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Diagnostic accuracies of endoscopic ultrasound-guided fine-needle aspiration with distinct negative pressure suction techniques in solid lesions: A retrospective study

RONGHUA WANG[1,2], JINLIN WANG[1], YAWEN LI[1], YAQI DUAN[3], XIAOLI WU[1] and BIN CHENG[1]

[1]Department of Gastroenterology and Hepatology, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, Hubei 430030, P.R. China; [2]Department of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA; [3]Department of Pathology, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, Hubei 430030, P.R. China

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Abstract. Endoscopic ultrasound (EUS)-guided fine-needle aspiration (EUS-FNA) is highly accurate in obtaining specific diagnoses for various diseases. The present study aimed to evaluate the diagnostic yields, accuracies and sampling adequacies, of slow-pull, 5 ml suction and 10 ml suction techniques in EUS-FNA of solid lesions. The present study was a retrospective comparative study, which was performed in tertiary academic centers, recognized for their expertise in EUS and EUS-guided FNA. The present study involved 149 patients who underwent EUS-FNA of solid masses. A total of 34 (22.8%), 37 (24.8%) and 78 (52.4%) patients underwent EUS-FNA with slow-pull, 5 ml suction and 10 ml suction techniques, respectively. The EUS-FNA cytology and histology results were compared with those from the gold standard of surgical histopathology [hematoxylin-eosin staining; immunohistochemical test of cluster of differentiation (CD) 79a, CD20 and flow cytometry test] or long-term clinical follow-up. The present retrospective comparative study demonstrated that the diagnostic yields and accuracies of EUS-FNA with slow-pull (86.1%) were significantly superior to those achieved with 5 ml suction (83.3%) or 10 ml suction (69.9%; P<0.0001; χ^2 test). Consistently, 86.5% (32/37) of the samples obtained from the 5 ml suction group were adequate for histological diagnosis. By contrast, 70.6 (24/34) and 85.9% (67/78) of samples from the slow-pull and 10 ml suction groups were adequate for histological diagnosis, respectively. The samples obtained using 10 ml suction contained more blood compared with those obtained via slow-pull and 5 ml suction (P=0.0056; χ^2 test). No complications were noted in any of the three groups. The samples that were obtained for histopathological diagnosis using 5 ml suction were superior to those obtained using slow-pull or 10 ml suction. Additional multi-central prospective studies in which EUS-FNA is performed with variable negative pressures are required to improve the defining of the diagnostic roles of those techniques.

Correspondence to: Dr Bin Cheng, Department of Gastroenterology and Hepatology, Tongji Hospital, Huazhong University of Science and Technology, 1095 Jiefang Avenue, Wuhan, Hubei 430030, P.R. China
E-mail: b.cheng@tjh.tjmu.edu.cn

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Introduction

Endoscopic ultrasound (EUS)-guided fine-needle aspiration (EUS-FNA) has been reported to be a sensitive method for tissue sampling of suspicious lesions of the gastrointestinal lumen and adjacent structures, including pancreaticobiliary and esophageal lesions, gastric malignancies and mediastinal and intra-abdominal lymphadenopathies (1-6). The diagnostic accuracy of EUS-FNA ranges between 60 and 90%, according to the site being evaluated (1,7-11). Cytological study of the material obtained by FNA allows for the evaluation of cellular findings that are indicative of malignancy. However, EUS-FNA has a number of limitations. Certain neoplasms, including lymphomas, stromal tumors and well-differentiated neoplasias are difficult to diagnose without histological samples, since tissue architecture and cell morphology are essential for accurate pathological assessments, which include immunohistochemical analyses in such cases (12-14). In addition, the accuracy of EUS-FNA depends on the presence of an on-site cytopathologist or cytotechnician to assess the specimen adequacy (15), and to determine whether additional samples are required to perform ancillary studies (16,17).

In an attempt to overcome these diagnostic limitations and optimize the accuracy, efficiency and quality of EUS-FNA specimens, various investigators have attempted to obtain tissue fragments with high negative pressure or with needles of varying diameters (18-21). The use of suction during FNA varies widely. No standard suction technique has been established. A randomized trial involving 52 patients compared suction and no suction during EUS-FNA of the pancreas (22). No significant differences in diagnostic yield were observed.

In a previous study, Kudo *et al* (23) utilized high negative pressure mechanical suction (35 ml of a 60 ml syringe) using a 22-gauge (G) needle, and this process yielded tissue cores that were adequate for histological evaluation in 96% of the solid masses, however, the approach was not advantageous compared with cytology alone. In addition, it may be assumed that suctioning dilutes the specimen with blood, and the stylet injures malignant cells. These assumptions raise the possibility of atypical results.

Therefore, a retrospective study was performed to investigate the feasibilities and yields of EUS-FNA combined with 10 ml suction (negative pressure applied with 10 ml syringes), 5 ml suction (negative pressure applied with a 5 ml syringe) and slow-pull (no stylet) techniques, and to compare characteristics of the samples obtained with each of the three techniques in terms of contamination with blood.

Materials and methods

Study design and patients. The present study was a retrospective, case-control study. A total of 149 patients who were referred for EUS-guided FNA tissue acquisition for the evaluation of intra-intestinal or extra-intestinal mass lesions and/or peri-intestinal lymph nodes between February 2013 and July 2014 were retrospectively identified from a prospectively collected endoscopy database at Tongji Hospital Endoscope Center (Wuhan, China). Patient characteristics are presented in Table I. Patients were classified into EUS/slow-pull, EUS/5 ml suction or EUS/10 ml suction groups (the patients who underwent EUS-FNA with the 22-G needle system with no stylet, with 5 ml negative pressure and with 10 ml negative pressure). Only patients with surgical pathology or with ≥6 months of clinical follow-up subsequent to EUS were included in the present study. The present authors reviewed the computerized patient record system to obtain patient demographics, lesion sites, EUS characteristics of the lesion and clinical follow-up information.

The EUS-FNA cytology and histology results were compared with those of the gold standard technique of surgical histopathology or long-term clinical follow-up. Intra-procedural and immediate post-procedural complications were monitored and recorded for all patients as part of a standard hospital protocol. The study protocol conformed to the guidelines of the 1975 Declaration of Helsinki (6th revision, 2008) and was approved by the Ethical Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (Wuhan, China). Written informed consent was obtained from all patients prior to undergoing EUS-FNA. Patients described in the present study provided written informed consent to publish their case details.

Procedural technique. The patients underwent EUS-FNAs with 22-G needles (EchoTip Ultra needle; Wilson-Cook, Winston-Salem, NC, USA) (24). These EUS-FNAs were performed by an experienced endosonographer (>150 EUS procedures/year; >10 years of experience). All procedures were performed with a standard technique, which utilized a linear array echoendoscope (Olympus GF-UCT 240; Olympus Corporation, Tokyo, Japan) and an Alpha 5 Aloka processor (Hitachi-Aloka Medical, Ltd., Tokyo, Japan). During the individual EUS-FNA passes, the stylet was reproducibly removed with a slow-pull technique, and a 10 ml syringe with 5 or 10 ml suction technique (25-27) was attached to the proximal end of the needle. The needle was then moved back and forth 12-16 times while applying suction. EUS-FNA was performed using fanning techniques. The lock of the syringe was finally closed prior to the withdrawal of the needle from the lesion. Needle aspirate was placed on glass slides. Ethanol-fixed smears (95% ethanol) were prepared, stained with Papanicolaou stain for 6 h at room temperature and evaluated the next working day by a cytopathologist to perform the preliminary diagnosis. Any visible core specimens and residual aspirate were collected into a liquid preservative (formalin) for subsequent preparation of histological analysis. Immunocytochemistry was performed within 24 h. No cytopathologist was present in the endoscopy room for the on-site sample evaluation.

Pathological assessments of the samples obtained. The pathologist evaluated the quantity and quality of each specimen and determined a histological diagnosis while blinded to the clinical information, cytology and final diagnoses. The quantities of the samples were assessed with the scoring system described by Gerke *et al* (28). Malignancies and borderline lesions were defined as positive for malignancy. Atypical cells and benign cells were defined as negative for malignancy.

An accurate diagnosis was defined as follows: Positive for malignancy with a final diagnosis of a malignant disease, including carcinoma, neuroendocrine tumor or solid pseudopapillary neoplasm (true positive); and negative for malignancy with the condition ultimately being diagnosed as a nonmalignant disease, including pancreatitis and non-neoplastic pancreatic tissue (true negative). Diagnostic accuracy was defined as the sum of the true positive and true negative values divided by the total number of samples. The adequacy rate was calculated with the following formula: Number of adequate samples/total number of samples.

Clinical diagnostic methodology used for the ultimate diagnosis. Malignant disease was ultimately identified in the patients according to the following criteria: Diagnosis at autopsy following pancreatic cancer-associated mortality; diagnosis based on histopathological analysis of surgically resected specimens; radiological or clinical data indicating evidence of disease progression; and diagnosis based on histopathological analysis of nodules in other organs that demonstrated metastatic progression. In the present study, benign disease was defined by a decrease or lack of change in mass and no change in the obtained clinical data for at least 6.5 months (23).

Outcome measurements. The primary objectives of the present study were to determine the adequacy of tissue acquisition via the EUS-FNA/high negative pressure (HNP) combined technique and to determine the accuracies of the histological diagnoses that were achievable using EUS-FNA combined with slow-pull, 5 ml suction and 10 ml suction. The secondary objectives of the present study were to assess the qualities and quantities of the obtained tissues and the potential for adverse events resulting from the application of this procedure.

Table I. Patient demographic and mediastinal and intra-abdominal lesion characteristics.

Characteristic	Total	0 ml	5 ml	10 ml	P-value
n		34	37	78	
Age, median	54	56	56	53	0.89[a]
Gender, n (%)					0.21[b]
Male	95	26 (76.5)	22 (59.5)	47 (60.3)	
Female	54	8 (23.5)	15 (40.5)	31 (39.7)	
Lesion location, n (%)					0.67[c]
Pancreatic mass	69 (46.3)	15 (10.1)	19 (12.8)	36 (24.2)	
Mediastinal nodes	33 (22.1)	9 (6.0)	7 (4.7)	17 (11.4)	
Retroperitoneal lesion	32 (21.5)	8 (5.4)	9 (6.0)	14 (9.4)	
Others[d]	15 (10.1)	2 (1.3)	2 (1.3)	11 (7.4)	
Needle passes (SD)	3.4 (0.7)	3.5 (0.7)	3.4 (0.8)	3.4 (0.6)	0.50[a]
Final diagnosis, n (%)					0.078[b]
Malignancy	102 (68.5)	26 (17.4)	29 (19.5)	47 (31.5)	
Benign processes	47 (31.5)	8 (5.4)	8 (5.4)	31 (20.8)	

[a]Mann-Whitney U-test; [b]χ^2 test; [c]Fisher's exact test; [d]Thickened esophagogastric wall, 8 patients; abdominal mass, 4 patients; liver mass, 2 patients; and left adrenal mass, 1 patient; SD, standard deviation.

Statistical analysis. Statistical analyses were performed with the SPSS (version 18.0; SPSS, Inc., Chicago, IL, USA) and MedCalc software packages (version 12.7.7; MedCalc Software bvba, Ostend, Belgium). The baseline characteristics of the patient population, mass lesions and technical details were calculated. Continuous variables were presented as medians and ranges of values. Categorical variables were reported as proportions with 95% confidence intervals where appropriate. Categorized variables were compared using the Fisher's exact or χ^2 two-tailed tests, as appropriate. Quantitative variables were analyzed by the two-sample Student's t-test/one-way analysis of variance (for normal distributions) or the Mann-Whitney U-test (for skewed distributions). $P<0.05$ was considered to indicate a statistically significant difference. Normally distributed data (n=149) are presented as the mean ± standard deviation.

Results

Patients and lesions characteristics. During the study period, 95 males and 54 females (149 patients) were enrolled. The median age of the patients was 54 years. All lesions were visible via EUS. There were 69 lesions in the pancreas, 33 in the mediastinum, 32 in the retroperitoneal area, 8 in the thickened esophagogastric wall, 4 in the abdominal cavity, 2 in the liver and 1 in the left adrenal gland (Table I). No significant differences were observed between the slow-pull, 5 ml suction and 10 ml suction techniques in terms of patient demographics or lesion locations. Surgical histopathological findings were available for corroboration in 49 (33%) of the cases, flow cytometry data collected following EUS-FNA were available for 6 (4%) patients, and the remaining cases (63%) were corroborated based on long-term clinical follow-up data. The mean clinical follow-up period following EUS was 6.5 months. The final histological diagnoses and diagnostic yields are shown in Tables II and III, respectively. All EUS-FNA procedures were performed with on-site cytopathology evaluations.

Accuracy. The final clinical diagnoses, the percentages of adequate histology samples and the numbers of correct diagnoses are listed in Table II. Of the 149 patients, the final diagnoses were: Malignancy in 82 patients; borderline lesions in 21 patients; and benign lesions in 46 patients. Of the patients with malignancies, 33 patients ultimately received a diagnosis of metastatic tumor, 22 exhibited pancreatic carcinomas, 9 exhibited lymphomas, 7 exhibited gallbladder and biliary cancer, 5 exhibited lung carcinomas, 5 exhibited gastroesophageal carcinomas and 1 exhibited an adrenal carcinoma. Of the patients with borderline lesions, 12 received a diagnosis of neuroendocrine tumors and 9 exhibited gastrointestinal stromal tumors. Among the benign patients, 12 patients received a diagnosis of pancreatitis, 11 exhibited tuberculosis, 16 exhibited benign lesions with histological types that could not be classified (without evidence of malignancy), 2 exhibited solid pseudo-papillaryneoplasma, and the remaining 4 cases exhibited 3 atypical hyperplasias and 1 reactive lymph node, and 1 patient exhibited Castleman disease. Representative cases of lymphoma (Fig. 1), tuberculosis (Fig. 2), pancreatic carcinoma and pancreatitis (Fig. 3) are presented in Figs. 1-3, respectively. Independent of the tissue biopsies, the final diagnoses were categorized as malignant or benign lesions.

Based on the locations, lesions were classified into 69 pancreatic lesions and 80 non-pancreatic lesions (Table III). The non-pancreatic lesion group consisted of 33 patients with mediastinal nodes, 32 patients with retroperitoneal lesions, 8 patients with thickened esophagogastric walls, 4 cases with abdominal masses, 2 cases with liver masses and 1 case with a left adrenal mass. Among the 69 pancreatic lesions that were detected with the normal, moderate and HNP suction techniques, the sensitivities of slow-pull (90%) and 5 ml suction

Table II. Final diagnosis, independent of tissue biopsies (EUS-FNA).

Diseases	Final diagnosis, n	Adequate histology sample, %	Correct diagnosis, %
Malignant	82	80.39	67.7
Secondary metastatic tumors	33	81.8	69.7
Pancreatic carcinoma	22	72.7	81.8
Lymphoma	9	100	77.8
Gallbladder and biliary cancer	7	57.1	57.1
Lung carcinoma	5	80	80
Gastroesophageal carcinoma	5	80	60
Adrenal carcinoma	1	0	100
Borderline lesions	21	90.5	90.5
Neuroendocrine tumor	12	77.8	77.8
Gastrointestinal stromal tumor	9	100	100
Benign	46	82.97	80.85
Pancreatitis	12	91.7	83.3
Tuberculosis	11	72.8	90.9
No evidence of malignancy	16	88.9	66.7
Solid pseudopapillary neoplasm	2	100	100
Others[a]	4	60	60

[a]Composed of 3 atypical hyperplasia, 1 reactive lymph node and 1 Castleman disease. EUS-FNA, endoscopic ultrasound-guided fine-needle aspiration.

Table III. Diagnostic yield and accuracy of normal, moderate and high negative pressure suction techniques in endoscopic ultrasound-guided fine-needle aspiration.

	Type of negative pressure			
Lesion location	0 ml, % (n=34)	5 ml, % (n=37)	10 ml, % (n=78)	P-value (χ^2 test)
Pancreatic lesion (n=69)				0.0005[a]
Sensitivity	90	86.7	64	
Specificity	75	100	88.2	
PPV	90	100	81.8	
NPV	75	60	75	
Accuracy	85.7	88.9	77.4	
Non-pancreatic lesion[b] (n=80)				0.0086[a]
Sensitivity	85.7	84.6	64.7	
Specificity	50	80	92.9	
PPV	92.3	91.7	94.4	
NPV	33.3	66.7	54.3	
Accuracy	81.2	83.3	71.9	
Total (n=149)				<0.0001[a]
Sensitivity	87.5	85.7	61.9	
Specificity	66.7	87.5	90.3	
PPV	91.3	96	89.7	
NPV	57.1	63.6	63.6	
Accuracy	83.3	86.1	69.9	

[a]P<0.05; [b]Non-Pancreatic lesion group consisted of 33 patients with mediastinal nodes, 32 patients with retroperitoneal lesion, 8 patients with thickened esophagogastric wall, 4 cases with abdominal mass, 2 cases with liver mass and 1 case with left adrenal mass. PPV, positive predictive value; NPV, negative predictive value.

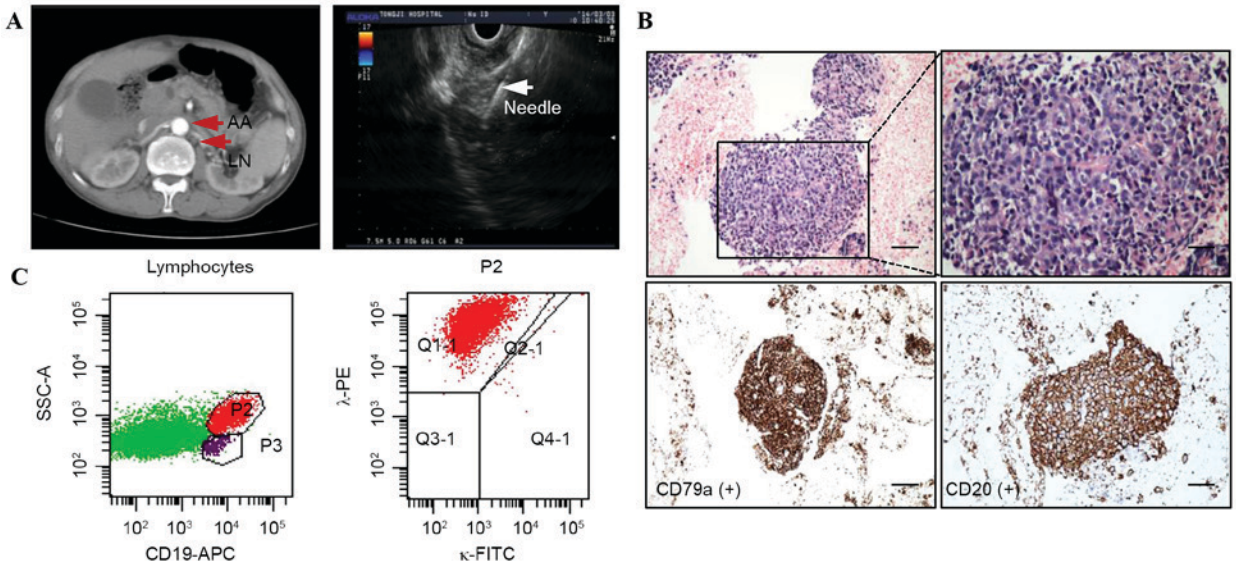


Figure 1. A representative case of lower para-aortic lymphoma. (A) Computed tomography revealed that there is a lymphadenopathy located in the lower para-aortic. Endoscopic ultrasound-guided fine-needle aspiration was performed on the lesion. The white arrow indicated the needle with no interposing vessels. (B) Histological findings demonstrated lymphoid follicles (H&E; magnification, x20; scale, 10 μm) and a monotonous population of small lymphoid cells (H&E; original magnification, x400; scale, 5 μm). These cells exhibited positive expression of CD79a and CD20 on immunohistological staining (original magnification; magnification, x400; scale, 5 μm). (C) The P2 subpopulation of lymphocytes with CD19-positive expression was isolated by flow cytometry, and λ monoclonal expression was analyzed. The patients received a final diagnosis of diffuse large B cell lymphoma. AA, abdominal aorta; LN, lymph nodes; H&E, hematoxylin and eosin; FITC, fluorescein isothiocyanate; CD, cluster of differentiation; APC, antigen-presenting cell; Q, quadrant.

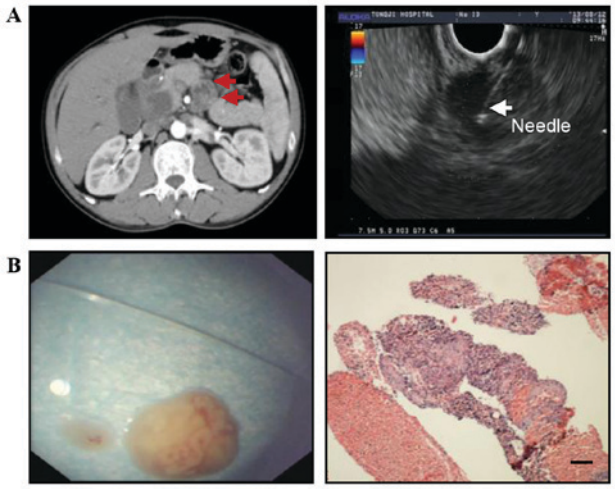


Figure 2. A representative case of pancreatic tuberculosis. (A) Computed tomography showed the diffuse enlargement of pancreas (red arrows). A linear endoscopic ultrasound image showed the fine-needle aspiration needle inside a round, well-defined lesion. (B) The specimen was composed of purulent material. A photomicrograph showed caseous necrosis (original magnification, x200; scale, 10 μm).

(86.7%) were increased compared with that of 10 ml suction (64%), but the specificity of slow-pull (75%) was worse than those of 5 ml (100%) and 10 ml suction (88.2%). Consequently, the accuracy of 5 ml suction (88.9%) was superior to those of slow-pull (85.7%) and 10 ml suction (77.4%). Similarly, among the non-pancreatic lesion cases, the sensitivities of slow-pull, 5 ml suction and 10 ml suction were 85.7, 84.6 and 64.7%, respectively, and the specificities were 50, 80 and 92.9%, respectively. The accuracy of 5 ml suction (83.3%) was superior to those of slow-pull (81.25%) and 10 ml suction (71.9%). Overall, the total accuracy of 5 ml suction (86.1%) was greater than those of slow-pull (83.3%) and 10 ml suction (69.9%). Collectively, these results indicated that the lesions were diagnosed more accurately with the EUS-FNA with 5 ml suction technique regardless of the lesion location.

Adequacy scores and tissue quality of specimens. The adequacy scores for histological diagnosis of the obtained tissues are shown in Fig. 4A. The numbers of adequate and inadequate samples in the slow-pull, 5 ml suction and 10 ml suction groups are provided in Fig. 4B. Among the samples obtained from the slow-pull group, 70.6% (24/34) were determined to be adequate for histological diagnosis. By comparison, 86.5 (32/37) and 85.9% (67/78) of the samples obtained from the 5 ml suction and 10 ml suction groups were found to be adequate for histological diagnosis. Therefore, the samples that were obtained for histopathological diagnosis using the 5 ml suction and 10 ml suction techniques were superior to those obtained using normal negative pressure (NNP), although no significant difference was observed (P=0.1118; χ^2 test). By contrast, the samples obtained using 10 ml suction contained more blood compared with those obtained using slow-pull or 5 ml suction techniques (P=0.0056; χ^2 test; Table IV).

Complications. Among the 149 enrolled patients with solid lesions, no complications developed following the EUS-FNA procedures.

Discussion

In the present retrospective comparative analysis, the use of the slow-pull and 5 ml suction techniques during EUS-FNA for pancreatic or non-pancreatic solid lesions with regular

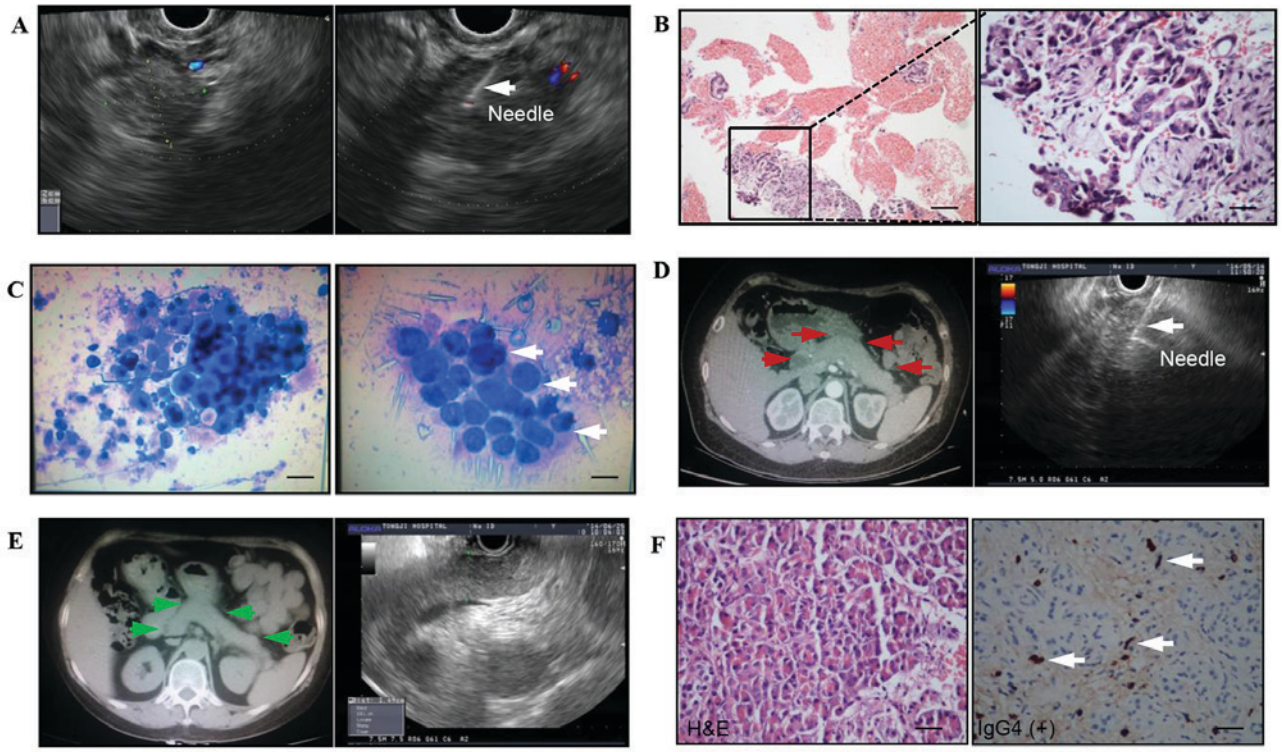


Figure 3. Patients with pancreatic carcinoma or autoimmune pancreatitis. (A-C) A representative case of pancreatic carcinoma. (A) A linear EUS image showed the FNA needle inside a round, undefined lesion (3.5 x3.0 cm), which was detected at the level of the pancreatic head and neck. The white arrow indicated the needle with no interposing vessels. (B) Histological specimen composed of sheets of neoplastic cells with hyperchromatic, molded nuclei and scant cytoplasm. The tissue architecture was recognizable (H&E; original magnification, x200; scale, 10 μm; original magnification, x400; scale, 5 μm). (C) Cytological diagnosis of adenocarcinoma cells (H&E; original magnification, x400; scale, 5 μm). (D-F) A representative case of autoimmune pancreatitis. (D) Computed tomography indicted the lesion in the pancreas head (red arrows). An EUS image showed the FNA needle (white arrow) following penetration into the target tissue. (E) The pancreas returned back to a normal size (green arrows) and normal echoes following immunotherapy. (F) A photomicrograph showed neoplastic cells with strong positive staining (brown areas) for immunoglobulin 4 (original magnification, x200; scale, 10 μm). EUS-FNA, endoscopic ultrasound-guided fine-needle aspiration; H&E, hematoxylin and eosin.

FNA needles (22-G) was associated with superior specificities and accuracies compared with the use of the 10 ml suction technique. Although the sensitivities of the cytological examinations conducted with 5 ml suction and 10 ml suction were worse than that of slow-pull, the increase in diagnostic yield based on histological examination resulted in improved overall diagnostic yields for the 5 ml suction and 10 ml suction techniques. Furthermore, the samples obtained using slow-pull and 5 ml suction contained less contamination with blood compared with those obtained with 10 ml suction. Collectively, these results indicated that the lesions were diagnosed more accurately using EUS-FNA with 5 ml suction techniques regardless of the lesion location.

The requirement for suction during EUS-FNA has been evaluated in previous reports but remains controversial (24,29,30). The application of suction in EUS-FNA was first investigated during the sampling of lymph nodes. In a previous study on the application of EUS-FNA to malignant lymph nodes that were dissected at autopsy (31), continuous and intermittent suction with syringes of between 10 and 30 ml were compared, and continuous low-level suction resulted in optimum cellularity. Another study by Wallace *et al* (32) compared the application of EUS-FNA with and without suction to lymph nodes, and the application of suction increased the cellularity but decreased the specimen quality due to blood contamination. In another previous randomized controlled trial on the application of EUS-FNA with and without suction to pancreatic solid masses (33), which utilized 22 and 25-G needles, the application of suction resulted in greater cellularity, bloodiness and sensitivity. Therefore, the effect of suction during EUS-FNA for pancreatic masses has not yet been fully elucidated. However, the use of suction during EUS-FNA is generally considered to increase the cellularity and blood contamination, which may hinder cytological interpretation.

The European Society of Gastrointestinal Endoscopy (Munich, Germany) technical guidelines advocate the use of suction for the EUS-FNA of solid masses/cystic lesions (34). However, regarding the application of EUS-FNA to lymph nodes (22), the types of negative pressure that should be used with pancreatic and non-pancreatic solid lesions remain vague. Therefore, three different types of negative pressure suction techniques were utilized: A normal condition without negative pressure or a stylet; a moderate negative pressure condition using a 5 ml syringe; and a HNP condition using a 10 ml syringe. The results of the present study revealed that EUS-FNA with the 5 ml suction technique enabled superior specificity and accuracy compared with the 10 ml suction technique, and greater sensitivity of cytological examination compared with the slow-pull technique.

Table IV. Degree of the amount of blood in the specimens.

Amount of blood	0 ml, n (%)	5 ml, n (%)	10 ml, n (%)	P-value (χ^2 test)
Minimal	12 (35.3)	13 (35.1)	10 (12.8)	0.0056[a]
Moderate	15 (44.1)	15 (40.5)	31 (39.7)	
Significant	7 (20.5)	9 (24.3)	37 (47.4)	

[a]P<0.01.

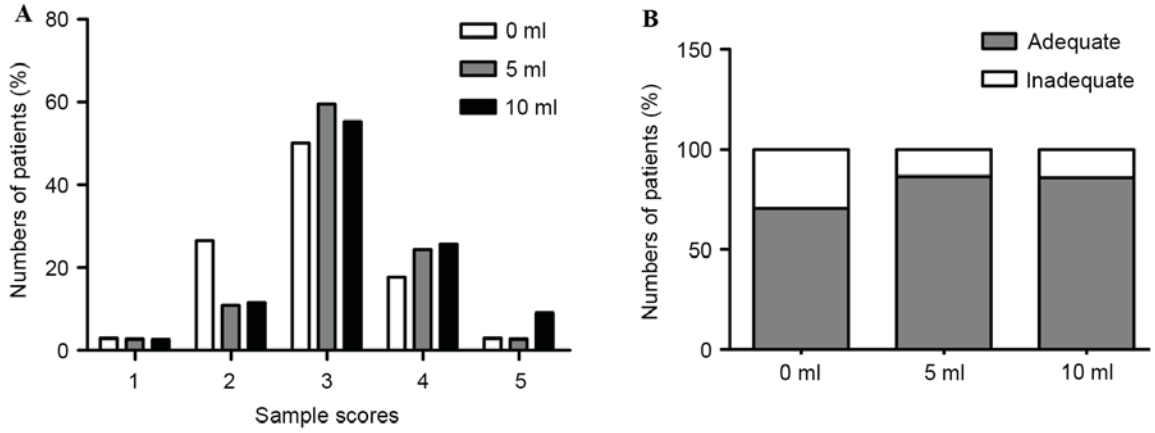


Figure 4. The adequacy of samples obtained for histological diagnosis based on the suction techniques. (A) Scores of 1-5 described the adequacy of samples for histological diagnosis. (B) The percentage of adequate and inadequate samples obtained for histological diagnosis.

A total of two previous studies have indicated that EUS-FNA approaches that employ HNP suction for the aspiration of tissue enable the acquisition of adequate tissue samples (24,28). In addition, a technique has been proposed that reportedly enables the acquisition of tissue cores for histological assessment with standard 22 or 25-G EUS-FNA needles (29,30). The needle is connected to a balloon inflation gun (Alliance II inflation system; Microvasive Endoscopy, Boston Scientific Corporation, Marlborough, MA, USA), which is turned into suction mode to apply HNP (35-60 ml). In a previous study, Larghi *et al* (24) applied this technique prospectively in 27 patients with solid masses. These authors reported that tissue samples for histological examination were obtained in 96% of the cases. Kudo *et al* (23) also used this system and confirmed that biopsy procedures involving the combination of EUS-FNA and HNP techniques of between 35 and 60 ml, are superior to EUS-FNA combined with 10 ml negative pressure procedures in terms of tissue acquisition. One identified problem with the use of EUS-FNA with HNP is that the obtained specimens contain more blood. However, there were no differences between HNP and NNP in terms of diagnostic accuracy. Consequently, as demonstrated in the present study, the samples obtained using 5 ml suction contained less blood contamination compared with those obtained using 10 ml suction. In addition, the samples obtained for histopathological diagnosis via 5 ml suction remained superior to those obtained using slow-pull, although this difference was not significant. Therefore, it appears that the application of EUS-FNA with 5 ml suction is preferable for the diagnosis of mediastinal and intra-abdominal lesions compared with techniques that employ negative pressure applied with slow-pull and 10 ml suction techniques.

There were a number of limitations in the protocol of the present study. One limitation was the relatively low number of cases. The low number of randomized lesions also led to uneven randomization of the different target lesions and diagnostic entities, which may have affected the results. The majority of the patients presented with malignancies and only a few had benign tumors. Specifically, only a few patients possessed hypervascular tumors (n=9, neuroendocrine tumors). Additionally, this is an observational and retrospective study. Although the majority of baseline characteristics are balanced, selective bias and heterogeneity could not be avoided. Although the evidence presented here indicated that EUS-FNA with 5 ml suction is feasible, an additional multicenter, prospective, double-blind, randomized, controlled crossover trial study will be performed to resolve these issues.

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