



Original Research

# Actual long-term outcome of T1 and T2 pancreatic ductal adenocarcinoma after surgical resection



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## HIGHLIGHTS

- Pancreatic ductal adenocarcinoma is not often diagnosed at an early stage.
- Retrospective analysis was performed for pancreatic ductal adenocarcinoma.
- T1/T2 pancreatic ductal adenocarcinoma showed good survival outcome.
- Additional efforts are needed to improve the screening for early detection.

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## ABSTRACT

**Background:** The prognosis for patients with pancreatic cancer is extremely poor. The diagnosis of pancreatic ductal adenocarcinoma at an early stage is uncommon. The purpose of this study was to analyze the clinicopathological characteristics of patients with pathologically proven pancreatic ductal adenocarcinoma following surgical resection and their actual 5 year survival rates, especially for those with T1 and T2 early stage cancer.

**Methods:** Retrospective analysis was performed for 433 patients with pancreatic ductal adenocarcinoma who underwent resection at Samsung medical center between May 1995 and December 2010. The actual 5 year survival rates and prognostic factors were analyzed.

**Results:** Multivariate analysis showed that positive resection margin, poor differentiation, large tumor size, large amount of blood loss, and T3/T4 were independent prognostic factors on overall survival. The median survival for T1/T2 stage was 71.7 months compared to 16.1 months for those with T3/T4 stage. The actual 5 year survival rates for T1/T2 and T3/T4 stages were 66.7% and 18.4%, respectively.

**Conclusions:** T stage is one of the strongest independent prognostic factor for overall survival of patients with pancreatic cancer. T1/T2 pancreatic ductal adenocarcinoma showed good survival outcome. Therefore, additional efforts are needed to improve the screening for early detection.

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## 1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) is a common cause of cancer related death. The incidence of PDAC is rising [1]. Surgical resection remains the only potentially curative treatment for patients with localized pancreatic cancer [2]. However, the prognosis for patients with pancreatic cancer underwent resection is

extremely poor, with actual 5-year survival rate ranging from 10 to 18% [3–6]. The poor prognosis is associated with the lack of early detection procedures [7]. Diagnosis of PDAC at an early stage is uncommon. It is related to the lack of specificity if symptoms are presented and frequently advanced disease at presentation [4].

The purpose of this study was to analyze the clinicopathological characteristics of patients with pathologically proven PDAC following surgical resection and their actual 5 year survival rates, especially for those with T1 and T2 early stage cancer.

## 2. Materials and methods

Retrospective analysis was performed for 433 patients with

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PDAC who underwent resection at Samsung medical center between May 1995 and December 2010. Institutional review board certificated this study (2016-10-050). The actual 5 year survival rates and prognostic factors were analyzed. All tumors were discussed at a multidisciplinary meeting with radiologists, to identify the location of tumor, staging, and resectability to rule out distant metastasis or major vascular encasements. Surgical strategy was based on the anatomical location of the tumor. Lymphadenectomy was performed, including dissection of the common hepatic artery. Lymph nodes and perineural tissue along the common bile duct, anterior and posterior pancreaticoduodenal nodes, nodes along the superior mesenteric vein and the right lateral wall of the superior mesenteric artery were removed. Pancreaticojejunal anastomosis was performed using a double layer duct to mucosa technique. All specimens were reviewed by dedicated pancreatic specialist pathologists. The pathologic stage was determined using the 7th edition of the American Joint Committee on Cancer staging system [8]. Patients were divided into two groups, T1/T2 and T3/T4. Clinical characteristics such as age, gender, BMI, preoperative serum CA19-9 level, operative procedures, and adjuvant therapy were evaluated. Pathological characteristics such as surgical margin status, size of the tumor, differentiation, TNM stage and perineural invasion were also analyzed. Tumor size was measured during macroscopic assessment of the specimen and reported as the greater diameter recorded. R0 resection was characterized by a specimen with clear resection margins without gross tumor mass remaining at the resection site. R1 resection was defined as microscopic involvement of the resection margin.

Statistical analyses were conducted using IBM SPSS Statistics 23.0. Categorical variables are presented as percentages. Continuous variables are presented as medians and ranges. Overall survival was calculated from the date of surgery to the date of death. Continuous variable were dichotomized at their median values for

statistical analysis. Survival probability was estimated using the Kaplan-Meier analysis and compared using the log rank test. Univariate and multivariate survival analysis was conducted using Cox proportional hazard model. Hazard ratios (HRs) were reported with 95% confidence intervals (CIs). Statistical significance was considered when  $p$  value was less than 0.05.

### 3. Results

#### 3.1. Clinicopathological characteristics

The characteristics of the 433 patients are summarized in Table 1. The median tumor size was 2.0 cm (range, 1.5–7.5 cm) in T1/T2 and 3.0 cm (range, 0.8–11.0 cm) in T3/T4 ( $p = 0.008$ ). In T1/T2 and T3/T4 patients, 16.7% and 63.4% ( $p = 0.002$ ) had positive lymph nodes, respectively. Perineural invasion was present in 16.7% of T1/T2 tumors and 39% ( $p = 0.004$ ) of T3/T4 tumors. Comparison of these two groups showed that small tumor size, absence of lymph node metastases and perineural invasion were associated with T1/T2.

#### 3.2. Prognostic factors of overall survival (OS)

The median survival for the overall study population was 16.4 months and the actual 5 year survival was 19.8%. Prognostic factors analyzed for all 433 patients are shown in Table 2. Positive resection margin (HR = 2.035, 95% CI = 1.521–2.724,  $p < 0.001$ ), poor differentiation (HR = 1.874, 95% CI = 1.484–2.366,  $p < 0.001$ ), large tumor size (>3 cm) (HR = 1.375, 95% CI = 1.099–1.719,  $p = 0.005$ ), large amount of blood loss (>500 ml) (HR = 1.505, 95% CI = 1.199–1.890,  $p < 0.001$ ), and T3/T4 stage (HR = 2.564, 95% CI = 1.130–5.818,  $p = 0.024$ ) were independent prognostic factors on overall survival.

**Table 1**  
Clinicopathological characteristics of patients with PDAC (n = 433).

	T1, 2 (n = 12)	T3, 4 (n = 421)	p value
Age, median (range), year	57 (41–70)	61 (32–81)	0.772
Gender (male:female)	7 (58.3%): 5	247 (58.7%): 174	0.981
BMI, median (range), kg/m <sup>2</sup>	22.84 (14.19–26.76)	22.68 (14.77–33.25)	0.869
ASA class (minimal/moderate/severe)	5/5/2	167/233/18	0.157
Co-morbidity (n,%)			
Diabetes mellitus	5 (41.7%)	135 (32.1%)	0.536
Hypertension	5 (41.7%)	110 (26.1%)	0.316
Pulmonary disease	1 (8.3%)	9 (2.1%)	0.247
Cardiovascular disease	1 (8.3%)	13 (3.1%)	0.329
Others	1 (8.3%)	9 (2.1%)	0.247
CA 19-9, median (range), U/ml	59 (10–360)	130 (0–40600)	0.108
Preoperative hemoglobin, median (range), g/dl	12.7 (8.6–16.0)	13.0 (7.0–16.5)	0.821
Preoperative bilirubin, median (range), mg/dl	1.1 (0.2–13.0)	1.5 (0.2–41.0)	0.734
Operative methods (PD: distal: other)	7: 4: 1	295: 88: 38	0.137
Operating time, median (range), min	330 (160–467)	330 (80–700)	0.632
Blood loss, median (range), ml	575 (200–3300)	500 (50–11000)	0.794
Hospital days, median (range)	16 (10–35)	14 (6–215)	0.127
Adjuvant therapy	4 (33.3%)	293 (69.6%)	0.100
Tumor size, median (range), cm	2.0 (1.5–7.5)	3.0 (0.8–11.0)	*0.008
Tumor differentiation			
Well-moderate	10 (83.3%)	283 (67.2%)	0.357
Poor	2 (16.7%)	129 (30.6%)	
Lymph node status			
Positive	2 (16.7%)	267 (63.4%)	*0.002
Negative	10 (83.3%)	154 (36.6%)	
Margin status			
Positive (R1,R2)	0 (0%)	74 (17.6%)	0.234
Negative (R0)	12 (100%)	347 (82.4%)	
Perineural invasion			
Present	2 (16.7%)	145 (39%)	*0.004
Absent	10 (83.3%)	227 (61%)	

\* $p < 0.05$  as statistically significant.

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