

# Portal-Mesenteric Vein Resection for Borderline / Locally Advanced Pancreatic Cancer: Over 2.5 year survival in patients with good performance status

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## ABSTRACT

**Background:** Pancreatectomy associated with resection of the involved portal-superior mesenteric vein, preceded by neoadjuvant chemotherapy, for locally advanced (LA) and borderline resectable (BR) pancreatic ductal adenocarcinoma (PDAC) is being performed in major pancreas referral centers globally, but its universal adoption faces challenges, notably in Greece. This study explores our center's experience with this particular group of patients.

**Materials and Methods:** Data from 43 consecutive patients undergoing pancreatectomy with superior mesenteric (SMV) and/or portal vein (PV) resection (January 2014 - January 2022) were analysed. Clinicopathologic information, perioperative details, complications, and follow-up through December 2023 were recorded. Statistical analyses employed Stata BE version 18.0.

**Results:** Forty-three patients (28 BR, 15 LA) underwent pancreatectomy with superior mesenteric and/or portal vein resection. Neoadjuvant therapy (NAT) was administered to 60.4%, correlating significantly with smaller tumour size (median: 3 cm vs. 5 cm,  $p = 0.009$ ), but not with overall survival (24 months vs. 26 months,  $p = 0.95$ ). Venous wall infiltration was present in 55.8%, with a significant correlation with NAT administration (40% vs. 82.3%,  $p = 0.006$ ). The extent of resection was substantial, with a median of 27 lymph nodes retrieved, 86% R0 resection rate, and a median length of resected vein segments measuring 3 cm, necessitating interposition grafts in 41.8% of cases. Postoperative mortality was 2.3%, with a median overall survival of 25 months. The two-, three-, and five-year overall survival rates were 51.1%, 31%, and 24.1%, respectively, surpassing established benchmark outcomes. Lower Eastern Cooperative Oncology Group (ECOG) status was significantly associated with longer survival (ECOG-0: 32 months, ECOG-1: 24 months, ECOG-2: 12 months,  $p = 0.018$ ), emphasising its prognostic importance in this context.

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Submission: 15.03.2024, Acceptance: 07.07.2024

**Conclusions:** This series of portomesenteric resection in BR or LA PDAC demonstrated a median survival of two years, extending to 31 months in patients with good performance status, which meet and often exceed established outcome benchmarks.

**Key Words:** *Borderline pancreatic cancer; portal vein resection; mesenteric vein resection; locally advanced pancreatic cancer; pancreaticoduodenectomy; benchmark outcomes*

## INTRODUCTION

Borderline resectable (BR) and locally advanced (LA) pancreatic ductal adenocarcinoma (PDAC) have been generally considered and managed as unresectable in Greece, since their possible resection should also involve resection of the portion of the superior mesenteric/portal vein involved by the tumour. This is probably because such a vascular resection is perceived to be associated with a prohibitive operative risk. However, major vascular resections have been regularly performed in pancreas referral centers over the last 15-20 years. At the same time, current neoadjuvant therapy (NAT) in such patients has increased resection rates with negative margins, as well as overall survival [1,2]. The pessimistic approach described, is especially highlighted in two recent Greek studies where patients with LA disease were grouped together with stage IV disease [3], indicating a palliative, and not curative intent, while in the other, out of 80 consecutive patients with Stage I-III PDAC, only one patient received NAT [4].

In this context, our group started performing portal/mesenteric vein resections in patients with BR/LA PDAC in 2012. Our initial results were promising [5] and were corroborated by our subsequent experience [6]. In this study, we present the complete data on our most recent group of such patients.

## MATERIALS AND METHODS

The study encompassed an analysis of data pertaining to 43 patients who underwent pancreatectomy involving resection of a segment of the superior mesenteric (SMV) and/or portal vein (PV) due to tumour involvement. The data collection was prospective and spanned for eight years (January 2014 to January 2022) and involved patients treated at our division. Solely patients diagnosed with PDAC were included in this retrospective analysis. Pertinent clinicopathologic information, details of the perioperative period, and comprehensive data on complications were meticulously recorded. The follow-up period extended through December 2023, ensuring a comprehensive view of patient outcomes of at least two years. Notably, this study stands as a continuation of our

previously published experience [5,6] and was conducted with the full approval of our Institutional Review Board.

Preoperative clinical staging of all patients was conducted using typical pancreatic protocol computerised tomography. The categorisation of PDAC into BR or LA adhered to the established criteria set forth by the National Comprehensive Cancer Network (NCCN) [7].

During the surgical procedures, a thorough skeletonisation of the PV, SMV, hepatic and celiac artery was undertaken, particularly in patients with pancreatic body tumours. Lymph node (LN) dissection encompassed all standard peripancreatic LN beds. In instances of limited venous involvement, a tangential longitudinal excision of the vein was performed, followed by transverse primary repair. For cases necessitating resection of a circumferential vein segment, the Cattell-Braasch maneuver (right-sided medial visceral rotation) facilitated the approximation of proximal and distal vein segments. This technique allowed for a primary end-to-end anastomosis in cases where the venous gaps were less than 4 cm. However, in instances where the gaps exceeded 4cm, interposition prosthetic polytetrafluoroethylene (PTFE) grafts were utilised. The preference for prosthetic over autologous venous interposition grafts was due to their immediate availability, thereby avoiding additional operative time for native vein retrieval. The established safety and long-term patency of prosthetic grafts in this context have been extensively documented [8–10]. Low molecular weight heparin was initiated the night of surgery, or the first postoperative day and continued for 28 days in all patients. In patients with primary vein reconstruction no further anticoagulation was administered. However, in patients where PTFE was utilised, aspirin was initiated at the third or fourth postoperative day and lifelong administration of daily aspirin was advised. Postoperatively, the patency of all prosthetic grafts was assessed via ultrasonography after a 2-month interval. Patients presenting with tumour involvement at the splenomesenteric venous confluence underwent total pancreatectomy (TP) with splenectomy, as did those with locally extensive disease.

Histopathologic evaluations of the pancreatectomy specimens were conducted in accordance with the stand-

ard guidelines outlined by the College of American Pathologists. The definition of R0 resection included negative margins exceeding 1 mm (<https://documents.cap.org/protocols/cp-pancreas-exocrine-17protocol-4001.pdf>).

Statistical analyses involved the use of Stata BE version 18.0 software. Descriptive statistics were employed for continuous data, presented as median and interquartile range (IQR). Normal distribution tests for numerical data were applied where applicable. Comparison of continuous variables between groups was performed using the Wilcoxon Mann-Whitney U-test. Categorical data were expressed as frequencies and percentages, and their comparison among groups predominantly involved Fisher's Exact test. The duration of follow-up was calculated using the reverse Kaplan-Meier method. Survival analysis, commencing from the time of diagnosis for all patients (including those subjected to neoadjuvant therapy), considered the time to death or last follow-up. Kaplan-Meier survival curves were generated, and differences in overall survival (OS) between groups were assessed using the log-rank test. Multivariate survival analyses were conducted using the backward conditional Cox regression method, with the proportional hazards assumption validated through graphical assessment of Kaplan-Meier curves. A significance level of  $p < 0.05$ , employing two-tailed tests, was deemed statistically significant for all analyses.

## RESULTS

### Demographic and perioperative data

Throughout the study period, a cohort comprising forty-three patients (28 categorised as BR and 15 as LA) underwent pancreatectomy with resection involving segments of the superior mesenteric (SMV) and/or portal vein (PV). Detailed clinicopathologic characteristics of these patients are presented in Table 1. Notably, the most prevalent procedure was total pancreatectomy (TP), accounting for 53.4% of cases. TP was performed in 11 patients diagnosed with neck tumours, in three with large body tumours extending towards the neck, and in five individuals with sizable head tumours infiltrating and extending beyond the neck. Additionally, 4 patients with uncinate tumours underwent TP due to their anterior extension involving the splenomesenteric venous junction. Nine patients with uncinate tumours and three with head tumours underwent a Whipple operation (30.2%). The remaining seven patients with body tumours underwent distal pancreatectomy (16.2%). Post-venous resection, the reconstruction of SMV-PV was executed through various methods: transverse lateral venorrhaphy in eight patients (18.6%), primary end-to-end anastomosis in 17 patients

(39.5%), and interposition polytetrafluoroethylene (PTFE) grafts in 18 patients (41.8%) (Table 1).

In our hospital records, the duration of the operation is documented not from "skin-to-skin" time but from the patients' entry into the operating room until exit from it. Consequently, the median operation time was recorded at 570 minutes (IQR: 475–675), equivalent to 9.5 hours (IQR: 7.9–11.25). Sixteen patients (37.3%) required no blood transfusions, whereas 27 (62.7%), received at least one unit of packed red blood cells (PRBCs), with a median of 2 units (IQR: 0–3).

Post-surgery, adjuvant chemotherapy (Gemcitabine alone) was administered to 15 out of 42 discharged patients (35.7%). The remaining 27 patients (64.2%) did not receive chemotherapy; among these, 18 had undergone neoadjuvant therapy (NAT), while the remaining nine were deemed medically unfit for chemotherapy.

### Neoadjuvant Chemotherapy

No patient received chemoradiation in this study. Among the cohort, 26 patients (60.4%) underwent NAT, with 10 receiving Gemcitabine/nab-paclitaxel, 14 undergoing FOLFIRINOX, and 1 patient receiving a combination of both regimens. Notably, 9 individuals (34.6%) received treatment elsewhere, involving 4 patients on Gemcitabine/nab-paclitaxel, 4 on FOLFIRINOX, and 1 receiving both regimens, although the specifics of their NAT regimen could not be thoroughly delineated. The remaining 17 patients (65.3%) underwent NAT within our institution, encompassing 7 on Gemcitabine/nab-paclitaxel and 10 on FOLFIRINOX, completing a median of 6 cycles (ranging from 2 to 12 cycles, IQR: 4–6 cycles). The decision to proceed with surgical intervention in patients having undergone NAT relied on either the completion of the 6-month protocol, or cessation due to their inability to continue, provided there was a concurrent decrease in CA 19–9 levels and no disease progression according to CT criteria.

Seventeen patients did not undergo NAT, or did not complete the full NAT protocol and they were categorised as undergoing pancreatectomy without prior NAT. This subgroup was comprised of some who were initially considered "upfront resectable" (and thus not considered for NAT preoperatively), but exhibited venous invasion intraoperatively, or had received disparate and inadequate chemotherapeutic regimens elsewhere, or declined appropriate NAT, or were reevaluated to have resectable disease based on CT and CA 19–9 criteria after prior self-referral.

The administration of NAT demonstrated significant association with smaller tumour size (median: 3 cm vs. 5 cm,  $p = 0.009$ ) and appeared to also have strong correlation

**TABLE 1.** Clinicopathologic characteristics of 43 patients who underwent pancreatectomy with PV/SMV resection for BR/LA PC.

		n (%)
Gender	Male	24 (55.8)
	Female	19 (44.2)
Age, years [median (IQR)]		65 (57-70)
ECOG	0	19 (44.2)
	1	14 (32.5)
	2	10 (23.3)
Location	Body	10 (23.3)
	Head	8 (18.6)
	Neck	12 (27.9)
	Uncinate	13 (30.2)
Neoadjuvant Chemotherapy	No	17 (39.5)
	Yes	26 (60.4)
Operation	Total Pancreatectomy	23 (53.4)
	Whipple	13 (30.2)
	Distal Pancreatectomy	7 (16.2)
Venous Reconstruction Type	Primary	17 (39.5)
	PTFE	18 (41.8)
	Lateral Venorrhography	8 (18.6)
Length resected, cm [median (IQR)]		3 (2-4)
ICU stay	No	33 (76.7)
	Yes	10 (23.2)
ICU stay, days [median (IQR)]		0 (0-0)
Transfused pRBC units [median (IQR)]		2 (0-3)
Postoperative hospital LoS, days [median (IQR)]		9 (7-14)
Adjuvant Chemotherapy	No	27 (64.2)
	Yes	15 (35.7)
Tumour size, cm [median (IQR)]		3.2 (2.5-4.2)
T	T1	8 (18.6)
	T2	15 (34.8)
	T3	18 (41.8)
	T4	2 (4.6)
N	N0	7 (16.2)
	N1	30 (69.7)
	N2	6 (14)
Resection	R0	37 (86)
	R1	6 (14)
	R2	0 (0)
Total LNs [median (IQR)]		27 (18-35)
Positive LNs [median (IQR)]		2 (1-5)
LN ratio, % [median (IQR)]		8 (4-20)
Vein Infiltration	No	19 (44.2)
	Yes	24 (55.8)
Complications	No	31 (72)
	Yes	12 (28)
Reoperation	No	38 (88.3)
	Yes	5 (11.4)

ICU: intensive care unit, LOS: length of stay, LN: lymph node.

with less frequent vein wall infiltration (40% vs. 82.3%,  $p = 0.006$ ). However, this correlation did not extend to the number of resected, or positive lymph nodes, lymph node ratio, type or length of vascular resection, Eastern Cooperative Oncology Group (ECOG) status, or overall survival rates (NAT vs. no NAT; 24 months vs. 26 months,  $p = 0.95$ ).

### Pathological Findings

The median size of tumours identified in this study was determined to be 3.2 cm (IQR: 2.5–4.2). Among the cohort, 17 individuals exhibited tumours smaller than 3 cm, with 13 of these patients (76.4%) having received NAT. The median count of harvested lymph nodes (LNs) was 27 (IQR: 18–35), with a median of two positive LNs (IQR: 1–5), yielding a median LN ratio of 8% (IQR: 4%–20%). Histological examination revealed that the resected veins displayed infiltration in the majority of patients (24 patients, 55.8%), while in the remaining 19 (44.2%), the vessel wall displayed dense adherence to cancer cells without evident infiltration. Intriguingly, among these 19 patients, 15 (78.9%) had undergone NAT. Notably, the occurrence of vein wall infiltration appeared to be less frequent in patients following NAT administration (40% vs. 82.3%,  $p = 0.006$ ). However, this observation did not exhibit a significant correlation with Eastern Cooperative Oncology Group (ECOG) status or tumour size.

Resection margins were identified as R0 in 37 patients (86%) and R1 in six patients (14%). Among those with R1 resections, three patients (or 6.9% of all patients) displayed positive (less than 1 mm) margins involving the portomesenteric vein.

### Morbidity and Mortality

The assessment of prosthetic graft patency during the two-month postoperative ultrasound revealed an excellent outcome, exhibiting 100% patency among the patients who underwent this assessment. However, within this group, one patient (6%) who received a polytetrafluoroethylene (PTFE) graft experienced an episode of upper gastrointestinal bleeding 19 months after surgery, necessitating hospital admission and blood transfusion. Subsequent imaging via CT scan unveiled graft occlusion, alongside dilated mesenteric veins and collaterals in the liver hilum. Although the patient did not encounter recurrent hemorrhage, her health deteriorated due to disease progression, resulting in her demise five months later. Among the remaining 17 patients who received PTFE grafts, no cases of infection, thrombosis, or anastomotic breakdown were reported.

Overall, 12 patients (27.9%) encountered at least one

major complication, classified as Clavien-Dindo grade  $\geq 3A$ . These complications included hemorrhage (one patient, or 2.5%), wound dehiscence (three cases), grade B pancreatic fistula (two out of 18 patients undergoing Whipple or distal pancreatectomy, accounting for 11%), bile leak (three cases), transverse colon necrosis (one case), gastric staple line leak (one case), delayed gastric emptying (two cases), and hepatic artery spasm leading to intrahepatic cholestasis and subsequent liver failure (one case).

Reoperation was required for five patients (11.6%), with one additional patient (2.3%) undergoing a major intervention. Notably, individuals who experienced postoperative hemorrhage, wound dehiscence, gastric leak, and colon necrosis underwent reoperation and displayed favourable recovery. However, the patient encountering hepatic artery spasm underwent an emergent hepatic artery stenting, unfortunately succumbing 30 days after the operation (mortality rate of 2.3%) due to rapidly progressing intrahepatic cholestasis and liver failure. Within the cohort of 42 discharged patients, 14 (32.5%) necessitated hospital readmission within a year following the operation.

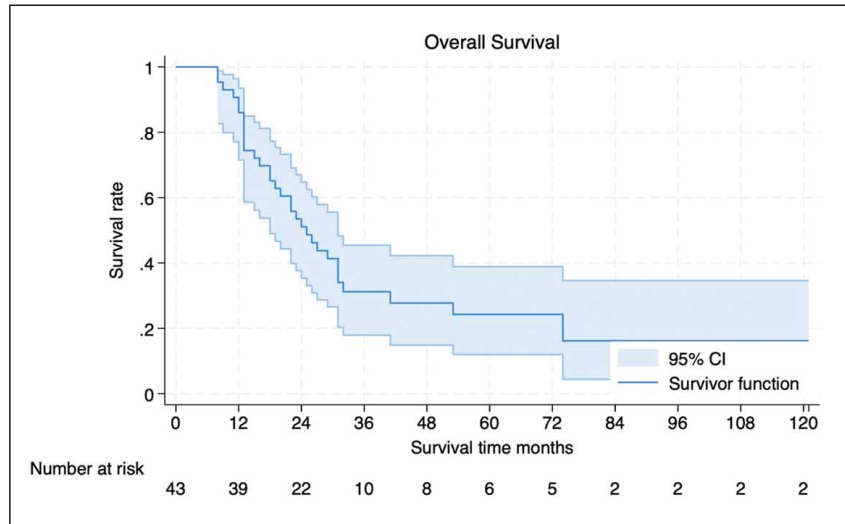
### Survival

The median duration of follow-up in this study spanned 25 months (IQR: 13–34). Among the 42 patients who were discharged, one succumbed to complications associated with COVID-19, not related to pancreatic cancer, while 24 patients passed away due to metastatic disease, with 80% attributed to liver metastases and the remaining 20% to peritoneal carcinomatosis. The observed one-, two-, three-, and five-year overall survival (OS) rates stood at 86%, 51.1%, 31%, and 24.1%, respectively. The median OS from the time of diagnosis was determined to be 25 months (Figure 1).

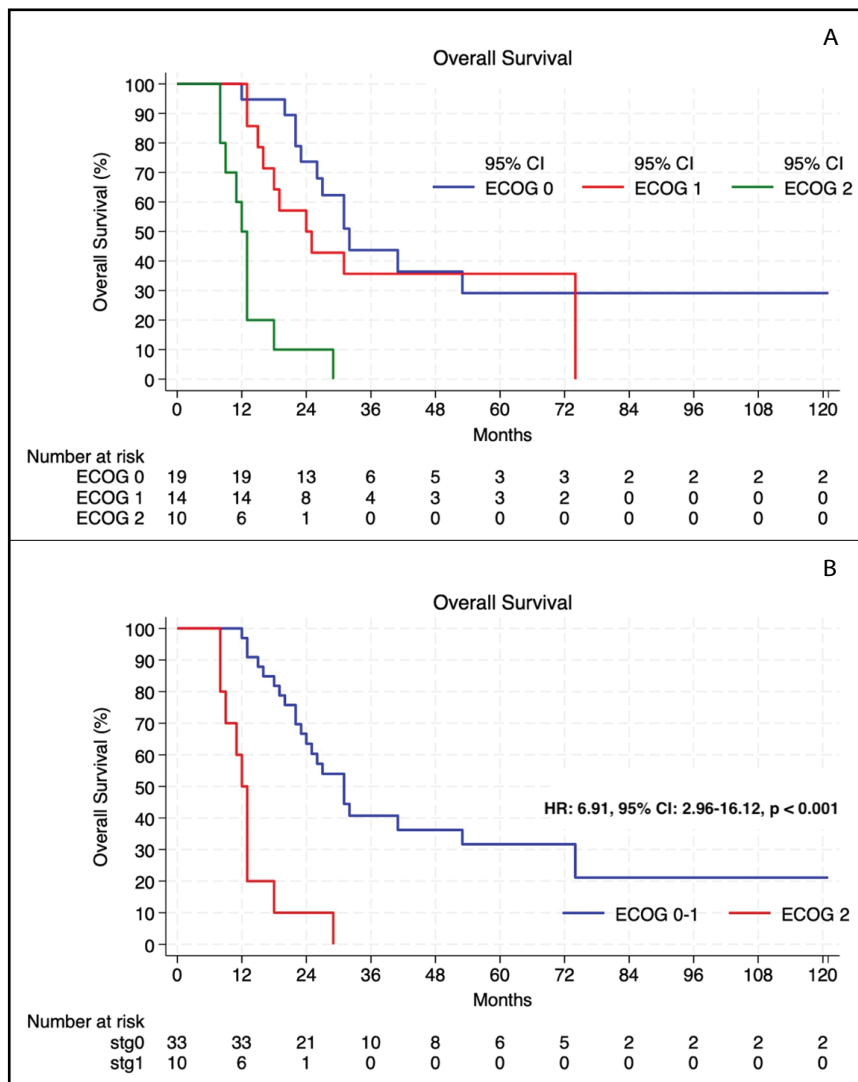
Upon univariate analysis, a significant association emerged between a higher Eastern Cooperative Oncology Group (ECOG) status and reduced survival rates (median OS [IQR]: ECOG-0: 32 months [23–53], ECOG-1: 24 months [16–48], ECOG-2: 12 months [9–15],  $p=0.018$ ) (Figure 2A). Furthermore, patients collectively categorised as ECOG-0 and ECOG-1, exhibited significantly improved survival compared to those in the ECOG-2 category, with median OS rates of 31 months [21–47] versus 12 months [9–15], respectively ( $p < 0.01$ ) (Figure 2B).

### DISCUSSION

The integration of NAT alongside superior mesenteric vein (SMV) and/or portal vein (PV) resection has marked a pivotal advancement in treating BR or LA PDAC. Several



**FIGURE 1.** Kaplan-Meier overall survival curve of 43 patients who underwent pancreatectomy with PV/SMV resection for BR/LA PC. Overall survival calculated since diagnosis.



**FIGURE 2.** (A) Kaplan Meier overall survival curves of 43 patients who underwent pancreatectomy with PV/SMV resection for BR/LA PC, by ECOG-0/1/2 category. (B) Kaplan-Meier overall survival curves of 43 patients who underwent pancreatectomy with PV/SMV resection for BR/LA PC, by ECOG-0 or -1 vs. ECOG-2 category. Overall survival calculated since diagnosis.

studies indicate that post-NAT, a notable 20%–60% of individuals diagnosed with LA disease have undergone resection, resulting in extended survival [11-15]. This approach aligns with the established guidelines of the International Study Group of Pancreatic Surgery (ISGPS) [16]. Notably, recent trends indicate an increasing adoption of more aggressive surgical procedures, including PV/SMV resection, contributing significantly to improved outcomes [13,17-22]. Pancreas referral centers have reported acceptable mortality rates (ranging between 3% and 5%) associated with this approach, showcasing survival rates comparable to pancreatectomy without vein involvement [12,17-19]. Benchmark outcomes have been established for pancreatoduodenectomy with portomesenteric vein resection by an international consortium of experts [23].

Despite these advancements, a sense of pessimism persists in Greece, where the majority of BR/LA PDAC patients are directed toward palliative chemotherapy as the solitary treatment option. It was within this context that our initiatives in vascular resection commenced in 2012. Initially, our efforts yielded promising outcomes, albeit involving a diverse patient cohort. In an unselected group with limited NAT administration, patients classified as ECOG-0 exhibited a median survival period of 33 months [5]. Subsequently, through the standardisation of patient selection criteria and refined surgical techniques, this report outlines our experiences with the most recent 43 patients diagnosed with BR/LA PC, undergoing significant vein resection from 2014 to 2022.

Within this cohort, the growing acceptance of NAT correlated with observed trends, such as smaller tumour sizes and reduced occurrences of vein wall infiltration. The scope of oncologic resections conducted was notably extensive, with the retrieval of 27 LNs, achieving an R0 rate of 86%. Noteworthy was the resection of lengthy vein segments, averaging 3 cm, with nearly half necessitating interposition grafts. The utilization of polytetrafluoroethylene (PTFE) grafts did not significantly elevate long-term morbidity rates. The postoperative mortality stood at 2.3%, while the median OS reached 25 months. These outcomes, while promising, were achieved without a universally uniform application of NAT.

It is essential to highlight that our study encompassed not only Whipple procedures, but also included total pancreatectomies (for highly extensive tumours) and only a limited number of distal pancreatectomies. Seven of our patients with body tumours required segmental PV/SMV resection and yet only a distal, but not total pancreatectomy, which may seem unusual. However, these seven patients had tumours extending to and involving the splenomesenteric venous junction, but did not extend

*beyond* that level to the right side. Thus, we were able to dissect the neck of the pancreas off of the SMV/PV at the level of 10 o'clock of the vein's circumference (having ligated and transected the gastroduodenal artery first, so we could create free space), then transected the pancreas at the level of the head (rather than the neck), at which point it became evident that the left side of the PV/SMV was involved in the tumour. We then excised the involved part of the vein and reconstructed it, with no need to go further to the right to remove the head as well. In cases of body tumours extending well beyond the neck towards the head, where we were not able to safely dissect off the pancreas from the SMV/PV, we proceeded with total pancreatectomy, which also explains the frequency (53%) of total pancreatectomies in our series.

Notably, our achieved outcomes either met or surpassed the recently established benchmarks for pancreatoduodenectomy involving PV/SMV resection [23]. This observation holds true across various benchmarked parameters encompassing hospital and ICU stays, significant postoperative complications, mortality rates, PV occlusion incidents, and OS outcomes (Table 2).

The extent of LN dissection has been standardised for a Whipple operation [24,25]. Typically, fifteen LNs are considered oncologically sufficient, with recommendations of 20 LNs for patients without prior chemotherapy exposure [22,25]. In our specimen analyses, the median retrieval of 27 LNs was achieved, ensuring extensive clearance of peripancreatic tissue, thereby favourably comparing to the LN retrieval at most other pancreatic centers [23].

The thoroughness of our resection procedures is evident in our achieved 86% R0 resection rate, aligning with the 55%–96% reported "negative microscopic margin" rates by other studies [11,26–28]. It is noteworthy that these referenced studies encompassed patients who all underwent NAT, in contrast to our cohort where only 58% received NAT. Moreover, some of these studies considered margins <1mm also as negative (R0), contributing to the reported rates. A significant portion of our patients, slightly over half, necessitated total pancreatectomy (TP) due to the extent of their tumours and the limited anatomic "downsizing". In the contemporary landscape of more extensive pancreatic surgery, TP has indeed become a more prevalent choice [29].

The absence of NAT in a considerable number of our patients, coupled with the presence of larger tumour sizes, likely contributed to the necessity for longer segments of SMV and/or PV resection. As a result, 41.8% of our patients required an interposition graft. In contrast, experiences at the Mayo Clinic [30] and Heidelberg [22] showed a lower incidence, with only 16% and 18% of patients respectively

**TABLE 2.** Comparison of our results with the benchmark outcome for pancreatoduodenectomy and PV/SMV resection. (Our “Operation duration” includes the total time of patients’ presence in the OR; not “skin-to-skin” time).

	Benchmark Cutoffs	Our Experience
Operation Duration	≤ 8h	(9.5h)
Intraop. Blood transfusion rate	≤ 27%	63%
ICU stay	≤ 1 day	0 days
Hospital stay	≤ 14 day	9 days
<b>Complications</b>		
Clavien – Dindo ≥3A	≤ 28%	27.9%
POPF – B/C	≤ 14%	10%
Postop Bleeding grade ≥ 3	≤ 7%	2.3%
In – Hospital Mortality	≤ 4%	2.3%
1-year Hospital readmission rate	≤ 32%	32.5%
Portal vein occlusion	≤ 4%	2.3%
<b>Resection Margins</b>		
R0	≥ 35%	86%
R1	≤ 63%	14%
R2	≤ 2%	0%
(+) PV margins	≤ 3%	4.6%
Total number of LNs resected	≥ 16	27
<b>Overall Survival Rate</b>		
1-year	≥ 68%	86%
2-year	≥ 37%	51%
3-year	≥ 21%	31%
5-year	≥ 9%	24%

having resected vein segments long enough to warrant a graft. Other reports have cited interposition graft usage in 33%–45% of patients [8,31]. The safety, effectiveness, and sustained patency of PTFE grafts have been extensively investigated and substantiated in existing literature (8-10). Our positive experience with PTFE application in cases involving significant venous gaps undoubtedly aligns with published findings.

Histological analysis revealed vein wall infiltration in 55.8% of cases within our group, mirroring the experiences of others, which reported rates between 51% and 93% [8,21,22,32]. Notably, among our cohort, patients naïve to NAT were more prone (p=0.006) to exhibit histological

vein infiltration upon resection (82.3% vs. 40%). Due to the known lack of consistent correlation between radiographic, operative, and pathologic findings following NAT [14,21,27,33], our strategy has pivoted toward proceeding with attempted resection, especially when significant decreases in CA 19–9 tumour markers are evident, despite the tumour appearing radiographically “stable” [26].

The median OS for patients undergoing upfront surgery without NAT ranged between 15 and 23 months [32,34]. Following the administration of NAT, this figure extended to a median of two years [28,35]. The consensus among experts strongly emphasizes NAT as an indispensable prerequisite in BR, or LA PDAC before contemplating resection [16]. Notably, in esteemed centers and within highly selective patient cohorts, median survival periods have now surpassed three years [12,15,27,36].

Our reported median OS of 25 months (32 months for patients classified as ECOG-0) stands favourably in comparison to existing literature, given that only 60.4% of our cohort received NAT. The lack of a universal and consistent application of NAT within our group might have contributed to its inability to significantly enhance survival outcomes. Furthermore, an Eastern Cooperative Oncology Group (ECOG) performance status of ≥2 has been acknowledged as a negative prognostic factor post-pancreatectomy [37]. Indeed, our findings align with this observation, as patients categorised as ECOG-2 exhibited significantly shorter survival (12 months) compared to those with ECOG-0 (32 months), ECOG-1 (24 months), or the combined ECOG-0 and ECOG-1 groups (31 months). Effective prehabilitation strategies may potentially improve ECOG status and contribute to prolonged postoperative survival [38].

Acknowledging several limitations within our study is imperative. The variation in patient numbers and the heterogeneity in prior receipt of NAT precluded a meaningful comparison of survival outcomes between patients who underwent NAT and those who did not (24 months vs. 26 months, p = 0.9). It is our firm conviction that all individuals diagnosed with LA/BR PDAC should undergo NAT before being considered for pancreatectomy. Extensive evidence from prospective studies with substantial patient cohorts robustly supports this assertion.

## CONCLUSIONS

Our recent experience involving pancreatectomy alongside portal vein (PV) and/or superior mesenteric vein (SMV) resection for BR or LA PDAC comprised a patient cohort, a substantial proportion of whom did not undergo NAT. These individuals underwent extensive dissections, circumvented ICU admission, necessitated minimal blood transfusions, and exhibited a mortality rate



of 2.3%, alongside a median OS of 25 months, extending to 32 months among patients categorised as ECOG-0. Our observed outcomes are in line with, or surpass outcomes reported by other institutions, often exceeding established outcome benchmarks.

While acknowledging the need for a more widespread application of NAT, improved patient selection criteria, and prehabilitation strategies for patients classified as ECOG-1/2, these results underscore the realistic potential for prolonged survival in individuals diagnosed with BR/LA PC following extensive resections. These findings should encourage a larger proportion of patients with BR/LA PC to undergo contemporary neoadjuvant protocols, with the primary aim of achieving a curative resection and further enhancing survival.

**Declarations of interest:** *None.*

**Funding:** *No funding was received for this work.*

**Data Statement:** *The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.*

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