. However, after multiple hemodialysis sessions, his renal function recovered to his normal level. Reoperation was performed in one patient due to bleeding from inferior pancreaticoduodenal artery. Subsequently the patient developed sepsis and died.

In the non VR group the majority of primary tumors were ampulla of Vater adenocarcinoma. The mean operative time was 390 minutes and mean blood loss was 373 mL. Two patients (11.5%) in this group died from septic shock and hospital-acquired pneumonia. A pancreatic fistula was observed in 3 patients (11.5 %) that were treated conservatively. All operative data is shown in Figures 1, 2 and Tables 1, 2, 3.

Figure 3 End to End anastomosis

Figure 4 Left renal vein graft

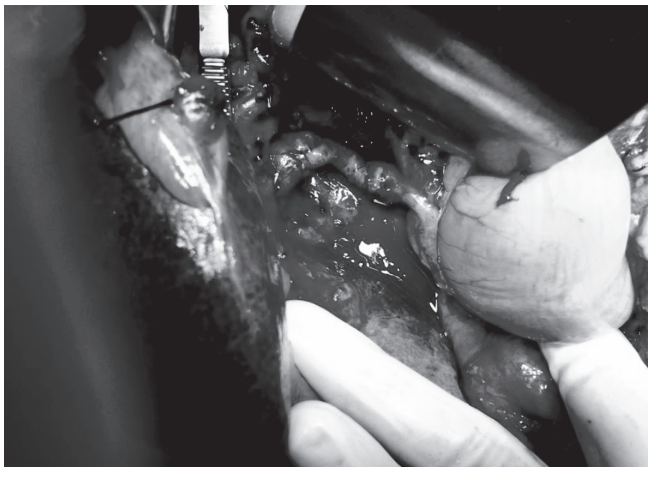

Figure 5 IMV graft

Table 4 Comparative survival data between non venous reconstruction (non VR) and venous reconstruction (VR) group

	non VR	VR
Median survival (month)	-	9
1 year survival (%)	83.3	27.3
Disease free survival (month)	12	6.5 _ 3.6
Metastatic site		
Liver (%)		4 (36)
Peritoneum (%)		2 (18)
Lung (%)		1 (9)
Node (%)		1 (9)

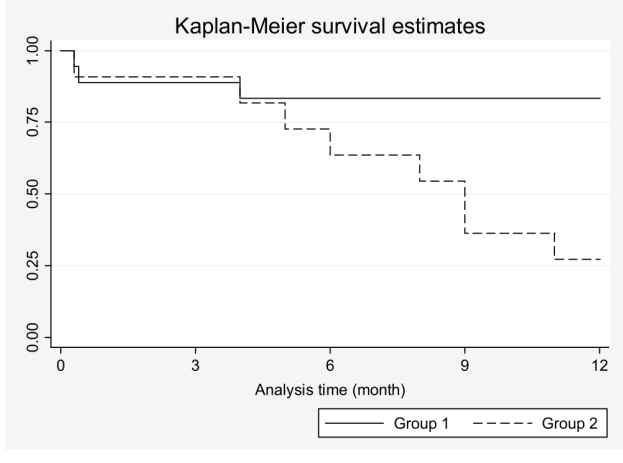

Figure 6 One-year survival graph of non VR and VR group. Group 1: non VR group, Group 2: VR group

Survival analysis

Survival data and survival curves are shown in Table 4 and Figure 6. There were significant differences in survival between both groups. In the VR group, the estimated one-year survival was 27.3% and median survival was 9 months. Median disease-free time is 6.5 months. None of the patients in the non VR group died in one year except for three patients who died in the early post-operative period. All of those who survived are still free of disease. The estimated one-year survival in the non VR group was 83.3%.

Discussion

SMV resection was first reported by Moore in 1951[9]. In 1956, Kikuchi described the use of a homologous vein graft and polyethylene splint for reconstruction of the portal vein. In 1963, Asada et al.[10] reported two cases of reconstruction with homologous vein grafts. In 1965, Siegel et al.[11] described autologous vein graft reconstruction. In 1966, Longmire[12] used a prosthetic graft for reconstruction. In 1973, Fortner proposed a regional pancreatectomy for removal of

peripancreatic soft tissue in conjunction with major vascular resection, but the frequency of complications was high, and there was no improvement in survival[13].

VR was initially performed with the objective to maximize soft tissue and lymphatic excision. However, from subsequent work done by Yeo et al.[14], it became evident that widening the surgical margins to include more lymphatic tissues had little impact on survival. One large series demonstrated that with proper patient selection and surgeon experience, VR can be performed safely with complication rates similar to standard pancreatic resections[15]. The low complication rate reported with vascular reconstruction and the improving operative morbidity and mortality after PD makes it reasonable to consider vascular resection to achieve an R0 resection[16].

Siriwardana et al. have reviewed the outcome of PV reconstruction during pancreatic resection for cancer[17]. Fifty two non-duplicated papers were reviewed. Pathological evidence of PV invasion was detected in 668 (63.4%) of 1,054 portal vein resection specimens. The rates of invasion ranged from 3% to 86% in 30 studies. PV margins were positive in 346 (39.8%) of 870 patients with PV resection in 23 studies, with a range of 0-85%. Postoperative morbidity ranged from 9% to 78%. There were 73 (5.9%) reported deaths among 1,235 patients in 39 studies that reported mortality after PV resection. The reported mortality rates in these studies ranged from 0 to 26%. However, the mortality rate has decreased to <5% in recent years. In this present study, mortality was found in 2 patients (11%) from the VR group which was more than many recent studies such as Nakao et al. (3.6% in VR group). These 2 patients died from gram negative sepsis on day 8 and 14 after surgery and we could not conclude that his death was correlated with the operation. Morbidity in the VR group was found in 2 patients (11%) that included pancreatic fistula, intra-abdominal fluid collection and acute renal failure. The interesting point from one patient in this group is that he developed acute renal failure after his left renal vein was sacrificed to be a substitution for SMV. Previous work demonstrated that good collateral flow and functional capacity of the left kidney was preserved despite ligation of the left renal vein. McCullough and colleagues[18] reported that after a right nephrectomy and ligation of the left renal vein for malignancy, only one of three patients experienced transient renal insufficiency. We suppose that because this patient had massive blood loss during the operation and this might be the cause that aggravated acute tubular necrosis. Finally, his normal renal function resumed after receiving hemodialysis for a couple of weeks. The left renal vein provides a graft with good length, optimal caliber, and is easily accessible. The left renal vein typically provides a graft of 3-4 cm in length when harvested from the junction of the left gonadal and left adrenal vein proximally and the inferior vena cava distally, although some reports have indicated lengths up to 6 cm[19]. The caliber of the graft allows for excellent flow. The ease of harvesting the graft is also an important consi-deration. Exposure of the left renal vein can be accomplished through a standard PD incision, without requiring any further prepping, an additional incision, or the need for an additional operating team. Furthermore, use of the left renal vein leaves the patient with all possible routes of central venous access. Inferior mesenteric vein (IMV) is another option for a venous graft for the distal SMV segment because the diameter of the IMV is usually smaller than the PV/SMV segment. The IMV can be harvested from a standard incision at the junction between the splenic vein and IMV. The length of an IMV graft can be 5-6 cm. However, the disadvantage of an IMV graft is interrupted collateral visceral venous drainage during the vascular reconstruction phase that may cause bowel congestion.

The major reconstruction technique in the VR group was primary end-to-end anastomosis. By complete mobilization of liver and colon, the gap between the anastomosis could be reduced approximately 2 to 3 cm. The Ligamentum Teres and Falciform ligament should be fixed in a proper position after all anastomoses are completed to reduce tension between vascular anastomoses. The intra-operative ultrasound was utilized to demonstrate patency of the anastomosis. We did not find any vascular complication in all patients. More invasive operations (concomitant arterial reconstruction and combine colectomy) have not shown a higher mortality. In case in which the RHA originated from the SMA and passed through the specimen, the RHA was divided and reconstructed by anastomosis to the gastroduodenal artery (GDA) or common hepatic artery proper (CHA). Indications for colectomy in PD are for achieved R0 resection and ischemia of colon. We preferred to perform colonic

anastomosis immediately after the colon was resected to minimize contamination in the operative field.

Histological evidence of true PV/SMV invasion was detected in 41.7% which was lower than many recent studies. However, the resection margin in the VR group was positive in 4 patients (23.5 %) which was better than nearly 40% (0-85 %) from the Siriwardana study[17]. Estimated blood loss and operative time in the VR group was statistically different from the non VR group but not far from Siriwardana study (median 1,750 ml). However, length of hospital stay in both groups showed no difference. These results showed that a PD with VR is safe and the mortality is not higher than in a non VR group. Our mortality rate in VR group was 11% which was comparable to the mortality rate in the current era from the Siriwardana study[17]. Two patients in non VR group who died in the early post-operative period were elderly (aged 70 and 80) which might be the risk factor for morbidity. Another patient in the non VR group had bleeding from GDA stump that was detected on post-operative day zero. We brought her back to the operative room to stop bleeding. However, massive blood loss resulted in acute renal failure and pancreatic anastomosis failure later. She had re-bleeding three times despite multiple attempts to embolize the vessel. Eventually, the patient died 120 days after surgery from hospital-acquired pneumonia. We realized that this is not a good result for PD in modern era which we should expect zero mortality in any kind of procedure.

Survival analysis shows that survival in the VR group was definitely worse than the non VR group. There was a 27.3% survival beyond one year. All patients in the non VR group except three patients who died in the early period achieved one year survival. However, 55% in the non VR group had ampulla carcinoma and we know that this type of tumor has a better prognosis than other periampullary carcinoma, particularly pancreatic cancer. We cannot conclude that the factors that impact survival is the type of operation because of the heterogeneity of the population in this study. However, we observed that aggressive tumors that need vascular reconstruction tend to have grave survival. The major limitation of this study is the retrospective nature that could result in variations in pre-operative selection criteria and mixed patient populations. The number of patients in this study is small. However, our study showed a one year result from a single center and operations by a single primary surgeon indicating a strong point in this study.

In summary, PD with VR is safe to perform. Morbidity and mortality is not different from standard PD in selected patients. However, survival in the VR group is small and significantly different from the non VR group that may be influenced by the type of primary tumor. Future studies may be needed to increase the number of patients and compare survival in a palliative group. Until then, we suggest that this type of procedure be performed by a hepatobiliary-pancreatic surgeon in high-volume centers.

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