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ORIGINAL ARTICLE

Extended left pancreatectomy: Postoperative and short-term oncologic outcomes: A prospective study (Spandispan project)

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Highlight box:

Key findings

- Extended left pancreatectomy represented 13.4% of left pancreatectomies and increased operative complexity (less minimally invasive surgery, longer operative time, higher blood loss).
- Despite comparable major morbidity and clinically relevant POPF rates, in-hospital mortality and failure-to-rescue were significantly higher after ELP, and the textbook outcome was lower with a longer length of stay.
- Early recurrence was more frequent after extended resections and was independently associated, in exploratory analysis, with surgical conversion and resection of additional organs other than the spleen; whether these predictors reflect tumor biology or unmeasured preoperative understaging could not be determined with the available data.

What is known and what is new?

- Known*:* Extended pancreatic resections may improve local clearance in selected patients but are often associated with greater surgical burden, and their oncologic benefit in left-sided resections remains uncertain.
- New*:* In a prospective multicenter Spanish cohort, ELP did not significantly increase major complications or POPF grade B/C but was linked to higher in-hospital mortality and lower textbook outcome. Early recurrence was independently predicted, in exploratory

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analysis, by surgical conversion and multiorgan resection; the absence of preoperative CA 19-9, neoadjuvant therapy, and NET grading data precludes determining whether these predictors reflect tumor biology, unrecognized preoperative understaging, or technical factors. Lymph node burden, although significant on univariate analysis, did not retain independence in the multivariate model.

What is the implication, and what should change now?

1. Extended left pancreatectomy can be considered feasible and safe in experienced centers, but patient selection and systemic disease control remain critical.
2. Patients undergoing extended resections should be recognized as high-risk for early recurrence; intensified multidisciplinary planning, nutritional/exocrine optimization, and timely systemic therapy pathways may be warranted.

Introduction

Pancreatic cancer (PC) is the fourth-leading cause of cancer-related death in the United States, with an incidence that increases by 1.03% per year of life.[1] It is projected to become the second-leading cause of cancer-related mortality by 2030.[2] PC remains one of the most lethal malignancies worldwide, with an overall 5-year survival rate of approximately 8%.[3] The most common histological subtype is pancreatic ductal adenocarcinoma, arising from the exocrine glands of the pancreas. Other tumor types may also occur, including pancreatic neuroendocrine tumors.[4]

Left pancreatectomy (LP) is defined as resection of the pancreas to the left of the splenoportal axis and is the standard surgical procedure for benign and malignant diseases involving the body and tail of the pancreas.[5] Although technically less complex than pancreaticoduodenectomy (PD), LP is not risk-free, with reported mortality rates ranging from 1% to 4% and morbidity rates between 30% and 50%.[6] While PC most commonly arises in the head of the pancreas,[1] tumors in the body and tail are associated with higher mortality, largely due to a more advanced stage at diagnosis.[7]

Surgical resection with negative margins remains the cornerstone of curative treatment for PC. However, only approximately 15% of patients are diagnosed with resectable disease and are candidates for potentially curative surgery.[8] In selected cases, achieving negative margins requires *en bloc* resection of adjacent organs; such procedures have been referred to as extended pancreatectomies since the work of Fortner et al. in 1977.[9]

In 2014, the International Study Group for Pancreatic Surgery (ISGPS) established a consensus definition of extended left pancreatectomy as a standard pancreatic resection combined with the removal of adjacent organs or structures involved in the disease.[10]

Extended resections have traditionally been described more often in the context of pancreaticoduodenectomy for PC located in the pancreatic head, given the head's proximity to major vascular and visceral structures. In contrast, the role and frequency of extended resections in LP (ELP) for tumors of the body and tail have been less consistently reported, and the available evidence remains limited and heterogeneous.[10]

Given the potential increase in morbidity associated with these procedures and the lack of robust prospective evidence supporting their oncologic benefit in the setting of LP, it is reasonable to question whether surgical extension confers a meaningful clinical advantage.

The aim of this prospective multicenter study was to evaluate the incidence of extended left pancreatectomy (ELP) and to compare perioperative outcomes and early oncologic recurrence between extended and standard left pancreatectomy.

Methods

A prospective, multicenter, observational snapshot study of LP was conducted at Spanish Hepato-pancreato-biliary (HPB) surgical units over a one-year period (1 February 2022 to 28 February 2023). The study was distributed via email to the 70 centers that had previously participated in the AEC/IHPBA Pancreatic Surgery Survey.[11] HPB units were also defined as high-volume if they performed more than 10 LP per year.[12] Each participating center appointed a local manager to oversee data and liaise with the overall study coordinator. Data were collected by the local managers at each hospital. A REDCap® (Research Electronic Data Capture, Vanderbilt University, Nashville, Tennessee, USA) database was created to conduct the study. The study is reported according to the STROBE guidelines.[13]

The inclusion criteria were LP for both benign and malignant lesions during the described period, and patients aged 18 years or older. Emergent LP, LP plus celiac trunk resections, and LP following pancreaticoduodenectomy were excluded.

Ethics

The study was conducted in accordance with the Declaration of Helsinki (2013) and approved by the institutional ethics committee of the Hospital General Universitario Dr. Balmis (Alicante, Spain) (CEIm: 28 April 2021, Acta 2021-04). The patients' informed consent was acquired previously. All data were collected anonymously, without patient identifiers. Participating centers were instructed to link patients' local medical record numbers to a pseudonymized study patient ID. All actions were logged in accordance with Good Clinical Practice guidelines.

Variables and definitions

The most notable variables studied were demographic data: age, gender, Body Mass Index (BMI), past abdominal surgeries, medications, and ASA score[14]; symptoms; biological, radiological, and surgical data: approach type (open/laparoscopy/robotic), conversion (defined as starting minimally invasive—MI - but undergoing laparotomy to end the procedure), clarifying that conversion in this study refers exclusively to intraoperative conversion from a minimally invasive approach to open laparotomy and is unrelated to oncologic conversion surgery, spleen preservation if the Warshaw or Kimura technique was performed, intraoperative blood loss and transfusion); and postoperative data. Morbidity and mortality complications were assessed at 90 days using the Clavien-Dindo classification, and those defined as Clavien-Dindo grade III or higher were considered major complications.[15] Data were prospectively collected and recorded using electronic medical and nursing records for each patient.

For complications specific to pancreatic surgery, we used the definitions from the International Study Group on Pancreatic Surgery (ISGPS) for delayed gastric emptying,[16] postpancreatic hemorrhage,[17] and postoperative pancreatic fistula (POPF).[18]

The resection margins of the specimen were categorized according to the Royal College of Pathologists' definitions: R0 (margin to the tumor $\geq$1 mm), R1 (margin to the tumor $<$1 mm), and R2 (macroscopically positive margin).[19] We staged invasive tumors according to the TNM classification (8th ed.).[20] Reoperation was defined as any unscheduled surgical intervention related to pancreatic resection. Hospital stays and readmissions were measured at 90 days. Tumor size on imaging refers to the maximum diameter measured on preoperative contrast-enhanced computed tomography (CT), used as the primary staging modality; magnetic resonance imaging (MRI) was used when CT was not performed or for complementary assessment. Histological data recorded included tumor size, R status, and resected pancreas size.

ELP was defined according to the criteria established by the ISGPS and published by Hartwig et al.[10] as a standard LP combined with resection of one or more of the following organs or

structures: any type of gastric resection; colon or major vascular structures of the transverse mesocolon (middle or left colic vessels); small intestine; portal vein, superior mesenteric vein, or inferior mesenteric vein; inferior vena cava; left adrenal gland; left kidney or its vascular structures; diaphragm; liver; arterial resections were not included because they were an exclusion criterion and are a well-known factor affecting outcomes.

Early recurrence was defined as recurrence within 90 days after surgery to identify extremely aggressive tumor biology and early systemic dissemination. Postoperative surveillance was not standardized across centers. Recurrence within 90 days was identified based on each center's institutional follow-up practice, which may have included scheduled cross-sectional imaging, tumor marker assessment, or clinically indicated imaging.

Statistical analysis

Descriptive statistics were calculated using frequencies and percentages for categorical data and medians and interquartile ranges (IQR) for continuous data. Differences between groups in quantitative variables were analyzed using the nonparametric Mann-Whitney U test, and differences in percentages or frequencies were analyzed using Pearson's Chi-square test or Fisher's exact test. A P-value < 0.05 was considered statistically significant.

Continuous variables were tested for normality using the Shapiro–Wilk test and missing data were handled by complete-case analysis.

Variables listed in Table 2 were analyzed as potential predictors of early disease recurrence using logistic regression. Variables that were statistically significant ($P \leq 0.05$) in the previous univariate analysis were entered into a multiple logistic regression analysis using backward stepwise selection. Logistic regression results are reported as odds ratios (ORs) and 95% confidence intervals (95% CI).

Note on denominators: conversion is, by definition, an event that can only occur in patients in whom a minimally invasive approach was attempted; it is not an applicable event for patients whose operation began open. Conversion rates and its regression coefficients are therefore expressed as a proportion of, and estimated within, the population who attempted a minimally invasive approach throughout this manuscript: 217/313 in the full cohort (Table 1) and 142/207 in the malignant histology subgroup (Tables 3-4). The multivariable model in Table 5 is further restricted to the 130 of these 142 patients with complete data on the number of positive lymph nodes. All other variables in Tables 3-5 are analyzed in the full malignant histology subgroup (n = 207, or n = 192 for positive lymph nodes owing to missing data). These sample sizes are now stated explicitly beneath each table.

Analyses were conducted using SPSS® for Mac, version 26.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Of the 313 patients from 41 centers who underwent left pancreatectomy, 42 (13.4%) were classified as extended left pancreatectomy (ELP), while 271 (86.6%) underwent standard left pancreatectomy (SLP). The characteristics of both groups are summarized in Table 1.

No statistically significant differences were observed between groups with respect to age, sex, BMI, ASA classification, comorbidities, or Charlson Comorbidity Index. However, tumor size on imaging was significantly greater in the ELP group (median 38 vs 27 mm; $P = 0.020$). Preoperative imaging in the ELP cohort (n = 37) included contrast-enhanced CT in 34 patients (91.9%), MRI in 16 (43.2%), and endoscopic ultrasound (EUS) in 18 (48.6%). The staging workup was not formally standardized across the 41 participating centers, which is an inherent feature of the real-world multicenter snapshot design.

Regarding intraoperative parameters, patients in the ELP group had a significantly lower rate of minimally invasive approach (42.9% vs 73.4%; $P < 0.001$), longer operative time (median

Table 1
Comparison between standard left pancreatectomy and extended left pancreatectomy.

Variable	SLP 271 (86.6%) n (%) / median (IQR)	ELP 42 (13.4%) n (%) / median (IQR)	*P-value*
Age	66 (55-75)	63 (55-71)	0.355
Sex (M/F)	129(47.6%) / 142(52.4%)	17(40.5%) / 25(59.5%)	0.389
BMI	27.55 (23.63-30.69)	27.2 (25.48-30.69)	0.29
ASA Classification			0.77
I	16 (5.9%)	1 (2.4%)	
II	128 (47.2%)	21 (50%)	
III	122 (45%)	19 (45.2%)	
IV	5 (1.8%)	1 (2.4%)	
Comorbidities	206 (76%)	31 (73.8%)	0.756
Charlson Comorbidity Index	4 (2-5)	4 (3-5)	0.135
Tumor size on imaging (mm)**	27 (16-40)	38 (23-50)	**0.020**
Minimally invasive approach	199 (73.4%)	18 (42.9%)	**<0.001**
Conversion*	22 (11.1%)	1 (5.6%)	0.701
Spleen preservation	40 (14.8%)	2 (4.8%)	0.077
Surgery time (min)	240 (180-288)	270 (215-325)	**0.012**
Blood loss (mL)	100 (50-250)	200 (100-350)	**0.014**
Intraoperative transfusion	16 (5.9%)	4 (9.5%)	0.324
Number of drains	1 (1-1)	1 (1-2)	**0.002**
Postoperative somatostatin use	88 (32.5%)	11 (26.2%)	0.415
Postoperative complications	155 (57.2%)	26 (61.9%)	0.565
Clavien-Dindo ≥ III	55 (20.3%)	11 (26.2%)	0.383
CCI	8.7 (0-20.9)	8.7 (0-26.2)	0.346
Pancreatic fistula	106 (39.1%)	14 (33.3%)	0.473
Grade B-C fistula	55 (20.3%)	8 (19%)	0.851
Delayed gastric emptying	9 (3.3%)	0 (0%)	0.614
Postpancreatectomy hemorrhage	17 (6.3%)	0 (0%)	0.142
Postpancreatectomy hemorrhage Grade C	3 (1.1%)	0 (0%)	1
Reintervention	22 (8.1%)	3 (7.1%)	1
Radiologic reintervention	4 (1.5%)	1 (2.4%)	0.516
Endoscopic reintervention	4 (1.5%)	1 (2.4%)	0.516
Surgical reintervention	19 (7%)	3 (7.1%)	1
ICU readmission	13 (4.8%)	4 (9.5%)	0.261
In-hospital mortality	1 (0.4%)	2 (4.8%)	**0.048**
Length of hospital stay (days)	7 (5-9)	8 (6-11)	**0.031**
Readmission	56 (20.7%)	13 (31%)	0.135
Histology (grouped)			**0.028**
Neuroendocrine tumor	89 (32.8%)	9 (21.4%)	
Adenocarcinoma	65 (24%)	19 (45.2%)	
IPMN + MCN	56 (20.7%)	5 (11.9%)	
Others	61 (22.5%)	9 (21.4%)	
Malignant histology	170 (62.7%)	37 (88.1%)	**0.001**
Resection margin			0.505
R0	251 (92.6%)	37 (88.1%)	
R1	19 (7.0%)	5 (11.9%)	
R2	1 (0.4%)	0 (0%)	
Number of lymph nodes retrieved	7 (3-14)	13 (6-22)	**0.001**
Number of positive lymph nodes	0 (0-0)	0 (0-2)	**<0.001**
Postoperative Diabetes Mellitus			0.354
No diabetes	192 (70.8%)	28 (66.7%)	
Worsening	42 (15.5%)	10 (23.8%)	
New onset	37 (13.7%)	4 (9.5%)	
Postoperative exocrine insufficiency	59 (21.8%)	9 (21.4%)	0.96
Recurrence	14 (5.2%)	11 (26.2%)	**<0.001**
Local recurrence	0 (0%)	4 (9.5%)	<0.001
Disease-free at 3 months	265 (97.8%)	35 (83.3%)	**<0.001**
Textbook outcome	158 (58.3%)	16 (38.1%)	**0.014**
FTR	1 (0.4%)	2 (4.8%)	**0.048**
High-volume center (≥10 cases/year)	128 (47.2%)	18 (42.9%)	0.597

* Conversion rate in Table 1 is expressed as a proportion of patients who underwent a minimally invasive approach. In Tables 3-5 (malignant histology subgroup), conversion is expressed as a proportion of the total subgroup regardless of initial surgical approach, as it was analyzed as an independent predictor variable.

** Tumor size measured on preoperative contrast-enhanced CT; MRI used when CT unavailable or as complementary assessment.

270 vs 240 minutes; $P = 0.012$), and greater intraoperative blood loss (median 200 vs 100 mL; $P = 0.014$). These differences did not translate into a significant increase in intraoperative transfusion rates between the two groups. The number of drains used was significantly higher in the ELP group ($P = 0.002$). In the ELP cohort (n = 37), the distribution of resected organs and structures beyond the pancreas was as follows (multiple possible per patient): spleen in 36 (97.3%), left adrenal gland in 13 (35.1%), stomach (partial) in 10 (27.0%), colon (partial) in 5 (13.5%), left kidney in 4 (10.8%), and small bowel in 2 (5.4%).

Analysis of postoperative complications revealed no statistically significant differences in overall complication rates (61.9% vs 57.2%; $P = 0.565$) or major complications (Clavien–Dindo $\geq$ IIIa: 26.2% vs 20.3%; $P = 0.383$). No significant differences were found in the incidence of clinically relevant postoperative pancreatic fistula (grade B/C: 19% vs 20.3%; $P = 0.851$), delayed gastric emptying (0% vs 3.3%; $P = 0.614$), postpancreatectomy haemorrhage (0% vs 6.3%; $P = 0.142$), or reintervention rates (7.1% vs 8.1%; $P = 1$). ICU readmission was numerically higher in the ELP group (9.5% vs 4.8%) without reaching statistical significance ($P = 0.261$); however, in-hospital mortality was significantly higher in the ELP group (4.8% vs 0.4%; $P = 0.048$), based on 2 deaths in the ELP group versus 1 in the SLP group. Length of hospital stay was significantly longer in ELP patients (median 8 vs 7 days; $P = 0.031$), and textbook outcome was achieved in a significantly lower proportion of this group (38.1% vs 58.3%; $P = 0.014$). The failure-to-rescue (FTR) rate was higher in the ELP group (4.8% vs 0.4%; $P = 0.048$). Readmission rates were numerically higher in the ELP group (31% vs 20.7%), although this difference did not reach statistical significance ($P = 0.135$).

From an oncologic perspective, patients in the ELP group more frequently presented with malignant pathology (88.1% vs 62.7%; $P = 0.001$), greater lymph node involvement ($P < 0.001$), and a significantly higher number of resected lymph nodes (median 13 vs 7; $P = 0.001$). Overall and local recurrence rates were significantly higher (26.2% vs 5.2%; $P < 0.001$ and 9.5% vs 0%; $P < 0.001$, respectively), and the 3-month disease-free survival rate was significantly lower (83.3% vs 97.8%; $P < 0.001$).

The oncologic analysis restricted to the subgroup of patients with malignant histology (n = 207; 170 SLP and 37 ELP) is presented in Table 2. The histological composition of the malignant ELP subgroup (n = 37) was as follows: pancreatic ductal adenocarcinoma (PDAC) in 19 patients (51.4%), pancreatic neuroendocrine tumor (NET) in 9 (24.3%), and other malignant neoplasms in 9 (24.3%). In this subgroup, adenocarcinoma was more frequent in the ELP group compared with SLP (51.4% vs 38.2%; $P = 0.003$), along with greater lymph node involvement (N1-N2 stage: 48.5% vs 23.4%; $P = 0.008$) and a higher proportion of metastatic disease (M1: 27.3% vs 5.2%; $P = 0.001$). Among the 9 M1 patients in the ELP cohort, the histological distribution was: PDAC in 5, NET in 3, and other histology in 1. Recurrence was 27% in the ELP group versus 7.6% in the SLP group ($P = 0.002$), local recurrence 10.8% vs 0% ($P = 0.001$), 3-month disease-free survival 83.8% vs 96.5% ($P = 0.009$), and 3-month mortality was significantly higher in the ELP group (16.2% vs 1.8%; $P = 0.001$). A sensitivity analysis restricted to confirmed M0 ELP patients (n = 24) identified 4 early recurrences (16.7%). In the specific PDAC subgroup (n = 19 ELP), early recurrence occurred in 6 patients (31.6%) and in-hospital mortality in 1 (5.3%).

To identify predictors of early recurrence (defined as recurrence within 90 days of surgery) the 207 patients with malignant histology were analysed, of whom 23 (11.1%) developed early recurrence. The comparative descriptive analysis between patients with and without early recurrence (Table 3) showed that patients who recurred had a higher Charlson Comorbidity Index (median 6 vs 4; $P = 0.007$), a lower rate of minimally invasive approach (43.5% vs 71.7%; $P = 0.006$), a higher conversion rate (50% vs 9.8%; $P = 0.003$), greater need for intraoperative transfusion (21.7% vs 4.9%; $P = 0.011$), a higher rate of resection of additional organs other than the spleen (43.5% vs 14.7%; $P = 0.002$), a higher number of positive lymph nodes (median 1 vs 0; $P < 0.001$), and greater use of adjuvant chemotherapy (60.9% vs 36.9%; $P = 0.028$). Postoperative exocrine pancreatic insufficiency showed a trend that did not reach statistical significance (39.1% vs 19.6%; $P = 0.056$).

Variables that were statistically significant in the descriptive analysis were included in the univariate logistic regression (Table 4). Factors significantly associated with early recurrence

Table 2
Oncologic outcomes in the malignant histology subgroup: comparison between standard left pancreatectomy and extended left pancreatectomy.

Variable	SLP (n = 170)	ELP (n = 37)	*P*-value
Histology (grouped)			**0.003**
Neuroendocrine tumor	89 (52.4%)	9 (24.3%)	
Adenocarcinoma	65 (38.2%)	19 (51.4%)	
IPMN + MCN	0 (0%)	0 (0%)	
Others	16 (9.4%)	9 (24.3%)	
T			0.057
1	57 (37%)	8 (24.2%)	
2	59 (38.3%)	9 (27.3%)	
3	31 (20.1%)	13 (39.4%)	
4	7 (4.5%)	3 (9.1%)	
N			**0.008**
0	118 (76.6%)	17 (51.5%)	
1	29 (18.8%)	10 (30.3%)	
2	7 (4.5%)	6 (18.2%)	
M			**0.001**
0	146 (94.8%)	24 (72.7%)	
1	8 (5.2%)	9 (27.3%)	
Resection margin			0.728
R0	151 (86.5%)	32 (88.6%)	
R1	18 (10.6%)	5 (13.5%)	
R2	1 (0.6%)	0 (0%)	
Adjuvant chemotherapy	57 (36.5%)	19 (54.3%)	0.053
Adjuvant radiotherapy	6 (3.9%)	2 (5.7%)	0.645
Deaths	3 (1.8%)	6 (16.2%)	**0.001**
Recurrence	13 (7.6%)	10 (27%)	**0.002**
Local recurrence	0 (0%)	4 (10.8%)	**0.001**
Liver recurrence	7 (4.1%)	3 (8.1%)	0.389
Pulmonary recurrence	5 (2.9%)	1 (2.7%)	1
Peritoneal carcinomatosis	3 (1.8%)	2 (5.4%)	0.218
Disease-free at 3 months	164 (96.5%)	31 (83.8%)	**0.009**
Alive at 3 months	168 (98.8%)	33 (89.2%)	**0.01**
FTR	1 (0.6%)	2 (5.4%)	0.083
Circumferential margin (mm)	2 (1-10)	1 (0.5-10)	0.579
Number of lymph nodes retrieved	8 (3-15)	13 (6-23)	**0.004**
Number of positive lymph nodes	0 (0-0)	0 (0-3)	**0.002**

were: minimally invasive approach (OR: 0.303; 95% CI 0.125-0.734; $P = 0.008$), conversion (OR: 9.154; 95% CI 2.337-35.859; $P = 0.001$), intraoperative transfusion (OR: 5.401; 95% CI: 1.633-17.862; $P = 0.006$), resection of organs other than the spleen (OR: 4.473; 95% CI 1.783-11.224; $P = 0.001$), number of positive lymph nodes (OR: 1.202; 95% CI: 1.033-1.399; $P = 0.017$), and adjuvant chemotherapy (OR: 2.659; 95% CI: 1.088-6.503; $P = 0.032$).

On multivariate analysis (Table 5), only surgical conversion (OR: 12.738; 95% CI 2.580-62.886; $P = 0.020$) and resection of additional organs other than the spleen (OR: 6.415; 95% CI 1.044-39.408; $P = 0.045$) remained as independent predictors of early recurrence.

Discussion

In patients with PC, achieving complete tumor resection with negative margins remains the only realistic hope for long-term survival. As pancreatic resections have become increasingly safe in specialized centers, surgeons have increasingly adopted more ELP in recent years.[21] Therefore, ELP should not be regarded merely as a technical enlargement of the standard resection but rather as the surgical expression of more locally advanced disease that compels the surgeon to go beyond conventional anatomical limits.

Table 3
Comparison of variables associated with early recurrence.

Variable	No Recurrence (184) n (%) / median (IQR)	Recurrence (23) n (%) / median (IQR)	*P-value*
Age	66 (58-75)	68 (63-78)	0.277
BMI	27.76 (23.98-30.85)	26.08 (25.1-28.48)	0.58
Charlson Comorbidity Index	4 (2-6)	6 (3-8)	**0.007**
Minimally invasive approach	132 (71.7%)	10 (43.5%)	**0.006**
Conversion	13 (9.8%)	5 (50%)	**0.003**
Surgery time (min)	240 (180-300)	246 (240-330)	0.082
Blood loss (mL)	150 (50-300)	150 (100-350)	0.12
Intraoperative transfusion	9 (4.9%)	5 (21.7%)	**0.011**
Organ resection (except spleen)	27 (14.7%)	10 (43.5%)	**0.002**
Clavien-Dindo ≥ III	35 (19%)	6 (26.1%)	0.413
CCI	8.7 (0-20.9)	8.7 (0-26.2)	0.49
Grade B-C fistula	41 (22.3%)	5 (21.7%)	0.953
Number of lymph nodes retrieved	8 (3-16)	8 (5-26)	0.237
Number of positive lymph nodes	0 (0-0)	1 (0-3)	**<0.001**
Postoperative exocrine insufficiency	36 (19.6%)	9 (39.1%)	0.056
Adjuvant chemotherapy	62 (36.9%)	14 (60.9%)	**0.028**
High-volume center (≥10 cases/year)	86 (46.7%)	7 (30.4%)	0.138

Note: the "Conversion" row reflects only the 142 patients (of 184 without early recurrence, n = 132; of 23 with early recurrence, n = 10) in whom a minimally invasive approach was attempted, since conversion is not an applicable event for patients started open; all other variables in this table are reported for the full malignant histology subgroup (n = 184 and n = 23, respectively). See note on denominators in methods.

Table 4
Univariate analysis for early recurrence predictors in patients with malignant histology.

Variable	OR (95% CI)	*P-value*
Charlson Comorbidity Index	1.008 (0.967-1.050)	0.708
Minimally invasive approach	0.303 (0.125-0.734)	**0.008**
Conversion	9.154 (2.337-35.859)	**0.001**
Intraoperative transfusion	5.401 (1.633-17.862)	**0.006**
Organ resection (except spleen)	4.473 (1.783-11.224)	**0.001**
Number of positive lymph nodes	1.202 (1.033-1.399)	**0.017**
Adjuvant chemotherapy	2.659 (1.088-6.503)	**0.032**

Note: analyses of conversion in this table were restricted to the 142 patients (of 207 in the malignant histology subgroup) in whom a minimally invasive approach was attempted; all other variables were analyzed in the full malignant histology subgroup (n = 207, or n = 192 for positive lymph nodes owing to missing data). See note on denominators in methods.

In this prospective multicentre series, 42 of 313 left pancreatectomies (13.4%) were ELP, a proportion that falls within the range reported in the literature, where the need for ELP in body and tail tumors ranges from 10% to 25% depending on the oncologic profile and institutional volume.[10,22,23] In contrast, Loos et al. reported a considerably higher rate (35.2%), likely attributable to selection bias at a high-volume center and to the inclusion criteria applied in that registry.[24] The median age in our ELP group was 63 years, with a female predominance (59.5%), findings comparable to those described in the main published series.[10,22,23,24]

From a technical standpoint, our data confirm that ELP is more technically demanding: lower rate of minimally invasive approach (42.9% vs 73.4%), longer operative time (270 vs 240 minutes), and greater blood loss (200 vs 100 mL).[22,23] This pattern is consistent with prior publications highlighting that ELP increases surgical complexity, particularly when vascular or retroperitoneal structures are involved,[10,12,22,23] and that minimally invasive surgery rates typically do not exceed 15% to 20% for these procedures.[22,24]

Table 5
Multivariate analysis of independent predictors of early recurrence in patients with malignant histology.

Variable	OR (95% CI)	*P-value*
Conversion	12.738 (2.580-62.886)	**0.02**
Organ resection (except spleen)	6.415 (1.044-39.408)	**0.045**
Number of positive lymph nodes	1.152 (0.968-1.372)	0.111

Note: this multivariable model was fitted in the 130 patients with complete data for all three variables shown (minimally invasive approach attempted and nonmissing positive lymph node count); it is not fitted in the full malignant histology subgroup (n = 207). See note on denominators in methods.

One of the most relevant findings of our series is that, despite this greater complexity, no significant differences were detected in overall postoperative complication rates or major complications (Clavien–Dindo ≥ IIIa: 26.2% vs 20.3%), nor in the incidence of clinically relevant postoperative pancreatic fistula (grade B/C: 19% vs 20.3%), postpancreatectomy haemorrhage (0% vs 6.3%), or delayed gastric emptying.[22] These data reinforce the feasibility and safety of ELP in experienced centres, in line with findings reported by Petrucciani et al. in their systematic review, where mortality does not increase significantly when surgery is performed in high-volume units.[23]

However, in contrast to the comparable morbidity profile, in-hospital mortality was significantly higher in the ELP group (4.8% vs 0.4%; $P = 0.048$), as was the FTR rate. It must be noted that this difference is supported by only 2 deaths in the ELP group versus 1 in the SLP group; although statistically significant by Fisher's exact test, this finding carries limited statistical robustness and should be interpreted with caution, as a single additional event in either group would substantially alter its significance. The same caveat applies symmetrically to the FTR rate. Nonetheless, the two in-hospital deaths in the ELP group had clearly distinct causes and merit individual description. The first patient had a pancreatic neuroendocrine tumor (pT1N0M0) resected with negative margins and no intraoperative conversion; death occurred from multiorgan failure secondary to respiratory sepsis (Clavien–Dindo grade V), representing a nonpancreatic, nonsurgical-field complication despite a technically successful resection. The second patient had PDAC (pT3N1M1) and underwent R0 resection including splenopancreatectomy, left adrenalectomy, and vascular resection; death occurred from septic shock secondary to a clinically relevant postoperative pancreatic fistula (grade B/C, Clavien–Dindo grade V), illustrating a classic failure-to-rescue scenario in which a manageable complication proved fatal in an M1 patient with already compromised physiological reserve following an extensive resection. These two cases, while numerically limited, reflect two distinct mechanisms by which ELP may narrow the margin for rescue: nonsurgical systemic complications and fistula-driven sepsis in physiologically vulnerable patients.

Loos et al. observed that overall morbidity and severe complications were significantly more frequent with ELP[24]; Hartwig et al. demonstrated that, although overall morbidity after any type of extended resection was higher than after standard procedures, mortality did not increase when complications were managed appropriately.[8] The partial discordance between our series and these reports may be explained in part by the sample size of the ELP group and by the intercenter heterogeneity inherent to multicenter studies. It is equally noteworthy that, despite comparable morbidity, the textbook outcome was significantly lower in ELP (38.1% vs 58.3%; $P = 0.014$), and the length of stay was longer (8 vs 7 days; $P = 0.031$).[25] This reflects that the accumulation of multiple deviations from the ideal postoperative course more frequently results in a globally suboptimal outcome in the ELP group.

From an oncologic perspective, the differences were more pronounced. The ELP group had a higher proportion of malignant tumours (88.1% vs 62.7%), particularly adenocarcinoma, greater lymph node involvement, and a higher number of retrieved lymph nodes (median 13 vs 7). These findings are consistent with the ISGPS definition of extended pancreatectomy: resection of adjacent organs implies contiguous tumour invasion and consequently more locally advanced disease.[10] In the malignant histology subgroup, higher early mortality (16.2% vs 1.8%)

and lower 3-month disease-free survival (83.8% vs 96.5%) likely reflect, at least in part, more advanced underlying disease in the ELP group; however, in the absence of preoperative CA 19-9, neoadjuvant therapy, and NET grading data, a purely biological interpretation cannot be distinguished from an effect of preoperative understaging or of the surgical procedure itself, and this should be regarded as an open question rather than an established finding. Loos et al. similarly observed that extended resections were associated with a higher frequency of malignant pathology and the use of neoadjuvant treatments.[24] In this context, the higher rates of overall and local recurrence in the ELP group may reflect aggressive underlying disease, technical factors related to the extended resection itself, or a combination of both that our data cannot disentangle.

The heterogeneous histological composition of the malignant ELP subgroup warrants specific consideration. In patients with NET, resection of the primary tumor in the presence of synchronous metastases is an accepted oncologic strategy given the frequently indolent biology of well-differentiated NETs.[26] In patients with PDAC resected despite M1 staging, metastatic disease was likely identified intraoperatively rather than on preoperative staging, a scenario recognized in multicenter real-world clinical practice studies. A sensitivity analysis restricted to confirmed M0 ELP patients (n = 24) identified 4 early recurrences (16.7%), with surgical conversion and resection of organs beyond the spleen remaining consistent predictors in terms of effect direction, although the limited number of events precludes formal multivariate analysis in this subgroup. In the specific PDAC subgroup (n = 19 ELP), 5 patients (26.3%) presented M1 disease at the time of surgery, early recurrence occurred in 6 patients (31.6%) and in-hospital mortality in 1 (5.3%), with a pattern of recurrence predictors consistent with the complete malignant subgroup analysis. As a descriptive, PDAC-restricted comparison requested during peer review, early recurrence occurred in 6 of 19 PDAC patients undergoing ELP (31.6%) versus 7 of 65 PDAC patients undergoing SLP (10.8%; Fisher's exact $P = 0.064$); restricted further to confirmed M0 PDAC patients, early recurrence occurred in 3 of 14 ELP patients (21.4%) versus 6 of 63 SLP patients (9.5%; $P = 0.352$). Given the small number of events in both comparisons, they cannot support a PDAC-specific multivariable model and are presented as descriptive, hypothesis-generating observations rather than confirmatory findings. These subgroup analyses should be considered exploratory and require validation in larger prospective series.

In the analysis of predictors of early recurrence in the malignant histology subgroup (n = 207), surgical conversion (OR: 12.738; $P = 0.020$) and resection of additional organs other than the spleen (OR: 6.415; $P = 0.045$) were identified as the only independent predictors on multivariate analysis (Table 5, Fig. 1).

Surgical conversion was associated with the greatest increase in the risk of early recurrence in the exploratory multivariable model (OR: 12.7; Table 5, n = 130). We had considered whether conversion might act as an indirect marker of greater tumor biological aggressiveness rather than a purely technical event. However, we cannot test this interpretation directly: preoperative CA 19-9, neoadjuvant/induction therapy, and detailed NET grading—the variables that would allow a biological interpretation to be distinguished from occult understaging at the time of surgery—were not collected in this prospective database, a design-stage limitation rather than one that emerged from the analysis. A sensitivity analysis restricted to confirmed M0 patients (n = 24, 4 recurrences) could not be formally tested owing to the small number of events, and therefore cannot confirm or refute the biological hypothesis. We have accordingly reframed this finding: conversion and multiorgan resection are strong exploratory correlates of early recurrence in this cohort, but whether they act as markers of tumor biology, of unrecognized preoperative understaging, or of some combination of both cannot be established from the present data. We regard this as an open question for future prospective studies that collect these biomarkers by design, rather than as a conclusion of the present study.

Concordantly, resection of additional organs other than the spleen was independently associated with early recurrence in the same exploratory model (OR: 6.4). This may reflect that the need to extend resection beyond the pancreas and spleen frequently follows direct tumor invasion of neighboring structures; however, as with conversion, we cannot distinguish a biological interpretation from confounding by unmeasured preoperative disease extent, and this finding

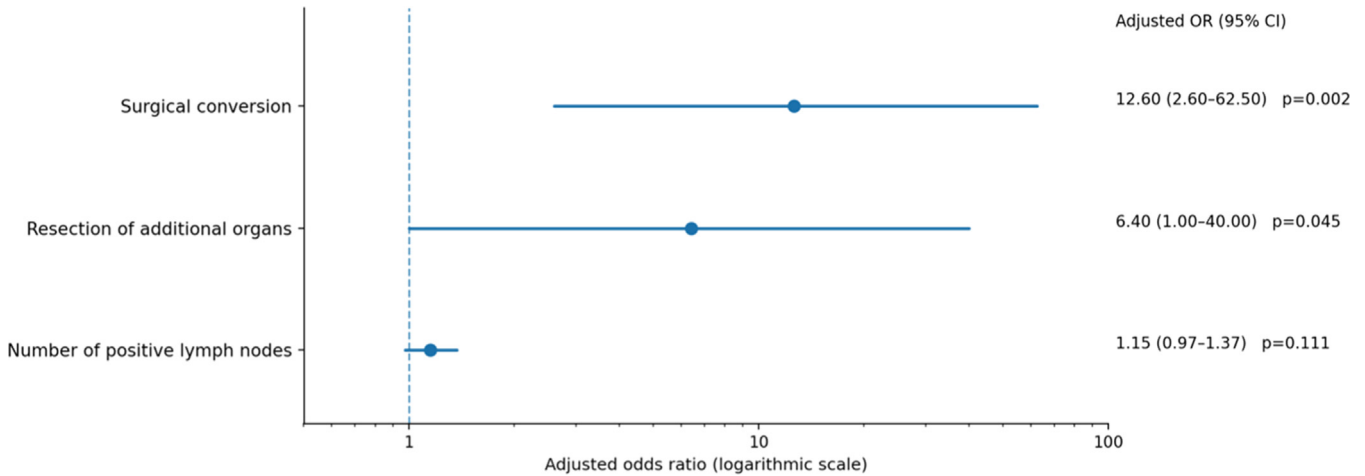


Fig. 1. Forest plot of multivariate analysis. Standard left pancreatectomy (SLP); Extended left pancreatectomy (ELP); CCI, comprehensive complication index; IPMN + MCN, intraductal papillary mucinous neoplasm + mucinous cystic neoplasm; FTR, failure to rescue.

should likewise be considered hypothesis-generating rather than a demonstrated marker of tumor biology.

Although the number of positive lymph nodes showed a significant association in univariate analysis (OR: 1.202; $P = 0.017$), this variable did not remain statistically independent in multivariate analysis (OR: 1.152; $P = 0.111$). This behaviour may be explained by the potential influence of other tumour-extension-related variables included in the model, as well as by the limited statistical power derived from the low number of events. Nevertheless, its trend toward significance retains clinical relevance and is consistent with the literature, which repeatedly identifies lymph node involvement as one of the main determinants of recurrence and survival in pancreatic adenocarcinoma.[20]

Intraoperative transfusion and adjuvant chemotherapy, although significant on univariate analysis, were not incorporated into the final multivariate model. In the case of adjuvant chemotherapy, its association with early recurrence most likely reflects a confounding-by-indication phenomenon: patients with more advanced tumours and a higher risk of recurrence are precisely those who most frequently receive adjuvant treatment, so this association reflects the patient's risk profile rather than an independent effect of the treatment itself. The same confounding-by-indication reasoning applies to the recurrence differences observed between groups. Patients with more advanced disease (reflected by higher N stage, M1 status, and greater locoregional extension) are precisely those who both underwent ELP and experienced higher recurrence rates. Consequently, the association between ELP and early recurrence should be interpreted as reflecting the patient's underlying oncologic profile rather than as a direct consequence of the extended procedure itself. The exclusion of these variables was based on the need to avoid redundancy among intraoperative variables and to prioritize those with greater clinical relevance and interpretability.

The main strengths of this study are its prospective design, which reduces the risk of information bias and improves data quality, and its combined evaluation of surgical and oncologic variables, which provides a comprehensive view of ELP; however, this strength was not fully realized for the oncologic endpoints specifically, since CA 19-9, neoadjuvant therapy status, and NET grading were not designated for mandatory prospective collection, which limits the interpretability of the recurrence predictors discussed above. The multicenter design enhances the external validity of the results by reflecting diverse real-world therapeutic approaches across participating centers, although this same feature may introduce intercenter heterogeneity. The main limitations of the study are the relatively small sample size of the ELP group ($n = 42$), which may limit statistical power to detect differences in certain outcomes, and the follow-up period limited to 90 days, which is insufficient to adequately assess long-term oncologic outcomes. Furthermore, the expanded limitations of this study include: the absence of preoperative CA 19-9 data, a key marker of tumor biology and a potential confounder of recurrence analyses; the absence of neoadjuvant or induction chemotherapy data, which may affect interpretation of early recurrence in borderline-resectable or locally advanced cases; the absence of detailed NET pathological grading (Ki-67, mitotic count, differentiation); and the nonstandardized postoperative surveillance protocol across centers, which may introduce detection bias in recurrence reporting.

Conclusion

ELP is a technically demanding procedure that, when performed in experienced hepatopancreatobiliary centers, does not significantly increase the rate of major morbidity or clinically relevant postoperative pancreatic fistula compared to standard left pancreatectomy. However, it is associated with significantly higher in-hospital mortality and lower textbook outcome, and these differences (while based on a limited number of events) carry important clinical implications for patient selection and perioperative planning. This perioperative profile constitutes the principal, best-supported finding of this study.

From an oncologic perspective, patients undergoing ELP more frequently presented with adenocarcinoma, greater lymph node involvement, synchronous metastatic disease, and higher rates of early recurrence than patients undergoing SLP. In exploratory multivariable analysis, surgical conversion and resection of organs beyond the spleen were independently associated with early recurrence; however, because preoperative CA 19-9, neoadjuvant/induction therapy, and detailed NET grading were not collected by design, we cannot determine whether these associations reflect underlying tumor biology, unrecognized preoperative understaging, or technical factors related to the extended resection itself. We therefore do not conclude that conversion or multiorgan resection are markers of tumor biology; we present them as exploratory, hypothesis-generating correlates of early recurrence that require confirmation in studies that prospectively collect these biomarkers, ideally with a histology-restricted design given the heterogeneity of this cohort.

In summary, ELP is feasible in selected patients at high-volume centers from a perioperative standpoint, which is the principal conclusion supported by these data. Its oncologic implications remain an open, hypothesis-generating question that requires dedicated prospective studies with standardized staging protocols, systematic biomarker collection (CA 19-9, neoadjuvant treatment status, NET grading), and longer follow-up, ideally restricted to a single predominant histology.

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Reporting checklist

The authors have completed the STROBE reporting checklist.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki (2013) and approved by the institutional ethics committee of the Hospital General Universitario Dr. Balmis (Alicante, Spain) (CEIm: 28 April 2021, Acta 2021-04). The patients' informed consent was acquired previously. All data were collected anonymously, without patient identifiers. Participating centers were instructed to link patients' local medical record numbers to a pseudonymized study patient ID. All actions were logged in accordance with Good Clinical Practice guidelines.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cpsurg.2026.102164.

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