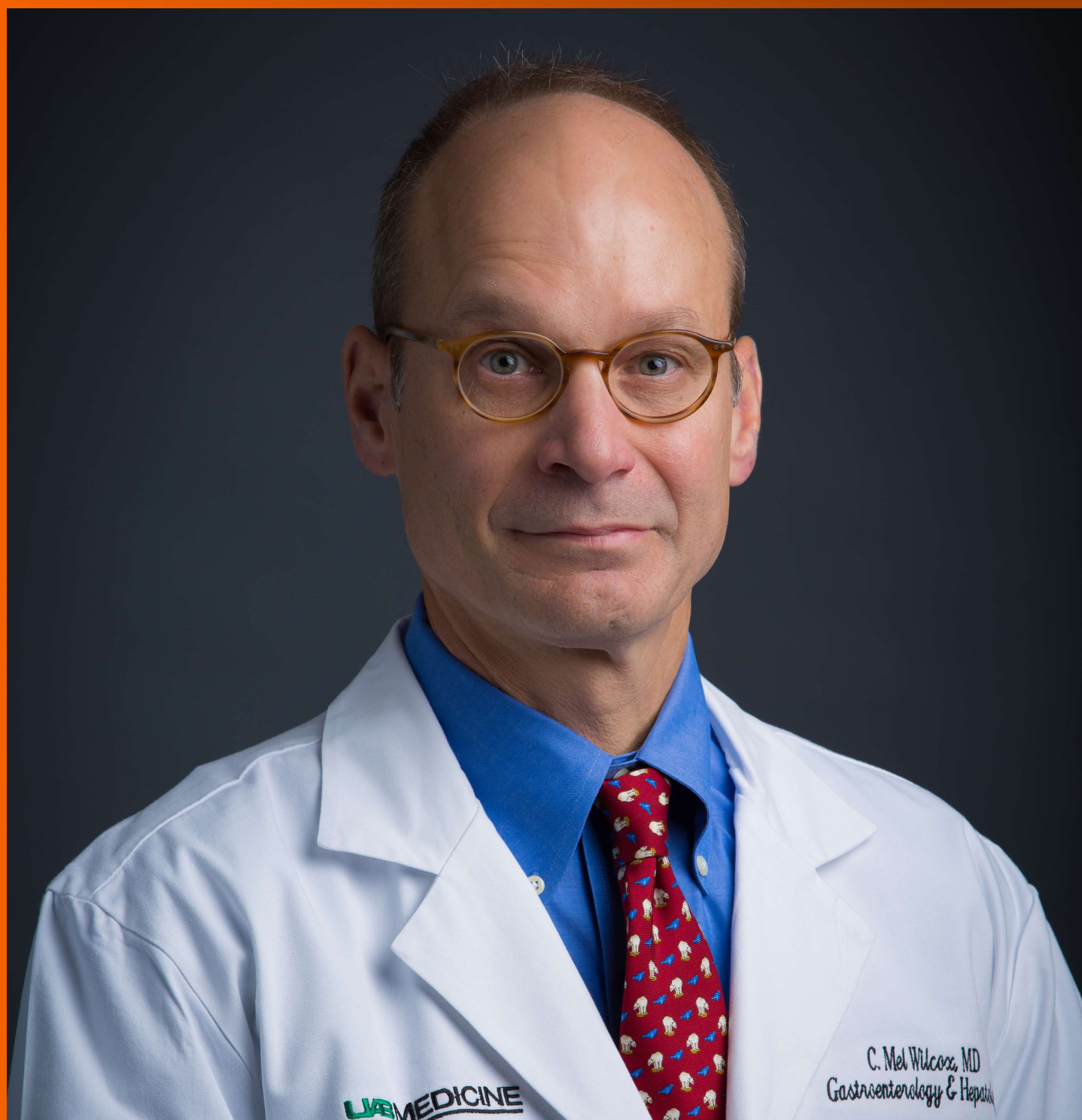


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Retrospective Study

Push *vs* pull method for endoscopic ultrasound-guided fine needle aspiration of pancreatic head lesions: Propensity score matching analysis

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Abstract

AIM

To evaluate the efficacy of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of pancreatic head cancer when pushing (push method) or pulling the echoendoscope (pull method).

METHODS

Overall, 566 pancreatic cancer patients had their first EUS-FNA between February 2001 and December 2017. Among them, 201 who underwent EUS-FNA for pancreatic head lesions were included in this study. EUS-FNA was performed by the push method in 85 patients, the pull method in 101 patients and both the push and pull methods in 15 patients. After propensity score matching (age, sex, tumor diameter, and FNA needle), 85 patients each were stratified into the push and pull groups. Patient characteristics and EUS-FNA-related factors were compared between the two groups.

RESULTS

Patient characteristics were not significantly different between the two groups. The distance to lesion was significantly longer in the push group than in the pull group (13.9 ± 4.9 mm *vs* 7.0 ± 4.9 mm, $P < 0.01$). The push method was a significant factor influencing the distance to lesion (\geq median 10 mm) ($P < 0.01$). Additionally, tumor diameter ≥ 25 mm (OR = 1.91, 95%CI: 1.02-3.58, $P = 0.043$) and the push method (OR = 1.91, 95%CI: 1.03-3.55, $P = 0.04$) were significant factors contributing to the histological diagnosis of malignancy.

CONCLUSION

The pull method shortened the distance between the endoscope and the lesion and facilitated EUS-FNA of pancreatic head cancer. The push method contributed to the histological diagnosis of pancreatic head cancer using EUS-FNA specimens.

Key words: Endoscopic ultrasound-guided fine needle aspiration; Pancreatic head; Pancreatic cancer; Push method; Pull method

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Core tip: Solid pancreatic head lesions are punctured by the push or pull method. We evaluated the efficacy of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) using the push and pull methods for pancreatic head cancer. After propensity score matching (age, sex, tumor diameter, and FNA needle), 85 patients each were stratified into the push and pull groups. Patient characteristics and EUS-FNA-related factors were compared between the two groups. The pull method shortened the distance between the endoscope and the lesion and facilitated EUS-FNA of

pancreatic head cancer. The push method contributed to the histological diagnosis of pancreatic head cancer using EUS-FNA specimens.

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INTRODUCTION

Endoscopic ultrasonography is superior to other imaging modalities for visualizing solid pancreatic lesions^[1,2]. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) plays an important role in the diagnosis of pancreatic cancer. The reported diagnostic sensitivity of EUS-FNA for solid pancreatic lesions is 79%-95.0%, the specificity is 75.0%-100%, and the accuracy is 78.0%-96.0%^[3-8]. The use of EUS-FNA is widespread irrespective of the type of hospital^[9].

However, EUS-FNA is difficult in some situations. Regarding the location of pancreatic lesions, some reports have described the difficulty of EUS-FNA for lesions in the pancreatic head. Haba *et al*^[10] reported that the pancreatic head was an independent factor affecting the accuracy of EUS-FNA for solid pancreatic lesions. Tadic *et al*^[11] reported that 69% of solid pancreatic lesions with intermediate or negative cytological diagnosis by initial EUS-FNA were localized in the pancreatic head. Varadarajulu *et al*^[12] reported that six pancreatic cancers with false-negative results by EUS-FNA were localized in the pancreatic head. A lesion in the pancreatic head was reported to be an independent factor for the requirement for multiple needle passes^[13].

There are two methods of puncturing the pancreatic head. Solid pancreatic head lesions are punctured in the duodenal bulb by pushing (push method) or pulling (pull method) the echoendoscope after it is inserted into the second portion of the duodenum. It is not apparent which of the two methods is more effective. Therefore, we evaluated the efficacy of EUS-FNA of pancreatic head lesions in patients who underwent the push and/or pull method.

MATERIALS AND METHODS

Study design

In this retrospective study, we compared the efficacy of EUS-FNA using the push and pull methods for pancreatic head lesions. This study was approved by the Institutional Review Board of Fukushima Medical University.

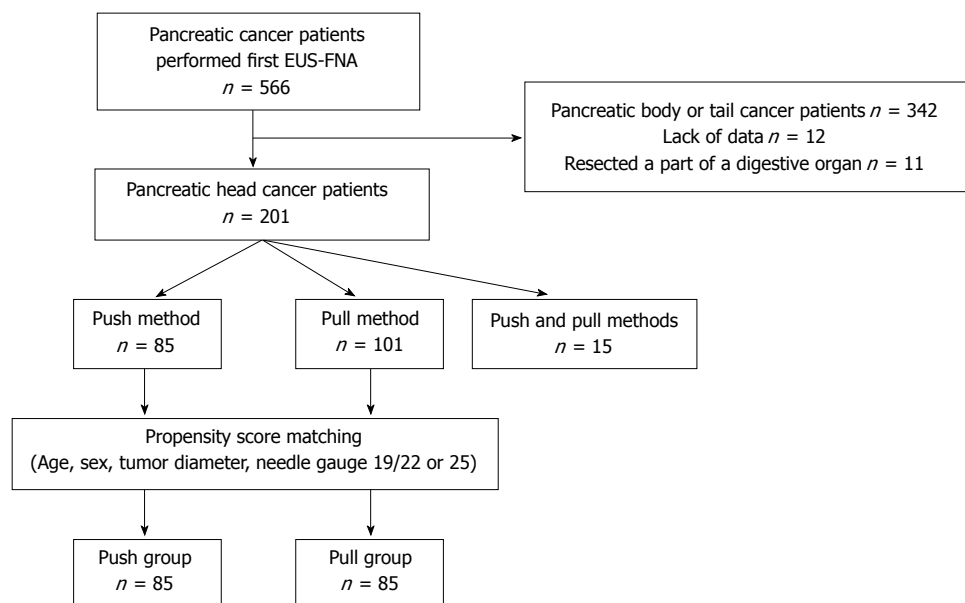


Figure 1 Subjects in this study. Propensity score matching was performed by using patient data [age, sex, tumor diameter, and needle gauge (19/22 or 25)]. After propensity score matching, 85 patients each were stratified into the two groups. EUS-FNA: Endoscopic ultrasound-guided fine needle aspiration.

Patients

In all, 566 pancreatic cancer patients underwent their first EUS-FNA between February 2001 and December 2017 at Fukushima Medical University (Figure 1). Among these patients, 201 who underwent EUS-FNA of the pancreatic head were included in this study. EUS-FNA was performed using the push method in 85 patients, the pull method in 101 patients, both the push and pull methods in 15 patients.

Because of the retrospective design of the study, the push or pull method was not randomly assigned. Therefore, propensity score matching was used to reduce selection bias derived from patient background (age, sex, tumor diameter, and FNA needle type—19/22 or 25 G). Regarding the FNA needle, a 19-G needle was used in only 3 patients. Therefore, propensity score matching was performed based on whether the needle was 25 G. The propensity score was calculated by using logistic regression analysis. After propensity score matching, 85 patients each were stratified into the push and pull groups.

EUS-FNA procedures

An echoendoscope was inserted into the patients after they were sufficiently sedated with midazolam. After the echoendoscope reached the antrum of the stomach or the duodenal bulb, pancreatic head cancer was visualized by pushing the echoendoscope (push method). In contrast, when the echoendoscope reached the descending part of the duodenum, pancreatic head cancer was visualized by pulling the echoendoscope (pull method). After the lack of blood flow was confirmed on the puncture line by Doppler ultrasound, needle passes were started. Rapid onsite cytology (ROSE) of the EUS-FNA specimen was performed by the

cytoscanner^[14-19]. If the amount of the specimen was sufficient, the procedure was completed. However, if the amount of specimen was insufficient, more punctures were performed until sufficient specimen was collected, as determined by the pathologist. Class IV and V disease was characterized as a malignancy by cytology. Histology specimens were fixed overnight in 10% formalin solution. Specimens were sectioned onto slides and stained with hematoxylin and eosin or prepared for immunostaining (p53 or Ki-67) as necessary. Patients not diagnosed with pancreatic cancer by EUS-FNA were eventually diagnosed by EUS-FNA of lymph node metastases, second EUS-FNA, surgery, pathological autopsy, or biliary juice cytology.

The echoendoscope used in this study was GF-Y0005-UCT, GF-UC240AL-5, GF-UCT240AL-5, or GF-UCT260 (Olympus Medical Systems, Tokyo, Japan). The ultrasonography equipment used in this study was EU-ME1 or EU-ME2 (Olympus Medical Systems) or SSD5000 or ALOKA ProSound α-10 (ALOKA, Tokyo, Japan). The biopsy needles were Expect 22 or 25 G or Acquire 22 G (Boston Scientific, MA, USA); EZ Shot 22 G, EZ Shot 2 22 G, EZ Shot 3 plus 22 G, or NA11J-KB (Olympus Medical System); EchoTip 19, 22, or 25 G or Quick-Core 19 G (Cook Medical Inc., NC, United States); or Sonotip 22 or 25 G (Medi-Globe GmbH, Achenmühle, Germany).

Examination items

Patient characteristics (age, sex, and tumor diameter) and factors related to EUS-FNA (needle gauge, number of needle passes, distance to lesion, diagnosis of malignancy by cytology, diagnosis of malignancy by histology, overall diagnosis of malignancy, and adverse events) were compared between the push and pull

Table 1 Comparison of patient characteristics and endoscopic ultrasound-guided fine needle aspiration results

	Push group (<i>n</i> = 85)	Pull group (<i>n</i> = 85)	<i>P</i> value
Patient characteristics			
Age (yr), mean ± SD	67.1 ± 10.2	67.6 ± 9.7	0.77
Sex (male/female)	48/37	46/39	0.88
Tumor diameter (mm), mean ± SD	25.9 ± 10.3	26.6 ± 10.1	0.67
EUS-FNA results			
Distance to lesion	13.9 ± 4.9	7.0 ± 4.9	< 0.01
No. of needle passes of pancreas, mean ± SD	2.4 ± 1.3	2.4 ± 1.3	0.86
Needle gauge			0.57
19	2	1	
22	32	38	
25	51	46	
Diagnosis of malignancy by cytology, <i>n</i> (%)	78 (91.8)	78 (91.8)	1
Diagnosis of malignancy by histology, <i>n</i> (%)	47 (55.3)	34 (40.0)	0.065
Overall diagnosis of malignancy, <i>n</i> (%)	80 (94.1)	80 (94.1)	1
Adverse events			
Abscess around pancreas, <i>n</i> (%)	0 (0)	1 (1.2)	1

EUS-FNA: Endoscopic ultrasound-guided fine needle aspiration.

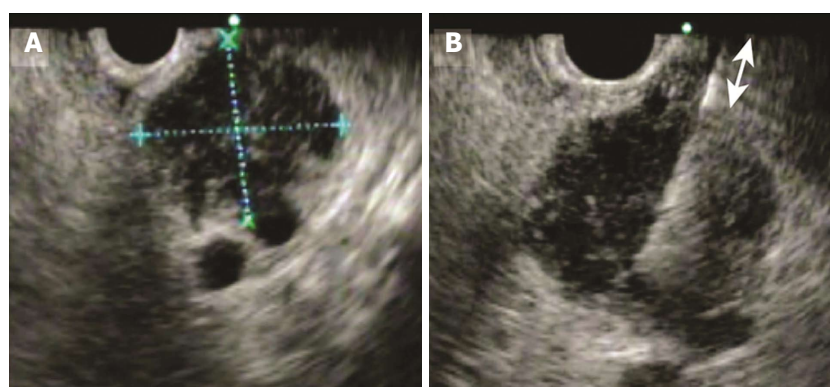


Figure 2 Measurement of tumor diameter and distance to tumor. A: The tumor diameter was measured by endoscopic ultrasonography; B: The distance to the tumor was measured between the upper end of the puncture line and the tumor.

groups. Tumor diameter and the distance to lesion were measured by EUS (Figure 2).

Statistical analyses

Student's *t* test was used to compare continuous variables. Fisher's exact test was used to compare nominal variables. Logistic regression was used to investigate factors that influenced the histological diagnosis of malignancy using EUS-FNA specimens. A *P* value < 0.05 indicated a significant difference. All statistical analyses were performed using the EZR platform (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, EZR is a modified version of the R commander that was designed to perform functions frequently used in biostatistics^[20].

RESULTS

Patient characteristics were not significantly different between the two groups (Table 1). Regarding the

factors related to EUS-FNA, the distance to lesion was significantly longer in the push group than in the pull group (13.9 ± 4.9 mm *vs* 7.0 ± 4.9 mm, *P* < 0.01). Other factors were not different between the two groups.

We investigated factors influencing the distance to lesion [≥ 10 mm (median)]. The push method was identified as significant in the univariate analysis (Table 2). Because no factors with *P* < 0.15 were identified, a multivariate analysis was not performed.

We investigated factors influencing the histological diagnosis of malignancy. Among factors potentially influencing the histological diagnosis of malignancy, tumor diameter ≥ 25 mm and the push method were identified as significant in the univariate analysis (factors with *P* < 0.15 were selected for the multivariate analysis) (Table 3). Logistic regression was performed using these two items, and independent factors included tumor diameter ≥ 25 mm [odds ratio (OR) = 1.91, 95% confidence interval (CI): 1.02-3.58, *P* = 0.043] and the push method (OR = 1.91, 95%CI: 1.03-3.55, *P* = 0.04) (Table 4).

Table 2 Factors influencing the distance to lesion *n* (%)

	Distance to lesion < 10 mm (<i>n</i> = 70)	Distance to lesion ≥ 10 mm (<i>n</i> = 100)	<i>P</i> value
Age ≥ 68 yr	32 (45.7)	56 (56.0)	0.21
Sex, male	35 (50.0)	59 (59.0)	0.28
Tumor diameter ≥ 25 mm	27 (38.6)	45 (45.0)	0.43
Push method	12 (17.1)	73 (73.0)	< 0.01
Needle gauge, 19 or 22 G	32 (45.7)	41 (41.0)	0.64

Table 3 Factors contributing to the diagnosis of malignancy by histology (univariate analysis) *n* (%)

	Malignancy by histology(-) (<i>n</i> = 89)	Malignancy by histology(+) (<i>n</i> = 81)	<i>P</i> value
Age ≥ 68 yr	50 (56.2)	38 (46.9)	0.28
Sex, male	50 (56.2)	44 (54.3)	0.88
Tumor diameter ≥ 25 mm	45 (50.6)	53 (65.4)	0.062
Push method	38 (42.7)	47 (58.0)	0.065
Needle gauge, 19 or 22 G	37 (41.6)	36 (44.4)	0.76
Needle passes ≥ 2	71 (80.0)	59 (72.8)	0.37

Table 4 Factors contributing to the diagnosis of malignancy by histology (multivariate analysis)

	OR	95%CI	<i>P</i> value
Tumor diameter ≥ 25 mm	1.91	1.02-3.58	0.043
Push method	1.91	1.03-3.55	0.040

DISCUSSION

In this study, we investigated which method (push or pull method) of EUS-FNA was more effective in diagnosing pancreatic head cancer. The distance to lesion was significantly longer in the push group than in the pull group, and the push method was an independent factor contributing to the histological diagnosis of malignancy using EUS-FNA specimens.

As mentioned above, the ability to diagnose pancreatic masses by EUS-FNA has been reported to be excellent^[3-8]. However, pancreatic head lesions were reported to be more difficult than lesions in other pancreatic locations to diagnose by EUS-FNA. Some reports have attempted to explain why EUS-FNA is difficult for pancreatic head lesions. One report indicated that pancreatic head lesions are visualized on the middle right of the EUS image, and the lesion is easily moved^[21]. Another report suggested that because the tip of the echoendoscope is flexed, the passage of the needle is more difficult^[22]. In this report, pancreatic head lesions were closer to the starting point when the needle was inserted by the pull method; however, the overall diagnosis of malignancy was not different between the push and pull groups. Thus, if a diagnosis of malignancy is needed or if the endoscopist is inexperienced, EUS-FNA of pancreatic head lesions should be performed by using the pull method.

The pull method better facilitates EUS-FNA for pancreatic head lesions than the push method; however, it has been reported that the echoendoscope position can

become unstable^[22]. In this report, the push method was an independent factor contributing to the histological diagnosis of pancreatic cancer. The direction in which the echoendoscope is pulled is opposite that of the lesion puncture, whereas the direction in which the echoendoscope is pushed is the same as that of lesion puncture. In addition, the echoendoscope is stable in the push method. These factors might explain why the push method contributed to the diagnosis of malignancy by histology of the EUS-FNA specimen. Therefore, the push method is recommended for patients requiring histology of EUS-FNA specimens, for example, patients who have a medical history of other cancers.

This study has some limitations. First, this study was retrospective and performed in a single center. We used propensity scoring to overcome this limitation; however, prospective and large-scale studies are warranted. Second, due to the retrospective nature of this study, EUS-FNA procedures were not performed by specific endoscopists. In this study, EUS-FNA was performed by specialists who had performed > 3000 pancreaticobiliary EUS procedures or by trainees under the guidance of specialists. Therefore, the quality of the EUS procedure was considered constant. Third, the difficulty of each method was not evaluated by Doppler ultrasound of blood flow on the puncture line. Because of the retrospective nature of this study, we were unable to identify the potential difficulty of either method by Doppler ultrasound of blood flow. Fourth, we used an EUS-guided trucut biopsy (EUS-TCB) needle or an EUS-guided fine needle biopsy (FNB) needle, such as the Quick-Core 19 G (Cook Medical Inc.) or Acquire 22 G needle (Boston Scientific). Although these needles have been reported to increase the yield of samples^[23,24], EUS-TCB and EUS-FNB needles were used in only two patients. A Quick-Core needle (Cook Medical Inc.) was used in a patient in the push group, and an Acquire needle (Boston Scientific) was used in a patient in the pull group. Therefore, we do not believe that the use of

EUS-TCB and EUS-FNB needles significantly influenced the results.

In conclusion, the pull method shortened the distance between the endoscope and the lesion and facilitated EUS-FNA of pancreatic head cancer. The push method contributed to the histological diagnosis of pancreatic head cancer using EUS-FNA specimens.

ARTICLE HIGHLIGHTS

Research background

Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) plays an important role in the diagnosis of pancreatic cancer. However, EUS-FNA of pancreatic head lesions is difficult. The pull and push methods are both used to diagnose pancreatic head lesions. It is unknown which method is more efficient.

Research motivation

We wanted to determine the appropriate puncture method for EUS-FNA of pancreatic head lesions.

Research objectives

The primary objective of this study was to reveal which method (push method or pull method) is more efficient for diagnosing pancreatic head cancer.

Research methods

We placed 85 patients in each group (push group and pull group) using propensity score matching. Patient characteristics and some EUS-FNA-related factors were compared between the push and pull groups.

Research results

The distance to the pancreatic cancer was significantly longer in the push group than in the pull group. The push method was identified as a significant factor contributing to the histological diagnosis of malignancy.

Research conclusions

The pull method shortened the distance between the echoendoscope and the lesion and facilitated EUS-FNA of pancreatic head cancer. The push method contributed to the histological diagnosis of pancreatic head cancer using EUS-FNA specimens.

Research perspectives

If only a diagnosis of malignancy is needed or if the endoscopist is inexperienced, the pull method is recommended. However, the push method is recommended for patients requiring histological analysis of EUS-FNA specimens. Further prospective and large-scale studies on these methods are warranted.

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