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Recurrence Timing and Survival After Pancreaticoduodenectomy for Pancreatic Ductal Adenocarcinoma: A Retrospective Cohort Study

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Abstract

Background and objective

Recurrence after pancreaticoduodenectomy for pancreatic ductal adenocarcinoma (PDAC) remains frequent; its timing and anatomical distribution depend on ascertainment and follow-up. The objective of this study was to characterize documented recurrence, recurrence-free survival (RFS), and post-recurrence survival (PRS) in a histopathologically confirmed PDAC cohort.

Methods

We retrospectively screened 141 operations at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Peshawar, from April 10, 2019, to March 1, 2025, with available follow-up reviewed through October 31, 2026. After excluding 32 neuroendocrine tumors and 13 other non-PDAC primary tumors, 96 patients were included. Early recurrence was defined as occurring within 12 months. RFS included recurrence or all-cause death; PRS was compared using the log-rank test.

Results

Recurrence was documented in 39/96 (40.6%) patients; 19 cases occurred within 12 months, and 20 occurred later. All 39 patients had a coded anatomical description of the first recurrence, including synchronous multisite disease. Kaplan-Meier RFS was 77.2% at 12 months, 67.3% at 24 months, and 51.2% at 36 months. The difference in PRS between the early- and late-recurrence groups was not statistically significant (log-rank p = 0.494).

Conclusions

Documented recurrence affected approximately two-fifths of patients with confirmed PDAC. The estimated recurrence burden may be affected by loss to follow-up and variations in surveillance; differences in PRS based on recurrence timing were not established.

Categories: Physical Medicine & Rehabilitation, Public Health, Oncology
Keywords: early recurrence, late recurrence, lymph node metastasis, pancreatic ductal adenocarcinoma, pancreaticoduodenectomy, post-recurrence survival, recurrence-free survival, vascular invasion

Introduction

Pancreatic cancer caused approximately 467,000 deaths worldwide in 2022 and was the sixth leading cause of cancer death globally [1]. Pancreatic ductal adenocarcinoma (PDAC) remains associated with frequent relapse after curative-intent surgery. Large series describe the liver and other distant sites as common initial recurrence locations, with differences in recurrence timing and subsequent survival [2-4]. Comparing recurrence frequencies across studies requires caution because of differences in treatment exposure, duration and completeness of follow-up, and surveillance practices [2-4].

Published studies use differing thresholds for early recurrence. A systematic review found that approximately 43.1% of included studies used a six-month cutoff and 52.3% used a 12-month cutoff [5]. We selected 12 months as the primary clinically interpretable threshold and additionally examined a six-month definition in a sensitivity analysis. Randomized trials establish the benefit of adjuvant systemic therapy after resection [6,7] but do not demonstrate the benefit of any particular imaging surveillance schedule.

The primary objective was to estimate the frequency and timing of documented recurrence in patients with pathology-confirmed PDAC after pancreaticoduodenectomy. Secondary objectives were to classify first

recurrence sites, describe patient and pathological characteristics, estimate recurrence-free survival (RFS) and post-recurrence survival (PRS), compare early and late recurrence, and explore nodal and lymphovascular associations with outcomes. As context, the multicenter recurrence literature and South Asian institutional surgical experiences were considered, without treating this single-center study as a population-representative estimate.

Materials And Methods

Study design and cohort

This retrospective observational cohort was assembled from the consecutive pancreaticoduodenectomy registry at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Peshawar, Pakistan. The surgical inclusion period was April 10, 2019, through March 1, 2025. Available outcome records were reviewed through the data cutoff of October 31, 2026; individual follow-up ended at death or the last verified contact, whichever applied. The screened registry comprised 141 unique operations. Thirty-two neuroendocrine tumors (NETs) were excluded on the basis of investigator-confirmed primary histology. The remaining 109 records underwent detailed reassessment of final tumor origin; nine ampullary adenocarcinomas, three duodenal adenocarcinomas, and one gallbladder carcinoma were excluded. All 96 remaining operations were for PDAC. Patient screening and inclusion are shown in Figure *1*. Inclusion was based on pathology, not on survival or recurrence outcome. Operative dates and last-contact dates were retained individually, and the duration of observed follow-up varied across patients. No intraductal papillary mucinous neoplasm (IPMN)-associated invasive carcinomas were included. No patient in the final PDAC cohort received neoadjuvant chemotherapy; four preoperative-treatment fields were corrected to “No” following investigator confirmation. Seven patients underwent portal or superior mesenteric vein resection and remained eligible. Patients who died within 90 postoperative days were not automatically excluded; death without prior recurrence counted toward the composite RFS endpoint.

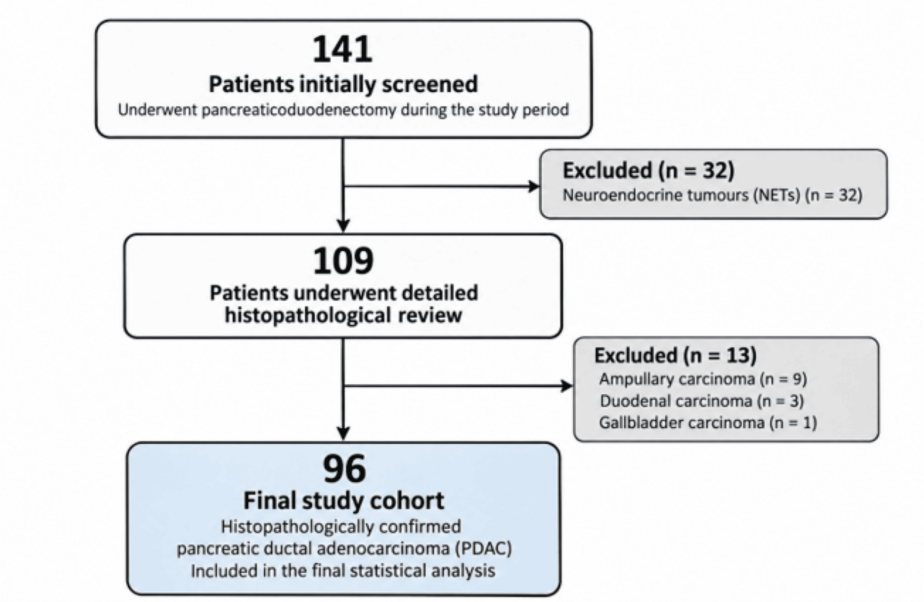


FIGURE 1: STROBE-style screening and pathology-confirmation flow diagram.

NET, neuroendocrine tumor; PDAC, pancreatic ductal adenocarcinoma; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology

[8]

Pathology, staging, surveillance, and event adjudication

Pathological staging followed the eighth edition of the AJCC criteria. A microscopically positive (R1) margin was defined as a tumor within 1 mm of the resection margin. The planned surveillance schedule consisted of cross-sectional imaging at six-month intervals for the first two postoperative years, followed by annual imaging through five years; serum CA19-9 testing and routine clinical reviews were generally scheduled every three to four months. Surgical consultations occurred in person for approximately six weeks after surgery and subsequently by telephone, where feasible; patients undergoing adjuvant treatment also attended medical oncology clinics. Actual adherence and scan completion were not fully captured. First

recurrence was classified using recorded imaging, clinical documentation, and, where available, cytology; malignant ascites was classified as peritoneal metastatic recurrence. Multiple-site disease at first recurrence was not incorrectly classified as isolated local relapse. Final histopathology was used to distinguish PDAC from pancreatobiliary-type ampullary, duodenal, gallbladder, and distal bile duct primaries. Tumor extension into the ampulla did not independently establish ampullary origin. The recorded margin classification was accepted without independent specimen re-inking. CA19-9 was interpreted cautiously given cholestasis and Lewis antigen-related nonsecretion. For patients with prior biliary stenting, available preoperative CA19-9 measurements were obtained after stenting, generally following referral; prestenting CA19-9 measurements were not available. The same 1-mm R1 definition was used throughout the study period.

Outcomes and statistical analysis

Early recurrence was defined as a first documented recurrence at or before 12 months after surgery, with a six-month sensitivity classification. RFS was measured from surgery to the first recurrence or death from any cause, whichever occurred first; event-free patients were censored at the latest verified contact. PRS was measured from first recurrence to death, with censoring at the last known follow-up. Kaplan-Meier curves were generated with confidence bands and numbers at risk. PRS between the early- and late-recurrence groups was compared using a log-rank test; all p-values are exploratory, and no correction for multiple comparisons was applied. For the recurrence-specific endpoint, death before recurrence was treated as a competing event using the cumulative incidence function. A parsimonious Cox proportional hazards analysis of composite RFS was attempted using nodal positivity and lymphovascular invasion and was restricted to complete cases; ties were handled using the Efron approximation. No missing data were imputed. Counts and denominators are stated explicitly. The two-by-two unadjusted exposure associations (if reported) were estimated using Fisher's exact tests rather than represented as regression-derived ORs. Missing-data denominators were retained separately for each analysis. No direct patient-level comparison with Western populations was undertaken. Statistical evidence was interpreted in light of the exploratory number of tests.

Ethics approval

The Institutional Review Board of Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, serves as the central IRB for the Peshawar site and granted an exemption (EX-05-05-26-10) dated June 3, 2026, with a waiver of informed consent for retrospective, de-identified record review.

Results

Cohort and recurrence

Among 141 initially screened surgical records, 32 NETs were excluded. After final primary-site verification of 109 records, 13 non-PDAC cancers were excluded, leaving 96 cases of PDAC. Recurrence was documented in 39/96 patients (40.6%); all 39 patients with recurrence had sufficient timing data for PRS analysis. Of these 39 cases, 19 (48.7%) had a first recurrence within 12 months, and 20 (51.3%) had a first recurrence after 12 months. A total of 19 patients were recorded as deceased in the available dataset. None of the 96 patients received neoadjuvant systemic therapy; seven underwent venous resection. All 32 initial NET exclusions were confirmed by the study investigators. The recorded Clavien-Dindo grades, adjuvant regimens, chemotherapy completion status, tumor stage, differentiation, and biliary drainage status are presented with explicit denominators in Tables *1*, *2*; missing values remain identifiable rather than being imputed.

Variable	Result
Screened operations	141
Initial NET exclusions	32
Detailed pathology review	109
Non-PDAC exclusions	Nine ampullary; three duodenal; one gallbladder
Final confirmed PDAC	96
Documented recurrence	39 (40.6%)
Deaths recorded	19
Early recurrence (≤12 months)	19
Late recurrence (>12 months)	20
Patients with usable RFS chronology	96

TABLE 1: Cohort flow and characteristics (n = 96).

NET, neuroendocrine tumor; PDAC, pancreatic ductal adenocarcinoma; RFS, recurrence-free survival

Characteristic	Category	Patients, n (%)
Postoperative Clavien-Dindo grade	I	64 (66.7%)
Postoperative Clavien-Dindo grade	II	26 (27.1%)
Postoperative Clavien-Dindo grade	III	3 (3.1%)
Postoperative Clavien-Dindo grade	IVB	2 (2.1%)
Postoperative Clavien-Dindo grade	V	1 (1.0%)
Adjuvant regimen	CAPOX (as recorded)	44 (45.8%)
Adjuvant regimen	Gemcitabine-capecitabine	27 (28.1%)
Adjuvant regimen	Not offered/missing	17 (17.7%)
Adjuvant regimen	mFOLFIRINOX	4 (4.2%)
Adjuvant regimen	Gemcitabine	4 (4.2%)
Adjuvant chemotherapy recorded	Yes	76 (79.2%)
Adjuvant chemotherapy recorded	No	19 (19.8%)
Adjuvant chemotherapy recorded	Missing/not applicable	1 (1.0%)
Adjuvant chemotherapy completed	Yes	65 (67.7%)
Adjuvant chemotherapy completed	No	13 (13.5%)
Adjuvant chemotherapy completed	Missing/not applicable	18 (18.8%)
Pathological T category	T3	45 (46.9%)
Pathological T category	T2	42 (43.8%)
Pathological T category	T4	5 (5.2%)
Pathological T category	T1	3 (3.1%)
Pathological T category	T0	1 (1.0%)
AJCC Eighth Edition N stage	N1	38 (39.6%)

AJCC Eighth Edition N stage	N0	33 (34.4%)
AJCC Eighth Edition N stage	N2	25 (26.0%)
Tumor differentiation	Moderately differentiated	62 (64.6%)
Tumor differentiation	Well differentiated	12 (12.5%)
Tumor differentiation	Poorly differentiated	12 (12.5%)
Tumor differentiation	Not specified	5 (5.2%)
Tumor differentiation	Mixed/intermediate differentiation	5 (5.2%)
Biliary stent/drainage	Yes	75 (78.1%)
Biliary stent/drainage	No	20 (20.8%)
Biliary stent/drainage	Missing/not applicable	1 (1.0%)
Portal/SMV vein resection	No	89 (92.7%)
Portal/SMV vein resection	Yes	7 (7.3%)

TABLE 2: Postoperative complications and treatment/pathological variables in the 96-patient PDAC cohort.

Descriptive categories were harmonized from free-text entries (e.g., pT3a and pT3b were grouped under T3); no hypothesis tests were performed. Missing data are reported rather than imputed. CAPOX is retained as recorded in the source file, without asserting guideline concordance.

AJCC, American Joint Committee on Cancer; CAPOX, capecitabine plus oxaliplatin; mFOLFIRINOX, modified fluorouracil, leucovorin, irinotecan, and oxaliplatin; PDAC, pancreatic ductal adenocarcinoma; SMV, superior mesenteric vein

Exploratory adjusted analysis

A complete-case Cox proportional hazards model included 94 patients with nodal and lymphovascular data. Adjusted HRs for the composite recurrence/death endpoint are presented in Table *3*. The small number of events, limited covariates, and possible violation of proportional hazards assumptions limit interpretation; HRs represent associations, not causal effects.

Covariate	Adjusted HR	95% CI	Wald p
Nodal positivity	3.18	1.31-7.72	0.011
Lymphovascular invasion	2.00	1.04-3.84	0.039

TABLE 3: Exploratory Cox proportional hazards model.

Cox proportional hazards regression (Efron method for tied event times); endpoint was recurrence or all-cause death. Complete-case analysis; exploratory, without multiplicity correction.

All 39 patients with recurrence had a first-recurrence description recorded in the source records. After mutually exclusive patient-level categorization, the initial recurrence was liver-only in 17 patients, isolated locoregional in seven, peritoneal-only in six, simultaneous locoregional and distant in three, multiple distant in five, and other distant in one. No first recurrence was recorded as isolated lung-only in the available structured fields. Multiple sites were counted once per patient, not as separate recurrence events (Tables *4*, *5*). Cytology-confirmed malignant ascites was classified as peritoneal metastatic disease.

First recurrence category	Patients, n (%)
Isolated locoregional	7 (17.9%)
Liver only	17 (43.6%)
Peritoneal only	6 (15.4%)
Locoregional and distant	3 (7.7%)
Multiple distant (liver/peritoneum)	1 (2.6%)
Multiple distant (other/unspecified)	4 (10.3%)
Other distant	1 (2.6%)

TABLE 4: First recurrence-site classification.

Patient-level descriptive counts of mutually exclusive first-recurrence patterns (n = 39). Patients with synchronous sites appear once in the appropriate combined category. No statistical hypothesis test is applicable to this descriptive table.

First recurrence category	Early ≤12 months (n = 19)	Late >12 months (n = 20)	Test statistic	p-value
Isolated locoregional	2	5	-	0.407
Liver only	7	10	-	0.523
Peritoneal only	4	2	-	0.407
Locoregional and distant	2	1	-	0.605
Multiple distant (liver/peritoneum)	0	1	-	1.000
Multiple distant (other/unspecified)	3	1	-	0.342
Other distant	1	0	-	0.487

TABLE 5: Early vs late first-recurrence patterns (exploratory comparison).

A two-sided Fisher's exact test was applied to each category vs all other categories; no t, χ^2, or F statistic is provided by this test. No multiplicity adjustment was applied; site-specific p-values are exploratory.

Supplementary unadjusted recurrence associations are presented in Table *6*; these analyses do not account for differences in follow-up duration.

Exposure	Recurrence (n/assessed)	No recurrence (n/assessed)	OR (2 × 2)	Test statistic	Fisher's p
Node positive (N1/N2 vs N0)	33/38	29/57	6.37	-	<0.001
Lymphovascular invasion (Yes vs No)	16/39	10/56	3.2	-	0.019
Adjuvant chemotherapy (Yes vs No)	28/38	48/57	0.53	-	0.295

TABLE 6: Unadjusted recurrence associations (supplementary exploratory analysis).

Counts represent the number of exposed patients among those with nonmissing data in each group. Two-sided Fisher's exact tests were used to calculate p-values; ORs were calculated from 2 × 2 tables (not from logistic regression). Reference categories were N0, no lymphovascular invasion, and no adjuvant chemotherapy. Fisher's exact test does not yield a separate t, χ^2, or F statistic. Missing values were excluded on a variable-by-variable basis. These ORs are descriptive and do not account for time at risk.

Time-to-event outcomes

All 96 patients had usable chronological data for the composite RFS analysis. Kaplan-Meier estimates at 12, 24, and 36 months were 77.2%, 67.3%, and 51.2%, respectively. The median RFS was 40.1 months (Figure 2). A competing-event analysis yielded estimated cumulative incidences of documented recurrence of 20.6%, 29.3%, and 45.4% at 12, 24, and 36 months, respectively. These estimates should not be confused with 1 - RFS because death without recurrence is treated differently. The early- vs late-recurrence PRS curves did not differ significantly (log-rank $\chi^2 = 0.47$, $p = 0.494$; Figure 3); the six-month sensitivity comparison yielded $p = 0.527$.

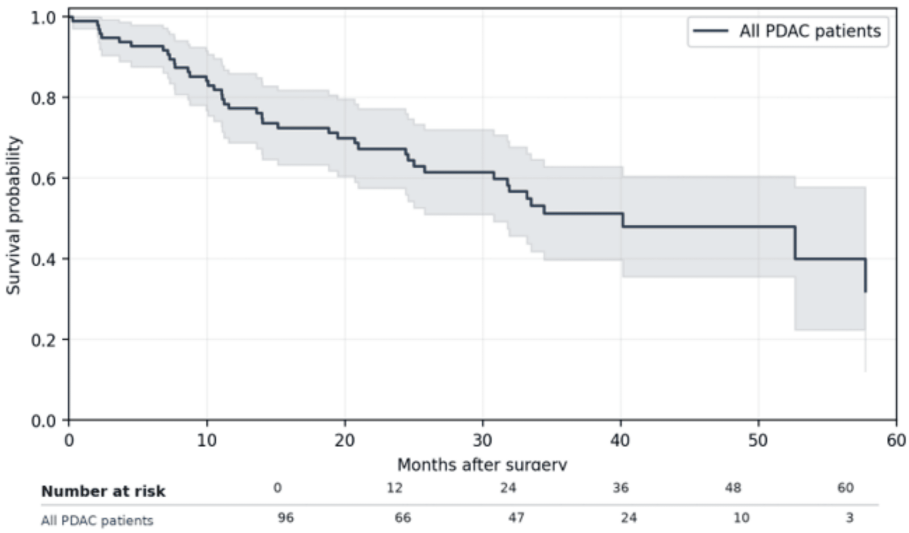


FIGURE 2: Kaplan-Meier RFS (n = 96).

Event: first recurrence or death; 95% confidence bands and numbers at risk are shown.

PDAC, pancreatic ductal adenocarcinoma; RFS, recurrence-free survival

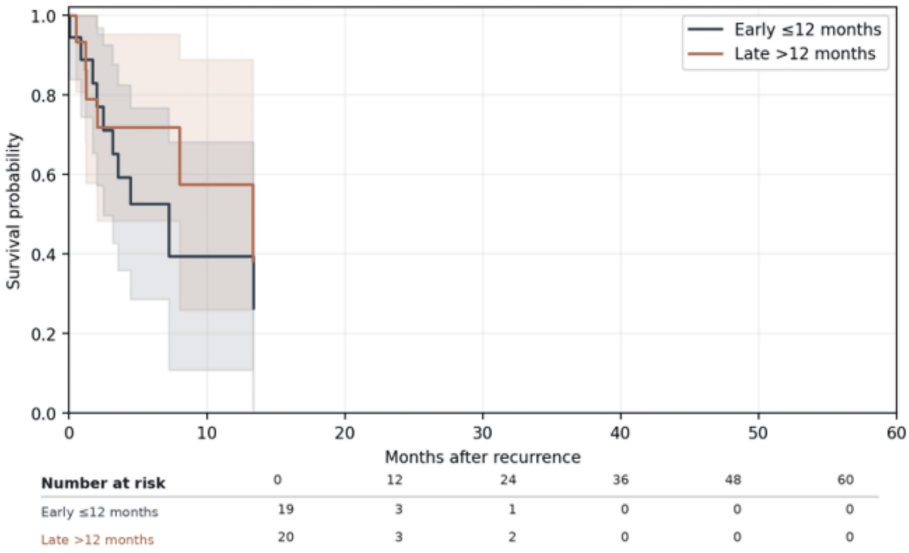


FIGURE 3: Kaplan-Meier PRS by 12-month recurrence threshold.

n = 39. Log-rank $\chi^2 = 0.47$; p = 0.494. Shaded areas indicate approximate 95% confidence bands; numbers at risk are shown.

PRS, post-recurrence survival

Discussion

This analysis excluded neuroendocrine, ampullary, duodenal, and gallbladder primaries and therefore describes a pathology-confirmed PDAC cohort. Recurrence was documented in 39 of 96 patients (40.6%). The anatomical first-event categories now account for all 39 patients, including combined and multisite recurrence, rather than treating unparsed clinical descriptions as missing. In Groot et al., recurrence was observed in 531 of 692 patients (76.7%) at a median follow-up of 25.3 months; direct comparison is limited by follow-up completeness, cohort selection, treatment exposures, and surveillance practices [2]. The lower observed fraction in this cohort should not be interpreted as a lower biological recurrence propensity. In Zhang et al., 530 of 634 patients experienced recurrence within or beyond the 12-month cutoff (83.6%), although that multicenter cohort differs materially in treatment and ascertainment [9]. In the ESPAC-4 secondary analysis by Jones et al., 479 of 730 patients (65.6%) developed recurrence, and the median follow-up from randomization was 43.2 months [10]. Related work also suggests that recurrence phenotype has prognostic implications after pancreatectomy [11]. Differences from the present observed recurrence rate of 40.6% require consideration of selection and differential follow-up rather than attribution to favorable biology.

Previous literature associates nodal involvement, tumor burden, and adjuvant therapy exposure with early recurrence [5]. Our adjusted analyses are necessarily parsimonious and exploratory; the estimates do not justify claims about independent mechanisms, escalation of surveillance, or treatment efficacy. The landmark randomized ESPAC-4 and PRODIGE-24 trials provide the therapeutic evidence base, whereas recurrence-specific observational results mainly inform hypothesis generation [6,7]. This upfront-surgery cohort predates routine institutional use of neoadjuvant chemotherapy for PDAC, whereas current international practice increasingly considers preoperative treatment in selected patients. The seven patients who underwent venous resection were not excluded.

Both six- and 12-month thresholds were assessed because these competing definitions were frequently used in published studies [5]. The late-recurrence subgroup is selected by remaining event-free long enough to enter that category; therefore, simple group-level PRS comparisons cannot establish a causal effect of recurrence timing. In this cohort, the PRS comparison was nonsignificant (p = 0.494). Surveillance scheduling is described for reproducibility, but its effectiveness was not evaluated.

Limitations

Limitations include the retrospective, single-institution design; modest sample size; varying surveillance adherence; possible detection bias; missing clinical covariates; loss to follow-up; and incomplete characterization of post-recurrence treatment. The 12-month recurrence threshold is clinically conventional but not unique; a six-month sensitivity analysis was conducted. Death without documented recurrence was

included in the composite RFS endpoint and treated as a competing event for recurrence-specific cumulative incidence. Analyses were exploratory, and multiple comparisons were not adjusted for; subgroup p-values should not be taken as confirmatory. First-recurrence categories were harmonized from available clinical entries, but detailed imaging or cytology was not independently re-reviewed for each patient. These limitations restrict causal and practice-changing conclusions.

Seventeen patients were explicitly marked as lost to follow-up, and one lacked a usable yes/no loss-to-follow-up designation in the analytic workbook; these fields reflect recorded status and may not capture all incomplete surveillance. Actual prescribed-vs-completed imaging intervals and all post-recurrence regimens could not be independently verified. No patients with IPMN-associated invasive PDAC or neoadjuvant-treated PDAC were included; this limits generalizability to contemporary mixed-treatment surgical populations. Margin positivity may be affected by specimen processing and the 1-mm definition, and the low recorded proportion should be interpreted cautiously. Postoperative mortality was not an exclusion criterion. Full independent verification of the Cox proportional hazards assumptions is not documented in this report; adjusted HRs should therefore be considered exploratory, and model-based inference should be interpreted conservatively.

Conclusions

After exclusion of non-PDAC primaries, documented recurrence occurred in 39 of 96 patients. Recurrence and death formed the composite RFS endpoint, and recurrence-specific cumulative incidence was estimated separately, accounting for death as a competing event. Early-vs-late PRS was not statistically different. Larger, systematically followed, multicenter cohorts are needed before translating these observations into surveillance or treatment recommendations.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Review Board, Shaukat Khanum Memorial Cancer Hospital and Research Centre issued approval EX-05-05-26-10. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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