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Research Article

Vascular Reconstruction (SM/PV) in Periampullary Tumors is there a Difference?

Yassein T[1], Eyoup E[1], Taha M[1], Mostafa A[1], Elshiekh E[2]*, Ibrahim T[1] and Schmidt J[3]

[1]Department of HBP Surgery, National Liver Institute, Monoufia University, Egypt

[2]Tanta Cancer Center, Egypt

[3]Surgical Clinic Heidelberg University, German

***Corresponding author:** Essam Elshiekh, Department of Surgical Oncology, Tanta Cancer Center, Egypt

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Abstract

Background: Surgical resection remains the treatment of choice and only hope for long-term survival for patients with pancreatic cancer. Numerous studies have supported the safety and feasibility of combining PD with vascular resection in an attempt to obtain negative margins.

Aim: To evaluate the impact of vascular reconstruction on the early postoperative outcome after resection of periampullary tumors.

Methods: From January 2010 to January 2016,114 patients underwent PD for periampullary tumors in National Liver Institute, Monoufia University. Patients who underwent PD with vascular resection (N=18) were compared to patients who underwent standard PD (N=96). Vascular reconstructions were performed due to: vascular invasion in 14 patients and vascular injury in another 4 patients. Vascular reconstructions were performed with resection of the involved vascular segment with: primary repair (N=12), vein patch (N=4), & interposition grafting in 2 patients.

Results: A total of 114 patients were included in this study. Vascular reconstructions were performed due to vascular invasion in 14 patients and vascular injury in another 4 patients. The mean operative time and blood loss were significant for group I. vascular invasion was significant for group I. There was no statistically significance difference between the group regarding surgical margin invasion. In group, I, complications occurred in 7 cases (38.8%) and for the group II without vascular resection, complications occurred in 37 cases (38.5%) with no statistically significance difference between the groups. There is no statistically significant difference between the postoperative 6 month's survival in patients with vascular reconstruction and those without vascular reconstruction (P value = 0.098).

Conclusion: Perioperative mortality, readmission rates, length of stay, and overall complication rates does not significantly differ between standard PD and PD with VR.

Keywords: Pancreaticodudenectomy; Vascular resection; Vascular reconstruction

Abbreviations

PV: Portal Vein; SMV: Superior Mesenteric Vein; SMA: Superior Mesenteric Artery; HA: Hepatic Artery; PD: Pancreaticodudenectomy; VR: Vascular Reconstruction

Introduction

Despite significant advances in the diagnosis and treatment of pancreatic adenocarcinoma, the prognosis for this disease remains relatively poor, representing the fourth most common overall cause of death due to cancer in the United States [1,2]. Surgical resection is the best line of treatment and offers the best survival outcome to patients with periampullary carcinoma amongst different treatment options [3]. However, the surgery remains a challenging operation, with hospital mortality rates ranging from 1% to 6% even at experienced centers [4,5]. Surgical resection remains the treatment of choice and only hope for long-term survival for patients with pancreatic cancer. Numerous studies have supported the safety and feasibility of combining PD with vascular resection in an attempt to obtain negative margins. Mortality rate of PV resection 30 years ago was >20% now decreased to 5%, requires suitable vein proximal and distal to tumor involvement for resection and reconstruction. Complete clearance of macroscopic tumor with negative microscopic resection margins is the main surgical objective, as patients with residual disease demonstrate survival rates similar to those treated palliatively [6].

Our aim in this study is to evaluate the impact of vascular reconstruction on the early postoperative outcome after resection of periampullary tumors.

Patients and Methods

From January 2010 to January 2016, 129 patients, with periampullary tumors were operated upon for PD, were retrospectively evaluated in Hepato-Pancreatico-Biliary Surgery and Liver Transplantation department, National Liver Institute,

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Monoufia University. All were operated and managed by a team of surgeons specialized in hepatopancreatic-biliary (HPB) surgery. Data on preoperative, intraoperative and postoperative care were collected and maintained on a secure database. Preoperative parameters included demographics, clinical presentation, preoperative risk factors, laboratory testing, and preoperative imaging modalities such as ultrasound, multi-detector abdominal CT with three-dimensional reconstructions and magnetic resonance cholangiopancreaticography is used to evaluate the periampullary tumors and its relation to vascular structures. CT accurately diagnoses mesenteric vein involvement, aiding in operative planning, endoscopic retrograde cholangiopancreaticography (ERCP) with or without endoscopic stent drainage and endoscopic ultrasound Intraoperative details such as operative time, total blood loss, transfusion needs and the type of surgical reconstruction were recorded. Postoperative events, complications, mortality, pathological data were also collected. According to CT criteria 33 patients were borderline for vascular invasion, From the 129 patients, 15 (19.3%) patients were inoperable due to either liver metastasis or locally advanced tumor due to portal and SMV and splenic vein involvement or celiac artery involvement and these patients offered bypass operation and excluded from our study. From the patients 114, Vascular reconstructions were performed with resection of the involved vascular segment with: primary repair (N=12), vein patch (N=4), & interposition grafting in 2 patients. So we divided our patients into 2 groups, Patients who underwent PD with vascular resection (N=18) Group I, were compared to patients who underwent standard PD (N=96) Group II.

According to the AHPBA/SSAT/SSO/NCCN definition, borderline resectable PDAC includes tumors (Figure 3) that display; (1) venous involvement of the SMV/PV demonstrating tumor abutment, encasement, or short segment venous occlusion, but with suitable vessel proximal and distal to the area of vessel involvement, allowing for safe resection and reconstruction; (2) gastroduodenal artery encasement up to the hepatic artery and short segment encasement/ direct tumor abutment of the hepatic artery with no extension to the celiac axis; or (3) tumor-SMA involvement < 180° [7]. Postoperative pancreatic fistula was defined as drainage of >50mL per 24 h of fluid, with amylase content >3 times serum amylase activity for >10 d after operation [8]. Perioperative mortality was defined as death in the hospital or within 30d [9]. Delayed gastric emptying (DGE) was defined to be present when nasogastric intubation was maintained for P10 d, combined with at least one of the following: vomiting after removal of the nasogastric tube, reinsertion of nasogastric tube, or failure to restore oral feeding [10].

Surgical technique

Midline or bilateral sub costal incision was used. Conventional or pylorus-preserving Pancreaticoduodenectomy was performed according to the decision of the responsible surgeon. Wedge or segmental resection (Figure 2) 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

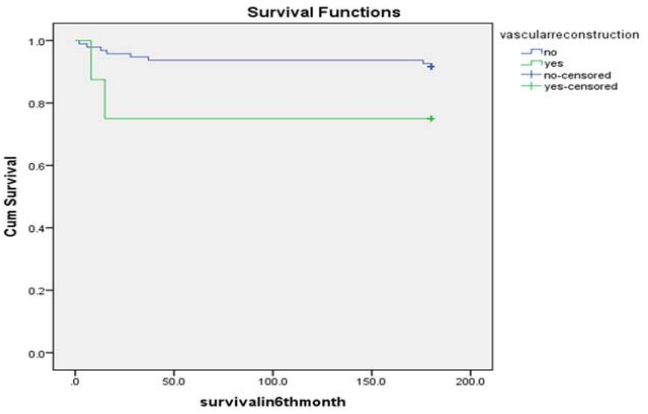

Figure 1: Survival analysis (Kaplan-Meier curve).
There is no statistically significant difference between the postoperative 6 month's survival in patients with vascular reconstruction and those without vascular reconstruction (P value = 0.098).

SMV shorter than 3cm, end-to-end anastomosis without the use of a graft was possible in 12 patients in group 1 after adequate mobilization of the SMV and the PV, while the saphenous vein graft was used in two patients only as the resection segment of Portal vein was more than 3cm. The anastomosis was continuously taken with 6/0 Prolene suture in the posterior layer and interrupted in the anterior layer to avoid narrowing of the vein. 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 [11].

Statistical analysis was done by SPSS statistical software package v21 (SPSS Inc., Chicago, Illinois, USA). The test, $\chi 2$-test, Fischer's exact test, and Monte Carlo exact test were used. Values were considered statistically significant when the P value was less than 0.05.

Results

Preoperative data

A total of 114 patients were included in this study; of these, 18(20.5%) received PD combined with vascular resection and reconstruction (group I) and 96 (79.5%) received traditional PD. The age of the patients of group (I) were ranged from 39 to 72 years, with a mean age of 56 years. Detailed patient information is listed in Table 1. Nine (50%) patients had one or more chronic co-morbid illnesses in group I, mostly COPD in (27.8 %), diabetes mellitus (22.2%) and hypertension (16.7%). In Group II, 38 (36.5%) patients had one or more chronic co-morbid illnesses, diabetes mellitus (36.5%) and hypertension (32.3%) and COPD in (32.3%) (Table 1).

Surgical data

Regarding the vascular reconstruction methods, vascular reconstructions were performed due to; vascular invasion in 14 patients and vascular injury in another 4 patients. Vascular reconstructions (Figure 2 and 3) were performed with resection of the involved vascular segment with primary repair (N=12 (66.6%), vein patch (N=4 (22.2%), & interposition grafting in 2 (11.1%) patients (Table1). The dilated pancreatic duct ≥3mm was presented in 12(66.7%) in group I and 39(40.6%) in group II. Type of Pancreaticoduodenectomy was pyloric preserve 15(83.3%) in group I and 27(28.1%) group II (Table 2). The operative time ranged

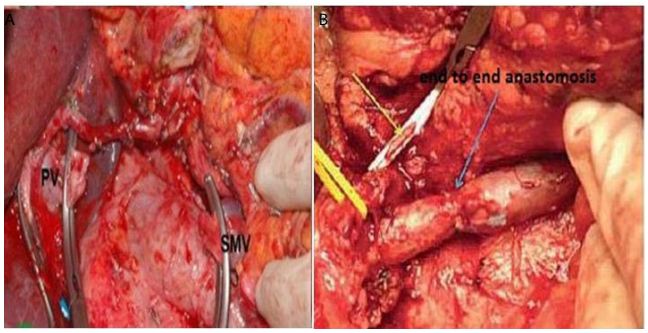

Figure 2A and 2B: Portal vein Resection with end-to-end anastomoses.

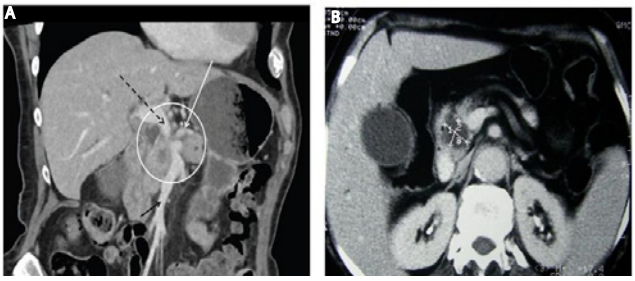

Figure 3: A) CT scans: Tumour infiltration of the PV confluence (white circle). SMV (black arrow), PV (broken black arrow), and SPV (white arrow) without thrombosis. B) Tumor not invading the superior mesenteric vessels.

from 4 to 8 hours with mean ± SD: 6.1±1.6 in group I and 4-10hours with mean 6.95±1.4 in group II which was statistically significant for group I, while blood loss was ranged 350-1300 ml with Mean ± SD 581.25±308.1 in group I while in group II was ranged 200-3000 with mean 948.8±526.6which was statistically significant for group I. The Intraoperative data is listed in Table 2.

Postoperative data

Pancreatic tumor 62(63.5%) was the most common tumor resected in group II. Vascular invasion was presented in 7 (38.8%) out 18 in group I and in 6(6.3%) out 96 in group II which was statistically significant for group I. The surgical margin was free in 15(83.4%) out 18 in group I and 84(87.5%) out 96 in group II with no statistically significance between both groups. The detailed pathology data are shown in Table 3.

For the combined vascular resection group I, complications occurred in 7 cases (38.8%). For the group II without vascular resection, complications occurred in 37 cases (38.5%). In Univariate analysis, there was no statistically significance difference between both groups in concern to pancreatic & biliary leakage, bleeding, wound infection and reoperation as P value not less 0.05 Table 5.

There is no statistically significant difference between the postoperative 6 month's survival in patients with vascular reconstruction and those without vascular reconstruction (P value = 0.098) Figure 1.

Discussion

Recently, many experienced centers advocated that the surgical approach of pancreatoduodenectomy (PD) combined with PV and

Table 1: Demographics data and Co-morbidities.

	PD+VR (G: I)	Standard PD(G:II)
	n=18	n=96
Gender, n (%)		
• Male	11(61.1%)	58(60.4%)
• Female	7(38.9%)	38(39.6%)
Age		
• Range	39-72	23-82
• Mean	56	52
Hospital stay		
• Range	2 -23 day	2-26 day
• Mean	15.3 ± 11.55	17.3 ± 13.75
Vascular Reconstruction		No
• Primary repair	12(66.6%)	no
• Vein patch	4(22.2%)	no
• Interposition graft	2(11.1%)	
Coronary Artery disease	2(11.1%)	4(4.2%)
Diabetes	4(22.2%)	35(36.5%)
COPD	5(27.8%)	31(32.3%)
Chronic Renal insufficiency	0	1(1 %)
Hypertension	3(16.7%)	31(32.3%)
Chronic liver disease	4(22.2%)	10(10.4%)

SMV resection and reconstruction has been widely applied in clinical practice to remove the tumor completely. Additionally, PD combined with vascular resection can consider for 20% to 25% of the total cases of PD surgery in a number of the large centers for pancreatic cancer treatment. Consequently, vascular invasion is no more a surgical contraindication, and the surgical resection rate has significantly increased [12-14].

There is now coming into view consensus that a subgroup of patients, previously deemed poor candidates for resection because of the relationship of their primary tumor to surrounding vasculature, may benefit from resection, in particular when preceded by neoadjuvant therapy. This stage of disease, described as borderline resectable pancreatic cancer, has become of increasing interest and is now the focus of a multi-centers clinical trial [15]. In our study there was 33 patients diagnosed as borderline resectable pancreatic cancer by CT, 15 (19.3%) patients were inoperable on exploration due to either liver metastasis or locally advanced tumor due to portal and SMV and splenic vein involvement or celiac artery involvement and these patients offered bypass operation and excluded from our study.

The definition of borderline resectability for pancreatic cancer remains controversial. Varadhachary et al. [16] Borderline tumor resectability dividing into: A, B and C. 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

Table 2: Intraoperative data.

		PD+VR (G I)	Standard PD (GII)	Chi-square	
		n=18	n=96	X^2	P value
Operative time	Range	4-8 hours	4-10 hours	2.311[t]	0.023*
	Mean ± SD	6.1±1.6	6.95±1.4		
Blood loss	Range	350-1300	200-3000	2.864[t]	0.005*
	Mean ± SD	581.25±308.1	948.8±526.6		
Blood transfusion	Yes	4(22.2%)	67(69.8%)	12.646	<0.001*
	No	14(77.8%)	29(30.2%)		
Dilated PD	>3mm	12(66.7%)	39(40.6%)	3.171	0.074
	3mm	6(33.3%)	57(59.4%)		
Pancreatic duct stent	Yes	3(16.7%)	32(33.3%)	1.273	0.259
	No	15(83.3%)	64(66.7%)		
Texture of Pancreas	Soft	8(44.5%)	61(63.5%)	1.584	1.584
	Firm	10(55.5%)	35(36.5%)		
Type of PD	Classic	3(16.7%)	69(71.9%)	17.554	<0.001*
	PPPD	15(83.3%)	27(28.1%)		
Type of Pancreatic-enteric anastomosis	PG	0	14(14.6%)	35.513	<0.001*
	PJ(Dunking)	0	16(16.7%)		
	PJ(End to side)	0	39(40.6%)		
	PJ(Duct to Mucosa)	18(100%)	25(26.2%)		
	Closure of PD	0	2(2.1%)		

Table 3: Pathological data.

		PD+VR	Standard PD	Chi-square	
		n=18	n=96	X^2	P value
Type of tumor	Malignant	18(100%)	85(88.5%)	1.158	0.282
	Benign	0	11(11.5%)		
Origin of the tumor	Pancreatic	8(44.4%)	62(63.5%)	14.553	0.002*
	Ampullary	4(22.3%)	25(26%)		
	Lower CBD	0	5(5.2%)		
	Duodenal	6(33.3%)	5(5.2%)		
LN involvement	Yes	10(55.6%)	38(39.6%)	0.999	0.318
	No	8(44.4%)	58(60.4%)		
Vascular invasion	Yes	7(38.8%)	6(6.3%)	12.916	<0.001*
	No	11(61.2%)	90(93.8%)		
Surgical margins	Invaded	3(16.6%)	12(12.5%)	0.01	0.92
	Free	15(83.4%)	84(87.5%)		

amenable to vascular resection and reconstruction because of a patent SMV and PV below and above the area of occlusion. B patients have tumors with extra pancreatic metastasis. 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% [17]. While not officially proposed in the literature until 2006, the concept of borderline resectability had its roots in early studies from the 1990s and early 2000s revealing that patients with pancreatic cancer involving venous structures such as the SMV/PV could be subjected to vascular resection with outcomes comparable to patients with localized disease undergoing typical resections, and superior to patients with locally advanced disease being managed non-operatively [18,19]. Although it might be effective for some patients, subjecting every patient with SMV or PV involvement to neoadjuvant therapy without considering

Table 4: Postoperative morbidity in both groups.

	No of patients 114 (%)
Pancreatic leakage	10(9.6%)
Bile leakage	7 (6.1%)
Delayed gastric emptying	10(9.6%)
Bleeding	9(7.9%)
Wound infection	27(23.7%)
Wound dehiscence	7(6.1%)
Reoperation	7(6.1%)

Table 5: Univariate analysis of vascular reconstruction and the incidence of postoperative complications.

	PD+VR (GI)	Standard PD (GII)	Chi-square	
	n=18	n=96	X^2	P value
Pancreatic leakage	1(5.5%)	9(9.3%)	0.943	0.636
Bile leakage	2(11.1%)	5(5.2%)	0.178	0.673
Delayed gastric emptying	0	10(10.4%)	0.96	0.327
Bleeding	0	9(9.3%)	0.77	0.38
Wound infection	3(16.6%)	24(25%)	0.213	0.645
Wound dehiscence	0	7(7.3%)	0.419	0.517
Reoperation	1(5.5%)	6(6.2%)	0.178	0.673

upfront surgery would allow progression of cancer in 40% of patients who would not respond well. 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 [20]. This is agreed with the current study in that Pancreaticoduodenectomy with vascular resection can be performed safely at our centers. The complications and pancreatic fistula rates in PD with VR (G:1) were not different those in group II. As there is no statistically signifience difference between the G I &GII in concern to pancreatic & biliary leakage, bleeding, wound infection and reoperation as P value 0.636.

Cheung et al. showed in their study that the medians for volume of blood loss (1200mL vs 800mL; $P < 0.05$) were significantly greater in PD with vascular resection group compared to PD group [20]. Gong et al. in their study showed that blood loss of patients who underwent combined vascular reconstruction the intraoperative blood loss decreased year after year, suggesting that the technique of combined vascular reconstruction has gradually matured. The median intraoperative blood loss in 2011 was 600ml, and the intraoperative blood loss of PD without vascular reconstruction was 500 ml; there was no significant difference between the two values [21]. This agreed with the current study as there is statistically difference in blood loss between the two groups and was significant greater in GII (without vascular reconstruction) (mean: 581ml vs 948ml: with P value 0.005).

In concern to the operative time there is statistically difference in operative time between the two groups and was significant greater in GII (without vascular reconstruction) (mean: 366 vs 417 min: with P value <0.023.). Cheung et al. in their study showed that operation time (715min vs 580min; $P <0.05$) were significantly greater in group with vascular resection compared to group without vascular resection [20]. Giovinazzo et al., recently published paper showed in their meta-analysis of 27 studies, Data on duration of surgery were available in 17 of 27 studies (6365 patients). The mean operating time for patients undergoing pancreatic resection with vascular resection was 550min, compared with 439min for those not having vascular resection (mean difference 72 ($P <0.001$) [22].

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 [23,24]. Also in our center we have a living related liver transplantation program since 2003 giving a good sense and experience in vessel reconstruction so we can do the vascular reconstruction with good technique and this explain the decreasing in operative time and blood loss in G I with vascular reconstruction in the current study.

In our study there is no statistically significance difference between the group I & group II in postoperative complications in concern to pancreatic & biliary leakage, bleeding, wound infection and reoperation and for the postoperative 6 month's survival. The incidence of postoperative complications remains relatively high at approximately 30% to 50%, as indicated by previous reports [25,26]. According to Pindak et al. experience [27], which in accordance with recently published single center studies by Flis et al. and Marsoneret al. [28,29] the postoperative morbidity, mortality and long term survival is equal in patients with/without venous resections in the treatment of localized pancreatic cancer. Moreover, the long term survival for the selected patient with PV-SMV resections after R0 resection followed with subsequent adjuvant chemotherapy is almost the same. On the other hand, study done by Gong et al. showed that for the combined vascular resection group, complications occurred in 28 cases (23.5%). For the group without vascular resection, complications occurred in 37 cases (8.2%). There was significant difference between the two groups [21]. The first two mentioned meta-analyses published in 2012 and 2014 by Zhou et al., and Yu et al., confirmed comparable morbidity, mortality and long term survival [22,30].

In our study there is no statistically significant difference between the postoperative 6 month's survival in patients with vascular reconstruction and those without vascular reconstruction. Cheung et al., [20] shown the short-term and survival outcomes with simultaneous vascular resection were not compromised when compared with that of standard Pancreaticoduodenectomy. Gong et al. in their study showed the median survival time of patients who underwent PD combined with vascular resection and reconstruction to achieve complete tumor resection was still lower than that of pancreatic cancer patients who did not experience vascular invasion. However, the most important finding is that its median survival time is higher than the median survival time of patients who received palliative treatment which has practical clinical significance [21].

Conclusion and Recommendations

Early detection and prevention of periampullary tumors are major rules in health programs to improve the life style of the population. Perioperative mortality, readmission rates, length of stay, and overall complication rates does not significantly difference between standard PD and PD with VR. High volume centers and surgeons together with good perioperative care are the mainstays to improve the outcome after standard PD and PD with VR.

Conclusion

Perioperative mortality, readmission rates, length of stay, and overall complication rates does not significantly differ between standard PD and PD with VR, with no statistically significant difference between the postoperative 6 month's survival in patients with vascular reconstruction and those without vascular reconstruction.

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