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ORIGINAL ARTICLE

Extended pancreatectomy as defined by the ISGPS: useful in selected cases of pancreatic cancer but invaluable in other complex pancreatic tumors

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Abstract

Purpose Extended pancreatectomy aimed at R0 resection of pancreatic tumors with adjacent vessel and organ involvement may be the only option for cure. This study was done with an objective to analyze the short- and long-term outcomes of extended pancreatic resections.

Methods All pancreatectomies performed between 2006 and 2015 were included. The pancreatectomies were classified as standard or extended, as per the International Study Group for Pancreatic Surgery. All surgical complications and terminologies were according to Clavien-Dindo classification and International Study Group for Pancreatic Surgery guidelines. Morbidity and mortality were primary outcomes and disease-free survival was a secondary outcome.

Results Sixty-three extended and 620 standard pancreatectomies were performed. Major morbidity (Clavien grades III, IV and V) (37 vs. 29%, $p = 0.21$) and mortality (6 vs. 4%, $p = 0.3$) for extended pancreatectomies were comparable to those for standard pancreatectomies. Blood loss > 855 ml, need for blood transfusion, and tumor size were independent risk factors for morbidity, and the latter two for mortality. Standard pancreatectomies were associated with better 3-year disease-free survival than extended pancreatectomies (67 vs. 41%, $p < 0.001$). Extended pancreatectomies resulted in a significantly better median disease-free survival for non-pancreatic adenocarcinoma vs. pancreatic adenocarcinoma (33.3 vs. 9.5 months, $p = 0.01$).

Conclusion Extended pancreatectomies resulted in similar peri-operative morbidity and mortality compared to standard pancreatectomies. Although the survival of patients undergoing these complex procedures is inferior to standard pancreatectomies, they should be undertaken not only in selected cases of pancreatic cancer but even more so in other complex pancreatic tumors.

Keywords Extended · Pancreatectomy · Outcome · Survival

Introduction

Experiments with extended resections date back to 1952, inspired by McDermott's thought, "with very rare exceptions, carcinoma of the pancreas is a fatal disease" [1]. With a dismal resectability rate, plateaued at 20–30% (1983 to 2007), many have challenged the anatomical limits of resection for pancreatic ductal adenocarcinoma (PDAC) [2, 3]. Locally advanced tumors, which account for 30% of all pancreatic tumors, are associated with a sinister prognosis. However, the long-term survival of this group can be improved by offering them extended resections, but with an acceptable peri-operative morbidity and mortality [4]. Although extended pancreatectomies (EP) were initiated as early as 1972 by Fortner under the helm of "regional pancreatectomy," it is the recent years that have seen an increasing acceptance for vascular resections, especially vein resections [2, 5]. With the International Study Group for Pancreatic Surgery (ISGPS) guidelines for EP published in 2014, many retrospective reviews have surfaced, implying that many have already pushed beyond standard

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resections under controlled settings, as surgery continues to be the only hope for cure [6–9]. We evaluated world literature in 2010 and now analyze our very own outcomes of EP as defined by the ISGPS to assess feasibility, safety, and benefit of these radical procedures [10, 11].

The primary objective of our study was to assess the peri-operative morbidity and mortality of EP compared to standard pancreatectomy (SP) and the secondary objective was to determine the long-term survival outcome following EP.

Patient and methods

Study design

A retrospective cohort analysis of a prospectively maintained database of pancreatic resections from January 2006 to August 2015 of the Hepato-Pancreato-Biliary Surgical Oncology Unit at Tata Memorial Centre (Mumbai, India) was performed. All patients undergoing EP and SP were included in the final analysis. Patients who were explored and were metastatic or inoperable due to locally advanced unresectable disease were excluded from the final analysis. All cases of EP were included as per the ISGPS definitions [11]. As per ISGPS consensus statement, EP is defined as resection of an adjacent organ or vasculature in addition to standard pancreatic resection [11].

Ethics

The data were collected prospectively during routine clinical practice, and accordingly, signed informed consent was taken from each patient before any surgical or clinical procedure. The study protocol conforms to the ethical guidelines of the "World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended in Fortaleza, Brazil, 2013 [12]. No dedicated approval was needed from the institutional review board.

Surgical considerations

Pre-operative Treatment plan for all patients was decided upon in a multi-disciplinary clinic. With regard to pancreatic adenocarcinoma, the patients were evaluated using a pancreatic protocol CT scan along with imaging of the thorax. Based on resectability, they were categorized as resectable, borderline resectable, locally advanced unresectable, and metastatic. Resectable cases were treated with upfront resection. Borderline resectable cases were treated with neoadjuvant therapy after confirming tissue diagnosis and reassessed for resection. Pre-operative biliary drainage was performed where indicated [13].

Surgery Staging laparoscopy was used selectively prior to curative resection in suspected pancreatic head adenocarcinoma patients with CA 19-9 > 100 U/ml without any concomitant obstructive jaundice or cholangitis and in all patients with suspected adenocarcinoma of the distal pancreas, irrespective of the CA 19-9 level. Pancreatoduodenectomies were routinely pylorus-preserving unless otherwise indicated, using appropriate approaches [14]. Alimentary continuity was maintained using a standardized duct-to-mucosa pancreato-jejunostomy, along with an end-to-side hepatico-jejunostomy and antecolic duodeno-jejunostomy [15]. Pancreatic stump closure was hand-sewn in distal pancreatectomies (DP). Spleen-preserving DP was performed in select situations. Peri-operative octreotide and prophylactic drains were used in all the cases. Intra-operative anticoagulation used in vascular resections was local use of heparinized saline. Primary end-to-end venous anastomosis was performed if the resected segment was < 4 cm. The threshold for using interposition graft was for vein resections > 4 cm to ensure a tension-free anastomosis. Vascular reconstructions were classified according to the ISGPS [16]. Nasojejunal tube was routinely placed intra-operatively for enteral nutrition. None of the colonic anastomoses were diverted.

Post-operative Drain and serum amylases were sent as per unit protocol on post-operative days 3 and 7, respectively. All complications were defined according to the ISGPS criteria and were graded according to Clavien-Dindo [17–20]. Major morbidity referred to any morbidity which was grade 3 and above. Mortality included all-cause death up to 90 days from surgery. Margin-positivity (R1) was defined according to the Royal College of Pathologists guidelines [21]. All resected patients were included in survival calculation, irrespective of their histopathological correlation of vessel/adjacent organ involvement.

Statistical analysis

Statistical analysis was done using a statistical software package, SPSS v.21.0 (SPSS Inc., Chicago, IL, USA). The data were represented as median (range) or frequency (%) as appropriate. Disease-free survival (DFS) was calculated from date of surgery to date of recurrence or last follow-up. The Kaplan–Meier method was used to estimate survival using two-sided log-rank for group comparison. Association was analyzed using Chi-square test or Fisher's exact test and Mann–Whitney U test for categorical and continuous variables, respectively. Factors contributing to peri-operative morbidity and mortality which were significant ($p < 0.05$) on univariate analysis were included in the multivariate model using logistic regression. p value < 0.05 was considered statistically significant for all comparisons.

Results

Patient characteristics and pre-operative details (Table 1)

A total of 683 patients underwent pancreatectomies during this period. There were 63 EP and 620 SP. During the same period, curative intent surgery was attempted for 92 patients but resection abandoned due to various reasons (Fig. 1). Pre-operative characteristics of the EP and SP patients are shown in Table 1. Seventy-three percent (46/63) of EP were operated in the time span 2012–2015. Significantly more patients were subjected to pre-operative biliary drainage in SP group (64 vs. 40%, $p < 0.001$). A significantly higher proportion was treated with neoadjuvant therapy in EP vs. SP (11 vs. 3%, $p = 0.002$). Neoadjuvant regimen amongst EP included chemoradiation in four, chemotherapy followed by chemoradiation in two, and chemotherapy in one patient. Among SP group regimen used included chemotherapy and chemoradiation in ten patients each.

Peri-operative details (Tables 1 and 2)

The median duration of surgery was significantly longer in EP (510 vs. 430 min, $p < 0.001$). Duration of hospital stay (13 vs. 13 days, $p = 0.69$) and re-admission rates (16 vs. 10%, $p = 0.16$) were similar between the two groups. EP was associated with a significantly higher median blood loss (1500 vs. 800 ml, $p < 0.001$), the percentage of patients requiring blood transfusion (56 vs. 20%, $p < 0.001$), and a median number of units transfused (2 vs. 1, $p < 0.001$). Of 31 VR patients, 29 underwent vein-only, 1 underwent vein and artery, and another underwent artery-only resection, comprising 32 vascular repairs in this VR group. Of the five MVR+VR, four underwent vein-only resection while one patient underwent vein and artery resection, comprising six vascular repairs in this MVR+VR group. The vein resected included segments of the portal vein (PV), superior mesenteric vein (SMV), or their confluence while the arterial segments resected were those of the common hepatic artery (CHA). The median length of vessel resected was 2 cm (0.5–8 cm) while the median vessel-clamp time was 10 min (6–35 min). There were 38 vascular reconstructions in all, performed in 36 patients of the VR and MVR+VR groups. Majority of reconstructions were Type 3 (55%). The remaining were Type 1 (26%) and Type 4 (18%) repairs. Interposition graft was used in seven patients. Six of these were prosthetic grafts and one was autologous saphenous vein graft. One of these patients succumbed. Of the remaining five in whom prosthetic grafts were used, three developed post-operative collections requiring intervention. However, no patient developed a graft infection. Table 3 shows the adjacent organs and vessels resected in the EP group.

Histopathology (Table 1)

Majority of the EP were for PDAC (27 of 63, 43%). Remaining histologies included 14 adenocarcinomas of non-pancreatic origin (22%), 5 solid pseudopapillary epithelial neoplasms (SPEN) (8%), 5 pancreatic neuroendocrine tumor (8%), 4 sarcomas (6%), 3 renal cell carcinomas (5%), 3 cystic pancreatic neoplasms (5%), and 2 gastrointestinal stromal tumor (GIST) (3%). Non-pancreatic origin adenocarcinoma included 6 colonic, 5 common bile duct, and 3 ampulla of Vater primaries. Median tumor size was significantly larger for MVR vs. VR cases. The tumors in the EP group were significantly larger in size and were associated with a higher lympho-vascular invasion (LVI) and peri-neural invasion (PNI) compared to those in the SP group. R1 resections were significantly higher in the EP group compared to the SP group. There was one case of R2 resection in the EP group—a patient in whom a PV resection was done but a major arterial resection was also required, and the latter was deferred due to inter-aorto-caval node positivity on frozen section.

Complications (Table 1; Fig. 2)

The bar graph in Fig. 2 shows the individual complications following SP and EP. Major morbidity for EP vs. SP in the PDAC group was 48.1% (13/27) vs. 23.2% (16/69) ($p = 0.01$) and that for non-PDAC group was 27.8% (10/36) vs. 29.8% (164/551) ($p = 0.8$). A univariate logistic regression was carried out of factors which might contribute to morbidity and mortality considering age, sex, American Society of Anesthesiologists (ASA) grade, pre-operative serum bilirubin and albumin, pre-operative biliary drainage, neoadjuvant therapy, surgical blood loss, need for blood transfusion, tumor size and type of pancreatic resection as the predictor variables, and morbidity and peri-operative mortality as the outcome. Of these, factors entered into multivariate analysis included age, blood loss, need for blood transfusion, and tumor size, which revealed that blood loss > 855 ml, need for blood transfusion, and tumor size were found to contribute significantly to major morbidity, and need for blood transfusion and tumor size were found to contribute significantly to peri-operative mortality.

Peri-operative mortality and survival (Table 1; Fig. 3)

During the 90-day peri-operative period, 4 (6%) of the patients in the EP group and 23 (4%) of the SP group ($p = 0.30$) died. Mortality for EP vs. SP in the PDAC group was 14.8% (4/27) vs. 2.9% (2/69) ($p = 0.03$) and that in the non-PDAC group was 0% (0/36) vs. 3.8% (22/551) ($p = 0.23$). Of the four EP who died, three were > 60 years of age. Two patients died of disseminated intravascular coagulation (DIC)—one had undergone right colonic resection along with PV resection and

Table 1 Peri-operative and post-operative characteristics

Characteristic	EP (*n* = 63)	%, range	SP (*n* = 620)	%, range	*p* value
Sex					
Male	36	57.1	399	64.4	0.25
Female	27	42.9	221	35.6	
Age, median (range), years	54	21–79	54	8–85	0.99
Pre-operative biliary drainage	25	39.7	394	63.7	< 0.001
Pre-operative stent					
Plastic	16	25.4	345	55.7	< 0.001
Metal	8	12.7	44	7.1	
Raised serum bilirubin (> 1.2 mg/dl)	12	19	210	34	0.01
Hypoalbuminemia (< 3.5 g/dl)	18	28.6	116	18.8	0.06
Elevated CA 19–9 (> 37)*	24	66.7	243	55.1	0.18
BMI					
< 18.5	5	11.6	31	10.4	0.96
18.5–24.9	24	55.8	171	57.4	
≥ 25	14	32.6	96	32.2	
ASA score ≥ 2	30	49.2	268	43.6	0.40
Type of pancreatectomy: no. (%)					
PD	42	66.7	562	90.6	< 0.001
DP	1	1.6	16	2.6	
DP-S	18	28.6	24	3.9	
Median/subtotal	1	1.6	12	1.9	
Total	1	1.6	6	1.0	
Type of pancreato-duodenectomy: no. (%)					
Pylorus-preserving	24	38.1	536	86.5	< 0.001
Classical	18	28.6	26	4.2	
Type of EP					
"Multivisceral"	27	42.9			–
"Vascular"	31	49.2			
Both	5	7.9			
Duration of surgery, median (range), min	510	235–645	430	210–630	< 0.001
Blood loss, median (range), ml	1500	400–23,000	800	50–23,000	< 0.001
Blood transfusion, no. (%)	35	55.6	123	19.8	< 0.001
Blood units transfused, median (range), no.	2	1–39	1	1–23	< 0.001
Hospital stay, median (range), days	13	4–59	13	1–69	0.69
Re-admission, no. (%)	10	15.9	63	10.2	0.16
Major Morbidity, no. (%)	23	36.5	180	29	0.21
Histopathology details[&]:					
Tumor size, median (range), cm	4.5	1–18	2	0–16	< 0.001
Differentiation, no. (%)					
Well	4	6.5	56	9.2	0.1
Moderate	28	45.2	341	56.1	
Poor	16	25.8	91	15	
Resection, no. (%)					
R0	50	79.4	530	85.5	< 0.001
R1	11	17.5	38	6.1	
R2	1	1.6	0	0	
Lympho-vascular invasion, no. (%)	25	39.7	104	16.9	< 0.001
Peri-neural invasion, no. (%)	25	39.7	109	17.7	< 0.001
Node positivity—N1, no. (%)	30	47.6	246	39.7	0.2
Lymph node yield, median (range), no.	14	2–38	11	0–53	.001

EP extended pancreatectomy, *SP* standard pancreatectomy, *BMI* body mass index, *ASA* American Society of Anesthesiology, *PD* pancreato-duodenectomy, *DP* distal pancreatectomy, *DP-S* distal pancreato-splenectomy, *mins* minutes, *no.* number

*Only adenocarcinoma

[&] All pathologies included

polytetrafluoroethylene (PTFE) graft repair, i.e., Type 4 repair, and the other after Type 3 repair between hepatic artery proper and splenic artery. The third patient died of hepatic failure after a PV and CHA resection and the fourth patient died after discharge due to a cardiac event, 22 days after surgery. The median disease-free survival (DFS) for patients with PDAC was 17.2 months with a median follow-up of 18.5 months. Among the EP group, median DFS for the non-PDAC cohort was 33.3 vs. 9.5 months for the PDAC cohort ($p = 0.01$). In the EP group, 29 (46%) patients had disease progression, i.e., 5 (8%) loco-regional failure, and 22 (35%) distant relapse, predominantly in the liver (11 of 22, 50%). The 3-year DFS

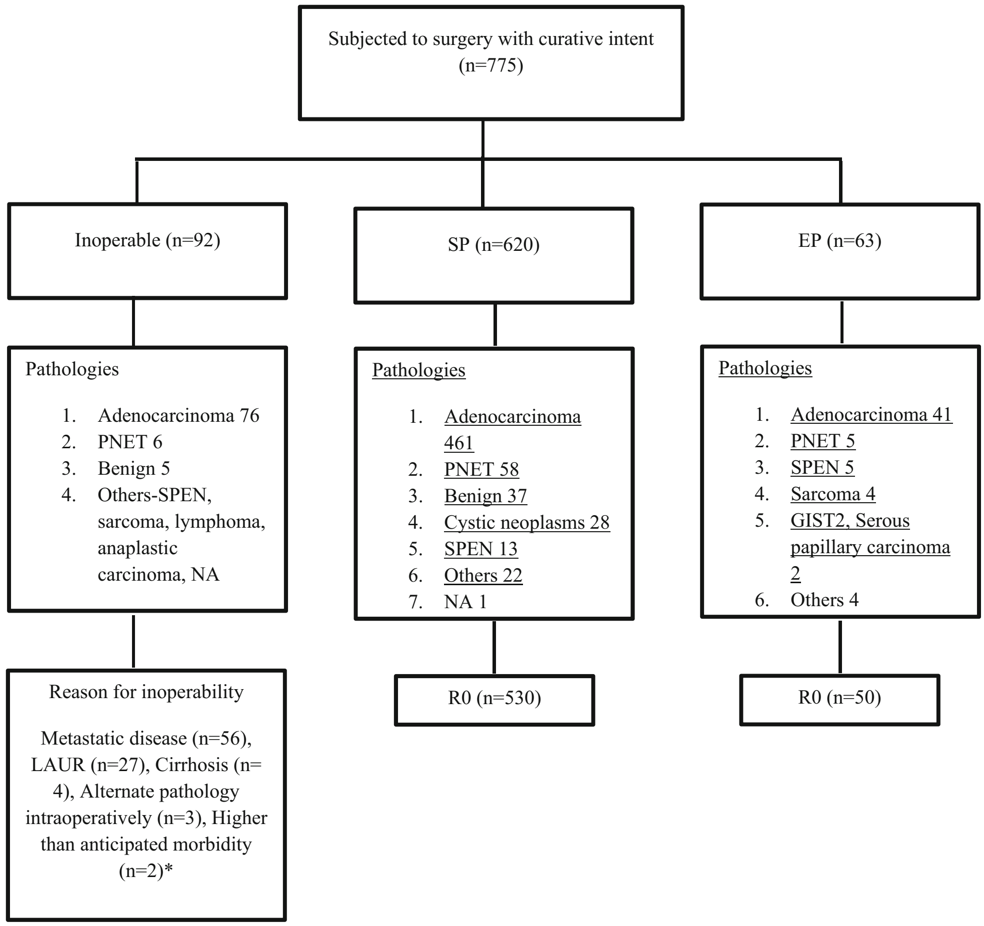


Fig. 1 Flowchart showing consort diagram of all the patients subjected to surgery. *2 patients; total pancreatectomy in a patient with cardiac co-morbidity (1) and technically difficult surgery due to highly friable tissues (?post-radiation) (1). *PNET* pancreatic neuroendocrine tumor, *SP* standard pancreatectomy, *EP* extended pancreatectomy, *NA* not available, *LAUR* locally advanced unresectable

for EP was 41 vs. 67% for SP ($p < 0.001$). The percentage of patients who received adjuvant chemotherapy in the SP vs. EP was 47 vs. 54% ($p = 0.29$). The median survival of SP vs. EP for PDAC was 19.5 vs. 9.5 months ($p = 0.06$). The 3-year DFS of SP vs. EP for the non-PDAC group was 71 vs. 49.5% ($p = 0.009$).

Discussion

The purpose of this study was to examine the outcomes of EP, grouping together the cohorts of VR and MVR, as recently advised by the ISGPS [11]. Currently, there is a lack of robust evidence comparing SP vs. EP, excluding extended lymphadenectomies [5]. Conducting a randomized control trial regarding the former would entail ethical issues, thus rendering importance to a retrospective analysis. The most pertinent issue with EP is if they can be performed with an acceptable morbidity, mortality, and survival outcome.

In our study, EP was associated with significantly higher blood loss, number of units of blood transfused, need for blood transfusion, and duration of surgery. However, overall, EP had a similar hospital stay, peri-operative morbidity and mortality, and re-admission rates as SP. The peri-operative mortality and morbidity for pancreatic adenocarcinoma patients undergoing EP were significantly higher than those undergoing SP. Significantly higher proportion of patients undergoing EP had LVI and PNI as well as R1 resections. EP was associated with a significantly lower DFS when compared to SP overall, for the PDAC and non-PDAC groups. However, following EP, patients with non-PDAC histology expectedly enjoyed a significantly better DFS as compared to PDAC.

The estimated blood loss and need for blood transfusion were significantly higher for EP in our study, similar to the observations by Shoup et al., two studies by Hartwig et al., and Burdelski et al., respectively, with the latter three including all types of pancreatic resections [22–25]. The blood loss for VR in our series is higher when compared to standard pancreatic resections (1300 vs. 800 ml). Similar results with regard to blood loss have been observed in another large single-institution series [26]. However, others have shown that concomitant vascular resections are associated with similar blood loss and transfusion requirement [27, 28]. Burdelski et al. and Hartwig et al. noted significantly increased morbidity (69 vs. 37% and 36.6 vs. 25.3%, respectively) but comparable in-hospital mortality (7 vs. 4% and 6.9 vs. 3.5%, respectively) when compared to SP, while the recent study by

Table 2 Comparison of vascular resections and multi-visceral resections

Characteristic	VR ($n = 31$)	MVR ($n = 27$)	Both ($n = 5$)	p value
Sex (M:F ratio)	7:8	2:1	4:1	0.14
Age, median (range), years	54 (21–78)	53 (29–79)	60 (54–72)	0.34
Surgery: no. (%)				
PD	27 (87.1)	11 (40.7)	4 (80)	< 0.05
DP/DP-S	2 (6.5)	16 (59.3)	1 (20)	
Subtotal	1 (3.2)	0	0	
Total	1 (3.2)	0	0	
Neoadjuvant treatment, no. (%)	4 (12.9)	1 (3.7)	2 (40)	0.054
Patients requiring blood transfusion, no. (%)	15 (48.4)	15 (55.6)	5 (100)	0.09
Estimated blood loss, median (range), ml	1300 (700–4000)	1700 (400–6500)	2500 (2000–23,000)	0.07
Blood units transfused, median (range), no.	2 (1–5)	3 (1–8)	3 (2–39)	0.22
Hospital stay, median (range), days	13 (5–59)	14 (7–42)	13 (4–48)	0.71
Re-admission, no. (%)	5 (16.1)	4 (14.8)	1 (20)	0.95
Tumor size, median (range), cm	3.5 (1–17)	7.5 (1–18)	4.5 (3–13)	0.003
Lymph node yield, median (range), no.	14 (3–30)	14 (2–38)	12 (7–24)	0.50
PDAC, no. (%)	15 (48.4)	10 (37)	2 (40)	0.67
Microscopic invasion of resected structures, no. (%)	12 (38.7)	22 (81.5)	4 (80)	0.003
R status, no. (%)				
R0	25 (80.6)	22 (81.5)	3 (60)	0.65
R1	4 (12.9)	5 (18.5)	2 (40)	
R2	1 (3.2)	0	0	
Major morbidity, no. (%)	11 (35.5)	10 (37)	2 (40)	0.97
Mortality, no. (%)	2 (6.5)	1 (3.7)	1 (20)	0.39
Adjuvant therapy, no. (%)	18 (60)	13 (54.2)	1 (20)	0.25

EP extended pancreatectomy, *SP* standard pancreatectomy, *PD* pancreato-duodenectomy, *DP* distal pancreatectomy, *DP-S* distal pancreato-splenectomy, *no.* number, *PDAC* pancreatic ductal adenocarcinoma, *OS* overall survival

Table 3 Adjacent organs and vascular structures resected in extended pancreatectomy group

Organs/vessel[$]	EP ($n = 63$)
Colon	20
Left adrenal	6
Kidney	5
Stomach	4
Diaphragm	3
Liver	2
Small bowel	2
PV	20
SMV	9
PV + SMV	6
CHA	2
RHA	1

EP extended pancreatectomy, *PV* portal vein, *SMV* superior mesenteric vein, *CHA* common hepatic artery, *RHA* right hepatic artery

[$] More than 1 organ and/or vessel resected in 14 patients

Hartwig et al. noted increased in-hospital and 90-day mortality [23–25]. Bhayani et al. observed significantly higher morbidity and mortality in patients who underwent MVR when compared to SP [29]. It was noted that our patients who underwent MVR+VR had a higher blood loss than those who underwent either alone. There are studies which have described comparable morbidity, as seen in our study. However, of these, Nikfarjam et al. and Seeliger et al. studied only MVR, and Dar et al. studied only VR and extended lymph node dissections [8, 30, 31].

In the studies by Hartwig, Burdelski, and Klempnauer et al., 28–38% of patients with MVR had concomitant distant metastases, making them unsuitable for comparison [23, 25, 32]. However, the recent publication by Hartwig had a cohort more comparable to ours, though in larger numbers [24]. Kulemann et al. reported higher peri-operative morbidity and mortality in MVR as compared to VR, in patients undergoing PD, a feature not seen in our study [9]. Comparable to the study by Temple et al. where 11% of patients who underwent EP with colonic resections received neoadjuvant therapy, 11% of our EP received neoadjuvant

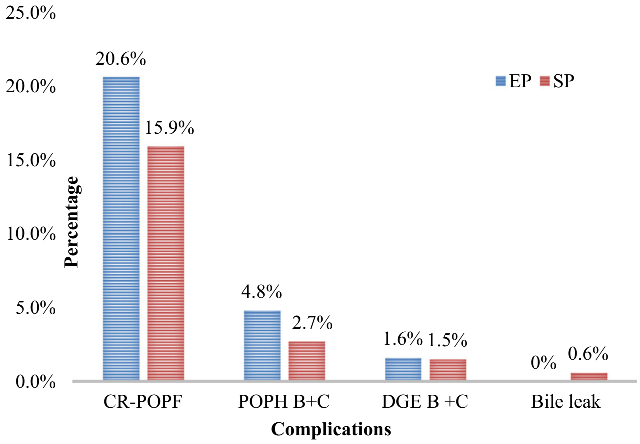


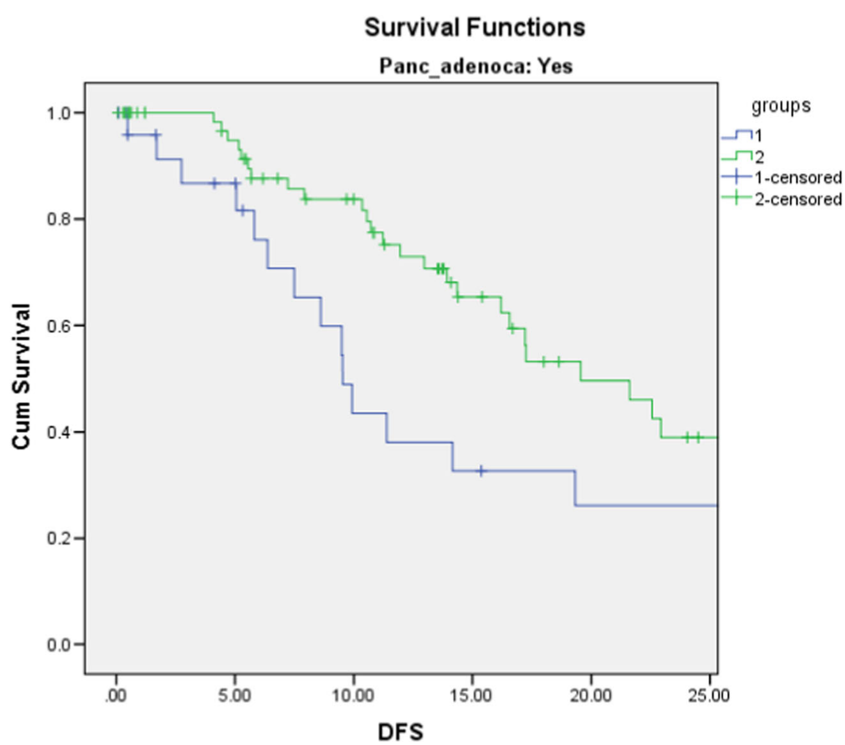
Fig. 2 Bar graph showing complications following EP and SP. *EP* extended pancreatectomies, *SP* standard pancreatectomies, *CR-POPF* clinically relevant post-operative pancreatic fistula, *POPH* post-operative pancreatic hemorrhage, *DGE* delayed gastric emptying

therapy [7]. While the majority of our VR were for pancreatoduodenectomies, MVR comprised more distal pancreatectomies. Also, EP had significantly more classical than pylorus-preserving surgeries, not found to influence morbidity.

Most studies differed from ours in that they either focused on left-sided [22, 31, 33, 34] or right-sided resections [7–9, 30]. Only the studies by Sasson et al. [35] and, recently, Hartwig et al. [24] had a study population most similar to ours that included all pancreatectomies, MVR, and VR. These studies differed from our study in that they included only PDAC, a more homogenous histology. The former had comparable morbidity (35 vs. 38%) and mortality (2.7 vs. 1.7%) for extended resections [35]. The significantly worse peri-operative morbidity and mortality seen in our study for PDAC undergoing EP are similar to the worse peri-operative outcomes following EP documented by Hartwig et al. [24].

One of the limitations of our study is the varied histology included. This was essential as our focus was mainly morbidity and mortality encountered in EP irrespective of tumor heterogeneity. A comparable morbidity and mortality for EP in our study reflects on a growing experience with complex pancreatic resections. Although the Indian setting entails a low incidence of PDAC, we do encounter neuroendocrine, cystic neoplasms, etc. with advanced presentation. The latter histologies may benefit more from radical surgeries than the otherwise traditionally aggressive PDAC. This is reflected in the survival difference we see between PDAC and their non-PDAC counterparts (median DFS 9.5 vs. 33.3 months, $p < 0.001$). Although histology of tumors and their corresponding survival has been analyzed, this was not our primary end-point. PDAC had inferior survival, trending towards significance, when they underwent EP when compared to SP (median DFS 9.5 vs. 19.5 months, $p = 0.06$). The inferior survival difference contradicts the ISGPS consensus [11] but is similar to the observations by De Reuver et al. [36] and recently by Hartwig et al. [24]. This may be the result of aggressive biology of tumors in the EP group, as reflected by their significantly larger size, higher PNI, and LVI. The other possible explanation may be significantly higher R1 resections

Fig. 3 Kaplan–Meier curve comparing disease-free survival (DFS) of extended (group 1; blue) vs. standard pancreatectomy (group 2; green) in the pancreatic adenocarcinoma group (9.5 vs. 19.5 months, $p = 0.06$)



seen in EP, in our series. These factors also explain the median DFS of 9.5 months following EP performed for PDAC. A larger cohort of PDAC followed up for a longer period can reflect the true picture. Contrastingly, Ravikumar et al. reported comparable PNI/LVI in patients undergoing VR [6]. Microscopic vascular invasion was noted in only 39% (12 of 31) of our VR patients. With vascular invasion ranging from 3 to 80%, it often occurs that tumors thought to have invaded the porto-mesenteric vasculature intra-operatively are often found to have only inflammatory adhesions to the resected vein on pathology [37–39]. Contrastingly, 82% (22 of 27) of our MVR demonstrated microscopic invasion of the additionally resected organs. Our EP had significantly more R1 resections (11 of 63, 18%) compared to SP (38 of 620, 6%) similar to Konstantinidis et al. who reported that patients with R1 resection had a longer survival compared with those who had locally advanced unresectable cancers (14 vs. 11 months; $p < 0.001$) [40]. Although R+ resections in EP ranges considerably from 9 to 39% [11], ESPAC-1 had initially suggested it to be a negative predictor of survival, only to be re-questioned by Tseng et al. as well as by the ESPAC-3 trial [41–43]. A significant proportion of our EP (73%) were operated over the last 3 years (2012–2015), indicating a combination of our growing experience with SP over a decade, coupled with the changing trends world over with more evidence-based acceptance for MVR and VR [7, 9, 11, 44–47]. More than 50% (36/63) of the resections in the extended pancreatectomy group were vascular resections. This is an indication of experience available at a high-volume center. Performing a vein resection vs. avoiding one is also a matter of experience which is difficult to document objectively, and a number of vein resections can be avoided with an increasing experience.

Another limitation of this study is the retrospective nature over a long study period of 9 years and the limited sample size of each cohort and type of surgery (PD vs. DP). Also, the smaller numbers of PDAC might under-power the study to detect smaller differences in outcome. While larger accrual would have facilitated more accurate survival data analyses, more MVR and VR would have allowed estimation of whether a specific organ (e.g., colon) or vessel (artery or vein), specifically contributed to increased morbidity. The VR and MVR clubbed together as “extended pancreatectomies” makes it a heterogeneous group. This along with the existing literature, which has inclusion and exclusion criteria similar and dissimilar to our own, precludes easy comparison [11].

Our study, however, provides evidence favoring EP, a procedure often condemned by surgeons. These resections can be performed with morbidity, mortality, hospital stay, and re-admission rates comparable to SP and also provide an acceptable long-term survival for non-PDAC histologies. This series, the first from India, clearly highlights the technical feasibility of these complex procedures. The study also underlines the importance of performing these demanding resections after careful patient selection and inexperienced high-volume units which are able to manage these demanding and challenging resections with their attendant problems. Future studies should aim at a larger accrual with mature long-term data and quality of life assessment, to further justify these radical procedures.

Conclusion

Extended pancreatectomies as defined by the ISGPS result in a similar peri-operative morbidity and mortality compared to standard pancreatectomies. Although the survival of patients undergoing these complex procedures is inferior to standard pancreatectomies for pancreatic ductal adenocarcinoma, they should be undertaken not only in selected cases of pancreatic cancer but even more so in other complex pancreatic tumors.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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