—Original Article—

Optimal number of needle passes during EUS-guided fine-needle biopsy of solid pancreatic lesions with 22G ProCore needles and different suction techniques: A randomized controlled trial

Wei Zhou[1,*], Shi-Yu Li[1,*], Hui Jiang[2], Li Gao[2], Jun Li[1], Xiang-Yu Kong[1], Li Yang[3], Ai-Qiao Fang[3], Zhen-Dong Jin[1], Kai-Xuan Wang[1]

[1]Department of Gastroenterology, Changhai Hospital, Second Military Medical University/Naval Medical University, Shanghai, China; [2]Department of Pathology, Changhai Hospital, Second Military Medical University/Naval Medical University, Shanghai, China; [3]Digestive Endoscopy Center, Changhai Hospital, Second Military Medical University/Naval Medical University, Shanghai, China

ABSTRACT

Background and Objectives: The sensitivity of EUS-guided fine-needle biopsy (EUS-FNB) varies considerably. The optimal number of passes through a solid pancreatic lesion with a 22G FNB needle during EUS-FNB is controversial. This prospective randomized controlled study aimed to determine the optimal number of needle passes during EUS-FNB of solid pancreatic lesions, with 22G FNB needles and different sampling techniques. **Methods:** Pancreatic masses were sampled using 22G FNB needles with either the stylet slow-pull (SP) technique or the standard-suction (SS) technique. We determined the number of needle passes required to obtain a diagnostic accuracy of >90%. Differences between the two techniques in terms of technical success rate, cytological acquisition, core tissue acquisition, sensitivity, specificity, accuracy, positive predictive value, negative predictive value, and complications were analyzed. **Results:** A total of 120 patients were randomly assigned to either SP or SS group. Three patients who were lost to follow-up and one who did not complete 5 passes due to bent needle head were excluded from the study. Fifty-six cases in the SP group and 60 cases in the SS group were included in the analysis. For SP technique, the cumulative accuracy of passes 1, 2, 3, 4, and 5 was 44.83%, 76.79%, 87.50%, 92.86%, and 94.64%, respectively. For SS technique, the cumulative accuracy of passes 1, 2, 3, 4, and 5 was 71.67%, 85.0%, 90.0%, 93.33%, and 95.0%, respectively. For each group, there was no statistically significant difference in accuracy after 3

How to cite this article: Zhou W, Li SY, Jiang H, Gao L, Li J, Kong XY, *et al*. Optimal number of needle passes during EUS-guided fine-needle biopsy of solid pancreatic lesions with 22G ProCore needles and different suction techniques: A randomized controlled trial. Endosc Ultrasound 2021;10:62-70.

Access this article online

Quick Response Code:

Website: www.eusjournal.com

DOI: 10.4103/EUS-D-20-00147

*Wei Zhou and Shi-yu Li contributed equally to this study and both are the first author.

Address for correspondence

Prof. Kai-Xuan Wang, Department of Gastroenterology, Changhai Hospital, Second Military Medical University/Naval Medical University, Shanghai, China. E-mail: wangkaixuan224007@163.com

Prof. Zhen-Dong Jin, Department of Gastroenterology, Changhai Hospital, Second Military Medical University/Naval Medical University, Shanghai, China. E-mail: zhendjin@126.com

Received: 2020-07-17; **Accepted:** 2020-12-01; **Published online:** 2021-02-11

and 4 passes. After 4 passes, the pooled sensitivity (92.59% *vs*. 93.10%), accuracy (92.86% *vs*. 93.10%), and specificity (100% *vs*. 100%) were similar ($P > 0.05$) in the SP and SS groups, respectively. In addition, positive cytological diagnoses (83.9% *vs*. 85.0%) and positive histological diagnoses (71.4% *vs*. 78.3%) were comparable ($P > 0.05$) in the SP and SS groups, respectively. No statistically significant factor was found associated with diagnostic sensitivity for each group. **Conclusion:** When on-site cytological evaluation is unavailable, we recommend that at least 3 passes with 22G ProCore needles be performed during EUS-FNB using the SS technique, at least 4 passes when using SP technique. The SS technique showed potential advantages over SP technique in tissue acquisition and diagnostic capabilities.

Key words: EUS, fine-needle biopsy, solid pancreatic lesion

INTRODUCTION

Pancreatic ductal adenocarcinoma is a highly lethal disease, for which mortality rates closely parallel incidence rates.[1,2] In 2018, there were an estimated 458,918 new cases of pancreatic ductal adenocarcinoma all over the world, along with an estimated 432,242 deaths.[3] EUS-guided fine-needle biopsy (EUS-FNB) is a widely used, reliable, and safe method for the diagnosis of pancreatic diseases, especially malignant diseases. The clinical practice guidelines proposed by the French Society of Gastroenterology[4] recommend EUS-FNB for differentiating pancreatic ductal adenocarcinoma from a benign lesion or another neoplasm, to ascertain malignancy before the initiation of chemotherapy for unresectable tumors, and before the commencement of neoadjuvant treatment for potentially resectable tumors. EUS-FNB for the detection of pancreatic ductal adenocarcinoma is reported to have widely varying sensitivity rates ranging from 70% to 100%[5-7] and specificity rates ranging from 86% to 100%.[5-8]

The sampling guidelines published by the European Society of Gastrointestinal Endoscopy (ESGE) in 2012 recommended performing at least 5 needle passes for solid pancreatic masses.[9] The 2017 update of the ESGE guidelines recommended performing 2–3 passes with an FNB needle when on-site cytological evaluation was not available.[10] However, some randomized controlled trials (RCTs) have reported that the use of only 3 needle passes does not produce high accuracy rates (defined as 90% or higher). A prospective multicenter RCT[11] reported that the diagnostic yield of EUS-FNB with the 22G FNB needle was 89.43% even after 4 needle passes had been performed through the lesion. Another prospective study[12] showed that after 3 needle passes, the diagnostic yield was only 83.3% for both fine-needle aspiration (FNA) and FNB.

Many RCTs and retrospective studies have analyzed the use of suction during EUS-FNA with different sizes of FNA needles.[13-16] However, as mentioned in the ESGE EUS-guided sampling guidelines,[9] no RCT has yet evaluated the impact of suction on the results of EUS-FNB, and it remains uncertain whether the results from studies using FNA needles can be extrapolated to sampling with FNB needles.

We decided to conduct this study because of three reasons. First, due to the shortage of pathologists in most centers in China and even around the world, rapid on-site evaluation cannot always be performed. As a result, the adequacy of samples cannot be determined on-site during the procedure. If the number of needle passes is insufficient, the diagnosis rate and the subsequent treatment of patients will be affected. Second, the bending of the needle tip and the displacement of the target organ caused by repeated punctures may limit the increase in accuracy derived from increasing the number of needle passes. Third, as the number of needle passes increases, the risk of complications may also increase.

Therefore, the aims of this prospective randomized study were as follows: (1) to determine the optimal number of needle passes that are required to produce high diagnostic accuracy rates of over 90% when performing EUS-FNB with a 22G FNB ProCore needle in patients with solid pancreatic lesions and (2) to compare the two most widely used sampling techniques, *i.e.*, the SP technique and the standard suction (SS) technique, in terms of diagnostic accuracy, tissue acquisition, and cytological diagnoses.

MATERIALS AND METHODS

Ethics statement

The study protocol was approved by the Ethics Committee of Changhai Hospital, Shanghai, China (approval number: CHEC2018-032), and the study was registered at the Chinese Clinical Trial Registry (ID: ChiCTR1800015328). Written informed consent was obtained from all patients.

Patients

A total of 120 patients in Changhai Hospital were enrolled in this study. All enrolled patients met the following criteria: (1) age between 18 and 75 years, (2) diagnosis or suspicion of a solid pancreatic lesion based on previous imaging examination (ultrasonography, computed tomography [CT], or magnetic resonance imaging [MRI]), (3) lesion diameter ≥2 cm, and (4) provision of informed consent. The exclusion criteria were as follows: (1) pregnancy, (2) cystic pancreatic lesion, (3) anticoagulant/antiplatelet therapy that could not be suspended, (4) inability or refusal to provide informed consent, (5) coagulation disorder (platelets $<50 \times 10^3/\mu L$ and international normalized ratio >1.5), (6) cardiorespiratory dysfunction leading to an inability to tolerate intravenous anesthesia, (7) history of mental disease, and (8) other medical conditions that were contraindications for EUS-FNB.

Data collection

The following data were collected from each enrolled patient before the study: baseline characteristics (age, gender, height, and weight), symptoms (pain, jaundice, and weight loss), lesion location, laboratory data (complete blood count, international normalized ratio, bilirubin, and carbohydrate antigen 19-9), and available imaging studies before EUS-FNB.

During the study, the following parameters were recorded: lesion location and size, number of needle passes, specimen adequacy for evaluation, cellularity, cytohistological analysis results, minimum number of needle passes for cytological or histological diagnosis, and procedure-related complications within 24 h after the intervention.

Follow-up evaluation was performed via telephone interviews and hospital visits until the patient's death or the termination of the study (but for at least 12 months in all patients). Symptoms, imaging tests, subsequent treatment, and results of postoperative pathological examinations were included in the follow-up assessments.

EUS-FNB procedure

All procedures were performed by two experienced endoscopists using a linear-array echoendoscope (EG-580UT; Fujifilm, Tokyo, Japan) and a 22G ProCore needle (Cook Medical, National Technology Park, Limerick, Ireland). Immediately before the procedure, patients were placed in the left lateral decubitus position and administered anesthesia-assisted sedation with intravenous propofol (2.0–2.5 mg/kg for initialization and then 8–10 mg/kg/h for maintenance).[17] Vital signs were continuously monitored during the procedure. The EUS-FNB procedure was performed as follows. First, the lesion was localized, and the echoendoscope was positioned. After inserting the needle into the echoendoscope, the lesion was located in the needle path. Under real-time ultrasound guidance, suction was applied as the needle was moved forward and backward within the lesion 10 times, by using a 10-mL syringe attached to the end of the needle (SS technique), or by slowly pulling the stylet out (SP technique). After completing a pass, the needle was completely withdrawn into the sheath. The obtained specimen was prepared by an assistant. Subsequent passes were carried out and processed in the same way. Five passes were carried out for each lesion. No on-site cytologist was available for any of the procedures. The suction technique (SS or SP) was applied in a randomized order determined using random numbers generated by a computer prior to the procedure. Odd numbers were assigned to the SP group, while even numbers were assigned to the SS group.

Specimen preparation

After each pass, the stylet was removed first. The material was completely flushed out with a saline solution. The tissue samples were picked out from the liquid and fixed in a container with formalin solution. The rest of the liquid sample was fixed in a single vial containing BD CytoRich non-gyn fixative (BD SurePath™, Franklin Lakes, NJ, USA) for SurePath processing. Containers with specimens from different passes were numbered accordingly.

The cytological and tissue samples were separately examined by two pathologists, who were blinded to the suction technique used. If the diagnoses were not consistent, the final diagnosis was decided by a pathological quality-control specialist.

Definitions

The cytological and histological findings were classified as positive if the result was "malignant" or "suspicious for malignancy." Pancreatic neuroendocrine

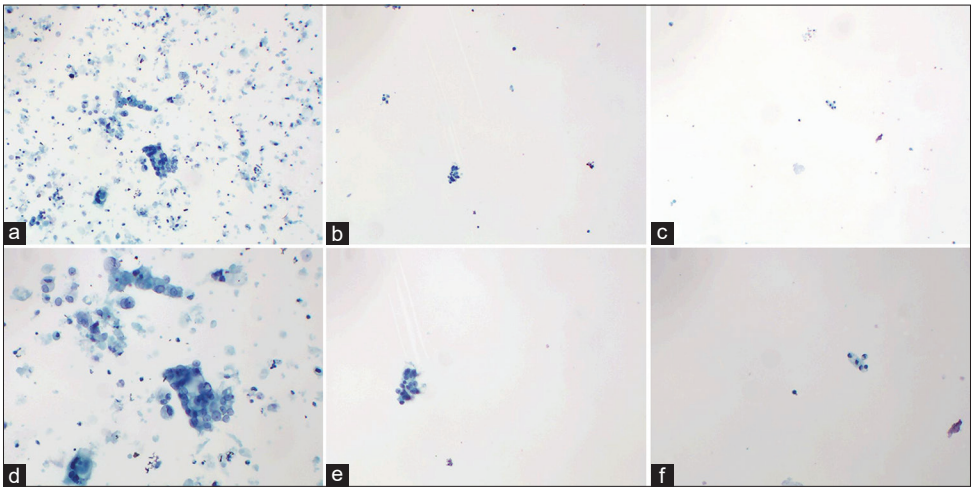

Figure 1. Cellularity of cytological specimens. Grade A: (a) ×100, (d) ×200, more than 4 cell clusters, with a minimum of 10 cells in each cluster, are seen. Grade B: (b) ×100, (e) ×200, 2 cell clusters are seen on the smear. Grade C: (c) ×100, (f) ×200, only 1 cluster of cells is seen on the smear

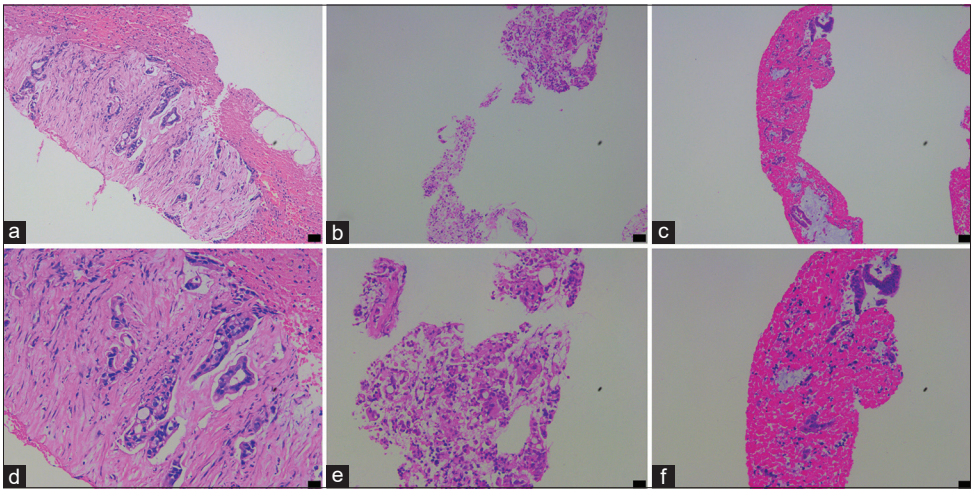

Figure 2. Integrity of tissue specimens. Grade A: (a) ×40, (d) ×100, the neoplastic glands are tubular or cribriform, with interstitial reactions; the diagnosis is pancreatic ductal adenocarcinoma. Grade B: (b) ×40, (e) ×100, scattered and broken heteromorphic glands are seen, with no mesenchymal fibers; the diagnosis is suspected pancreatic ductal adenocarcinoma. Grade C: (c) ×40, (f) ×100, a few heterotypic glands and a small amount of mucus are found in a blood clot; a definite diagnosis cannot be made

tumors (PanNETs) and intraductal papillary mucinous neoplasia were included in the malignant diagnoses for the purpose of analysis. The cellularity of the cytological specimens was graded into 3 levels[18] as follows [Figure 1]: Grade A, more than 4 clusters, with a minimum of 10 cells in each cluster; Grade B, approximately 2–4 clusters, with a minimum of 10 cells in each cluster; and Grade C, fewer than 2 clusters or no cellular smear.

The tissue integrity on histological analysis was also graded into 3 levels[7,19] [Figure 2]: Grade A, existing core tissue (defined as an architecturally intact piece of tissue with a long axis measuring at least 550 μm), which can clearly characterize the lesion, and is sufficient for diagnosis; Grade B, existing core fragments, which does not meet the criteria for architecturally intact histology, but can still yield a diagnosis based on cell morphology; and Grade C, no lesion tissue found, and a diagnosis cannot be made based on the sample.

Complications were defined as unexpected events occurring during or after the procedure and causing morbidity or mortality. Complications included but were not limited to pancreatitis, abdominal pain, fever, gastrointestinal bleeding, and pancreatic leakage.

For patients who underwent surgery, the final diagnosis was based on the definite histological diagnoses obtained from the surgically resected specimens. For patients who did not undergo surgery, the final diagnosis was based on the biopsy findings, postoperative pathological

examination, and follow-up clinical observations. A final diagnosis of a benign lesion was based on the progression of the lesion on radiological studies performed over at least 12 months.[20]

Statistical analysis

Descriptive statistics for continuous variables are presented as means and standard deviations (SDs) or medians and ranges. Continuous variables are expressed as mean (range) and SD and were analyzed using the *t*-tests or Wilcoxon rank-sum test. Categorical variables are expressed as counts and percentages and were analyzed using the Chi-square test. The diagnostic yield is presented as a proportion and was evaluated using the Chi-square test. The tissue integrity and cellularity of specimens in the SP and SS groups were divided into three levels (Grades A, B, and C), and the McNamara test for correlated proportions was used to evaluate these two parameters. The level of statistical significance for all the above tests was defined at a probability value of less than 0.05 ($P < 0.05$). All statistical analyses were performed using IBM SPSS Statistics *v*22.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Patient characteristics

Between April 2018 and May 2019, 120 consecutive patients from Changhai Hospital who met the inclusion criteria were enrolled into the study. Of these, 59 patients were randomly allocated to the SP group, while 61 patients were randomly assigned to the SS group. Four cases were excluded during the study, 3 of whom were lost to follow-up, and 1 case did not complete 5 needle passes due to the needle tip bending. Fifty-six cases in Group A and 60 cases in Group B were included in the analysis. A flowchart of the study is shown in Figure 3. Among the enrolled patients, 67.2% were male, and the mean age of the patients was 60 years. The baseline characteristics of the patients as well as the lesion characteristics are summarized in Table 1. No statistically significant differences were found between the two study groups in terms of age, gender ratio, height, weight, and lesion location and size.

Sample adequacy and complications

Technical success was achieved in all cases. Samples (cytological or histological) of Grades A or B were considered satisfactory. In every patient, at least 1 of the 5 passes yielded a sufficient cytological specimen. After the first pass, the sample adequacy rates were lower in the SP group than in the SS group for both

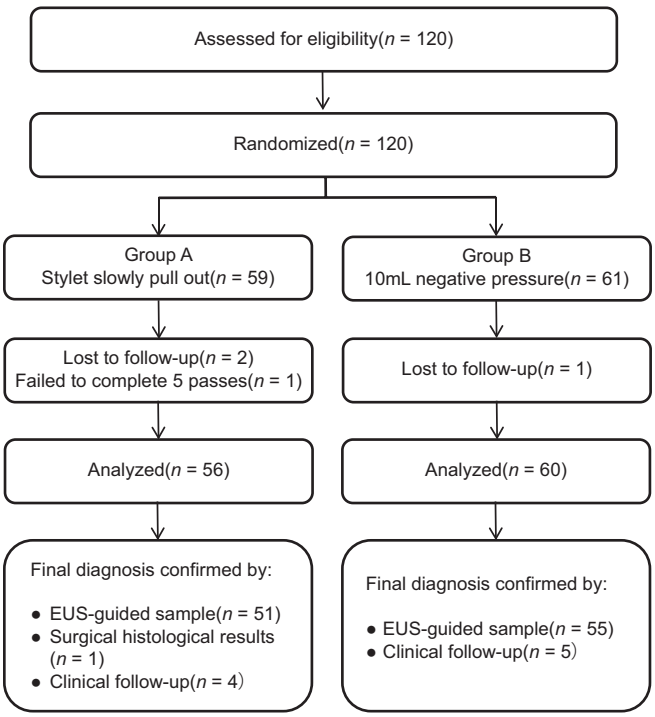

Figure 3: Flowchart of the study

Table 1. Baseline characteristics

	SP	SS	All participants	*P*
Patients, *n*	56	60	116	
Age (years), median (quartile)	61.5 (52-66)	58 (51-64)	60 (52-65)	0.462
Gender (male/female)	35/21	43/17	78/38	0.293
Height (cm), median (quartile)	168 (160-172)	169 (160-172)	168 (160-172)	0.934
Weight (kg), mean±SD	60.1±11.51	63.3±11.04	61.9±11.31	0.617
Lesion location				
Head/uncinate	13	23	36	0.079
Neck/body/tail	43	37	80	
Lesion size (cm), *n*				
2-4	42	43	85	0.685
>4	14	17	31	

SP: Slow pull; SS: Standard suction; SD: Standard deviation

Table 2. Pooled diagnostic parameters after each pass

Number of passes	SP					SS				
	1	2	3	4	5	1	2	3	4	5
Positive diagnoses (*n*)	24	41	47	50	51	41	49	52	54	55
Adequate cytological sample, *n* (%)	38 (67.9)	50 (89.3)	54 (96.4)	55 (98.2)	56 (100)	51 (85.0)	57 (95.0)	59 (98.3)	60 (100)	60 (100)
Adequate histological sample, *n* (%)	17 (30.4)	29 (51.8)	37 (66.1)	43 (76.8)	44 (78.6)	30 (50.0)	38 (63.3)	46 (76.7)	49 (81.7)	52 (86.7)
Positive cytological diagnoses, *n* (%)	21 (37.5)	35 (62.5)	43 (76.8)	47 (83.9)	48 (85.7)	34 (56.7)	44 (73.3)	49 (81.7)	51 (85.0)	52 (86.7)
Positive histological diagnoses, *n* (%)	13 (23.2)	24 (42.9)	33 (58.9)	40 (71.4)	43 (76.8)	26 (43.3)	35 (58.3)	43 (71.7)	47 (78.3)	48 (80.0)
Sensitivity (%)	44.4	75.9	87.0	92.6	94.4	70.7	84.5	89.7	93.1	94.8
Specificity (%)	100	100	100	100	100	100	100	100	100	100
Accuracy (%)	46.4	76.8	87.5	92.9	94.6	71.7	85.0	90.0	93.3	95.0
PPV (%)	100	100	100	100	100	100	100	100	100	100
NPV (%)	6.7	13.3	22.2	33.3	40	10.5	18.2	25	33.3	40

PPV: Positive predictive value; NPV: Negative predictive value; SP: Slow pull; SS: Standard suction

Table 3. Comparison of tissue materials obtained from each needle pass

	Macroscopic tissue acquisition			Histological sample adequacy			Positive diagnoses		
	SP	SS	*P*	SP	SS	*P*	SP	SS	*P*
1st	17	33	0.007	15	30	0.010	11	21	0.064
2nd	23	32	0.186	20	27	0.309	16	23	0.266
3rd	29	38	0.208	24	36	0.065	22	31	0.181
4th	28	32	0.72	25	30	0.564	23	27	0.669
5th	30	38	0.286	27	32	0.582	23	28	0.544

SP: Slow pull; SS: Standard suction

histological testing (30.4% *vs.* 50.0%, $P = 0.029$) and cytological testing (67.9% *vs.* 85.0%, $P = 0.031$). After the second to fifth passes, the cumulative sample adequacy rates for both histological testing and cytological testing were similar in the two groups. The sample adequacy rates for both the groups are shown in Table 2.

The rates of macroscopic tissue acquisition, histological sample adequacy, and positive diagnoses obtained from each single pass in both the groups are shown in Table 3. For the first needle pass, the SS technique acquired more macroscopic tissue material than the SP technique ($P = 0.017$). Similar results were found for the macroscopic tissue acquisition rate. For the other needle passes also, the SS technique showed a potential advantage over the SP technique in terms of tissue sample acquisition.

No complications occurred in any patient after the procedure.

Final diagnoses

Final diagnoses were confirmed using definitive EUS-FNB results ($n = 106$), postoperative pathological results ($n = 1$), and clinical follow-up for more than 12 months ($n = 9$). On May 1, 2020, the follow-up duration for the last enrolled patient was more than 11 months. Patients ($n = 10$) who failed to receive a positive diagnosis after EUS-FNB were followed up for 8–25 months (the follow-up period was calculated until the day of the patient's death or until May 1, 2020). In 4 of the 10 patients who did not receive any treatment, CT or MRI showed no significant change or reduction in lesion size and no distant metastatic lesions after over 17 months of follow-up (17–25 months). We characterized these lesions as benign. Another 5 patients died of pancreatic cancer during the follow-up period. One patient underwent pancreaticoduodenectomy, and the postoperative pathological examination confirmed the diagnosis of pancreatic ductal adenocarcinoma. The follow-up data of these 10 patients are shown in Table 4.

Pancreatic ductal adenocarcinoma was diagnosed in 88 (75.86%) of the study patients: 44 (78.57%) patients in the SP group and 44 (73.33%) patients in the SS group. PanNET was the second most common diagnosis, with 3 (5.36%) patients in the SP group and 6 (10.0%) patients in the SS group. The other diagnoses were adenosquamous carcinoma, lymphoma, acinar cell carcinoma, and undifferentiated carcinoma. There were also 2 cases of benign lesions in each group. The number of cases of each diagnosis is shown in Table 5.

Diagnostic parameters

After each pass, the cumulative sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated [Table 6]. After the first pass, the diagnostic sensitivity and accuracy

Table 4. Follow-up data of patients without a definitive diagnosis after EUS-FNB

Sex	Age (year)	Follow-up period (months)	Therapy	Imaging	Outcomes	Benign or malignant
Female	64	25	None	No significant change	Survival	Benign
Male	66	12	Chemotherapy	Unknown	Death	Malignant
Female	62	10	Chemotherapy	Progression	Death	Malignant
Male	50	20	None	No significant change	Survival	Benign
Male	70	8	Chemotherapy	Progression	Death	Malignant
Male	75	19	None	Lesion shrinkage	Survival	Benign
Male	51	18	Surgery+chemotherapy	Shrinkage of liver lesion	Survival	Malignant
Female	47	10	Chemotherapy	Progression	Death	Malignant
Male	29	17	None	No significant change	Survival	Benign
Male	58	8	Chemotherapy	Progression	Death	Malignant

Table 5. Number of diagnoses (*n*, %)

Diagnosis	SP	SS	All participants
PDAC	44 (78.57)	44 (73.33)	88 (75.86)
PanNET	3 (5.36)	6 (10.0)	9 (7.76)
IPMN	1 (1.79)	0 (0)	1 (0.86)
Adenosquamous carcinoma	2 (3.57)	3 (5.0)	5 (4.31)
Lymphoma	0 (0)	1 (1.67)	1 (0. 86)
Acinar cell carcinoma	1 (1.79)	0 (0)	1 (0. 86)
Undifferentiated carcinoma	0 (0)	1 (1.67)	1 (0. 86)
Benign	2 (3.57)	2 (3.33)	4 (3.45)
False negative	3 (5.36)	3 (5.0)	6 (5.17)
Total	56	60	116

PDAC: Pancreatic ductal adenocarcinoma; PanNET: Pancreatic neuroendocrine tumor; IPMN: Intraductal papillary mucinous neoplasia; SP: Slow pull; SS: Standard suction

were significantly lower in the SP group than in the SS group (P = 0.005 and 0.006, respectively). The difference in NPV between the two groups was not statistically significant (P = 0.636). From the second to the fifth passes, there was no statistically significant difference in the cumulative sensitivity, specificity, accuracy, NPV, and PPV between the two groups.

For the SS group, 3 passes could yield 90% diagnostic accuracy, while for the SP group, at least 4 needle passes were required to yield an accuracy rate of over 90%. In the SP group, the accuracy after 3 and 4 passes was 87.50% and 92.86%, respectively (P = 0.341). In the SS group, the accuracy after 3 and 4 passes was 90.0% and 93.33%, respectively (P = 0.509). The specificity for both the groups was 100%.

Univariate and multivariate analyses to identify factors associated with the diagnostic sensitivity of the SP and SS techniques are shown in Tables 7 and 8. No factor was found to be significantly associated with diagnostic sensitivity in either group.

DISCUSSION

We found that after 3 passes, the diagnostic accuracy rates in the SP and SS groups were 87.50% and 90.0%, respectively; after 4 passes, the diagnostic accuracy rates were 92.86% and 93.33%, respectively. In the SS group, there was no significant difference between the cumulative diagnostic accuracy rates after 3 and 4 passes, and a diagnostic accuracy of 90% was obtained after 3 passes. The present prospective study demonstrated that to obtain a diagnostic accuracy of 90% when performing EUS-FNB with the 22G ProCore needle, a minimum of 4 needle passes were required for the SP technique and at least 3 needle passes were required for the SS technique. This finding contradicts part of the ESGE sampling guidelines,[10] which recommend 2–3 needle passes with an FNB needle in the absence of on-site cytological evaluation. However, this recommendation was based on low-quality evidence. Two previous prospective studies have claimed that 1 or 2 needle passes are sufficient to establish a diagnosis;[19,21] however, the number of patients participating in these studies was small. One multicenter RCT has indicated that 3 passes were required to generate a diagnostic rate of nearly 90%,[22] and two other prospective studies from Chinese medical centers[11,12] have reported that 3 needle passes are insufficient to obtain a diagnostic yield of over 90%. These findings are consistent with our results. Few of the prospective studies on the diagnostic efficacy of EUS-FNB for solid pancreatic lesions conducted in China have had large sample sizes, in spite of the immense popularity of this procedure. The present study reflects the current situation and experience in tertiary hospitals in China well.

In a previous retrospective study in our center,[23] we found that liquid-based cytology (LBC) was superior to

Table 6. Comparison of cumulative diagnostic parameters between the two groups (%, 95% confidence interval)

	Pass 1			Pass 2			Pass 3		
	SP	SS	*P*	SP	SS	*P*	SP	SS	*P*
Sensitivity	44.44 (31.16-58.51)	70.69 (57.09-81.54)	0.005	75.93 (62.06-86.08)	84.48 (72.07-92.23)	0.255	87.04 (74.48-94.2)	89.65 (78.16-95.72)	0.666
Specificity	100 (19.79-100)	100 (19.79-100)	-	100 (19.79-100)	100 (19.79-100)	-	100 (19.79-100)	100 (19.79-100)	-
Accuracy	44.83 (31.96-58.38)	71.67 (58.36-82.18)	0.006	76.79 (63.27-86.60)	85.00 (72.92-92.5)	0.259	87.50 (75.31-94.41)	90.0 (78.83-95.87)	0.670
PPV	100 (82.83-100)	100 (89.33-100)	-	100 (89.33-100)	100 (90.94-100)	-	100 (90.59-100)	100 (91.43-100)	-
NPV	6.25 (1.09-22.22)	10.53 (1.84-34.54)	0.623*	13.33 (2.34-41.61)	18.18 (3.21-52.25)	1.000*	22.22 (3.95-59.81)	25 (4.45-64.42)	1.000*
	Pass 4						Pass 5		
	SP	SS	*P*				SP	SS	*P*
Sensitivity	92.59 (81.26-97.60)	93.10 (82.45-97.77)	1.000*				94.44 (83.66-98.55)	94.83 (84.70-98.65)	1.000*
Specificity	100 (19.79-100)	100 (19.79-100)	-				100 (19.79-100)	100 (19.79-100)	-
Accuracy	92.86 (81.87-97.69)	93.33 (82.99-97.84)	1.000*				94.64 (84.20-98.61)	95.00 (85.18-98.70)	1.000*
PPV	100 (91.11-100)	100 (91.73-100)	-				100 (91.27-100)	100 (91.88-100)	-
NPV	33.33 (6.00-75.89)	33.33 (6.00-75.89)	1.000*				40 (7.26-82.96)	40 (7.26-82.96)	1.000*

SP: Slow pull; SS: Standard suction; PPV: Positive predictive value; NPV: Negative predictive value

Table 7. Diagnostic sensitivity-related factors using the standard suction technique

	OR	*P*
Male gender	0.052	0.819
Lesion size (≤4 cm)	0.025	0.875
Pancreatic head/uncinate	1.933	0.164
Age (≤60 years)	0.222	0.637
BMI (<24)	1.665	0.197

BMI: Body mass index; OR: Odds ratio

Table 8. Diagnostic sensitivity-related factors using the slow-pull technique

	OR	*P*
Male gender	0.041	0.839
Lesion size (≤4 cm)	0.091	0.763
Pancreatic head/uncinate	0.227	0.634
Age (≤60 years)	0.072	0.788
BMI (<24)	0.227	0.634

BMI: Body mass index; OR: Odds ratio

smear cytology (SC) in terms of sensitivity, accuracy, and PPV for pancreatic samples obtained by EUS-FNA/FNB. Furthermore, the combination of SC and LBC was superior to LBC alone in terms of sensitivity, accuracy, and PPV. Considering that EUS-FNB samples from each pass would be sent for testing separately, we tested the cytological samples using LBC only, rather than SC, to ensure that there were enough cytological samples and to improve the diagnostic yield.

The SP technique is considered to perform better for SC, as it involves less blood contamination.[13] Some studies have shown a potentially higher diagnostic yield with the SP technique than with the SS technique for certain needles.[13,14,24] However, two prospective studies[15,25] and a multicenter randomized trial[26] have indicated that there are no significant differences between the SS and SP techniques in terms of diagnostic accuracy. It should be noted that two[25,26] of the above four studies were recent studies involving FNB needles. In our study, the diagnostic yield was comparable between the two suction techniques, but there was a potential trend for the SP technique being inferior to the SS technique in terms of tissue sample acquisition and histological diagnoses, although no statistical significance was found for our current sample size. A possible reason for the above results maybe that the suction force generated by the SP technique was far less than that generated by the SS technique. Katanuma *et al.*[27] compared the suction forces generated by different needles and different sampling techniques. They found that the suction forces for different needles were similar at stylet-pulling speeds of 100 mm/s, 50

mm/s, and 25 mm/s. The suction force generated using the SP method was estimated to be only 3% of the force generated using the SS method for the 22G FNA and FNB needles. Low pressure may be the cause of the relatively poor tissue sample quality.

No factor was found to be significantly associated with diagnostic sensitivity in either group. The main reason might be that after 5 passes, the pooled sensitivity of either group was over 94%, and the regression analysis was affected by the limit number of false-negative cases.

Our study has certain limitations. First, it was a single-center study, and the results may not reflect the practices or techniques used at other institutions. Second, we applied 10 back-and-forth needle movements for each pass, which may reduce the quality of the tissue sample.

CONCLUSION

When on-site cytological evaluation is unavailable, we recommend that at least 3 passes with 22G ProCore needles be performed during EUS-FNB when using the SS technique and at least 4 passes be performed when using the SP technique. The SS technique showed potential advantages over the SP technique in terms of tissue acquisition and diagnostic capabilities.

Financial support and sponsorship

This study was funded by Construction of Shanghai Pancreatic Diseases Medical Center (Grant No. 2017ZZ01009).

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Jia X, Du P, Wu K, *et al*. Pancreatic cancer mortality in China: Characteristics and prediction. *Pancreas* 2018;47:233-7.
2. Kamisawa T, Wood LD, Itoi T, *et al*. Pancreatic cancer. *Lancet* 2016;388:73-85.
3. IARC, GLOBOCAN 2018. Available from: http://globocan.iarc.fr. [Last accessed on 2019 Nov 21].
4. Neuzillet C, Gaujoux S, Williet N, *et al.* Pancreatic cancer: French clinical practice guidelines for diagnosis, treatment and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, ACHBT, AFC). *Dig Liver Dis* 2018;50:1257-71.
5. Ramesh J, Bang JY, Magee HS, *et al*. Randomized trial comparing the flexible 19G and 25G needles for endoscopic ultrasound-guided fine needle aspiration of solid pancreatic mass lesions. *Pancreas* 2015;44:128-33.
6. Berzosa M, Villa N, El-Serag HB, *et al.* Comparison of endoscopic ultrasound guided 22-gauge core needle with standard 25-gauge fine-needle aspiration for diagnosing solid pancreatic lesions. *Endosc Ultrasound* 2015;4:28-33.
7. Fabbri C, Luigiano C, Maimone A, *et al.* Endoscopic ultrasound-guided fine-needle biopsy of small solid pancreatic lesions using a 22-gauge needle with side fenestration. *Surg Endosc* 2015;29:1586-90.
8. Varadarajulu S, Bang JY, Hebert-Magee S. Assessment of the technical performance of the flexible 19-gauge EUS-FNA needle. *Gastrointest Endosc* 2012;76:336-43.
9. Polkowski M, Larghi A, Weynand B, *et al.* Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European society of gastrointestinal endoscopy (ESGE) technical guideline. *Endoscopy* 2012;44:190-206.
10. Polkowski M, Jenssen C, Kaye P, *et al.* Technical aspects of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European society of gastrointestinal endoscopy (ESGE) technical guideline-march 2017. *Endoscopy* 2017;49:989-1006.
11. Cheng B, Zhang Y, Chen Q, *et al.* Analysis of fine-needle biopsy vs. fine-needle aspiration in diagnosis of pancreatic and abdominal masses: A Prospective, multicenter, randomized controlled trial. *Clin Gastroenterol Hepatol* 2018;16:1314-21.
12. Tian L, Tang AL, Zhang L, *et al*. Evaluation of 22G fine-needle aspiration (FNA) versus fine-needle biopsy (FNB) for endoscopic ultrasound-guided sampling of pancreatic lesions: A prospective comparison study. *Surg Endosc* 2018;32:3533-39.
13. Nakai Y, Isayama H, Chang KJ, *et al.* Slow pull versus suction in endoscopic ultrasound-guided fine-needle aspiration of pancreatic solid masses. *Dig Dis Sci* 2014;59:1578-85.
14. Saxena P, El ZM, Stevens T, *et al*. Stylet slow-pull versus standard suction for endoscopic ultrasound-guided fine-needle aspiration of solid pancreatic lesions: A multicenter randomized trial. *Endoscopy* 2018;50:497-504.
15. Kin T, Katanuma A, Yane K, *et al.* Diagnostic ability of EUS-FNA for pancreatic solid lesions with conventional 22-gauge needle using the slow pull technique: A prospective study. *Scand J Gastroenterol* 2015;50:900-7.
16. Sahai AV, Paquin SC, Gariépy G. A prospective comparison of endoscopic ultrasound-guided fine needle aspiration results obtained in the same lesion, with and without the needle stylet. *Endoscopy* 2010;42:900-3.
17. Wang KX, Jin ZD, Du YQ, *et al.* EUS-guided celiac ganglion irradiation with iodine-125 seeds for pain control in pancreatic carcinoma: A prospective pilot study. *Gastrointest Endosc* 2012;76:945-52.
18. Lee JK, Choi JH, Lee KH, *et al.* A prospective, comparative trial to optimize sampling techniques in EUS-guided FNA of solid pancreatic masses. *Gastrointest Endosc* 2013;77:745-51.
19. Iwashita T, Nakai Y, Samarasena JB, *et al.* High single-pass diagnostic yield of a new 25-gauge core biopsy needle for EUS-guided FNA biopsy in solid pancreatic lesions. *Gastrointest Endosc* 2013;77:909-15.
20. Yeon MH, Jeong HS, Lee HS, *et al*. Comparison of liquid-based cytology (CellPrepPlus) and conventional smears in pancreaticobiliary disease. *Korean J Intern Med* 2018;33:883-92.
21. Leung Ki EL, Lemaistre AI, Fumex F, *et al.* Macroscopic onsite evaluation using endoscopic ultrasound fine needle biopsy as an alternative to rapid onsite evaluation. *Endosc Int Open* 2019;7:E189-94.
22. Cho E, Park CH, Kim TH, *et al.* A prospective, randomized, multicenter clinical trial comparing 25-gauge and 20-gauge biopsy needles for endoscopic ultrasound-guided sampling of solid pancreatic lesions. *Surg Endosc* 2020;34:1310-7.
23. Zhou W, Gao L, Wang SM, *et al*. Comparison of smear cytology and liquid-based cytology in EUS- guided fine-needle aspiration of pancreatic lesionexperience from a large tertiary center. *Gastrointest Endosc* 2020;91:932-42.
24. Chen JY, Ding QY, Lv Y, *et al.* Slow-pull and different conventional suction techniques in endoscopic ultrasound-guided fine-needle aspiration of pancreatic solid lesions using 22-gauge needles. *World J Gastroenterol* 2016;22:8790-7.
25. El Haddad R, Barret M, Beuvon F, *et al.* The slow-pull capillary technique increases the quality of endoscopic ultrasound fine needle biopsy samples in solid pancreatic lesions. *Eur J Gastroenterol Hepatol* 2016;28:911-6.
26. Di MR, Mocciaro F, Antonini F, *et al*. Stylet slow-pull vs. standard suction technique for endoscopic ultrasound-guided fine needle biopsy in pancreatic solid lesions using 20 Gauge Procore needle: A multicenter randomized trial. Dig Liver Dis 2020;52:178-84.
27. Katanuma A, Itoi T, Baron TH, *et al.* Bench-top testing of suction forces generated through endoscopic ultrasound-guided aspiration needles. J *Hepatobiliary Pancreat Sci* 2015;22:379-85.