Artery First Pancreaticoduodenectomy Versus Conventional Whipple Procedure in Pancreatic Head Adenocarcinoma

Original Article

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ABSTRACT

Background: Surgical resection remains the only potentially curative treatment for pancreatic ductal adenocarcinoma, provided that negative surgical margins (R0) are achieved, in conjunction with appropriate adjuvant therapies. In particular, the margin adjacent to the superior mesenteric artery has been frequently identified as the most common site for positive margins (R1) in tumors located in the pancreatic head. Recently, the adoption of the 'artery-first' approach (AFA) during pancreaticoduodenectomy has gained global attention. This technique involves prioritizing the dissection of the connective tissues surrounding the superior mesenteric artery early in the procedure. The primary goals are to allow for an early assessment of tumor resectability and to minimize intraoperative blood loss.

Patients and Methods: This The study evaluated two surgical techniques for managing pancreatic head adenocarcinoma: the conventional approach and the artery-first (posterior) approach.

Results: Receiver A total of 32 patients were included, with 15 undergoing the AFA and 17 treated via the conventional approach. Analysis revealed no statistically significant differences between the two groups in the majority of evaluated parameters.

Conclusion: The AFA proves to be a valuable surgical technique, particularly in patients with borderline resectable tumors and those who have undergone neoadjuvant therapy. However, the conventional approach remains a viable option, with satisfactory outcomes in appropriately selected cases.

Key Words: Adenocarcinoma, Approach, Artery, Pancreatic.

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INTRODUCTION

Among gastrointestinal cancers, pancreatic cancer is known to have the worst prognosis [1]. Even when categorized as 'radical' resection (R0), about one-third of patients experience local recurrence after pancreaticoduodenectomy (PD) [2]. There have been attempts in recent years to enhance surgical methods, especially about the removal of the retroduodenal (superior mesenteric artery, or SMA) margin. Incomplete resection at this margin was long thought to be the result of a surgical mistake. Regretfully, these improvements by themselves have not been enough to drastically cut positive margins [2].

The soft tissue that surrounds the proximal 3–4cm of the right lateral border of the SMA and contains autonomic nerves is referred to as the retroperitoneal, mesenteric, or uncinate margin by the American Joint Committee on Cancer. Despite being called the retroperitoneal margin in the past, 'SMA margin' is now thought to be a more accurate word [3]. The SMA margin cannot be re-excised, but re-resection is permitted if intraoperative frozen section analysis shows positive pancreatic or bile duct transection margins. As a result, following PD, the SMA margin usually stays positive [3].

Prior to undergoing irreversible surgical procedures, the 'artery-first approach' (AFA) to pancreatoduodenectomy (AFA-PD) entails the early dissection of arterial planes and clearing of retropancreatic tissue, enabling an early

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assessment of significant arterial involvement [4]. The mesenteric approach as an artery-first technique was initially presented by Nakao *et al.,* [5]. The AFA has two objectives: (1) to minimize intraoperative blood loss by early division of the inferior pancreaticoduodenal artery and (2) to assess resectability early by assessing the extent of tumour invasion into the SMA plexus, a critical site for potential positive margins [5,6].

A trial dissection is frequently required to assess the degree of tumour involvement in patients with tumours that are just borderline resectable. In this patient group, neoadjuvant treatment use is anticipated to rise [7]. The artery-first technique is especially beneficial in these situations because it maximizes surgical results and allows for early resectability decision-making [6].

Aim

The objective of the present study is to assess the oncological and surgical outcomes of the AFA during PD for patients with pancreatic ductal adenocarcinoma compared with the conventional surgical approach.

The primary endpoint will be the rate of negative (R0) and positive (R1) surgical margins. Secondary endpoints will include various intraoperative and postoperative measures such as total operative time, time from skin incision to specimen removal, intraoperative blood loss volume, and the need for blood transfusions. Postoperative complications within 90 days of surgery, including clinically significant pancreatic fistula (grade B or C), delayed gastric emptying, intra-abdominal hemorrhage, and the incidence of diarrhea, along with overall morbidity and mortality rates within the same time frame, will also be evaluated.

Additional secondary endpoints include the distance from the tumor to the closest resected margin in cases of R0 resection, the number of lymph nodes harvested, disease-free survival, and overall survival.

PATIENTS AND METHODS:

This prospective study was conducted from March 2021 to November 2023. Patients diagnosed with pancreatic head cancer who presented to the Upper Gastrointestinal and Liver Surgery Unit at the Main Alexandria University Hospital were randomized into two groups: group A, treated with the AFA, and group B, treated with the conventional approach. The primary population analysis will follow the ‘intention-to-treat’ principle.

Patients clinically and radiologically confirmed to have resectable or borderline resectable pancreatic head cancer were included in the study.

Exclusion criteria included:

(a) Patients with advanced or metastatic pancreatic head cancer.

(b) Patients deemed poor candidates for surgery.

(c) Patients found to have distant metastases and/or peritoneal deposits during surgery.

(d) Patients with macroscopic positive surgical margins (R2).

(e) Patients requiring a change in the planned procedure intraoperatively, such as combined resection of other organs.

(f) Patients with a pathological diagnosis other than pancreatic ductal adenocarcinoma.

Randomization (conducted via REDCap) was performed after surgical exploration and exclusion of metastatic or advanced disease, with a 1 : 1 allocation ratio between the two groups. The study population was further stratified based on resectability (resectable vs. borderline resectable) and preoperative neoadjuvant therapy (yes or no), ensuring a 1 : 1 ratio between both study groups across these variables.

In this study, patients were treated using either the AFA or the conventional approach, depending on their assigned group.

The conventional approach depends on cutting the stomach midway in its length while in pylorus-preserving pancreaticoduodenectomy we cut the duodenum 2-3cm distal to the pylorus. The neck of the pancreas is dissected from the portal vein and SMV “tunnelling” then the pancreatic neck is divided and this is considered an irreversible step in PD. Subsequently, the specimen is separated from the surrounding structures, and only at this latter stage do we begin to separate the head of the pancreas from the superior mesenteric artery by dividing and excision of the mesopancreas [8]. In 2007 mesopancreas was first anatomically defined and it included tissues containing fat, nerves, blood vessels and lymphatics in conjunction with the posterior wall of the pancreas and SMV and surrounding SMA on both sides down to the inferior vena cava and the aorta. The space between the uncinate process and SMA which is part of the mesopancreas could contain tumour cells and so could be responsible for R1 resection. [9] The artery-first approach helps elimination of all the nerves, the minor vessels, and the lymphatic nodes and networks within the retroperitoneal adipose tissue and is referred to as the total mesopancreatic excision due to the elevated negative resection margins rate. Hence, it may reduce the local recurrence rate as well as enhance the survival rate [10].

The artery-first technique can be executed through several variations, including the posterior approach, medial uncinate approach, inferior infracolic approach, left posterior approach, inferior supracolic approach, and superior approach. The specific choice of the artery-first

method was left to the surgeon's discretion. In this study, the posterior approach was selected as the artery-first method.

The posterior approach involves the dissection and exposure of the SMA at its origin, where it passes anterior to the left renal vein and the abdominal aorta. The procedure begins with extensive Kocherization of the duodenum and firm lateral retraction of the pancreatic head towards the left. The dissection starts with the incision of the perivascular connective tissue around the SMA, which is then carried out in a caudal direction, following the SMA posterior to the pancreatic head until it crosses the duodenum.

During this approach, the attachments between the SMA and the uncinate process of the pancreas are carefully separated to expose the lateral boundary between the portal vein (PV) and the superior mesenteric vein. The dissection also allows for the identification and ligation of the superior and inferior pancreaticoduodenal artery as they enter the pancreatic head and uncinate process [6]. Although division of the jejunum is not always necessary in this approach, it can facilitate better exposure of the SMA when required (Figs. 1-5).

RESULTS:

There were no significant difference between the two groups according to age, sex, CA19-9, history of chronic illness, preoperative laboratory assessment, preoperative staging, and one case in each group had neoadjuvant therapy. The following table shows the different in tra-operative parameters in both groups.

The following Tables 1–3 show different intra-operative parameters, hospital stay and the different postoperative complications in the two groups while Table 4 describes the pathological staging and number of lymph nodes retrieved.

Table 1: Different intra-operative parameters.

Variables	**Total (*n*=32)**	**Artery first (*n*=15)**	**Conventional (*n*=17)**	**Test of significance**	***P***
Operative time (h)					
Min–max	5.0–8.0	5.0–7.0	5.0–8.0	t=0.762	0.452
Mean±SD.	6.36±0.87	6.23±0.78	6.47±0.96		
Median (IQR)	6.50(5.75–7.0)	6.50(5.50–7.0)	6.50(6.0–7.0)		
Blood loss (cc)					
Min–max	400.0–1000.0	400.0–850.0	450.0–1000.0	t=1.018	0.317
Mean±SD	618.8±150.1	590.0±135.2	644.1±161.9		
Median (IQR)	600.0(500.0–700.0)	600.0(500.0–675.0)	600.0(500.0–750.0)		
Intraoperative blood transfusion (RBCs)					
Min–max	1.0–4.0	1.0–4.0	2.0–4.0	U=109.500	0.502
Mean±SD.	2.47±0.92	2.33±0.90	2.59±0.94		
Median (IQR)	2.0(2.0–3.0)	2.0(2.0–2.0)	2.0(2.0–4.0)		
Intraoperative plasma transfusion					
Min–max	4.0–10.0	4.0–8.0	4.0–10.0	U=95.000	0.230
Mean±SD.	5.31±1.49	4.93±1.28	5.65±1.62		
Median (IQR)	6.0(4.0–6.0)	4.0(4.0–6.0)	6.0(4.0–6.0)		
Intraoperative SMA contact, *n* (%)					
Absent	32(100.0)	15 (100.0)	17(100.0)	–	–
Present	0	0	0		
Intraoperative SMV contact, *n* (%)					
Absent	27(84.4%	13(86.7)	14(82.4)	χ^2=0.112	^{FE}P=1.000
Present	5(15.6)	2(13.3)	3(17.6)		

(t): Student t-test; (U): Mann–Whitney test; (FE): Fisher Exact test; (P): Probability Value; (X^2): Chi-square Test.

Table 2: Postoperative ICU, hospital stay, and postoperative leak.

	Total (n=32) *N* (%)	Artery first (n=15) *N* (%)	Conventional (n=17) *N* (%)	Test of significance	*P*
Post-operative complications					
Absent	19(59.4)	8(53.3)	11(64.7)	χ^2=0.427	0.513
Present	13(40.6)	7(46.7)	6(35.3)		
Post-operative ICU admission days					
Min–max	2.0–10.0	2.0–10.0	2.0–6.0	*U*=98.500	0.278
Mean±SD.	3.0±1.83	3.53±2.36	2.53±1.07		
Median (IQR)	2.0(2.0–3.0)	2.0(2.0–4.50)	2.0(2.0–3.0)		
Total days of hospital stay (days)					
Min–max	6.0–15.0	7.0–15.0	6.0–12.0	*U*=102.00	0.350
Mean±SD.	8.44±2.55	9.13±3.20	7.82±1.67		
Median (IQR)	7.0(7.0–9.50)	7.0(7.0–11.0)	7.0(7.0–8.0)		
Postoperative isolated pancreatic leak					
Absent	29(90.6)	13(86.7)	16(94.1)	χ^2=0.521	^{FE}P=0.589
Present	3(9.4)	2(13.3)	1(5.9)		
Isolated biliary leak					
Absent	31(96.9)	14(93.3)	17(100.0)	χ^2=1.170	^{FE}P=0.469
Present	1(3.1)	1(6.7)	0(0.0)		
Isolated leak of gastrojejunostomy					
Absent	32(100.0)	15(100.0)	17(100.0)	–	–
Present	0(0.0)	0(0.0)	0(0.0)		

(*U*): Mann–Whitney test; (FE): Fisher Exact test; (*P*): Probability Value; (X^2): Chi-square Test.

Table 3: Other postoperative complications.

	Total (n=32) *N* (%)	Artery first (n=15) *N* (%)	Conventional (n=17) *N* (%)	χ^2	^{FE}P
Delayed gastric emptying	1(3.1)	1(6.7)	0	1.170	0.469
Use of Erythromycin	1(3.1)	1(6.7)	0	1.170	0.469
Hemorrhage	2(6.3)	1(6.7)	1(5.9)	0.008	1.000
Denovo DM	1(3.1)	0	1(5.9)	0.911	1.000
Diarrhea	2(6.3)	2(13.3)	0	2.418	0.212
Wound infection	4(12.5)	1(6.7)	3(17.6)	0.878	0.603
Incisional hernia	0	0	0	–	–
Renal insufficiency	0	0	0	–	–
DVT	0	0	0	–	–
Ascites	2(6.3)	1(6.7)	1(5.9)	0.008	1.000
Lower limb edema	8(25.0)	3(20.0)	5(29.4)	0.376	0.691

(FE): Fisher Exact test; (*P*): Probability Value; (X^2): Chi-square Test.

Table 4: Pathological staging.

	Total (n=32) *N* (%)	Artery first (n=15) *N* (%)	Conventional (n=17) *N* (%)	Test of significance	*P*
Stage of specimen					
T1	2(6.3)	1(6.7)	1(5.9)	χ^2=2.778	^{MC}P=0.293
T2	11(34.4)	3(20.0)	8(47.1)		
T3	19(59.4)	11(73.3)	8(47.1)		
N0	21(65.6)	12(80.0)	9(52.9)	χ^2=2.773	^{MC}P=0.185

	Total (*n*=32) *N* (%)	Artery first (*n*=15) *N* (%)	Conventional (*n*=17) *N* (%)	Test of significance	*P*
N1	10(31.3)	3(20.0)	7(41.2)		
N2	1(3.1)	0	1(5.9)		
Number of lymph nodes retrieved					
Min–max	1.0–24.0	8.0–24.0	1.0–18.0	*t*=1.126	1.126
Mean±SD.	14.13±4.15	15.0±4.17	13.35±4.09		
Median (IQR)	14.0(12.0–16.50)	14.0(12.50–17.0)	14.0(12.0–16.0)		
Number of lymphnodes retrieved ‘ positive’					
Min–max	0.0–5.0	0.0–5.0	0.0–5.0	*U*=91.500	0.176
Mean±SD	0.91±1.49	0.53±1.36	1.24±1.56		
Median (IQR)	0.0(0.0–2.0)	0	0.0(0.0–2.0)		

Figure 1: The picture is of an Artery first PD showing superior mesenteric artery passing into a tunnel made by the uncinate process of pancreas.

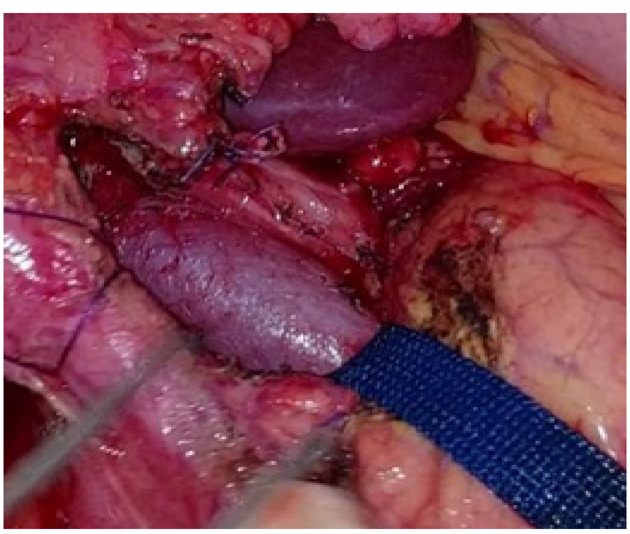

Figure 2: The picture is showing dissected CHA with ligated GDA, dissected CBD, and the upper part of the tunnel made posterior to the neck of pancreas.

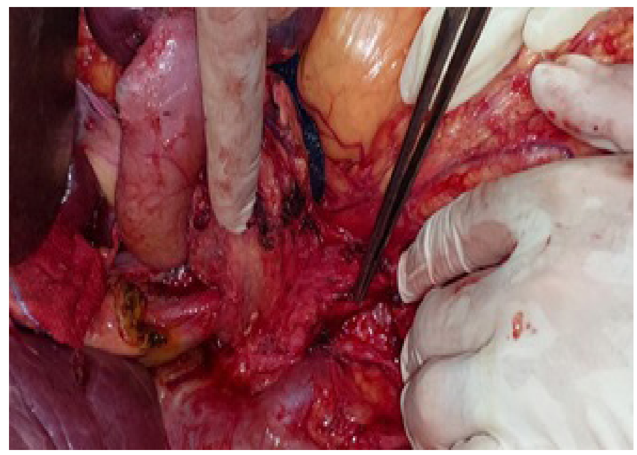

Figure 3: A picture of an Artery first PD showing dissected superior mesenteric artery from the uncinate process along its course from Aorta until it gives the middle colic artery while preserving the neck of pancreas making the procedure a reversible one.

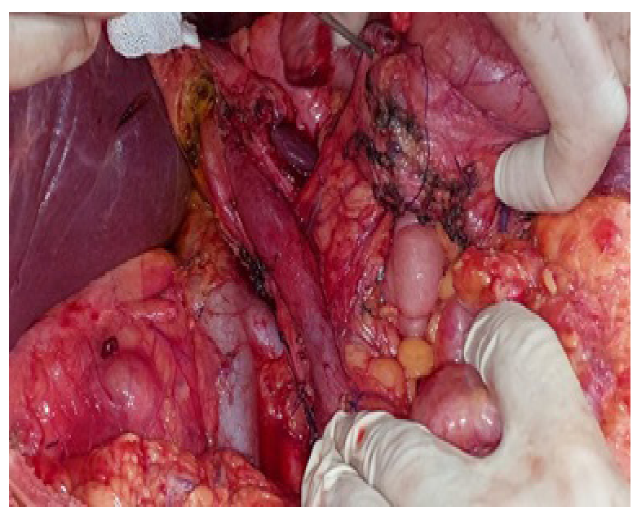

Figure 4: A picture of an Artery first PD showing continuation of dissection from the adventitia of superior mesenteric artery along portal vein till we reached the tunnel made posterior to the neck of pancreas while neck of pancreas is still intact.

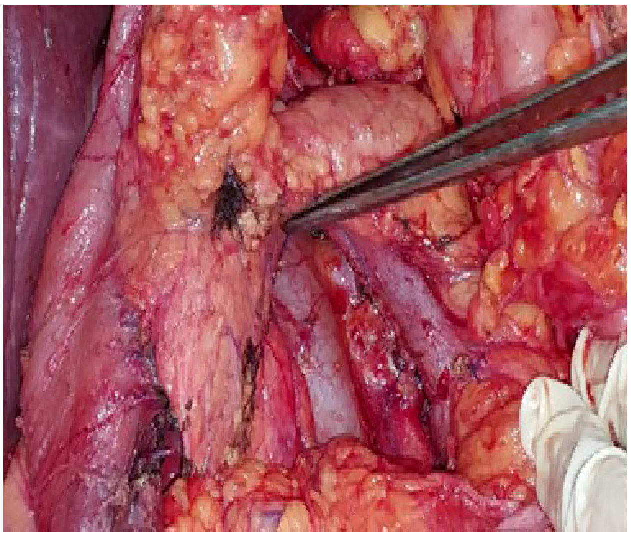

Figure 5: A picture of an artery first PD showing completely separated head (with the mass), uncinate process and neck of pancreas from superior mesenteric artery, superior mesenteric vein, and portal vein with preservation of the first jejunal branch.

DISCUSSION

This study was conducted on 32 patients: 15 in the AFAPD group and 17 in the conventional PD group, focusing on pancreatic head cancer as the primary pathological diagnosis. In terms of sample size, Aimoto *et al*., conducted a study on 38 patients, with 19 in each arm, utilizing the left posterior approach, while Dumitrascu et al. included 21 cases in each group, of which 11 were pancreatic head cancer patients, using the posterior approach [11].

In our study, the mean length of hospital stay was 9.13±3.20 days for the AFAPD group and 7.82±1.67 days for the conventional PD group, with a similar median of 7 days for both groups, showing no significant difference between them (*P*=0.350).

Similar findings were reported by other authors, who observed shorter hospital stays in patients treated with the mesenteric approach [12]. Another study found the mean hospital stay to be 19.57 days (±12.89) in the posterior approach PD group and 19.90 days (±12.87) in the conventional PD group, with no significant difference in postoperative hospitalization time between the two groups (*P*=0.9336, NS) [13].

In some studies, the operative time was longer in the mesenteric group compared with the conventional group, which was attributed to the learning curve associated with the AFA [12]. However, others found that the mean operative time was shorter in the posterior approach PD group compared with the conventional PD group [13]. In our study, the mean operative time was slightly shorter in the AFAPD group (6.23±0.78h) than in the conventional PD group (6.47±0.96h), with a median of 6.5h for both groups, but the difference was not statistically significant (*P*=0.452).

Regarding intraoperative blood loss, several studies have demonstrated reduced blood loss and lower transfusion requirements with the AFA, with reported ranges between 700 and 1,500ml [13]. A meta-analysis found that SMA-first PD was associated with significantly less intraoperative blood loss, with a mean difference of 345.3ml (*P*<0.01), and fewer blood transfusions (*P*<0.01) [11]. In our study, the mean blood loss was lower in the AFAPD group (590.0±135.2ml) compared with the conventional PD group (644.1±161.9ml), with a similar median of 600ml for both groups, but this difference was not statistically significant (*P*=0.317).

According to reports, AFA-PD has a 93% R0 resection rate, while standard PD has a 60% rate [11]. According to other research, the retroperitoneal margin is involved in 80% of cases, with overall R1 resection rates of 35% [14]. R0 resection rates were 67.9% for AFA-PD and 77.3% for traditional PD, according to another study. R0 rates for conventional PD and AFA-PD in patients with pancreatic cancer (*n*=87) were 57.9% and 58.8%, respectively. The posterior circumferential margin was most frequently impacted, with 88% in conventional PD and 56% in AFA-PD (*P*=0.069) in 17(22.7%) patients undergoing conventional PD and 25(32.1%) patients undergoing AFA-PD [11]. There was no discernible difference in the R0 resection rate between the two groups in our trial, which was 100%.

A meta-analysis reported that the number of lymph nodes resected did not significantly differ between SMA-PD and conventional PD groups (*P*>0.05) [8]. In our series, the median number of lymph nodes harvested was comparable: 14.0(12.50–17.0) for the AFAPD group and 14.0(12.0–16.0) for the conventional PD group (*P*=1.126). The rate of superior mesenteric vein or PV resections was higher in the SMA-PD group in previous studies (*P*=0.02) [11]. In our study, four patients underwent lateral wall resection and reconstruction of the PV, and one patient had vascular resection with a saphenous vein graft, with similar rates between the two groups: two (13.3%) patients in the AFAPD group versus three (17.6%) patients in the conventional PD group (*P*=1.00).

Studies on postoperative morbidity found no significant differences in the following: pancreatic fistula, hemorrhage, delayed gastric emptying, biliary leak, severity of complications, reoperation, readmission, or postoperative hospital stay. Overall morbidity rates were 73.3% in the conventional PD group and 67.9% in the AFA-PD group (*P*=0.484). Compared with 8% of instances after AFA-PD, diarrhoea was seen in 4% of patients after traditional PD (*P*=0.495). Throughout the series, the 90-day mortality rate was 5.8%; the traditional PD group experienced a mortality rate of 4%, whereas the AFA-PD group experienced a mortality rate of 7.7% (*P*=0.267) [4]. There were no statistically significant variations in the postoperative morbidity and mortality rates between the two groups in our study. In certain studies, postoperative rates of pancreatic fistulas were greater for conventional PD than for posterior approach PD (42.85 vs. 23.80%); nevertheless, this difference was not statistically significant (*P*=0.3264) [10]. There was no significant difference (*P*=0.589) between the three pancreatic leak cases we saw in our series: two in the artery-first group (13.3%) and one in the traditional group (5.9%).

Limitations of the study

One of the limitations of this study is that the study does not account for long-term survival data, focusing instead on immediate postoperative outcomes such as blood loss and hospital stay, which may not fully capture the potential oncological benefits of the AFA. The single-institution nature of the study might also limit its generalizability to other settings.

Recommendations

Future studies should aim to include larger, multicenter patient populations to increase the generalizability of the findings and enhance the statistical validity. It would also be beneficial to incorporate long-term oncological outcomes, such as overall survival and disease-free survival, to evaluate the full impact of the AFA on cancer control. Furthermore, exploring the use of more advanced imaging techniques to better assess tumor involvement with surrounding vasculature before surgery could improve patient selection for the AFA, potentially leading to better surgical outcomes.

CONCLUSION

(a) AFAPD is a valuable technique that should be learned and practiced, particularly in cases of borderline resectability and in patients receiving neoadjuvant therapy. It allows for early assessment of arterial involvement, which is critical for determining the feasibility of resection.

(b) AFA-PD provides significant benefits in reducing intraoperative blood loss and the need for blood transfusions, contributing to a reduction in postoperative morbidity and mortality. This technique facilitates better hemostasis by controlling the blood supply early during the procedure.

(c) Computed tomography remains indispensable in the preoperative assessment of resectability, as well as in the evaluation of the vasculature and potential vascular anomalies. It serves as a crucial tool in planning both AFA-PD and conventional PD.

(d) Conventional PD continues to be a reliable option with acceptable outcomes in terms of resectability, blood loss, length of hospital stay, and postoperative morbidity and mortality, making it a viable alternative in appropri ately selected patient s.

CONFLICT OF INTEREST

There are no conflicts of interest.

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