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Long-term Outcomes and Prognostic Factors in pT1N0 Pancreatic Ductal Adenocarcinoma: A Retrospective Analysis of Real-World Institutional Data

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1. Abstract

1.1. Background

The prognostic significance of neoadjuvant chemotherapy in patients with down staged stage IA (T1N0) pancreatic ductal adenocarcinoma (PDAC) remains unclear.

1.2. Methods

We retrospectively reviewed 31 patients with pathologic T1N0 PDAC who underwent curative-intent resection at a single tertiary center between March 2005 and February 2025. Overall survival (OS) and recurrence-free survival (RFS) were the primary endpoints.

1.3. Results

Median follow-up was 22.6 months. The ypT1N0 group demonstrated higher R0 resection rates (95.1% vs. 87.3%; p = 0.013) and smaller residual tumor size (1.24 cm vs. 1.62 cm; p < 0.001). OS did not differ significantly between ypT1N0 and pT1N0 patients (median not reached vs. 71.6 months; p = 0.077), but RFS was shorter in the ypT1N0 group (33.6 vs. 50.2 months; p = 0.029). On multivariate analysis, NAC was not an independent predictor of OS (HR 1.21; 95% CI 0.78–1.89; p = 0.39) and RFS (HR 1.43; 95% CI 0.95–2.14; p = 0.085).

1.4. Conclusion

In resected stage IA PDAC, NAC group showed no significant difference in survival compared with US group. Further prospective study is needed for validation.

2. Introduction

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, with an overall 5-year survival rate below 10% [1-3]. Late presentation, aggressive tumor biology, and limited effective systemic therapies contribute to poor outcomes. However, tumors ≤2 cm without nodal involvement (T1N0) is associated with markedly better survival, with reported 5-year overall survival rates approaching approximately 70% following curative resection [3,4]. Despite this improvement, recurrence still occurs in a substantial proportion of patients, highlighting the need to refine risk stratification within this “favorable” subgroup.

Neoadjuvant chemotherapy (NAC) has emerged as an important strategy in PDAC management, offering potential benefits of early treatment of micro metastatic disease, improved patient selection, and higher R0 resection rates [5-8]. Several randomized trials, retrospective studies, and meta-analyses have demonstrated that NAC can downstage tumors, increase the likelihood of margin-negative

resection, and in some series improve both disease-free and overall survival compared with upfront surgery [9-13]. On this basis, guidelines increasingly support NAC for borderline and even respectable tumors in selected high-risk patients.

Nonetheless, the prognostic implications of NAC in patients whose final pathology demonstrates T1N0 disease remain poorly defined. [14,15] While NAC may convert a subset of larger or node-positive tumors into T1N0 at the time of surgery, it is unclear whether these down staged cases achieve outcomes equivalent to those presenting de novo as T1N0. Existing reports often group all resected cases together, limiting our ability to distinguish whether NAC-treated T1N0 tumors represent a distinct biological subset with different recurrence patterns or survival trajectories.

In this study, we therefore compared clinicopathologic features and long-term outcomes of patients with T1N0 PDAC treated with upfront surgery versus those down staged to T1N0 by NAC. By focusing exclusively on the T1N0 cohort, we sought to clarify whether neoadjuvant treatment confers equivalent, superior, or inferior prognosis in this early-stage population and to identify factors that may guide personalized treatment strategies.

3. Materials & Methods

This retrospective cohort study was conducted at Severance Hospital, Yonsei University College of Medicine, Seoul, Korea. We reviewed electronic medical records of patients who underwent surgical resection for pancreatic cancer between March 2005 and February 2025. Inclusion criteria were: (1) pathological stage IA PDAC according to the 8th edition of the American Joint Committee on Cancer (AJCC) staging system; [16] (2) curative-intent resection perform upfront or after neoadjuvant chemotherapy, either pancreaticoduodenectomy (PD) or distal pancreatectomy (DP); and (3) complete follow-up da-ta including recurrence and survival outcomes. Exclusion criteria were: (1) had other pathological diagnosis rather than PDAC (2) pathological stages other than stage IA; or (3) Operations other than PD or DP.

Patients' baseline characteristics were collected including operative outcome and pathologic outcome. The baseline characteristics were divided into four group; preoperative outcome, intraoperative outcome, pathologic outcome, and postoperative outcome and were compared between upfront surgery (US) group(pT1N0) and neoadjuvant chemotherapy (NAC) group(ypT1N0). Patients who achieved pathologic stage IA without neoadjuvant chemotherapy were defined as the upfront surgery (US) group, and those whose final pathologic stage was IA after neoadjuvant chemotherapy were defined as the NAC group. The primary outcomes of survival were overall survival (OS) and recurrence-free survival (RFS). Overall survival (OS) was defined as the interval from the date of surgery to death from any cause or last follow-up. Recurrence-free survival (RFS) was de-fined as the interval from the date of surgery to the first documented recurrence or death, whichever occurred first.

Categorical variables were compared via the chi-square test or Fisher's exact test. Continuous variables were expressed as mean or median, depending on the distribution of the data, and were compared using the Student's t-test or Mann–Whitney U test, as ap-propriate. Survival curves were estimated via the Kaplan–Meier method and compared via the log-rank test. Cox proportional hazards regression was used to identify factors associated with RFS and OS, adjusting for potential confounders. Subgroup analyses were per-formed according to surgical approach (PD vs. DP) and chemotherapy status. A p-value < 0.05 was considered statistically significant. All the statistical analyses were performed via Jamovi statistical software (version 2.6.26, The Jamovi project, Sydney, Australia; https://www.jamovi.org).

4. Results

4.1. General Characteristics of the Patients

The patients' characteristics are summarized in Table 1 with comparison between upfront surgery group and neoadjuvant group. Of 1463 resected PDAC patients, 310 had pT1N0 disease (20%). The patient selection algorithm is shown in figure 1. The mean age was 63.2 years, and 154 patients (49.7%) were male. Of the 310 patients, 110 (35.5%) underwent upfront surgery and 200 (64.5%) received chemotherapy prior to surgery. All patients in the NAC group underwent biopsy prior to treatment, whereas 69.1% (76/110) of patients in the US group underwent biopsy. One hundred ninety-three patients (62.3%) had right-sided tumors, and 136 (43.9%) underwent minimally invasive surgery. Twenty-four patients (7.7%) had a microscopically positive margin. Median follow-up was 22.6 months (range, 0.2–210.5). Median OS for the entire cohort was 71.6 months, and median RFS was 33.6 months.

4.2. Short-Term Outcomes; Pt1n0 Vs Ypt1n0

Relative to the US group, patients in the NAC group tended to be younger (64.6 vs. 62.4 years; $p = 0.045$), yet had higher ASA scores (Table 1). More patients underwent preoperative drainage for cholangitis (19/110 [17.3%] vs. 72/200 [36%]; $p = 0.001$). The preoperative CA 19-9 level measured immediately before surgery was significantly higher in the US group (29.9 U/mL [10-1-97.5]) than in the NAC group (16.5 U/mL [8.9-32.5]; $p < 0.001$). Pancreatic head tumors were more frequent in the NAC group (140/200 [70%]) than in the US group (53/110 [48.2%]; $p < 0.001$). The proportion of borderline-respectable and locally advanced disease was higher in the NAC group ($p < 0.001$). Final tumor size was smaller in NAC group (1.24 ± 0.563 cm vs. 1.62 ± 0.318 cm; $p < 0.001$), perineural invasion was more common (67/105 [63.8%] vs. 87/190 [45.8%]; $p = 0.004$), and R0 resection was achieved more frequently (95% vs. 87.3%; $p = 0.027$). Incidence of POPF grade B/C were no different between two groups. There were no significant differences in complication rates or length of hospital stay.

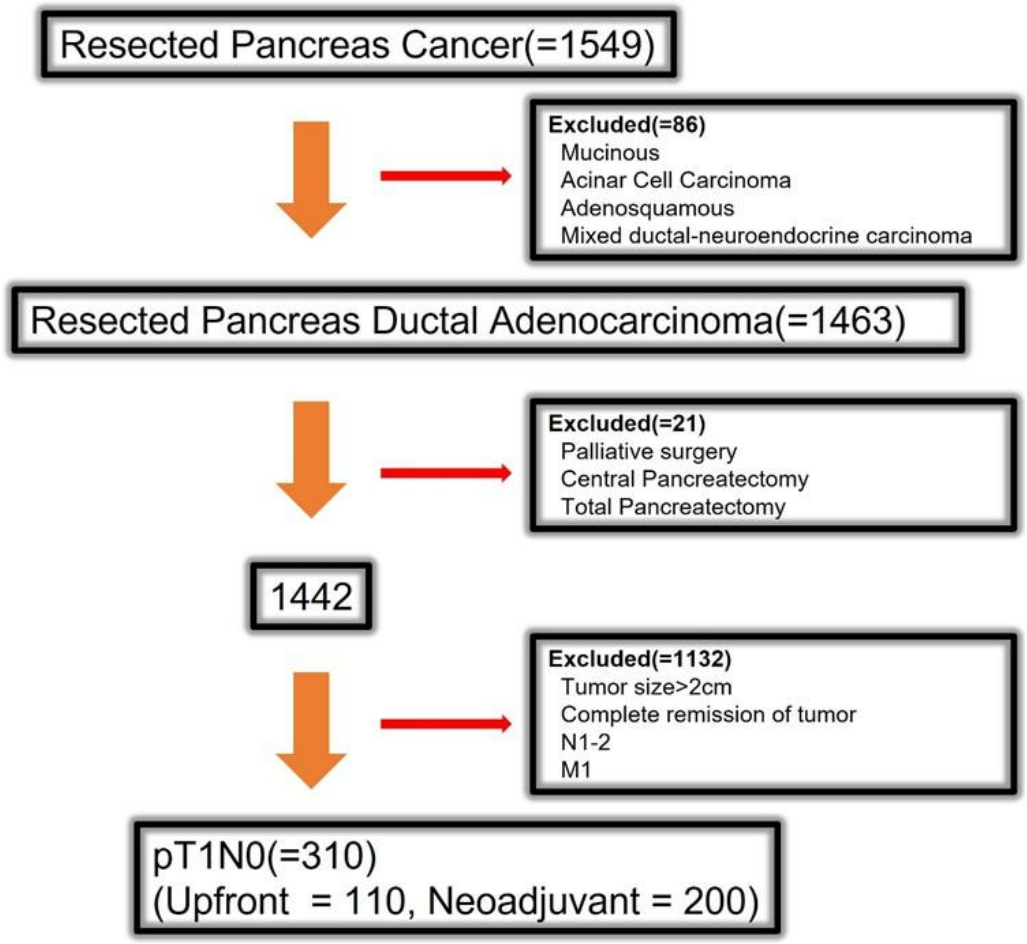

Figure 1. Patient Selection Algorithm

Flowchart illustrating the identification of 314 patients with resected stage IA (pT1N0) pancreatic ductal adenocarcinoma from 1,463 surgically treated cases between 2005 and 2025.

Table 1. Baseline characteristics of patients with resected stage IA (pT1N0) pancreatic ductal adenocarcinoma

Clinicopathologic features of the cohort stratified by treatment group (upfront surgery vs. neoadjuvant chemotherapy). Values are expressed as mean ± standard deviation or number (%).

	Total(n=310)	US n=110	NAC n=200	**p-value**
Patient Characteristics				
Age, mean (SD*)	63.2(9.3)	64.6(8.5)	62.4(9.6)	**0.045**
Male, n (%)	154(49.7)	61(55.5)	93(46.5)	0.165
BMI*, mean (SD)	23.2(3.2)	23.6(3.9)	23.0(2.8)	0.11
1	38(12.3)	21(19.1)	17(8.4)	**0.013**
2	129(41.7)	47(42.7)	82(41.2)	
3	142(46)	42(38.2)	100(50)	
Hypertension, n (%)	130(41.9)	43(39.1)	87(43.5)	0.527
Diabetes mellitus, n (%)	112(36.1)	34(30.9)	78(39.0)	0.195
Pre-operative drainage, n (%)	91(29.4)	19(17.3)	72(36)	**0.001**
CEA*, median (range, IQR)	2.4(1.6-3.4)	2.2(1.5-3.4)	25(1.6-3.5)	0.275
CA19-9*, median (range, IQR)	18.2(9.2-49.6)	29.9(10.1-97.5)	16.5(8.9-32.5)	**0.001**
Resectability				**<0.001**
Borderline, n (%)	77(24.8)	5(4.5)	72(36)	
Locally advanced, n (%)	29(9.4)	0	28(14)	
Intraoperative outcome				
Operation type, n (%)				
Pancreaticoduodenectomy	193(62.3)	53(48.2)	140(70)	**<0.001**

Distal Pancreatectomy	117(37.7)	57(51.8)	60(30.0)	
Minimally invasive surgery, n(%)	136(43.9)	54(49.1)	82(41)	0.21
Operation time, mean(SD)	342.2(143)	306.4(128.2)	343.2(143)	**0.001**
Intraoperative blood loss, mean(SD)	347.7(351.8)	320.1(296.7)	362.9(378.5)	362.9(378.5)
Vascular resection, n(%)	51(16.5)	10(9.1)	41(20.5)	**0.015**
Pathological outcome				
Tumor size, cm(SD)	1.37(0.525)	1.62(0.318)	1.24(0.563)	**<0.001**
Cell differentiation, n(%)				
Well	50(16.9)	15(13.6)	35(18.8)	0.165
Moderate	205(69.5)	83(75.5)	122(65.9)	
Poor	39(13.2)	11(10)	28(15.1)	
Undifferentiated	1(0.3)	1(0.9)	0	
Retrieved Lymph node, mean(SD)	15.5(9.64)	13.94(9.405)	16.39(9.683)	**0.031**
CAP* score, n(%)				
1			7(5.1)	
2			95(69.3)	
3			35(25.5)	
Lymphovascular invasion, n(%)	24(8.1)	10(9.5)	14(7.4)	0.67
Perineural invasion, n(%)	154(52.2)	67(63.8)	87(45.8)	0.004
Margin status(R1), n(%)	24(7.7)	14(12.7)	10(5.0)	**0.027**
Postoperative Outcome				
Complication, n(%)	160(51.6)	62(56.4)	98(49)	0.262
POPF* grade B/C, n(%)	14(4.5)	5(4.5)	9(4.5)	1
Delayed gastric emptying, n(%)	25(8.1)	12(10.9)	13(6.5)	0.18
Postoperative Bleeding, n(%)	6(1.9)	2(1.8)	4(2)	0.93
CD* score IIIa and over, n(%)	27(8.7)	8(7.3)	19(9.5)	0.649
Hospital stay, mean(SD)	15.31(10.8)	14.34(8.11)	15.8(12)	0.245
In hospital mortality	0	0	0	
90-day mortality	1(0.3)	0	1(0.5)	0.462
90-day readmission, n(%)	43(13.9)	20(18.2)	23(11.5)	0.145
Neoadjuvant chemotherapy, n(%)				
Gemcitabine based			35(17.5)	
5-FU based			26(13)	
FOLFIRINOX			139(69.5)	
Adjuvant Chemotherapy, n(%)	233(71.9)	81(73.6)	142(71)	0.717
Recurrence pattern, n(%)				0.691
Local	31(23.5)	11(23.4)	20(23.5)	
Systemic	83(62.9)	28(59.6)	55(64.7)	
Local and Systemic	18(13.6)	8(17)	10(11.8)	
Median OS, mo	71.6	80.9	63.3	0.078
Median RFS, mo	33.6	60.8	24.1	**0.03**

SD* : standard deviation, BMI* : Body Mass Index, ASA*: American Society of Anesthesiologists physical status classification, CEA*: Carcinoembryonic antigen, CA19-9*: Carbohydrate antigen 19-9, POPF* : Postoperative pancreatic fistula, CD* : Clavien–Dindo, CAP* : College of American Pathologists tumor regression grade.

4.3. Long-Term Outcomes; Pt1n0 Vs Ypt1n0

OS did not differ significantly between groups (p = 0.077), whereas RFS was significantly shorter in the NAC group (p = 0.029) (Figure 2). When compared with FOLFIRINOX group with US group, there were no significant difference in RFS and OS (Figure 3). Table 2 presents Cox regression results for OS and RFS in the overall cohort. On multivariable analysis, independent factors associated with OS were older age (HR 1.05 per year; 95% CI 1.02–1.08; p = 0.001), female sex (HR 0.57; 95% CI 0.34–0.88; p = 0.011), minimally invasive surgery(MIS) (HR 0.50; 95% CI 0.28–0.91; p = 0.022), combined-organ resection (HR 2.15; 95% CI 1.20–3.84; p = 0.010), and receipt of adjuvant chemotherapy (HR 0.47; 95% CI 0.29–0.77; p = 0.003). For RFS, adjuvant chemotherapy was the only independent factor (HR 0.65; 95% CI 0.43–1.00; p = 0.049). Notably, gemcitabine-based NAC was associated with poorer outcomes for both OS (HR 2.12; 95% CI 1.00–4.48; p = 0.050) and RFS (HR 2.26; 95% CI 1.16–4.37; p = 0.016).

Table 2: Cox regression analyses of survival outcomes in stage IA PDAC.

Univariate and multivariate Cox proportional hazards regression analyses of (a) OS and (b) RFS in the entire cohort.

	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)	p-value
Age	1.05 (1.02-1.08)	<0.001	1.05 (1.02-1.08)	0.001
Female	0.61 (0.40-0.93)	0.02	0.57 (0.37-0.88)	0.011
Pre operative CEA	1.02 (0.95-1.09)	0.66		
Pre-operative CA19-9	1.00 (1.00-1.00)	0.19		
Symptom	1.79 (1.18-2.71)	0.006	1.30 (0.78-2.17)	0.316
Pre-operative drainage	1.52 (0.99-2.31)	0.053	1.14 (0.68-1.91)	0.626
Resectability	Ref			
	1.22 (0.73-2.02)	0.451		
	1.59 (0.87-2.90)	0.133		
MIS*(vs open)	0.40 (0.24-0.70)	0.001	0.50 (0.28-0.91)	0.022
Vascular resection	1.54 (0.95-2.48)	0.079	0.82 (0.47-1.45)	0.501
Combined resection of organ	1.85 (1.08-3.17)	0.026	2.15 (1.20-3.84)	0.01
Tumor size(cm)	1.10 (0.74-1.64)	0.639		
Tumor location(left)	0.92 (0.60-1.42)	0.714		
Cell differentiation				
well	ref			
moderate	0.91 (0.49-1.70)	0.764		
poor	1.05 (0.47-2.34)	0.903		
undifferentiated	0.00 (0.00-Inf)	0.995		
LVI*	1.21 (0.58-2.52)	0.614		
PNI*	1.40 (0.90-2.18)	0.132		
Margin positive	0.54 (0.22-1.32)	0.176		
POPF*	0.29 (0.07-1.18)	0.083	0.34 (0.08-1.44)	0.143
Upfront surgery			Ref	
FOLFIRINOX	0.94 (0.53-1.67)	0.844	1.13 (0.62-2.07)	0.684
Gemcitabine-based	2.64 (1.60-4.37)	<0.001	2.12 (1.00-4.48)	0.05
5-FU based	1.23 (0.62-2.42)	0.555	1.01 (0.41-2.47)	0.988
NAR*	1.75 (1.14-2.68)	0.01	1.19 (0.59-2.41)	0.628
Adjuvant CTx*	0.45 (0.29-0.70,)	<0.001	0.47 (0.29-0.77)	0.003
(b) Recurrence-Free Survival				
	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)	p-value
Age	1.02 (1.00-1.04)	0.055	1.02 (1.00-1.04)	0.07
Female	0.85 (0.60-1.19)	0.342		
Pre operative CEA	1.04 (0.99-1.09)	0.121		
Pre-operative CA19-9	1.00 (1.00-1.00)	0.274		
Symptom	1.42 (1.01-2.00)	0.046	1.13 (0.79-1.63)	0.5
Pre-operative drainage	1.15 (0.80-1.66)	0.456		
Resectability	ref			
	1.09 (0.71-1.67)	0.69		
	1.49 (0.90-2.49)	0.121		
MIS*(vs open)	0.67 (0.46-0.97)	0.033	0.73 (0.49-1.08)	0.116
Vascular resection	1.46 (0.95-2.23)	0.082	1.12 (0.71-1.78)	0.625
Combined resection of organ	1.43 (0.86-2.39)	0.167		
Tumor size(cm)	1.02 (0.74-1.40)	0.926		
Tumor location(left)	1.33 (0.94-1.88)	0.105		
Cell differentiation				
well	Ref			

moderate	1.23 (0.73-2.07)	0.436		
poor	0.82 (0.40-1.67)	0.587		
undifferentiated	0.00 (0.00-Inf)	0.994		
LVI*	0.89 (0.45-1.75)	0.73		
PNI*	1.10 (0.77-1.58)	0.582		
Margin positive	1.06 (0.60-1.87)	0.85		
POPF*	0.32 (0.10-1.00)	0.051	0.38 (0.12-1.21)	0.102
Upfront surgery	ref		ref	
FOLFIRINOX	1.31 (0.86–1.98)	0.209	1.39 (0.91-2.12)	0.132
Gemcitabine-based	2.49 (1.56–3.98)	<0.001	2.26 (1.16-4.37)	0.016
5-FU based	1.02 (0.53-1.96)	0.957	0.98 (0.42-2.06)	0.849
NAR	1.50 (1.03-2.19)	0.036	0.95 (0.52-1.73)	0.869
Adjuvant CTx*	0.56 (0.38-0.83)	0.003	0.61 (0.40-0.94)	0.024

MIS*: Minimally invasive surgery, LVI*: Lymphovascular invasion, PNI* : Perineural invasion, POPF* : Postoperative pancreatic fistula, NAR* : Neo-adjuvant radiotherapy, CTx* : Chemotherapy.

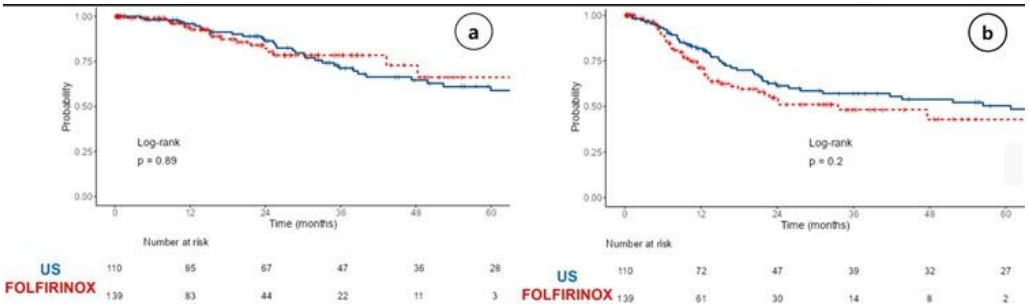

Figure 2. Kaplan–Meier survival comparing US and NAC

Survival outcomes of patients with resected stage IA (pT1N0) pancreatic ductal adenocarcinoma according to treatment group. (a) OS (b) RFS.

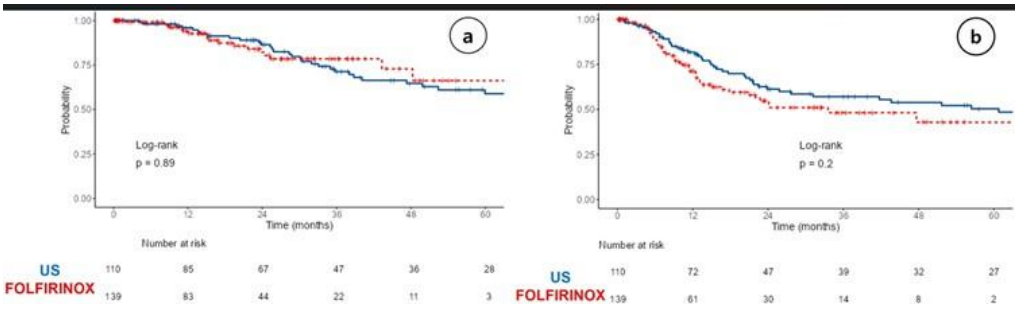

Figure 3. Kaplan–Meier survival comparing US and FOLFIRINOX

Survival outcomes of patients with resected stage IA (pT1N0) pancreatic ductal adenocarcinoma stratified by treatment with upfront surgery or FOLFIRINOX-based neoadjuvant chemotherapy. (a) OS (b) RFS.

5. Discussion

In this single-center cohort of patients with pathologic stage IA (T1N0) PDAC, crude survival analyses showed that patients in the neoadjuvant chemotherapy (NAC) group had shorter recurrence-free survival (RFS) than those who underwent upfront surgery. However, after adjustment for baseline clinicopathologic and treatment-related factors in multivariable Cox models, receipt of NAC was not independently associated with either RFS or overall survival (OS). These findings suggest that, among patients who ultimately achieve pathologic T1N0 status, downgraded tumors may have comparable survival outcome as upfront surgery group. In the overall T1N0 population, adjuvant chemotherapy emerged as the most consistent determinant of both OS and RFS, while minimally invasive surgery and avoidance of combined-organ resection were also associated with favorable long-term outcomes. Of note, gemcitabine-based neoadjuvant regimens were associated with inferior survival compared with non-gemcitabine regimens, although this finding should be interpreted cautiously.

There are only a few reported study comparing characteristics and survival outcome of ypT1N0 and pT1N0. One study conducted by Sekiguchi et al [15]. Compared oncologic outcome of pstage I and ypstage I in pancreatic cancer. In this study, despite a higher proportion of borderline or locally advanced disease at diagnosis in the ypStage I cohort, postoperative overall survival (OS) (median OS 40 vs 47 months, p=0.461) and recurrence-free survival (RFS) (median RFS 21 vs 23 months, p=0.625) did not differ significantly

from those in the pstage I group. Kim et al. likewise reported no significant difference in outcomes between pStage I and ypStage I PDAC, with 2-year OS rates of 82.4% in the pStage I group (n=53) and 76.2% in the ypStage I group (n=191) (p=0.577). [17] In a large SEER-based retrospective cohort of 13 674 patients, Zou et al. [18] reported that in clinical Stage IA PDAC, neoadjuvant therapy followed by surgery was associated with a non–statistically significant overall survival both before (median OS 53 vs. 35 months; P = 0.396) and after propensity score matching (49 vs. 35 months; P = 0.306). Despite a few prior reports, there is still no dedicated evidence directly comparing outcomes of ypStage IA and pStage IA pancreatic cancer, highlighting the novelty and rationale of our study. Notably, however, gemcitabine-based chemotherapy was associated with poorer outcomes; however, this finding should be interpreted with caution given the small sample size and the fact that most treatments were administered earlier in the study period, raising the possibility of selection bias.

Nonetheless, the role of adjuvant chemotherapy in early-stage PDAC remains to be fully established. Zhang et al. analyzed the effect of adjuvant chemotherapy in stage IA PDAC patients using both the SEER database and a multi-institutional cohort, and found no significant survival differences with or without adjuvant chemotherapy in either dataset [19]. Reported that, although adjuvant chemotherapy did not significantly affect outcomes in the overall stage IA cohort, it was associated with improved overall survival in a selected high risk subgroup [20]. Shaib et al. conducted a study on the effect of adjuvant chemotherapy in stage IA PDAC patients by collecting data from the National Cancer Data Base (NCBD) [21]. They reported a statistically significant effect of postoperative chemotherapy in patients with stage IA disease. In our study, adjuvant chemotherapy was associated with improved both OS and RFS on multivariable analysis. Although these results should be interpreted with caution, they suggest that even in stage IA PDAC-which is generally considered the most favorable subgroup-adjuvant chemotherapy should be actively considered, and clinicians must carefully individualize these decisions in the outpatient setting to ensure the best possible outcomes for each patient.

In our cohort of pathologic stage IA (T1N0) PDAC, minimally invasive surgery (MIS) emerged as an independent favorable factor for overall survival. Given that pathologic stage, margin status, and receipt of adjuvant chemotherapy were accounted for in the multivariable model, this association is unlikely to reflect technical "superiority" of MIS alone and is more plausibly explained by a complex interplay of patient selection, perioperative recovery, and the delivery of systemic therapy. Our findings are in line with large database and systematic analyses showing that MIS pancreatectomy achieves oncologic equivalence to open surgery in terms of margin status, lymph node yield, and survival, while consistently reducing length of stay and accelerating postoperative recovery [22]. Notably, national data indicate that patients undergoing minimally invasive distal pancreatectomy are more likely to receive adjuvant chemotherapy than those treated with an open approach, even when overall survival remains similar [23]. Together with prior reports that MIS pancreatectomy is associated with shorter time to adjuvant treatment or lower rates of failure to deliver planned chemotherapy, these observations support the concept that MIS can function as an "enabler" of multimodal therapy in pancreatic cancer.

These considerations may be particularly relevant in the context of truly early-stage disease. Stage I PDAC still represents only a small fraction of all pancreatic cancers, and stage IA accounts for an even smaller subset; however, multicenter data already show that patients with tumors ≤2 cm experience substantially better survival than those with larger lesions, and that even within stage I, aggressive pathological features such as perineural invasion mandate active adjuvant therapy [24]. Ongoing advances in cross-sectional imaging, surveillance of high-risk lesions such as IPMN, and development of blood-based and AI-assisted diagnostic tools are expected to progressively increase the proportion of patients diagnosed at stage IA rather than at locally advanced or metastatic stages. In such a future landscape, the ability to offer a minimally invasive pancreatectomy with rapid postoperative recovery may become an important prerequisite for ensuring that a higher proportion of "favorable-stage" patients actually receive and complete guideline-recommended adjuvant chemotherapy.

Several limitations warrant consideration. First, this study was conducted at a single high-volume tertiary center in Korea, raising the possibility of selection bias and limiting the generalizability of our findings. Second, its retrospective design without a prospective element may introduce information bias, and treatment heterogeneity over the long accrual period (2005–2025) further complicates interpretation. Third, although the overall sample size of 310 patients is relatively large for this rare stage IA PDAC cohort, the lack of an ex-ternal, multi-institutional validation cohort restricts the broader applicability of our results. Future multi-center prospective studies incorporating molecular profiling are war-ranted to validate and extend our results.

6. Conclusion

In conclusion, among patients with pathologic stage IA (T1N0) PDAC, neoadjuvant chemotherapy was not independently associated with recurrence-free or overall survival, suggesting that down staged ypT1N0 tumors can achieve outcomes comparable to de novo pT1N0 disease. Adjuvant chemotherapy was the most important modifiable factor for both survival endpoints, and minimally invasive surgery was independently associated with improved overall survival, likely by facilitating recovery and delivery of systemic therapy. As earlier detection increases the proportion of stage IA cases, these findings support an individualized treatment strategy that integrates pre-treatment stage, surgical approach, and perioperative chemotherapy, and they warrant confirmation in larger, multi-institutional prospective studies.

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text to ensure accuracy and take full responsibility for the content of this publication.

8. Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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