Preoperative EUS-guided FNA: effects on peritoneal recurrence and survival in patients with pancreatic cancer CME

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Background and Aims: EUS-guided FNA (EUS-FNA) is an accurate and relatively safe tissue confirmation method for pancreatic cancer. However, there is concern that this procedure may spread tumor cells along the needle track or within the peritoneum. We aimed to estimate the effect of preoperative EUS-FNA on the risk of peritoneal recurrence and long-term outcomes in resected pancreatic cancer.

Methods: We retrospectively reviewed records of patients diagnosed with pancreatic cancer who had undergone curative resection between 2009 and 2013 to investigate the overall survival, cancer-free survival, and peritoneal recurrence. Peritoneal recurrence was diagnosed based on image findings or cytology-confirmed ascites.

Results: Of 411 patients, 90 underwent preoperative EUS-FNA (EUS-FNA group), whereas 321 did not (non–EUS-FNA group). The median length of follow-up was 16.2 months (range, 2-46). Peritoneal recurrence occurred in 131 patients: 30% (27/90) in the EUS-FNA group versus 32% (104/321) in the non–EUS-FNA group ($P = .66$). Cancer-free survival or overall survival was not significantly different between the 2 groups: median overall survival of 25.3 months in the EUS-FNA group versus 23.7 months in the non–EUS-FNA group ($P = .36$) and median cancer-free survival of 12.7 months in the EUS-FNA group versus 11.6 months in the non–EUS-FNA group ($P = .38$).

Conclusions: Preoperative EUS-FNA for pancreatic cancer was not associated with an increased rate of peritoneal recurrence or mortality. Therefore, EUS-FNA is an accurate and safe method to obtain suspicious pancreatic mass tissue. (Gastrointest Endosc 2018;88:926-34.)

Surgery is the only potential cure for resectable pancreatic cancer.[1-3] However, pancreatic resections including pancreaticoduodenectomy have shown high morbidity and mortality since their introduction.[4-7] Some reviews have reported that approximately 10% of resected pancreatic specimens have benign or non-neoplastic conditions.[8] Therefore, the decision to perform surgery on a suspicious pancreatic mass should be undertaken cautiously. Obtaining an accurate preoperative diagnosis has become very important because neoadjuvant therapy can facilitate the possibility of surgery in borderline resectable pancreatic cancer.[9-13]

EUS-guided FNA (EUS-FNA) is an accurate diagnostic tool with an overall sensitivity and specificity of 85% and 98%, respectively. It is a relatively safe method for tissue confirmation of pancreatic cancer with an overall morbidity and mortality of .98% and .02%, respectively.[14-18] It is also helpful in ruling out malignancy in autoimmune pancreatitis patients.[19] Patients who undergo EUS-FNA rarely have serious adverse events.[20,21] However, there have been concerns that this diagnostic tool might risk tumor cell dissemination along the needle track or within the peritoneum.[22-25] Theoretically, a pancreatic cystic lesion is more likely to develop cancer seeding than a solid

Abbreviations: CA 19-9, carbohydrate antigen 19-9; EUS-FNA, EUS-guided FNA.

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malignancy.[26] Cancer seeding may occur more frequently in the body or the tail of a lesion through a transgastric approach than that in the head of a lesion through a transduodenal approach.[26] This is because the EUS-FNA tract to the head portion occurs within the pancreaticoduodenectomy region, whereas the EUS-FNA tract for the body or the tail portion lies outside the surgical resection region. Some surgeons and physicians hesitate to confirm the histopathologic diagnosis of a pancreatic mass preoperatively using an EUS-FNA approach. The aim of this study was to investigate the effect of preoperative EUS-FNA on the frequency of peritoneal recurrence and long-term prognosis in patients with pancreatic cancer who underwent curative-intent surgery.

METHODS

Study population and data source

This retrospective, single-center study was approved by the Institutional Review Board of Samsung Medical Center. Data were obtained through computerized medical record reviews. Patients with a histopathologic confirmation of pancreatic cancer from surgical resection with curative intention between January 2009 and December 2013 were included. We defined resectable pancreatic tumor as having no distant metastasis, no localized tumor expansion in the celiac axis or hepatic artery, and no invasion of superior mesenteric vasculature.

Patients with any synchronous double primary neoplasms, distant metastatic cancer, carcinoma in situ or high-grade dysplasia, or short-term follow-up period of less than 30 days were excluded. Tumor staging was assessed according to the American Joint Committee on Cancer manual (8th edition). The date of death was obtained from the Social Security Death Index in 2017.

Measurements

Baseline characteristics of patients, tumor markers, type of surgery, margin status, nodal involvement, use of chemotherapy and radiotherapy, and characteristics of the EUS-FNA group were reviewed. Peritoneal recurrence was defined as the presence of peritoneal nodules or infiltrations detected using imaging studies or malignant ascites confirmed using cytology. The follow-up period was measured from the date of surgery to the date of the last hospital visit. Overall survival was estimated from the date of surgery to the date of death or the last hospital visit. Cancer-free survival was calculated from the period between the operation date and the date of recurrence of cancer in any organ.

EUS-FNA was performed through inserting either a 22-gauge or a 25-gauge needle into the lesion in real time while viewing the US image. After puncture, specimens were obtained using a slow pull-back technique with a minimum of 2 passes attempted. Diagnostic accuracy was evaluated through comparing results of aspiration in the EUS-FNA group with the pathologic diagnosis of resected specimens. Levels of amylase and lipase were routinely checked for all patients who underwent the EUS-FNA. Patients usually visited the medical center 1 month after the discharge date and every 3 months thereafter if there were no specific medical problems. At each visit, blood test and image study were conducted. If there was no recurrence for 2 years, follow-up was performed every 6 months.

Statistical analysis

All data were analyzed using the Statistical Analysis System, version 9.4 (SAS Institute, Cary, NC). Baseline characteristics between the 2 groups were compared using Mann-Whitney test, χ^2 test, or Fisher exact test as appropriate. Analyses of cancer-free survival and overall survival were performed using the Kaplan-Meier method and log-rank test. Univariate analyses were performed using the Cox proportional hazard model to identify the prognostic factors associated with decreased cancer-free survival and overall survival after adjusting for age, sex, tumor size, tumor location, histologic pathology, tumor grade, tumor stage, lymph node involvement, margin status, undergoing EUS-FNA, chemotherapy, and radiotherapy. Variables with $P < .2$ in univariate analyses were used for multivariate analyses. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated. The significance level for all tests was 2-sided with $P < .05$.

RESULTS

In total, 546 patients underwent curative-intent surgery for pancreatic neoplasm between January 2009 and December 2013 at Samsung Medical Center. Among them, 135 patients were excluded because they met the exclusion criteria or because resected specimens revealed other pancreatic neoplasms such as neuroendocrine tumor or squamous cell carcinoma. Our study population comprised 411 patients: 90 patients who had undergone preoperative EUS-FNA were included in the EUS-FNA group and 321 patients who did not receive preoperative EUS-FNA were included in the non–EUS-FNA group (Fig. 1).

Characteristics of patients in EUS-FNA and non–EUS-FNA groups are summarized in Table 1. The median follow-up period was 18.0 months for the EUS-FNA group and 15.1 months for the non–EUS-FNA group ($P = .18$). The most frequent tumor site was located at the pancreatic head in both groups (EUS-FNA group, 66%; non–EUS-FNA group, 69%). The most common type of surgery in both groups was the pylorus-preserving pancreaticoduodenectomy. Histopathologic results revealed that moderately differentiated tubular adenocarcinoma was the most common type of cancer in both groups (EUS-FNA group,

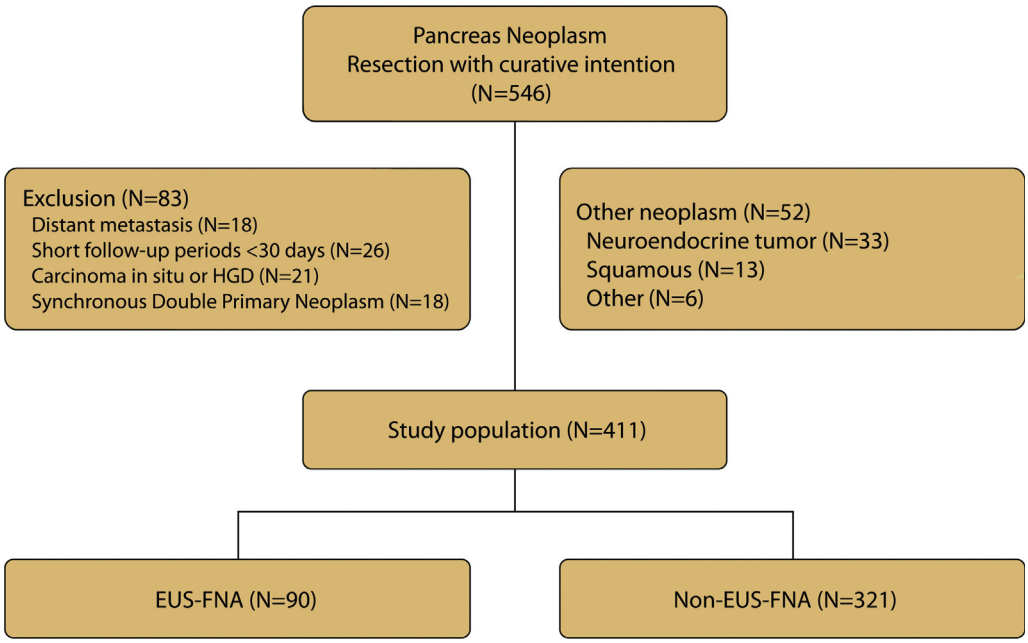

Figure 1. A total of 546 patients underwent curative-intent surgery for pancreatic neoplasm, and 135 patients were excluded because 83 patients met the exclusion criteria and 52 resected specimens revealed other pancreatic neoplasms. The remaining 411 patients included in the study were divided into 2 groups: 90 patients in the EUS-FNA group and 321 patients in the non–EUS-FNA group. *HGD*, High-grade dysplasia; *EUS-FNA*, EUS-guided FNA.

69%; non–EUS-FNA group, 62%). Lymph node involvement was evident in both the EUS-FNA group (34%, 31/90) and the non–EUS-FNA group (38%, 122/321) ($P = .53$). There was a 22% (20/90) positive surgical margin in the EUS-FNA group and a 17% (55/321) positive surgical margin in the non–EUS-FNA group ($P = .26$). Chemotherapy had been completed in 56 patients (62%) in the EUS-FNA group and 180 patients (56%) in the non–EUS-FNA group ($P = .29$). Radiotherapy was administered to 46 patients (51%) in the EUS-FNA group and 165 patients (51%) in the non–EUS-FNA group ($P = .96$). Preoperative carcinoembryonic antigen level was at 6.54 ng/mL in the EUS-FNA group and 3.01 ng/mL in the non–EUS-FNA group ($P = .04$). Preoperative carbohydrate antigen 19-9 (CA 19-9) level was at 467.15 U/mL in the EUS-FNA group and 1266 U/mL in the non–EUS-FNA group ($P = .19$) (Table 1).

Outcomes

The median overall survival was 25.3 months (95% CI, 21.7-32.1) in the EUS-FNA group and 23.7 months (95% CI, 20.0-27.1) in the non–EUS-FNA group ($P = .36$) (Fig. 2). In the univariate Cox regression model, variables associated with unfavorable overall survival were older age, increased tumor size, poorly differentiated ductal adenocarcinoma-type cancer, positive lymph node involvement, and positive resection margin ($P < .2$). Undergoing EUS-FNA was not significantly associated with unfavorable overall survival (HR, .88; 95% CI, .67-1.15; $P = .36$). In the multivariate Cox regression model after adjusting for other variables, significant variables associated with unfavorable overall survival were older age (HR, 1.02; 95% CI, 1.01-1.04; $P = .00$), increased tumor size (HR, 1.17; 95% CI, 1.06-1.28; $P = .00$), poorly differentiated tumor grade (HR, 1.79; 95% CI, 1.38-3.00; $P = .00$), and positive lymph node involvement (HR, 1.67; 95% CI, 1.28-2.17; $P = .00$). A positive resection margin also showed statistical significance (HR, 1.33; 95% CI, .99-1.78; $P = .05$) (Table 2).

The median cancer-free survival was 12.7 months (95% CI, 9.5-16.8) in the EUS-FNA group and 11.6 months (95% CI, 9.4-14.2) in the non–EUS-FNA group ($P = .38$) (Fig. 3). In the univariate Cox regression model, variables associated with poorer cancer-free survival were pancreatic head-portion cancer, increased tumor size, poorly differentiated ductal adenocarcinoma-type cancer, positive lymph node involvement, and positive resection margin ($P < .2$). Univariate analyses suggested that EUS-FNA for pancreatic cancer was not an adverse prognostic factor (HR, .88; 95% CI, .66-1.17; $P = .38$). In the multivariate Cox regression model after adjusting for other variables, significant variables associated with poorer cancer-free survival were increased tumor size (HR, 1.20; 95% CI, 1.09-1.32; $P = .00$), poorly differentiated tumor grade (HR, 1.87; 95% CI, 1.20-2.93; $P = .00$), and positive lymph node involvement (HR, 1.56; 95% CI, 1.19-2.03; $P = .00$) (Table 3).

A total of 289 patients (70%) had recurrence during the follow-up period. Among them, 27 patients (30%) in the EUS-FNA group and 104 patients (32%) in the non–EUS-FNA group had peritoneal recurrence ($P = .66$). In the univariate Cox regression model, variables associated with peritoneal recurrence were positive lymph node involvement and a history of chemotherapy and radiotherapy ($P < .2$)

TABLE 1. Baseline characteristics of patients who underwent pancreatic surgery for suspicious pancreatic mass in each group

	EUS-FNA (n = 90)	Non–EUS-FNA (N = 321)	*P* value
Age, mean (SD), y	67.62 (10.93)	63.63 (9.88)	.53
Sex, male	53 (59)	191 (60)	.91
Carcinoembryonic antigen, mean (SD), ng/mL	6.54 (27.65)	3.01 (5.10)	.04
CA 19-9, mean (SD), U/mL	467.15 (1117.65)	1266.58 (7905.82)	.19
Tumor location			.09
Head	59 (66)	223 (69)	
Neck	4 (4)	2 (1)	
Body	20 (22)	67 (20)	
Tail	7 (8)	29 (9)	
Tumor size, mean (SD), cm	3.07 (1.33)	3.13 (1.52)	.86
Tumor histology			1
Ductal adenocarcinoma	87 (97)	306 (95)	
Mucinous cystic adenocarcinoma	1 (1)	6 (2)	
Invasive carcinoma because of intraductal papillary mucinous neoplasm	2 (2)	9 (3)	
Tumor grade			.01
Well differentiated	9 (10)	29 (9)	
Moderately differentiated	63 (69)	200 (62)	
Poorly differentiated	14 (16)	86 (27)	
Undifferentiated	4 (5)	26 (12)	
Nodal involvement	31 (34)	122 (38)	.53
Surgical margin (R0/R1)	70/20 (78/22)	266/55 (83/17)	.26
Stage			.20
I	1 (1)	12 (4)	
IIA	30 (33)	109 (34)	
IIB	57 (63)	199 (62)	
III	2 (2)	1 (0)	
Type of surgery			.18
Whipple's operation	8 (8)	10 (3)	
Pylorus-resecting pancreaticoduodenectomy	15 (17)	65 (29)	
Pylorus-preserving pancreaticoduodenectomy	33 (37)	129 (40)	
Subtotal pancreatectomy	4 (4)	20 (6)	
Medial pancreatectomy	0 (0)	2 (1)	
Distal pancreatectomy	22 (24)	79 (25)	
Total pancreatectomy	8 (9)	16 (5)	
Chemotherapy	56 (62)	180 (56)	.29
Radiation therapy	46 (51)	165 (51)	.96
Length of hospital stay, mean (SD), days	14.19 (8.92)	15.50 (45.59)	.35
Follow-up period, mean (SD), months	25.23 (20.84)	23.86 (22.45)	.18
Recurrence	63 (70)	226 (70)	.94
Peritoneal recurrence	27 (30)	104 (32)	.66

Values are n (%) unless otherwise defined.
SD, Standard deviation; *CA 19-9*, carbohydrate antigen 19-9.

(Table 4). In univariate analysis, undergoing an EUS-FNA was not an independent risk factor for peritoneal recurrence (HR, .88; 95% CI, .53-1.46; $P = .66$). In the multivariate Cox regression model after adjusting for other variables, no significant variable associated with peritoneal recurrence was found.

The mean number of needle passes performed for diagnosis was 3 (range, 2-4) in the EUS-FNA group. EUS-FNA

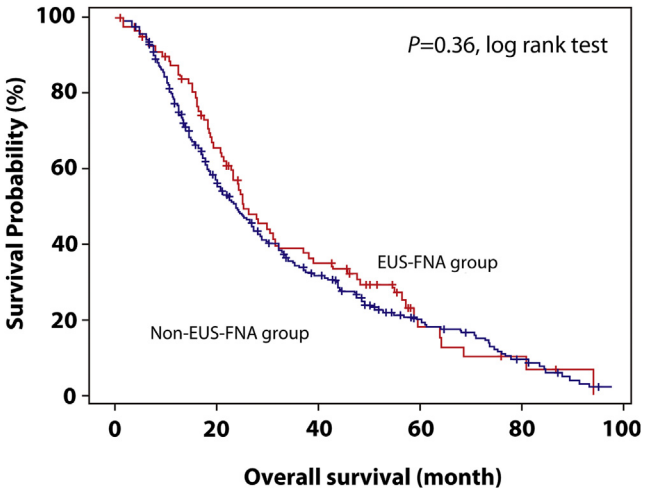

Figure 2. This Kaplan-Meier curve depicts overall survival in patients undergoing surgery for pancreatic cancer. The *red line* represents the EUS-FNA group and the *blue line* the non–EUS-FNA group. The median overall survival was 25.3 months in the EUS-FNA group and 23.7 months in the non–EUS-FNA group (log rank test; $P = .36$). There was no statistically significant difference in overall survival between the 2 groups. *EUS-FNA*, EUS-guided FNA.

was performed through either a transduodenal approach (71%) or a transgastric approach (29%). Peritoneal recurrence was more frequently found in 16 patients (25%) with the transduodenal approach than 11 patients (42%) with the transgastric approach ($P = .10$) (Fig. 4). Diagnostic accuracy of EUS-FNA for pancreatic cancer was 82.2%. EUS-FNA was not repeated for patients with negative results because malignancy was strongly suspected in the image study. Amylase and lipase levels were routinely checked for all patients who underwent EUS-FNA regardless of abdominal pain. Postprocedural amylase or lipase elevation occurred in 13 patients (15.4%). One patient (1.2%) complained of abdominal pain after EUS-FNA, which was treated conservatively (Table 5).

DISCUSSION

Pancreatic cancer is known as one of the most fatal neoplasms.[27] Recently, neoadjuvant chemotherapy has emerged as an innovative way to enable surgery for initially inoperable pancreatic cancer. It has become very important to accurately diagnose pancreatic neoplasm before starting neoadjuvant chemotherapy.[9-13] Although imaging modalities for pancreatic lesions are notably improving, the diagnostic accuracy for pancreatic neoplasm using imaging studies alone remain unsatisfactory.[8,28] Approximately 10% of surgical specimens preoperatively diagnosed as malignant pancreatic neoplasms are subsequently confirmed to be benign diseases, such as chronic pancreatitis or autoimmune pancreatitis.[29-31] Moreover, the overall mortality after pancreatic surgery ranges from 0% to 10%.[32,33] Therefore, operations for patients with a suspicious pancreatic mass should be undertaken with caution. A correct preoperative diagnosis is essential to reduce morbid pancreatic surgery.

EUS-FNA has shown a high diagnostic accuracy of 75% to 95% for pancreatic mass evaluation, with mild postprocedural adverse events mostly involving pancreatitis.[14-18] However, several instances of tumor dissemination resulting in a very poor prognosis after undergoing EUS-FNA have been reported.[22-25] Paquin et al[25] first reported tumor seeding of the gastric wall as a result of EUS-FNA for pancreatic adenocarcinoma in 2005. Kita et al[24] also reported a case of needle tract seeding after EUS-FNA in pancreatic cancer detected by serial positron emission tomography/CT. Katanuma et al[23] encountered a case in which tumor cells were noted in the puncture line in a surgically resected specimen after EUS-FNA, in which dissemination in the posterior wall of the upper gastric body was later observed. Chong et al[22] experienced a similar case of tumor seeding at the gastric wall after EUS-FNA of a pancreatic tail mass. Ngamruengphong et al[34] reported on 13 patients (7.7%) with gastric or peritoneal recurrence after performing EUS-FNA for resectable pancreatic cancer. Gastric wall recurrence post–EUS-FNA has been reported in 6 patients worldwide.[34] Among them, 5 patients had cystic lesion or intraductal papillary mucinous neoplasm, whereas 1 patient had a solid lesion.[34] It appears that a solid pancreatic lesion has less gastric wall recurrence. After that, Ngamruengphong et al[35] again showed that preoperative EUS-FNA was not associated with increased risk of mortality using a large number of patients in 2015. Therefore, EUS-FNA seems to be a safe technique to obtain suspicious tissue from a solid pancreatic mass. However, if the diagnosis is definite and the patient is scheduled for surgery, performing an EUS-FNA for pancreatic cystic lesion may be unnecessary.

To the best of our knowledge, this is the third study that investigates the effects of EUS-FNA for resectable pancreatic cancer on overall survival and peritoneal recurrence between an EUS-FNA group and a non–EUS-FNA group after 2 previously published articles by Ngamruengphong et al.[34,35] Our study included a sizable number of patients (n = 411). Our results demonstrated that the performance of preoperative EUS-FNA did not adversely affect overall survival, cancer-free survival, or peritoneal recurrence in the EUS-FNA group compared with those without EUS-FNA after a mean follow-up of 16.2 months. Although not statistically significant, overall survival and cancer-free survival were better in the EUS-FNA group with fewer peritoneal recurrences. Tumor stage, surgical margin status, perineural invasion, the performance status of the patient, treatment effect, and CA 19-9 levels are known to be prognostic factors for pancreatic cancer.[36] In our study, unfavorable overall survival was strongly associated with older age, increased tumor size, poorly differentiated

TABLE 2. Univariate and multivariate analyses of factors affecting overall survival

	Univariate analyses		Multivariate analyses	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Age	1.02 (1.01-1.03)	.00	1.02 (1.01-1.04)	.00
Male (vs female)	1.05 (.83-1.32)	.67		
Tumor location				
Head/neck (vs body/tail)	1.00 (.78-1.28)	.87		
Tumor size	1.10 (1.02-1.19)	.01	1.17 (1.06-1.28)	.00
Tumor grade				
Moderately differentiated (vs well differentiated)	1.01 (.69-1.47)	.94	1.13 (.77-1.66)	.51
Poorly differentiated (vs well differentiated)	1.49 (0.98-2.27)	.05	1.79 (1.38-3.00)	.00
Undifferentiated (vs well differentiated)	.79 (.30-2.03)	.62	.70 (.27-1.82)	.47
Nodal involvement (vs none)	1.81 (1.41-2.31)	.00	1.67 (1.28-2.17)	.00
Resection margin, R1 (vs R0)	1.55 (1.17-2.05)	.00	1.33 (.99-1.78)	.05
Chemotherapy (vs none)	.92 (.73-1.17)	.52		
Radiotherapy (vs none)	.37 (.70-1.10)	.26		
EUS-guided FNA (vs non–EUS-guided FNA)	.88 (.67-1.15)	.36		

CI, Confidence interval; *R1*, microscopic residual tumor; *R0*, resection for cure or complete remission.

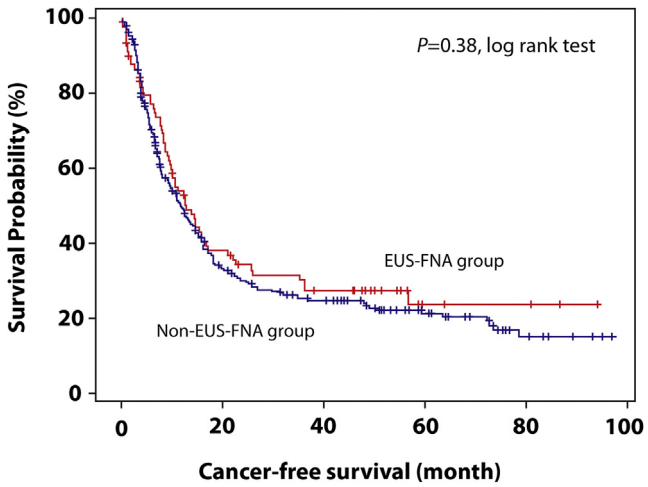

Figure 3. This Kaplan-Meier curve depicts cancer-free survival in patients undergoing surgery for pancreatic cancer. The *red line* represents the EUS-FNA group and the *blue line* the non–EUS-FNA group. The median cancer-free survival was 12.7 months in the EUS-FNA group and 11.6 months in the non–EUS-FNA group (log rank test; $P = .38$). There was no statistically significant difference in cancer-free survival between the 2 groups. *EUS-FNA*, EUS-guided FNA.

ductal adenocarcinoma-type cancer, positive lymph node involvement, and positive resection margin. Increased tumor size, poorly differentiated ductal adenocarcinoma-type cancer, and positive lymph nodal involvement decreased cancer-free survival. Interestingly, older patients were less likely to have peritoneal recurrence, although the odds ratio did not indicate statistical significance. There was no significant difference in the development of peritoneal recurrence between patients with the transduodenal approach and those with the transgastric approach.

Our study has some limitations. First, this was a single-center retrospective study. Mean CA 19-9 level was higher in the non–EUS-FNA group than that in the EUS-FNA group. There is not agreement on a level of CA 19-9 that would obviate the need for preoperative EUS-FNA. Whether patients belonged to the EUS-FNA group or the non–EUS-FNA group depended on whether patients visited the department of internal medicine first or the surgical department first. When patients first visited the internal medicine department for suspicious pancreatic mass, physicians implement EUS-FNA. When patients visited the surgical department first, surgeons often preferred to operate without performing EUS-FNA, because of concerns about tumor seeding. There was also controversy within the department of internal medicine regarding the implementation of EUS-FNA according to physicians' propensity or experience. There were no significant differences in baseline characteristics between the 2 groups except carcinoembryonic antigen level. Second, not all patients undergoing follow-up received the same thorough follow-up examinations. In addition, the recurrence time may not have been accurate. Patients usually visited the hospital 1 month after the discharge date and every 3 months thereafter if there were no specific medical problems. At each visit, blood tests and image study were conducted. If there was no recurrence for 2 years, follow-up would be performed every 6 months. However, depending on the doctor's judgement, there were differences in follow-up period and type of tests. In addition, EGD was not performed routinely. Therefore, we might have missed transgastric recurrence. Third, it was difficult to distinguish whether peritoneal tumor seeding was because of the procedure or cancer progression. There may have been some differences in follow-up imaging

TABLE 3. Univariate and multivariate analyses of factors affecting cancer-free survival

	Univariate analyses		Multivariate analyses	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Age	1.00 (.99-1.01)	.82		
Male (vs female)	1.08 (.85-1.37)	.49		
Tumor location				
Head/neck (vs body/tail)	1.23 (.94-1.60)	.12	1.31 (.98-1.75)	.06
Tumor size	1.05 (1.00-1.11)	.04	1.20 (1.09-1.32)	.00
Tumor grade				
Moderately differentiated (vs well differentiated)	1.02 (0.69-1.53)	.89	1.23 (.82-1.85)	.31
Poorly differentiated (vs well differentiated)	1.57 (1.01-2.44)	.04	1.87 (1.20-2.93)	.00
Undifferentiated (vs well differentiated)	.50 (.15-1.66)	.26	.56 (0.17-1.86)	.34
Nodal involvement (vs none)	1.98 (1.54-2.55)	.00	1.56 (1.19-2.03)	.00
Resection margin, R1 (vs R0)	1.22 (.91-1.65)	.17	.98 (.72-1.34)	.92
Chemotherapy (vs none)	.97 (.77-1.23)	.83		
Radiotherapy (vs none)	.91 (.72-1.14)	.42		
EUS-guided FNA (vs Non–EUS-guided FNA)	.88 (.66-1.17)	.38		

CI, Confidence interval; *R1*, microscopic residual tumor; *R0*, resection for cure or complete remission.

TABLE 4. Univariate and multivariate analyses of factors affecting peritoneal recurrence

	Univariate analyses		Multivariate analyses	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Age	.96 (.94-.98)	.00	.97 (.95-.99)	.00
Male (vs female)	1.18 (.77-1.81)	.36		
Tumor location				
Head/neck (vs body/tail)	.92 (.58-1.44)	.85		
Tumor size	1.01 (.88-1.17)	.87		
Tumor grade				
Moderately differentiated (vs well differentiated)	1.41 (.65-3.05)	.37		
Poorly differentiated (vs well differentiated)	1.50 (.65-3.46)	.33		
Undifferentiated (vs well differentiated)	1.40 (.22-8.85)	.72		
Nodal involvement (vs none)	1.64 (1.05-2.56)	.01	1.52 (.97-2.39)	.06
Resection margin, R1 (vs R0)	1.07 (.62-1.82)	.76		
Chemotherapy (vs none)	1.60 (1.04-2.46)	.03	1.29 (.68-2.44)	.43
Radiotherapy (vs none)	1.51 (1.51-2.30)	.06	1.10 (.59-2.06)	.74
EUS-guided FNA (vs non–EUS-guided FNA)	.88 (.53-1.46)	.66		

CI, Confidence interval; *R1*, microscopic residual tumor; *R0*, resection for cure or complete remission.

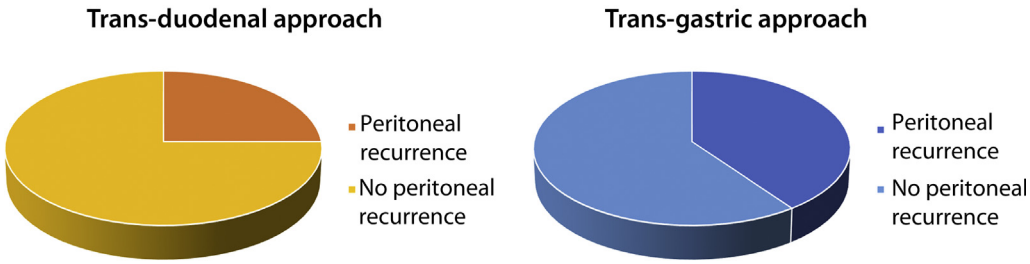

Figure 4. Peritoneal recurrence in patients with the transduodenal approach group or the transgastric approach group. EUS-guided FNA was performed using either a transduodenal approach (71%) or a transgastric approach (29%). Peritoneal recurrence occurred in 16 patients (25%) with the transduodenal approach and 11 patients (42%) with the transgastric approach ($P = .10$).

TABLE 5. Characteristics of patients in the EUS-guided FNA group

	EUS-FNA (n = 90)
Total needle passes, mean (SD)	3.17 (.86)
Site	
Samsung Medical Center	81 (90)
Other hospital	9 (10)
Doctor	
Endoscopist 1	58 (65.9)
Endoscopist 2	26 (29.5)
Endoscopist 3	2 (.22)
External doctor	4 (4.5)
EUS-guided FNA approach	
Transduodenal approach	64 (71)
Transgastric approach	26 (29)
ERCP	25 (28)
Diagnosis of cytology	
Ductal adenocarcinoma	58 (65.1)
Suspicious adenocarcinoma	14 (15.7)
Negative for malignant cell	14 (15.7)
Other malignancy	3 (3.3)
Diagnostic accuracy	74 (82.2)
Amylase/lipase elevation (× 3 WNL)	13 (15.4)
Post–EUS-guided FNA abdominal pain	1 (1.2)
Peritoneal recurrence	27 (30)

Values are n (%) unless otherwise defined.
SD, Standard deviation.

intervals and limitations of imaging distinguishing whether peritoneal cancer was from the disease process or the EUS-FNA approach. The impact of seeding may not be easily observed in this biologically aggressive disease with short overall survival. Also, peritoneal seeding could recur because of existing subclinical metastasis not appreciated at the time of surgery. Definite conclusions would require further evaluation in larger studies.

In conclusion, preoperative EUS-FNA for pancreatic mass is unlikely to increase the frequency of peritoneal seeding. It does not negatively affect overall survival or cancer-free survival. In patients with potentially resectable pancreatic cancer, preoperative EUS-FNA was found to be a highly accurate and relatively safe diagnostic method. Therefore, EUS-FNA should be performed for suspicious pancreatic mass evaluation to avoid unnecessary and morbid pancreatic surgery.

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