

Superior Mesenteric Artery First Approach versus Conventional Pancreaticoduodenectomy in Periampullary Adenocarcinomas: A Single Institutional Observational Study

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ABSTRACT

Introduction: Periampullary malignancies represent a group of malignancies at and around the ampulla of Vater, whose clinical features and management are similar, with Pancreaticoduodenectomy (PD, Whipple procedure) being the standard surgical treatment. Superior Mesenteric Artery (SMA) first approach to PD (smaPD) is a modification of conventional PD (cPD) in which the SMA is assessed early in the surgery. This improves the assessment of intraoperative resectability, reduces bleeding during surgery and enhances the dissection of retroportal tissues, resulting in a greater number of resections with no residual tumour (R0).

Aim: To compare smaPD with cPD with respect to clinical, perioperative, histological, oncological and survival outcomes.

Materials and Methods: This was a retrospective observational study conducted at the Department of General Surgery at North Bengal Medical College and Hospital, West Bengal, India. A total of 58 patients with periampullary adenocarcinomas who had undergone PD from 1 May 2018 to 30 November 2023 were studied. The retrospective data of 58 matched patients (smaPD vs cPD) with n=29 in each group were retrieved from the records. They were compared with respect to clinical and intraoperative findings, postoperative complications, in-hospital mortality,

Overall Survival (OS) and pathology parameters. Continuous data were analysed using Student's t-test and categorical data using the Chi-square test. OS was plotted using Kaplan-Meier survival curves and compared using the log-rank test. Results were considered statistically significant when p-value <0.05. Statistical software used: GraphPad Prism 10 (San Diego, USA) and Epi Info version 7.4.6 (Atlanta, Georgia, USA).

Results: The mean operative time in group A (smaPD) was 391.74 ± 32.15 minutes whereas in group B (cPD) it was 306.55 ± 39.57 minutes (p-value <0.0001). The mean blood loss in group A was 365.52 ± 108.97 mL and in group B 424.14 ± 58.34 mL (p-value=0.0162). R0 resection was higher in smaPD but this was not statistically significant (p-value=0.315). There was not much difference in terms of postoperative complications, length of hospital stay, pathology and OS (p-value=0.4034). Vascular anomalies were observed in four patients in group A.

Conclusion: The operative time was significantly longer in group A, but intraoperative blood loss was significantly lower, with more R0 resections. Advanced Multidetector Computed Tomography (MDCT) can accurately predict resectability preoperatively. In a rural setup, pursuing the smaPD technique for intraoperative assessment appears useful.

Keywords: Artery first, Resectability, Residual, Retroportal, Whipples

INTRODUCTION

Periampullary cancers arise at or around the ampulla of Vater. The most common are pancreatic ductal adenocarcinoma, ampullary adenocarcinoma, distal cholangiocarcinoma and duodenal adenocarcinoma, in that order. The rest include neuroendocrine tumours, intraductal papillary mucinous neoplasms, mucinous cystic neoplasms, gastrointestinal stromal tumours, acinar cell tumours, solid pseudopapillary tumours, sarcomas and metastases. The clinical presentations are similar, as is their surgical management. The most common symptom is painless obstructive jaundice, often associated with recent weight loss, fatigue and pain [1]. MDCT detects the tumour, assesses resectability and spread [1,2]. Three-dimensional vascular reconstruction can reveal the relationship to the SMA, Celiac Axis (CA), Common Hepatic Artery (CHA), Superior Mesenteric Vein (SMV) and Portal Vein (PV). Magnetic Resonance Cholangiopancreatography (MRCP) is very useful in distal cholangiocarcinomas. Diagnosis is essentially clinicoradiological. A biopsy is considered (preferably endoscopic ultrasound-guided) only if the tumour is unresectable, has metastasised, is a candidate for neoadjuvant chemotherapy, or has a high index of suspicion of lymphoma [1,2]. PD is the only known potentially curative measure for periampullary carcinomas [1,3]. William Halstead, in 1898 at

Johns Hopkins Hospital, performed the first successful surgery for periampullary cancer, in which he performed a local wedge resection of the periampullary duodenum with reimplantation of the bile and pancreatic ducts. Alessandro Codivilla performed the first resection of the duodenum with the head of the pancreas, but the patient died soon after. Walter Kausch performed a two-stage PD in 1909. Hirschel, in 1914, performed a one-stage PD who survived one year. However, PD became the mainstay surgical management of periampullary cancers since 1935 after Allen Oldfather Whipple refined the technique [1].

A tumour is resectable when there is no arterial tumour contact (CA, SMA, CHA) and no tumour contact with the SMV/PV or $\leq 180^\circ$ contact without vein contour irregularity [2]. There is often incomplete oncological clearance around the mesopancreas and the tissues to the right of the SMA. Also, when the pancreas is transected, profuse blood loss makes the dissection even more difficult, increasing the possibility of a non R0 resection. To counteract this, the SMA-first approach is applied, wherein the SMA is referenced early in the operation to assess resectability before taking an irreversible step such as pancreatic transection and discovering that the tumour has irresectably involved the SMA and/or other vessels. Also, early ligation of the Inferior Pancreaticoduodenal Arteries (IPDA) prevents

the pancreatic head from becoming congested with blood. All this reduces peroperative blood loss, improves retroportal tissue dissection and nodal clearance, increases R0 resection and prolongs long-term survival [3-5]. Given the advances in radiological evaluation by MDCT, a routine SMA-first approach is not required for assessment of unresectability [4]; but in a rural setup like ours, with radiological and logistical constraints, we feel the need for SMA-first approach to PD (smaPD).

The smaPD technique was first documented by Pessaux P et al., in their publication in 2006 [6]. Six different smaPD techniques exist [7]. Schneider M et al., described a technique of harvesting lymphatic and neural tissue in the triangle between the CA, SMA and PV, enabling the removal of possibly tumour-infiltrated tissue, thus potentially reducing the risk of local recurrence [8]. Gagner M and Pomp A first described laparoscopic PD in 1994. Though it is practised in many high-volume centres, many meta-analyses have obtained similar oncological results [9,10].

Comparative studies between smaPD and cPD have been conducted from across the globe [3,5-7]. However, no such comparative study has thus far been conducted from our sub-Himalayan region of West Bengal, India. Therefore, the aim of the present study was to compare smaPD and conventional PD (cPD) approaches with respect to the clinical, perioperative, histological, oncological and survival outcomes.

MATERIALS AND METHODS

This was a single-institution retrospective observational study conducted in the Department of Surgery at a rural tertiary care centre of Eastern India. Institutional Ethics Committee clearance was obtained (Memo no. IEC/NBMC/M-04/F-03/2022). Data of patients who underwent PD from 1 May 2018 to 30 November 2023 for periampullary adenocarcinomas were retrieved from records. The cut-off date for follow-up data collection was 30 November 2024. The retrospective data were collected from records, compiled and analysed from 1 December 2024 to 15 January 2025. Patients had been followed-up routinely postoperatively at the third, sixth and twelfth months of the first postoperative year and then semi-annually. Every six months, MDCT abdomen and serum CA19-9 were observed.

Inclusion criteria: The retrospective data of 58 matched patients (29 in each group) were retrieved from the records.

Exclusion criteria: Patients with intraoperative findings of metastases/irresectability and those who were histologically negative for adenocarcinoma and who had received neoadjuvant therapy were excluded from our study. Irresectability was decided according to National Comprehensive Cancer Network (NCCN) guidelines Version 3.2024 [2].

Study Procedure

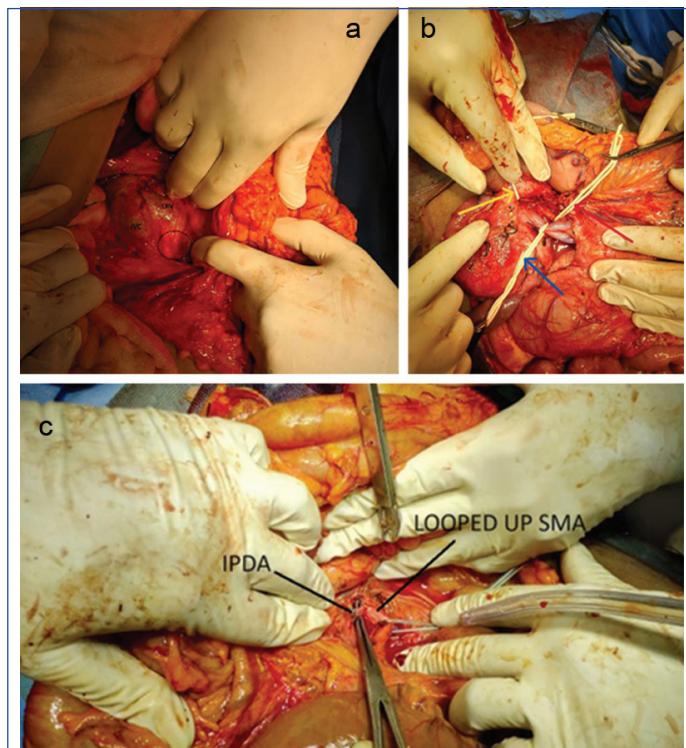
This study had two groups: Group A (reference group) smaPD and Group B (control group) the matched cPD group. The groups were matched by age, sex, location of tumour and follow-up time postsurgery. The clinical data/investigations, intraoperative parameters (operative time, intraoperative blood loss), postoperative complications (Delayed Gastric Emptying (DGE), Postoperative Pancreatic Fistula (POPF), Upper Gastrointestinal Bleeding (UGIB), Biliary Fistula (BF), Surgical Site Infection (SSI), diarrhoea and intra-abdominal haemorrhage), in-hospital mortality and OS were compared. Resection rates and nodal positivity were also compared. SMV/PV involvement was assessed preoperatively using pancreatic protocol CT and classified according to the Chaoyang classification [11].

All patients received adjuvant chemotherapy, except those with poor general condition or who refused chemotherapy. Venous Resection (VR) types, as described by the International Study Group

of Pancreatic Surgeons (ISGPS), were performed at the institution: Type 1, partial venous excision with direct closure by suture; Type 2, partial venous excision using a patch; Type 3, segmental resection with primary venovenous anastomosis; and Type 4, segmental resection with an interposed venous conduit [12].

POPF was defined according to the International Study Group of Pancreatic Fistula [13].

In smaPD, we first dissect out 16B1 for a frozen section to exclude metastasis [Table/Fig-1a]. Then we reference the SMA early and ligate the IPDA [Table/Fig-1b,c].



[Table/Fig-1]: a) 16B1 nodal station (black circle), IVC is inferior vena cava, LRV is left renal vein; b) SMA looped up; c) IPDA referenced.
LRV: Left renal vein; IVC: Inferior vena cava; Encircled area- is 16B1 station of lymph node; Yellow arrow- looped up neck of pancreas; Red arrow- looped up superior mesenteric artery; Blue arrow- looped up Superior Mesenteric Vein (SMV); IPDA: Inferior pancreaticoduodenal artery; SMA: Superior mesenteric artery

STATISTICAL ANALYSIS

The collected data were tabulated in Microsoft Excel. Continuous quantitative variables were expressed as mean \pm SD and categorical qualitative variables as absolute frequencies (numbers) and relative frequencies (percentages). Categorical data were analysed using the Chi-square test and continuous data using the unpaired t-test. OS was plotted using Kaplan-Meier survival curves and compared with the log-rank test. A p-value <0.05 was considered statistically significant. Statistical software used: GraphPad Prism 10 (San Diego, USA) and Epi Info version 7.4.6 (Atlanta, GA, USA).

RESULTS

Demographic and intraoperative data: The mean age was 48.83 \pm 6.53 years in group A and 50.38 \pm 7.17 years in group B. Sex distribution was equal in both groups. The mean operative time was shorter in group B: group A 391.74 \pm 32.15 minutes vs group B 306.55 \pm 39.57 minutes (p-value <0.001). The mean blood loss was lower in group A: 365.52 \pm 108.97 mL (range 250-600 mL) vs group B 424.14 \pm 58.34 mL (range 360-550 mL) (p-value=0.0162). Intraoperative incidents were not significantly different in both groups. Classical PD and PPPD were performed in 20 and 9 patients respectively in group A, whereas in 19 and 10 patients in group B (p-value=0.779, NS). Tumour location was similar in both groups, the most common being the head of the pancreas. Co-morbidities were also similar between groups [Table/Fig-2].

Pathology Data [Table/Fig-3]

There were no significant differences between the two groups regarding tumour type, staging, or grade [Table/Fig-2,3]. R0 resection (no residual tumour) was more frequent and R1 resection (microscopic residual tumour) was less frequent in group A, although this difference was not statistically significant (p -value=0.315). Thus, with similar prognostic factors influencing survival, we can assess the impact of the type of approach (group A vs group B) on survival. The SMA margin was positive in four cases of group B but none in group A. The mean lymph nodes retrieved was 12.69 ± 5.54 (range 6-22) in group A and 10 ± 2.59 (range 5-14) in group B (p -value=0.1782); mean nodal positivity was 1.65 ± 1.88 (range 0-6) and 1.24 ± 1.15 (range 0-4), respectively (p -value=0.32).

Factor	Group A	Group B	χ^2/p -value
Age (years)	48.83 ± 6.53	50.38 ± 7.17	0.3931
Sex, N (%)	Male	21 (72.4)	1
	Female	8 (27.6)	
Tumour location, N (%); TNM Stage (I,II,III), N (%)	Pancreatic head	12 (41.4); 3(25), 9 (75), 0(0)	1
	Distal CBD	9 (31); 3 (33), 6 (67), 0 (0)	
	Duodenum	6 (20.7); 2 (33.33), 2 (33.3), 2 (33.33)	1
	Ampulla of vater	2 (6.9); 1 (50), 0 (0), 1 (50)	
Operative time (minutes)	391.74 ± 32.15	306.55 ± 39.57	<0.0001 S
Intraoperative blood loss (mL)	365.52 ± 108.97	424.14 ± 58.34	0.0162 S
Postoperative stay	15.14 ± 5.23	16.51 ± 2.94	0.224
Co-morbidities N (%)	DM	8 (27.6)	0.0364/ 0.981966
	HTN	7 (24.1)	
	Pulmonary	2 (6.9)	
Type of PD N (%)	Classical	20 (69)	0.078/ p 0.7797
	ppPD	9 (31)	

[Table/Fig-2]: Distribution of the patient and operative variables.

Qualitative variables- Sex, Tumour location, Comorbidities, Type of PD; Others-Quantitative; t test used for continuous data, chi square for categorical data

Variables	Group A	Group B	χ^2/p -value
Grade N (%)	Well differentiated	8 (27.6)	0.0959/ p 0.9532
	Moderately well differentiated	14 (48.3)	
	Poorly differentiated	7 (24.1)	
Resection N (%)	R0	25 (86.20)	1.010/ p 0.3150
	R1	4 (13.80)	
Margin positive N (%)	Bile duct margin	0	NS
	Neck pancreas margin	0	
	Uncinate margin	2 (6.9)	
	SMA margin	0	
	SMV margin	0	
Lymph nodes mean (SD)	Retrieved	12.69 ± 5.54	0.1782
	Positive	1.65 ± 1.88	0.3207

[Table/Fig-3]: Pathology information in the two groups.

Qualitative variables- Grade, Resection, Margin positivity; Quantitative-Lymph nodes; t test used for continuous data, chi square for categorical data

Postoperative Events [Table/Fig-4]

In group A, POPF occurred in eight patients: seven were grade A and one was grade B (all conservatively managed). POPF types followed the ISGPS classification [13]. There was haemoperitoneum from the pancreatic stump, but it was managed by transfusion (4 units each of packed red blood cells, fresh frozen plasma and platelets)

in one patient who developed grade B POPF. Post-pancreatectomy haemorrhage presented as UGIB in two patients and intra-abdominal bleeding in four patients; these occurred after 24 hours and were managed with blood transfusions. Bronchopneumonia was observed in five patients and treated with antibiotics; one patient developed massive lung collapse and succumbed after one month. There were two additional in-hospital mortalities at one week and two weeks due to pulmonary embolism. SSI occurred in seven cases and intra-abdominal abscesses were seen in three patients. Diarrhoea and biliary leaks were observed in seven cases each. DGE was the most common complication, occurring in 13 patients. The average postoperative stay was 15.14 ± 5.23 days (range 7-30 days).

In Group B too, DGE was the most common complication, occurring in 12 patients, followed by POPF in 11 and SSI in 10. Grade A fistula occurred in eight patients (all conservatively managed), two patients had grade B fistula (conservatively managed) and one patient developed a grade C POPF (this patient had a soft pancreas with a pancreatic duct caliber of about 1 mm) and subsequently died after two weeks despite aggressive conservative management (nil per os, total parenteral nutrition, enteral nutrition via feeding jejunostomy and subcutaneous octreotide). Two patients developed haemoperitoneum and three had upper gastrointestinal bleeding (UGIB); all were managed conservatively. Bronchopneumonia and intra-abdominal abscesses were observed in four patients each and recovered with antibiotics. Diarrhoea and biliary leaks were found in five and six patients, respectively. The mean postoperative stay was 16.51 ± 2.94 days (range 7-22 days). There was an elderly lady who developed a massive myocardial infarction one week postoperatively and succumbed to it.

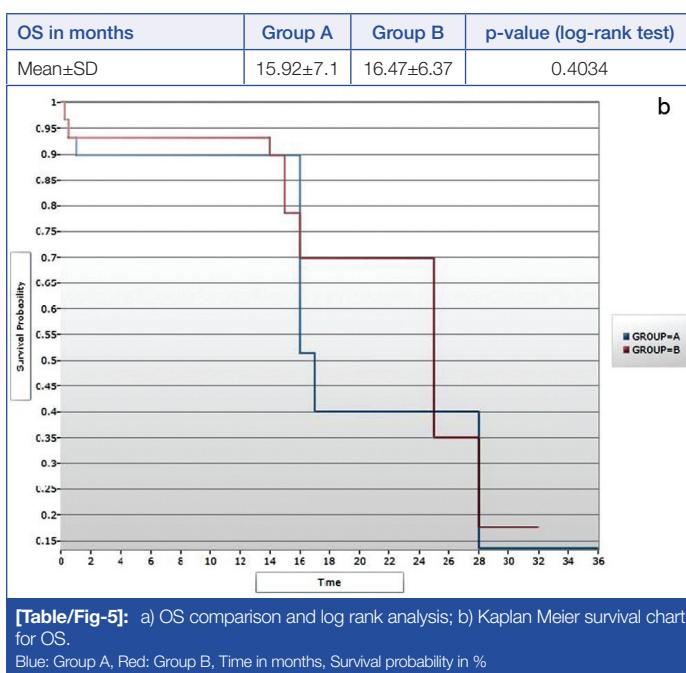
Overall, there was no statistically significant difference between the two groups regarding postoperative complications [Table/Fig-4].

Variables N (%)	Group A	Group B	χ^2/p -value
Delayed Gastric Emptying (DGE)	Yes	13 (44.83)	0.070/ 0.7909
	No	16 (55.17)	
Surgical Site Infection (SSI)	Yes	7 (24.1)	0.749/ 0.3868
	No	22 (75.9)	
Postoperative Pancreatic Fistula (POPF)	Yes	8 (27.6)	0.704/ 0.4013
	No	21 (72.4)	
Biliary leak	Yes	7 (24.1)	0.099/ 0.7529
	No	22 (75.9)	
Intrabdominal haemorrhage	Yes	4 (13.8)	0.744/ 0.3885
	No	25 (86.2)	
Upper Gastrointestinal Bleeding (UGIB)	Yes	2 (6.9)	0.219/ 0.6399
	No	27 (93.1)	
Diarrhoea	Yes	7 (24.1)	0.420/ 0.5168
	No	22 (75.9)	
Bronchopneumonia	Yes	5 (17.2)	0.132/ 0.7169
	No	24 (82.8)	
Intra-abdominal abscess	Yes	3 (10.3)	0.162/ 0.6869
	No	26 (89.7)	
In hospital mortality	Yes	3 (10.3)	0.219/ 0.6399
	No	26 (89.7)	

[Table/Fig-4]: Postoperative events in the two groups.

Patient Survival

The mean OS was 15.92 ± 7.1 months in group A and 16.47 ± 6.37 months in group B. There was no statistically significant difference between the two groups in OS (p -value=0.4034), with a similar median survival of 16 months [Table/Fig-5]. Follow-up lasted until the death/cut-off date of November 30, 2024.



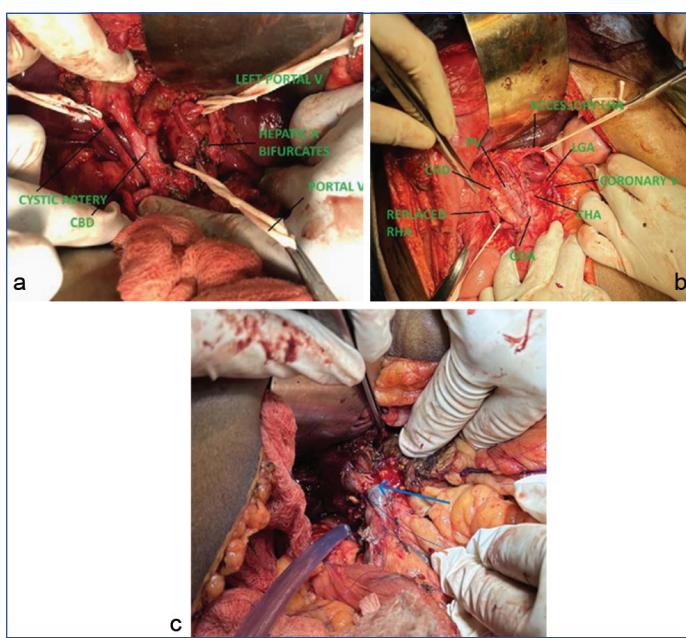
Müller PC et al., found no difference in operative time [17]. Müller PC et al., documented lesser blood loss (p-value <0.001), similar operative time (p-value=0.58) and a lower overall complication rate (p-value=0.001) in smaPD. There were fewer POPF (p-value=0.001) and fewer DGE (p-value=0.001) and more postoperative diarrhoea (p-value=0.03), with no difference in postoperative blood loss (p-value=0.32). However, mean intraoperative blood loss was significantly lower in present study group A (p-value=0.0162). Several studies have demonstrated a similar finding, attributable to earlier vascular control [13,15]. Postoperative stay was similar in both groups (p-value=0.224). Different hospital stays have been demonstrated in different studies. There was no significant difference in the studies by Dumitrascu T et al., and Tohamy AZ et al., [15,16]. SSI (7 vs 10 cases), POPF (8 vs 11 cases), diarrhoea (7 vs 5 cases) and intra-abdominal abscess (3 vs 4 cases) were observed in group A and group B, respectively. DGE, the most common complication, was similar in the two groups (13 vs 12 cases). UGIB, biliary leak and bronchopneumonia were similar between the groups. DGE has been reported in 12-15% in most studies, though a few have reported up to 45%, whereas POPF has been recorded in 3-28% [1,18]. Mirrielees JA et al., observed that the most relevant postoperative complications were DGE (17.3%), POPF (10.1%), incisional SSI (10.0%) and organ/space SSI (6.2%) [19]. Although mortality rates in PD have dropped in high-volume centres, the complication rate remains as high as 25-70% [20]. Venous involvement, when reconstructible, is no longer a contraindication to resection [3]. In present study, author performed partial right lateral circumference removal of the PV and direct repair in four cases, two in each group (ISGUPS Type 1 VR). Author encountered all the vascular variations in group A. Noussios G et al., reported an incidence of 0.35% of Michel Type VIII in 19,013 subjects [21]. Andall RG et al., reported a 0.29% incidence of a cystic artery origin from the SMA in 9,836 subjects [22]. R0 resection was observed in 25 group A cases versus 22 group B cases, whereas R1 resection was achieved in four group A cases and seven group B cases (p-value=0.315). Jiang X et al., and Müller PC et al., documented increased R0 rates in smaPD (p-value=0.001) [2,17].

The medial and posterior margins are the most commonly involved margins [12,14]. Warschkow R et al., reported that a higher nodal yield increased diagnostic accuracy and survival [23]. Eskander MF et al., confirmed that no additional benefit is achieved beyond 30 nodes [24]. In the present study, nodal retrieval and positivity were not statistically significant between the two groups.

In present study, there was no statistical difference regarding OS (p-value=0.4034). This perhaps indicates that OS is more dependent on tumour biology and other factors. Earlier control of the IPDA may not prevent micrometastatic spread. Wang X et al., realised that TNM stage, resection margin, overall complications and adjuvant therapy were independent risk factors affecting OS [25]. Pandanaboyana S et al., documented a 1- and 3-year OS of 90% and 53% (group A) versus 80% and 16% (group B); p-value=0.04 [5]. The mean OS in group A was 26.9±7.78 months and 24.8±9.48 in group B, with no significant difference (p-value=0.35) in the study by Tohamy AZ et al., [16]. Wang X et al., found that the median OS was 21.8 months in smaPD, whereas it was 19.8 months in cPD (p-value=0.900); also the number of nodes harvested was greater in the smaPD group (19 vs 15, p-value=0.021). The R0 resection rate was higher (93.3% vs 82.6%, p-value=0.197) and SMA margin positivity was lower (0 vs 13%). There were no differences regarding complication rates and mortality [25].

Limitation(s)

Since this was a retrospective study, there might be selection bias because non randomised groups were compared. It was conducted at a single centre. Prospective multicentre studies can improve the results.



DISCUSSION

Present study compared two groups of smaPD and cPD and found that smaPD offered lesser blood loss at the cost of a longer operative time. In the present study, the mean operative time was significantly greater in group A (p-value <0.0001). This finding was concordant with most studies and may be related to the learning curve of the technique [14]. However, Dumitrascu T et al., and Tohamy AZ et al., reported shorter operative times in the smaPD group [15,16].

CONCLUSION(S)

Both groups in present study had similar postoperative complications, mortality and OS. At sophisticated centres, current-generation MDCT with 3D reconstructions and maximum intensity projections can identify subtle vascular involvement and determine resectability preoperatively. But at a rural centre like ours with limited resources, smaPD is a very useful approach to appreciate intraoperative resectability and achieve better R0 resection rates, notwithstanding significantly reduced intraoperative blood loss. Furthermore, when SMV/PV invasion is detected, smaPD is useful as it decreases intraportal tumour dissemination and makes vascular repair technically easier.

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