Is pancreaticoduodenectomy with vascular resection a safe procedure in developing country? Early outcomes and review of national literature

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**HIGHLIGHTS**
- Impact of extended lymphadenectomy (EL) in pancreatic cancer remains unknown.
- Role of vascular resections is also ill defined.
- Should extended procedures be performed in developing countries?
- Current study shows low complication rate associated with EL or vascular resections.

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**Abstract**

Introduction: Safety of extended lymphadenectomy (EL) ± vascular resection in patients undergoing pancreatectoduodenectomy (PD) in resource limited settings is not well established. The objective of this study was to report outcomes of PD resection with EL ± vascular resection from Pakistan and review national literature.

Methods: Data of patients who underwent PD between 2011 and 2014 was reviewed. A total of 66 patients were included in the study. Primary outcome was 90 day morbidity and mortality. Secondary objective was 2 year overall survival.

Results: Median age was 57 (32–82) years. Majority patients had locally advanced (pT3/T4) tumors and nodal involvement i.e. 44 (71%) and 42 (67.8%). Mean number of excised lymph nodes and positive lymph nodes was 28.2 ± 12.8 (range 3–62) and 4.8 ± 6.9 (range 0–27) respectively. There were 13 vascular resections including 3 arterial resections. Overall 90 day morbidity was 31.8% and mortality was 3%. No difference in complication rate was observed in patients who did and did not undergo vascular resection i.e. 18% versus 34.5% (P = 0.1). Similarly, median survival was 11 (3–24) months and 11 (1–36) months and not significantly different (P = 0.5).

Conclusion: In developing countries, extended lymphadenectomy with vascular resection can be safely performed with pancreatectoduodenectomy in specialized hepatobiliary units.

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1. Introduction

Pancreatectoduodenectomy (PD) remains one of the most formidable abdominal surgical procedures. Refinement in surgical technique, better understanding of anatomy and improvement in preoperative imaging and ancillary care has yielded impressive peri-operative outcomes [1]. The hospital mortality has reduced and now ranges between 1 and 6% in experienced centers [2,3]. Emergence of high volume centers has played a significant role in improving outcomes [4]. The idea of centralization is yet to be embraced in developing countries. In particular for pancreatic
malignancy; which is not very common in the sub-continent, regionalization and achievement of high volumes is yet to be realized [5]. A recent study demonstrated acceptable outcomes in a select group of patients who underwent PD in a low volume center in Pakistan. In this study, extent of surgery was limited to standard lymphadenectomy while vascular resections were not performed [6].

High volume HPB centers all over the world have pushed boundaries and have become more aggressive in surgical resection of periampullary/pancreatic tumors. Whether extended PD ± vascular resection offers any survival benefit over standard resection remains controversial due to problems with study designs and characteristics of patient cohorts. It also remains unclear if extended PD has an impact on short term morbidity and mortality [7–10]. The argument is further intricated due to lack of standard definition of EL. More recently, an attempt has been made by international study group on pancreatic surgery (ISGPS) to standardize definition of EL [11].

It is logical to ask if centers in developing countries should embark upon extended PD with vascular resection and expect outcomes comparable to high volumes centers in the developed world. Here, we report outcomes of PD with EL ± vascular resection from a high volume albeit new HPB center in Pakistan. We have also attempted to review literature on PD outcomes in Pakistani population.

2. Methods

We retrospectively reviewed patients who underwent pancreaticoduodenectomy (PD) in department of hepato-pancreato-biliary (HPB) surgery and liver transplantation at Shifa international hospital between February 2011 and August 2014. A total of 66 patients who underwent PD with EL were included in the study.

Patients were initially seen at the gastroenterology clinic or HPB surgery out-patient department (OPD). Baseline investigations, liver function tests, clotting profile, ultrasound exam and dynamic CT scan with pancreatic protocol was performed on all patients with obstructive jaundice or suspected peri-ampullary malignancy. Patients with symptoms of cholangitis were offered pre-operative biliary drainage via endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC). Patients with resectable and borderline resectable tumors were offered upfront surgery. These included patients with patent superior mesenteric-portal vein junction even if there was suspicion of vascular invasion. Also, patients with involvement of short segment of superior mesenteric or common hepatic artery were candidates for surgical intervention. Neoadjuvant chemotherapy was reserved for patients with locally advanced irresectable tumors. All patients were discussed in multi-disciplinary team before treatment plan was formulated. Preoperative histological diagnosis was not mandatory if imaging was clearly suggestive of a malignancy.

All surgeries were performed by or supervised by single surgeon (FSD). A transverse upper abdominal incision was used in most cases. Peritoneal and visceral metastases were ruled out on diagnostic laparotomy. Resection was performed in standard fashion. Lymphadenectomy involved removal of lymph nodes in the following areas;

1) Around right and left hepatic artery
2) Proper and common hepatic artery
3) Right side of superior mesenteric artery
4) Aorto caval window extending from inferior mesenteric artery (IMA) to root of superior mesenteric artery (SMA) and bilateral renal hilum

For segmental resection of PV or SMV <2 cm, end to end anastomosis was performed while for >2 cm resections, PTFE graft was used as conduit for anastomosis. After arterial resection, a microvascular anastomosis was performed with 8/0 prolene sutures. We routinely used Roux-en-Y bowel loop for reconstruction. A duct to mucosa end to side pancreatico jejunoanostomy was performed with PDS sutures. A single layer interrupted hepatojejunostomy (HJ) was fashioned with 4/0 PDS sutures. A two layer hand sewn end to side retrocolic gastrojejunostomy was performed with PDS 3/0 sutures. Two drains were placed; one adjacent to PJ and second close to HJ.

Patients were shifted to surgical ICU or Step Down as required. If post operative recovery was uneventful, they were shifted to floor on day 1. Aggressive chest physiotherapy, incentive spirometry and calf compression exercises were a routine. Naso-jejunal feeding was started 12 h after surgery. Patients were usually taking soft diet on day 3. Drain serum amylase was performed on day 4 as a matter of routine. Octreotide was administered in cases of soft parenchyma and small ducts. Patients were seen at 3, 6 and 12 months post op and then yearly with baseline investigations.

Demographics, clinicopathological variables and post-operative course were assessed. Patients were followed until January 2015 to ensure at least 90 day follow up. The primary objective of the study was to evaluate 30 and 90 day morbidity and mortality. All grade II and above complications on Clavien Dindo grading system were noted if imaging was 3 times normal on day 4 and/or CT findings of peripancreatic collection. Gastraparesis was defined as failure to remove nasogastric tube after 7 post-operative days or failure to wean off parenteral nutrition. We also determined estimated 2 year over-all survival in our patient cohort. Overall survival was calculated by subtracting date of death/last follow-up from date of surgery. For calculation of estimated survival, Kaplan—Meier curves were generated and Log rank test was used to determine significance. Fisher’s exact test and chi square test were used for categorical variables while T test was applied for interval variables. All analysis was performed on SPPS version 20.

3. Results

3.1. Patient characteristics

Median age was 57 (32–82) years. Male to female ratio was 1.8:1. Preoperative biliary drainage was performed in 33 (50%) patients. Out of which 36 had ERCP while 2 underwent PTC. Ampullary and pancreatic adenocarcinoma were the most common underlying etiologies in 27 (40.9%) and 26 (39.5%) patients. Table 1 represents patient characteristics.

3.2. Operative variables

Standard Whipple’s procedure was performed in 49 (74.3%) patients. Right hemicolectomy was performed in 3 patients secondary to tumor invasion. One patient required total pancreatectomy and splenectomy due to friable pancreatic parenchyma. Vascular resection was performed in 11 patients. There were 10 venous and 3 arterial resections. Primary resection and anastomosis was performed in 6 patients, PTFE graft was used in 2 patients and lateral venoplasty was performed in 2 patients. Replaced right hepatic artery was resected and reconstructed with gastro-duodenal artery stump in 2 patients. In 1 patient with involvement of CHA, arterial resection was performed and PTFE graft was used as a conduit from infra renal aorta to common hepatic artery. One patient had pT2, 6 had pT3 and 3 patients had pT4 tumors. Drain
lymph nodes removed was 28.2 ± 12.8 (range 3–62). Mean number of positive nodes was 4.8 ± 6.9 (range 0–27) as shown in Table 3.

### 3.3. Histological variables

Majority of patients i.e. 44 (71%) and 42 (67.8%) tumors and nodal involvement were pT3/T4 and N0, respectively. Estimated overall survival was 11 (1–36) months. There was no difference in median survival between patients who did 11 (3–24) months and did not 11 (1–36) months undergo vascular resection. Estimated 2 year overall survival was 43%. Estimated 2 year overall survival for early and advanced tumors was 80% and 20% and was significantly different (P = 0.01) as shown in Fig. 1.

### 3.4. Primary outcomes

Table 4 demonstrates 90 day morbidity in our patients. Overall 90 day morbidity was 31.8%. Most common complications were gastroparesis and chyle leak in 7 (10.6%) and 5 (7.5%) patients respectively. PJ leak was confirmed in 2 (3%) patients. Re-exploration was performed in 1 patient with PJ leak and abdominal washout with drain placement was performed. Ureteric injury was identified intra-operatively and managed with a nephrostomy tube with delayed repair. One patient with burst abdomen required secondary closure. All other complications were managed conservatively. There was no significant difference in complication rate between patients who did and did not undergo vascular resection. In fact, lower morbidity was observed in patients who had vascular resection i.e. 2/11 (18%) versus 19/55 (34.5) (P = 0.1). Out of 11 patients who underwent vascular resection, 6 patients were alive at last follow up. Overall 90 day mortality was 3%. Two patients developed myocardial infarction and succumbed to their cardio-vascular event.

### 3.5. Secondary outcomes

A total of 15 (22.7%) patients relapsed during the follow up period as shown in Table 5. Liver was the site of first relapse in 11 (16.6%) patients. A total of 21 deaths were observed. Underlying cause of death was disease relapse in 15, MI in 2 and chemotherapy induced liver failure in 2 patients. In 2 patients, a definite cause could not be identified. Median overall survival was 11 (1–36) months. There was no difference in median survival between patients who did 11 (3–24) months and did not 11 (1–36) months undergo vascular resection. Estimated 2 year overall survival was 43%. Estimated 2 year overall survival for early and advanced tumors was 80% and 20% and was significantly different (P = 0.01) while median overall survival was 12 (6–36) and 9 (1–26) months respectively. Estimated overall survival for pancreatic and non-pancreatic tumors was 33% and 64% (P = 0.1) as shown in Fig. 1.

### 4. Discussion

The present study reports operative outcomes in 66 patients who underwent PD with EL. This is the second largest study on PD...
outcomes from Pakistan but signifies the first report on PD outcomes with EL and vascular resection [13]. Our center has sustained a decent number of (>15) resections per year for three consecutive years and results achieved are comparable to high volume centers in the developed world [1–3]. The limitations of this study are inherent in nature and stem from its retrospective design. We could have missed significant post-operative events. A prospective database however has now been developed to avoid this problem. Outcome is relatively short considering that a number of patients had non-pancreatic tumors and are known to have better survival. It is possible that significance between some variables could not be reached due to relatively smaller sample size.

The complication rate reported in literature depends greatly on post-operative time period (30 days versus 90 days) and grade of complications and can vary between 15 and 60% [14,15].

It is also believed that for high volume centers not performing vascular resections, a mortality rate of 3–5% is acceptable [2]. A 90 day morbidity of 31.8% and mortality of 3% in the current study is very much comparable to international high volume HPB centers [1–3]. It has been shown previously that acceptable outcomes can be achieved after PD in a developing country with careful patient selection [6].

Being one of the few centers in country with HPB expertise, we did not have the option of choosing patients with favorable outcomes. In fact, the oldest patient to undergo PD at our center was 82 years old. There were 15 patients with borderline resectable tumors; visceral resection was performed in 4 patients and 13 vascular resections were performed of which 3 were arterial. The low morbidity and mortality in our patient cohort can be attributed to positive influence of a simultaneous living donor liver transplant (LDLT) program in our center [1]. Microvascular techniques are frequently practiced in LDLT and their replication in PD probably yielded better outcomes. In addition, our primary surgeon underwent six years of extensive training in HPB and liver transplantation in top centers in United Kingdom (UK). We believe that to achieve good results, extensive training in high volume HPB centers is the most critical aspect determinant of outcomes. Standard of ancillary care improved reflecting upon complex nature of care involved in an LDLT program and patients who underwent PD were also benefited.

Since LDLT requires outstanding technical skills and meticulous post-operative care to be successful; our medical and para medical staff underwent extensive training in international high volume HPB/transplant centers before the unit was established. It has been shown that complex vascular skills learned in LDLT can be safely and effectively transferred to HPB surgery [1,16].

So far we have performed more than 150 LDLT’s and we believe that a successful transplant program has greatly facilitated achievement of comparable outcomes for PD in our center.

Most frequent complications in our series were gastroparesis and chyle leak. Low numbers of PPPD and high rates of EL respectively are probably responsible. We are already performing more PPPD’s now and have started carefully ligating/clipping lymphatics to decrease chyle leak in our patients. A PJ leak around 10–28% has been reported after PD [15,17]. The PJ leak in current study was significantly low and a clinical leak was detected only in 2 (3%) patients. Although, 8 patients had raised drain amylase levels, it was not more than 3 times normal in 6 patients. They were not found to have intra-abdominal collections and did not require additional treatment or prolongation of hospital stay. A duct to mucosa technique, adequate blood supply at pancreatic resection margin and sharp dissection with knife or scissors might have contributed to this.

Whether EL improves survival in periampullary/pancreatic tumors is debatable. However, it definitely improves staging [11]. Many factors have been shown to impact survival after PD and include tumor size, grade and nodal involvement [18,19]. Mean number of LN removed in the current study was 28.2 ± 12. This is a significantly high nodal yield when compared with reports on standard PD where on average <20 LN were removed [6,20]. Out of 66 patients in our series, 15 (24%) had aortocaval lymph node involvement; nodes that are generally not removed in standard PD. Majority patients in our patient cohort had advanced tumors. We did not experience any increase in complication rate for patients who underwent vascular resections and we believe in experienced hands vascular resections can be embarked upon safely and provide a chance of cure to patients otherwise deemed irresectable [1]. Our median overall survival was 12 months and estimated 2 years overall survival of 43% is also comparable to published literature [1,6].

Table 6 demonstrates previous reports from Pakistan on outcomes of PD. Only 8 studies were published in the last 15 years on PD outcomes from Pakistan. Outcomes from a study by Haq and colleagues could not be included in our review due to non-availability of results [26].

Overall, 255 patients underwent curative resection for periampullary malignancy in 15 years. Note ably, majority of reports were from low volume centers, vascular resection/EL was not attempted and only short term outcomes reported. Together, all

![Fig. 1. Estimated 2 year overall survival for pancreatic versus non-pancreatic tumors.](image)

**Table 6**

<table>
<thead>
<tr>
<th>Author</th>
<th>Duration</th>
<th>Number of patient s</th>
<th>Resections per year</th>
<th>Vascular resection</th>
<th>Extended lymphadenectomy</th>
<th>Morbidity</th>
<th>Post opmortality</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pal et al [13], 2011</td>
<td>23 years</td>
<td>121</td>
<td>5</td>
<td>None</td>
<td>None</td>
<td>54%</td>
<td>10%</td>
<td>NR</td>
</tr>
<tr>
<td>Bhatti et al [22], 2014</td>
<td>13 years</td>
<td>12</td>
<td>&lt;1</td>
<td>None</td>
<td>None</td>
<td>41.6%</td>
<td>NR</td>
<td>5 year ~ 21%</td>
</tr>
<tr>
<td>Bhatti et al [6], 2014</td>
<td>13 years</td>
<td>39</td>
<td>3</td>
<td>None</td>
<td>None</td>
<td>48.7%</td>
<td>15%</td>
<td>5 year ~ 38%</td>
</tr>
<tr>
<td>Aziz et al [23], 2005</td>
<td>NR</td>
<td>18</td>
<td>NR</td>
<td>None</td>
<td>None</td>
<td>59.2%</td>
<td>NR</td>
<td>6 months ~ 90%</td>
</tr>
<tr>
<td>Aslam et al [24], 2005</td>
<td>2 years</td>
<td>30</td>
<td>15</td>
<td>None</td>
<td>None</td>
<td>76.4%</td>
<td>10%</td>
<td>NR</td>
</tr>
<tr>
<td>Gondal et al [24], 2002</td>
<td>3 years</td>
<td>15</td>
<td>5</td>
<td>None</td>
<td>None</td>
<td>–</td>
<td>17.4%</td>
<td>NR</td>
</tr>
<tr>
<td>Tufail et al [25], 2000</td>
<td>5 years</td>
<td>20</td>
<td>4</td>
<td>None</td>
<td>None</td>
<td>–</td>
<td>20%</td>
<td>4 year ~ 20%</td>
</tr>
</tbody>
</table>
these reports represent only three major cities of the country (Karachi, Lahore, and Multan). The post-op mortality was high (10% or more) in these studies compared to recent standards. It is surprising that a country with a population over 180 million people, surgical outcomes on only 255 patients with peri-ampullary malignancy have been reported. Low prevalence, late presentation with advanced stage and limitations in surgical expertise/peroperative care can only partially account for this underreporting. PD resection has generally been performed by general surgeons and HPB surgery only accounts for part of their surgical practice. This lack of site specific focus has not allowed them to push boundaries and undertake EL or vascular resections. According to estimates, there are around 139, 200 new cancer patients annually in Pakistan and only 0.5% of these are pancreatic in origin [27,28].

This translates into 10,000 cases of pancreatic cancer alone in 15 years. Assuming that only 20% of these cases are potentially resectable at the time of presentation, it still translates into 2000 cases of resectable pancreatic tumors in Pakistan over a period of 15 years [29]. Obviously the numbers will be even higher if other peri-ampullary tumors are included in the list. We believe that poor surgical outcomes in the hands of occasional Whipplists and a lack of research culture are equally responsible for this dearth of literature on PD outcomes from Pakistan [30,31].

In recent years, there has been a trend towards site specific surgery and at present there are 4 centers in the country with designated HPB departments. However, results from these centers remain to be reported. The current study reports outcomes of EL along with PD in Pakistani population. Results comparable to international high volume centers were possible owing to high level of surgical expertise and impressive perioperative care facilities. Vascular resections did not entail additional risk to our patients and extended nodal dissection allowed better staging.

Unfortunately, there is very limited literature on PD outcomes from Pakistan and we are hopeful that recent development of specialized HPB centers will nourish refinement in HPB surgery and produce literature of international quality in near future.

Ethical approval

The research was performed in accordance with declaration of Helsinki. It is retrospective, non interventional and subjects are not identifiable.

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Author contribution

FSD, AHB, AWD: design, writing draft, critical review.
AHB.HZ, IH, AR: Data collection, analysis, design.
AL, MS, NHS: Design, final revision of draft, critical analysis.

Conflict of interest statement

We have no conflict of interests.

Guarantor

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References
