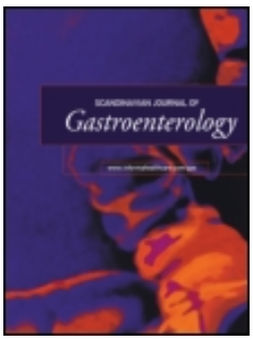

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ORIGINAL ARTICLE

Yield of endoscopic ultrasound-guided fine needle aspiration and endoscopic retrograde cholangiopancreatography for solid pancreatic neoplasms

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ABSTRACT

Objective: Both endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) and endoscopic retrograde cholangiopancreatography (ERCP) cytology may provide tissue diagnoses in solid pancreatic neoplasms. However, there are scant data comparing these two methods. This study aims at retrospectively comparing EUS-FNA and ERCP tissue sampling and ability of cytopathological diagnosis in solid pancreatic neoplasms and to determine usefulness and adverse events of combining both procedures. *Material and methods:* Two hundred and thirty four patients suspected to have solid pancreatic mass on abdominal ultrasound and/or computed tomography (CT) were enrolled. EUS-FNA (group A), ERCP cytology (group B) and combined procedures (Group C) performed in 105, 91 and 38 cases, respectively. *Results:* Sensitivity, specificity and accuracy were 98.9%, 93.3% and 98.1% for group A, and 72.1%, 60% and 71.4% for group B. Those for group C were all 100%. Sensitivity for malignancy in the pancreas head was 100% for group A and 82.4% for group B, and in the pancreas body and tail, 97.6% for group A and 57.1% for group B. EUS-FNA was more sensitive than ERCP cytology in diagnosing malignant pancreatic neoplasms 21–30 mm in size ($p = 0.0068$), 31–40 mm ($p = 0.028$) and $\geq$41 mm ($p < 0.0001$). Sensitivity for pancreatic malignancy with group C was 100% regardless of mass location or size. Adverse events were 1.9%, 6.6% and 2.6% following EUS-FNA, ERCP and combined procedures, respectively. *Conclusions*: EUS-FNA is superior to ERCP cytology for diagnosis of solid pancreatic neoplasms. Although combination of both procedures provide efficient tissue diagnosis and with a minimal adverse events rate, a prospective study including larger number of patients is required.

KEYWORDS

cytopathological diagnosis, endoscopic ultrasound-guided fine needle aspiration, endoscopic retrograde cholangiopancreatography, pancreatic neoplasm

HISTORY

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Introduction

Pancreatic cancer is a significant cause of morbidity and mortality, with a reported five-year survival rate of less than 5%. Therefore early and accurate diagnosis of pancreatic neoplasms is of clinical benefit for determining therapeutic strategy [1]. However, differentiating between malignant and benign pancreatic neoplasms by imaging modalities alone is sometimes challenging. Histopathological evidence is therefore needed [2–4].

Endoscopic ultrasound (EUS) is a highly accurate modality for assessing the pancreatic parenchyma and ductal system and provides detailed assessment for the presence of pancreatic neoplasms, nodal or hepatic metastases and local vascular staging [5]. EUS-guided fine needle aspiration (EUS-FNA) is a well-established modality to obtain pancreatic tissue samples [6,7]. Diagnostic yield of EUS-FNA is previously reported as 78–95% and 75–100% in sensitivity and specificity, respectively [8–13]. On the other hand, it is often difficult to detect carcinoma in situ (CIS) or faint infiltrations without the presence of a formed mass by other cross-sectional modalities [10,14,15], and to detect the mass located in an area inaccessible from the digestive tract with EUS. Moreover, EUS-FNA cannot be performed in cases with a high risk for bleeding or those with intraductal papillary mucinous neoplasm with an associated invasive carcinoma (IPMN-IC), because of the risk of needle track seeding [16,17].

Prior to the development of EUS, endoscopic retrograde cholangiopancreatography (ERCP) with brush cytology and/or aspiration of pancreatic juice was the initial investigation of choice for cytopathological diagnosis in patients with pancreatic neoplasm. Although the specificity of this technique is approaching 100%, its sensitivity has been reported as only 33.3–67%, generally

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lower than that of EUS-FNA [9,18–20], ERCP also carries a risk of acute pancreatitis.

The present study aims to compare the diagnostic yield and adverse events of EUS-FNA with those of ERCP cytology for pancreatic neoplasms, and also to evaluate the usefulness and adverse events of combining both procedures in clinical practice.

Patients and methods

Patients

In the current study, from January 2001 to August 2013 in Osaka Medical College hospital, a total of 234 patients suspected to have solid pancreatic mass by abdominal ultrasound and/or computed tomography (CT) were enrolled. We retrospectively analyzed these subjects by classifying them into three groups, group A underwent EUS-FNA only, group B underwent ERCP cytology and/or biopsy only, and group C underwent both EUS-FNA and ERCP in the same session. The final diagnosis was based on the pathological examination of specimens obtained by surgical resection and/or clinical follow-up for at least one year. If signs of malignancy were absent at the end of follow-up (disease regression or lack of evidence of disease progression), pancreatic cancer was ruled out. Hence, the final diagnosis was a benign disorder if the clinical course of the patient was consistent after follow-up for at least one year. Patients with pancreatic neuroendocrine tumors were excluded from this study.

Methods

Our algorism for diagnosis of a solid pancreatic mass

Before the introduction of EUS-FNA to our hospital, we performed ERCP with pancreatic cytology and/or biopsy for definite diagnosis of solid pancreatic mass lesions following cross-sectional imaging (Figure 1). After the introduction of EUS in 2010, EUS-FNA was performed as the first endoscopic procedure and also for cases in which cytology on ERCP was negative and those in which histological evidence of malignancy was needed before chemotherapy. In Group C, ERCP performed besides EUS-FNA in patients who provided consent for combined procedures to maximize the diagnostic accuracy. In all patients with risk factors such as diabetes mellitus and chronic pancreatitis, MPD dilatation by trans-abdominal ultrasound and tumor markers or pancreatic enzymes elevation we performed a multidetector pancreatic protocol computed tomography (MDCT) study, magnetic resonance imaging (MRI) and positron emission tomography (PET) prior to ERCP and EUS-FNA.

All subjects provided written informed consent before the procedures. Study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and its later amendments and approved by the institutional review board of Osaka Medical College.

EUS-FNA procedure

EUS-FNA was performed using a linear array echo-endoscope (GF-UCT 240 and GF-UCT 260; Olympus

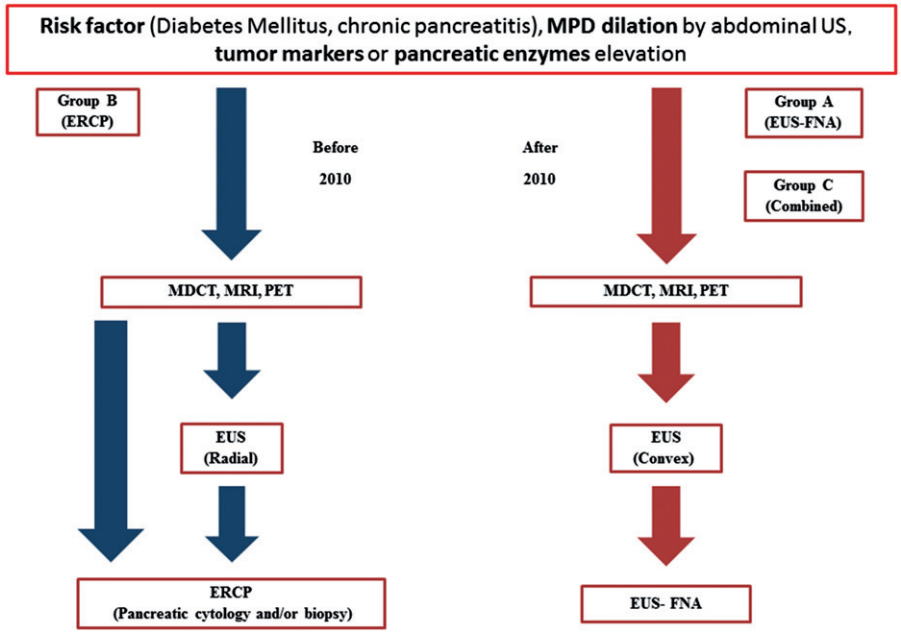

Figure 1. Flowchart of our algorism to diagnose solid pancreatic neoplasms.

Optical Co., Ltd., Tokyo, Japan) connected to an ultrasound device (EUM 2000, α 10; Aloka, Tokyo, Japan) and 22-G or 25-G puncture needles (Sono Tip Pro Control; Medi-Globe GmbH, Rosenheim, Germany; Medico's Hirata Inc., Osaka, Japan, or Expect; Boston Scientific Japan, Tokyo, Japan). After 1–5 needle passes with moving the needle back and forth 10–15 times per pass, the puncture needle was removed. We first requested the cytopathologists to perform rapid on-site cytological evaluation with part of the aspirated material by modified Gimsa stain (Cyto-Quik, Muto Chemicals Co, Ltd., Tokyo, Japan), or Gill-Schorr stain (Schorr, Muto Chemicals Co, Ltd., Tokyo, Japan); the remaining material was then submitted for cell-block evaluation.

ERCP procedure

ERCP was performed using a side-viewing duodenoscope (JF 260V, JF 240 and TJF 240), an ERCP cannula, and a hydrophilic guidewire (0.025, 0.035 inch). An ERCP cannula was inserted to the main pancreatic duct from ampulla at first, then introduced to the upstream side if any stenosis or obstruction of the main pancreatic duct was present, and pancreatic juice was sampled by the inserted ERCP cannula or 5 Fr endoscopic naso-pancreatic drainage (ENPD) tube to the main pancreatic duct. If possible, pancreatic duct biopsy was performed at the site of stenosis. Pancreatic juice cytology and/or biopsy obtained under ERCP were evaluated by a cytopathologist.

Interpretation of cytological samples

The cytological samples obtained by EUS-FNA and ERCP were reported as positive, suspicious, atypical, negative, or insufficient. Cytopathological results in malignant lesions were considered positive when the cytological or histological results of EUS-FNA or ERCP were positive or suspicious, and those in benign lesions were considered negative when cytological or histological results were atypical, negative or insufficient. In group C, criteria of diagnosing malignancy were, when the cytological or histological results of EUS-FNA or ERCP were positive or suspicious, cytopathological results in malignant lesions were considered positive, and, when both cytological and histological results of EUS-FNA and ERCP were atypical, negative, or insufficient, cytopathological results in malignant lesions were considered negative.

Evaluation of adverse events

All patients were observed for adverse post-endoscopic events. Clinical symptoms after the procedures were carefully evaluated. Blood samples were also obtained to measure the serum amylase level, an inflammatory maker (C-reactive protein) and hematologic profiles before and 24 h after EUS-FNA or ERCP. Follow-up radiological imaging (MDCT and MRI) is done at six-month intervals to detect the course of benign lesions or the recurrence of pancreatic malignancies after surgical resection. All the patients were followed up for at least one year after endoscopic procedures.

Statistical analysis

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated. Diagnostic power between study groups and subgroups (mass size and location subgroups) was compared with the χ^2 test and a p value less than 0.05 was considered significant. Statistical analysis was performed using the JMP® pro 11 software program (SAS Institute, Japan, Tokyo, 2013).

Results

Patient characteristics

A total of 234 patients (144 males and 90 females, mean age 67.8 ± 9.6 years) with solid pancreatic mass were enrolled in this study. Group A included 105 patients, group B included 91 patients and group C included 38 patients. The characteristics of the three groups are summarized in Table I. Mean sampling number on ERCP was 2.0 ± 1.5 (range 1–8) and mean puncture passes on EUS-FNA were 2 ± 0.04 (range 1–5).

Final diagnoses of pancreatic neoplasms were as follows: 207 patients had malignant neoplasm and 27 patients had benign neoplasm (Table II).

Comparison of diagnostic yield between groups A and B

The results in group A were: sensitivity 98.9%, specificity 93.3%, PPV 98.9%, NPV 93.3% and accuracy 98.1%, while the results in group B were: sensitivity 72.1%, specificity 60%, PPV 96.9%, NPV 11.1% and accuracy 71.4%. There is significant difference in sensitivity ($p < 0.0001$), specificity

Table I. Patient characteristics among the three groups.

	Group A	Group B	Group C
Number of patients	105	91	38
Age (years) (Mean ± SD)	68.9 ± 9.1	65.5 ± 9.8	70.2 ± 9.3
Gender (Male:Female)	66:39	54:37	24:14
Tumor location (Ph:Pbt)	53:52	55:36	30:8
Tumor size (mm) (Mean ± SD)	39.5 ± 26.1	31.9 ± 16	35.3 ± 25.7
Final diagnosis M:B	90:15	86:5	31:7

Ph: pancreas head; Pbt: pancreas body and tail; M: malignancy; B: benign.

Table II.Final diagnoses in solid pancreatic neoplasms.

	No
Malignant neoplasm	207
Pancreatic cancer	173
Malignant lymphoma	9
Metastatic pancreatic mass	9
IPMN-IC	13
CIS	3
Benign neoplasm	27
Autoimmune pancreatitis	15
Mass forming pancreatitis	7
Pancreatic abscess	3
Pancreatic accessory spleen	2
†otal	234

Table III. Comparison of diagnostic yield among groups A and B for solid pancreatic neoplasms.

	Group A (No = 105)	Group B (No = 91)	*p* Value
Sensitivity % (no)	98.9% (89/90)	72.1% (62/86)	<0.0001
Specificity % (no)	93.3% (14/15)	60% (3/5)	0.001
PPV % (no)	98.9% (89/90)	96.9% (62/64)	0.37
NPV % (no)	93.3% (14/15)	11.1% (3/27)	<0.0001
Accuracy % (no)	98.1 (103/105)	71.4 (65/91)	<0.0001

PPV: positive predictive value; NPV: negative predictive value.

($p = 0.001$), NPV ($p < 0.0001$) and accuracy ($p < 0.0001$) between groups A and B (Table III).

Diagnostic sensitivity for pancreatic malignancies according to mass size was 100% for carcinomas ≤10 mm, 100% for 11–20 mm, 96.4% for 21–30 mm, 100% for 31–40 mm and 100% for carcinomas ≥41 mm in group A; and 75% for carcinomas ≤10 mm, 92.9% for 11–20 mm, 69.7% for 21–30 mm, 70% for 31–40 mm and 61.9% for carcinomas ≥41 mm in group B. There were significant differences in diagnostic sensitivity in pancreatic carcinomas size 21–30 mm ($p = 0.0068$), 31–40 mm ($p = 0.028$) and ≥41 mm ($p < 0.0001$) between groups A and B (Table IV). When sensitivity for pancreatic malignancy was investigated according to mass location, it was 100% in the head and 97.6% in the body and tail in group A; and 82.4% in the head 57.1% in the body and tail in group B. There were significant differences in diagnostic sensitivity at pancreatic head malignancies ($p = 0.0023$) and body/tail malignancies ($p < 0.0001$) between groups A and B (Table IV).

Sufficient specimens were obtained in 100% in pancreatic head carcinomas and 100% in pancreatic body/tail carcinomas in group A, while sufficient specimens were obtained in 98.1% in pancreatic head carcinomas and 85.3% in pancreatic body/tail carcinomas in group B. There were significant differences in obtaining sufficient specimens in pancreatic body/tail carcinomas ($p = 0.0093$) (Table V).

Table IV. Diagnostic sensitivity among groups A and B in subgroups of pancreatic malignancy.

Subgroups	Group A (Number of patients with positive pathology = 90)	Group B (Number of patients with positive pathology = 86)	*p* Value
Location†			
Head	48/48 (100%)	42/51 (82.4%)	0.0023
Body, Tail	41/42 (97.6%)	20/35 (57.1%)	<0.0001
Size‡			
≤10 mm	3/3 (100%)	6/8 (75%)	0.52
11–20 mm	11/11 (100%)	13/14 (92.9%)	0.36
21–30 mm	27/28 (96.4%)	23/33 (69.7%)	0.0068
31–40 mm	14/14 (100%)	7/10 (70%)	0.028
≥41 mm	34/34 (100%)	13/21 (61.9%)	<0.0001

†‡Location and size based on MDCT and EUS findings.

Table V. Rate of sufficient sampling among groups A and B in pancreatic malignancy.

	Group A (Number of patients with positive pathology = 90)	Group B (Number of patients with positive pathology = 86)	*p* Value
Head	47/47 (100%)	51/52 (98.1%)	0.913
Body, Tail	43/43 (100%)	29/34 (85.3%)	0.0093

Table VI. Diagnostic yield of combined EUS-FNA and ERCP (group C) for solid pancreatic neoplasms (no = 38).

	EUS-FNA	ERCP	*p* Value
Sensitivity % (no)	100% (31/31)	67.8% (21/31)	0.0006
Specificity % (no)	85.7% (6/7)	100% (7/7)	0.29
PPV % (no)	96.9% (31/32)	100% (21/21)	0.41
NPV % (no)	100% (6/6)	41.2% (7/17)	0.012
Accuracy % (no)	97.4 (37/38)	73.7 (28/38)	0.0033

PPV: positive predictive value; NPV: negative predictive value.

Time from mass detection to definite diagnosis was 29.8 ± 3.9 days in group A and 42.5 ± 3.6 days in group B. This was statistically significant ($p = 0.02$).

Diagnostic yield of combined EUS-FNA and ERCP cytology (group C)

The results in group C were as follows: sensitivity 100%, specificity 85.7%, PPV 96.9%, NPV 100% and accuracy 97.4% with EUS-FNA; and sensitivity 67.8%, specificity 100%, PPV 100%, NPV 41.2% and accuracy 73.7% with ERCP. There was significant difference in sensitivity ($p < 0.0006$), NPV ($p < 0.012$) and accuracy ($p < 0.0028$) between EUS-FNA and ERCP cytology (Table VI). When the cytopathological results of EUS-FNA and ERCP were combined, the results improved as follows: sensitivity, specificity, PPV, NPV and accuracy were all 100%. Sensitivity for pancreatic malignancy was 100% regardless of pancreatic mass location or size with combined EUS-FNA and ERCP cytology. Sufficient specimens were

obtained in 100% of cases with pancreatic head and body/tail carcinoma. Time from mass detection to definite diagnosis was 30.6 ± 6.2 days.

Adverse events

Two patients (1.9%) developed mild pancreatitis in group A and six (6.6%) suffered adverse events in group B (five cases mild pancreatitis and one of acute cholangitis), all were resolved with conservative treatment. There was no significant difference in adverse events between groups A and B ($p = 0.09$). One case developed mild pancreatitis in group C (2.6%).

Possibility of pancreatic malignancy recurrence after surgical resection (57 patients) was evaluated by CT, MRI and PET follow-up. There was no significant difference in the recurrence rate between group A (7/20 patients) and group B (23/37), ($p = 0.08$). Also there was no recurrence at the gastrointestinal wall (at the location of the EUS-guided fine needle track).

Discussion

Obtaining a cytopathological diagnosis of pancreatic neoplasms is crucial for selecting the appropriate strategy of therapy. ERCP cytology and EUS-FNA are currently preferred as endoscopic cytological methods for diagnosis of solid pancreatic neoplasms.

The diagnostic ability of cytology under EUS-FNA for pancreatic neoplasms was previously reported as having sensitivity, specificity, PPV, NPV and accuracy of 78–95%, 75–100%, 98–100%, 46–80% and 78–95%, respectively [8–13]. ERCP cytology has yielded sensitivity, specificity, PPV, NPV and accuracy of 33.3–67%, 100%, 100%, 27.3–98% and 46.7–93%, respectively [9,10,20]. The present results are similar to those previously reported, and show that EUS-FNA is a more sensitive and accurate modality of cytopathological diagnosis for pancreatic neoplasms than ERCP.

EUS-FNA for pancreatic lesions of less than 10 mm is thought to be technically challenging. In the present study, our data shows that EUS-FNA was accurate in the evaluation of pancreatic neoplasms regardless of size; these results are superior to those of ERCP, particularly in tumors of more than 20 mm in size. This may be due to the possibility of presence of tight strictures in the main pancreatic duct in case of ERCP. Our results are consistent with Uehara et al. [22], who showed that EUS-FNA sensitivities of 100%, 92%, 95% and 100% were yielded for lesions of less than 10 mm, 11–20 mm, 21–30 mm and more than 31 mm, respectively. In contrast, Agarwal et al. [8] reported that the diagnostic sensitivity of EUS-FNA was lower for suspected pancreatic cancer <20 mm in diameter (75%) than for lesions ≥21 mm (92%). Haba et al. [23] reported diagnostic sensitivities of 73%, 81% and 93.5% for pancreatic lesions less than 10 mm, 11–20 mm, and more than 20 mm, respectively. However, these results may have been underestimated because suspicious cytology results were counted as negative for malignancy and excluded from calculation. Another reason is that EUS-FNA of small pancreatic lesions should be performed by experienced endosonographers; in a multicenter study, one of the factors that enhanced the accuracy of EUS-FNA in malignant lesions was operator technique, which improved with experience [24].

Although pancreatic lesions located in the head may prove more difficult to biopsy at EUS-FNA than those in other locations, in the present study EUS-FNA was accurate in the evaluation of pancreatic neoplasms regardless of location and its diagnostic sensitivity was superior to that of ERCP cytology, particularly at pancreas body lesions; this may be due to the difficulty of obtaining sufficient samples from the upstream pancreatic duct. These results are consistent with Uehara et al. [22], which showed that the diagnostic sensitivity of EUS-FNA was not influenced by the location, yielding sensitivities of 94% and 95.5% in pancreas head and body/tail neoplasms, respectively. However, Ushijima et al. [21] reported poorer diagnostic sensitivity for pancreatic head lesions (67.9%) compared to body and tail lesions (83.3%) in the EUS-FNA group, while diagnostic sensitivities in the ERCP group were 61% in pancreatic head lesions and 59.5% in body and tail lesions. EUS-FNA for lesions located in the head may be challenging because the approach to the head from the long position exerts sharp angulation and torque on the needle, which leads to difficulty in advancing it. Successful FNA for the pancreas head would be brought about by approaching it from the short position. In addition to operator technique, using a more flexible needle type and choosing a suitable needle size improved technical success rates for head lesions in our study.

In the present study, EUS-FNA provided sufficient samples more readily than ERCP, especially from pancreatic body and tail carcinoma. In cytology by ERCP, this may be due to the difficulty of obtaining sufficient samples from the upstream pancreatic duct because of the presence of tight strictures in the main pancreatic duct. In cytology by EUS-FNA, the availability of on-site cytological evaluation leads to a lower rate of insufficient sampling. Moreover, using appropriate needle size and changing between suction and slow pulling techniques increased the rate of sampling. These results are similar to those previously reported [13,23,25].

Moreover, time from pancreatic mass detection to definite diagnosis was significantly shortened in group A compared to that in group B; this may be due to the fact that the patients who underwent ERCP had a lower diagnosis rate and thus underwent other forms of biopsy that took longer.

The number of studies evaluating the use of combined EUS-FNA and ERCP to increase the diagnostic yield for pancreatic neoplasms is relatively small. Cytology using a combination of EUS-FNA and ERCP was previously reported as having sensitivity, specificity, PPV, NPV and accuracy of 92.5%, 100%, 100%, 91.7% and 95.9%, respectively. Sensitivity for malignancy was 95% in the head, 96.7% in the body, and 97.3% in the tail of the pancreas. Sensitivity was 90.6% for carcinomas $\leq$20 mm, 97.4% for 21–40 mm, 100% for 41–60 mm, and 100% for carcinomas $\geq$61 mm [14]. In the present study, the results of combined EUS-FNA and ERCP were of higher diagnostic ability; sensitivity, specificity, PPV, NPV and accuracy were all 100%. Sensitivity for pancreatic malignancy was 100% regardless of pancreatic mass location or size, moreover adequate samples were achieved from 100% of pancreatic head and body/tail carcinomas, and time from pancreatic mass detection to definite diagnosis was significantly shortened in the combined EUS-FNA and ERCP group compared to the ERCP group. To the best of our knowledge, these results show the greatest accuracy ever reported for cytopathological examinations for pancreatic neoplasms. Success rate and diagnostic accuracy increased with improved operator experience and the availability of rapid on-site cytological evaluation. Combining the two procedures expedited the patient evaluation, eliminated the need for a second endoscopy session, and reduced demand on endoscopic and anesthetic resources. Our study provides further evidence that EUS-FNA and ERCP can be effectively performed together to diagnose patients with pancreatic neoplasms.

The rate of significant adverse events with EUS-FNA for pancreatic lesions reported to be between 2.5% and 5%. Massive bleeding, pancreatitis, infection, duodenal perforation and needle track seeding are the major adverse events and the risk of pancreatitis is 0.5% to 2.0% [6,26,27]. The risk of pancreatitis with a diagnostic ERCP is reported to be 5% [28]. The rate of reported adverse events with combined procedures is 4–10% and includes pancreatitis, cholangitis, bleeding, bile leak and asymptomatic pneumoperitoneum [10,28,29]. In our series, two patients (1.9%) developed acute pancreatitis following EUS-FNA, six (6.6%) suffered adverse events (five cases acute pancreatitis and one of acute cholangitis) following ERCP, and one developed acute pancreatitis following combined EUS-FNA and ERCP (2.6%). These figures are within the range of reported complication rates; there is thus no significant difference in the adverse events rate in combined procedures than an individual one. A simultaneous approach therefore appears to be feasible and safe [29]. Tumor seeding at the gastric wall via the needle track following EUS-FNA has been described in multiple case reports [17]. In the present study, EUS-FNA is not associated with an increased risk of needle track seeding during follow up of resected pancreatic cancers, but as some seeding cases were reported, we should be careful about EUS-FNA for suspected pancreas body cancer. Our results are consistent with Ngamruengphong et al. [30], who state that EUS-FNA was not associated with an increased rate of gastric or peritoneal cancer recurrence in patients with resected pancreatic cancer.

This study has several limitations, such as patient selection bias, its retrospective nature, the small sample size of group C, and the fact that it was a single-center study. We conclude that EUS-FNA is a more sensitive and accurate modality of cytopathological diagnosis than ERCP cytology for solid pancreatic neoplasms, particularly in tumors located at the pancreas body and tail, and in tumors more than 2 cm in size. Although diagnosis in pancreatic lesions less than 10 mm in size and lesions located at pancreas head and uncus is thought to be technically challenging, our data shows that EUS-FNA was accurate in the evaluation of pancreatic neoplasms regardless of size and location. Combined EUS-FNA and ERCP may maximize diagnostic accuracy especially in difficult cases of EUS-FNA, and highly suspicious lesions with previous repeated negative EUS-FNA. Another indication of combined procedures is to detect CIS or faint infiltrations without the presence of a formed mass. We do not fundamentally intend to recommend combined procedures for diagnosis of solid pancreatic mass, because sensitivity, specificity, and accuracy is high enough in group A, combined procedures are not the standard, they can be performed only by endoscopists experienced in both EUS and ERCP and there is a risk of post-ERCP pancreatitis. But fortunately sensitivity, specificity and accuracy of combined procedures (Group C) were high and moreover adverse events rate were similar among the three procedures, EUS-FNA, ERCP and combined. Recommendation of combined EUS-FNA and ERCP will require analyzing larger number of cases in a prospective study.

Declaration of interest: The authors declare that they have no conflict of interest.

All procedures performed were in accordance with the ethical standards of the institutional review board of Osaka

Medical College and with the 1975 Helsinki declaration and its later amendments.

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