Comparison of specimen quality among the standard suction, slow-pull, and wet suction techniques for EUS-FNA: A multicenter, prospective, randomized controlled trial

Tian-Yin Chen¹, Ji-Wang Cao², Chen Jin³, Yuan Ji⁴, Liang Zhong⁵, Li-Mei Wang⁶, Ning Cui⁶, Yang Di⁶, Yun Bao⁷, Ning Zhong⁶, Yi-Qun Zhang¹, Ping-Hong Zhou¹

¹Endoscopy Centre and Endoscopy Research Institute, Zhongshan Hospital, Fudan University, Shanghai, China; ²Department of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan, Hubei Province, China; ³Department of Pancreatic Surgery, Pancreatic Disease Institute, Huashan Hospital, Fudan University, Shanghai, China; ⁴Department of Pathology, Zhongshan Hospital, Fudan University, Shanghai, China; ⁵Department of Gastroenterology, Huashan Hospital, Fudan University, Shanghai, China; ⁶Department of Gastroenterology, Laboratory of Translational Gastroenterology, Qilu Hospital of Shandong University, Jinan, Shandong Province, China; ⁷Department of Pathology, Huashan Hospital, Fudan University, Shanghai, China

ABSTRACT

Background and Objectives: Standard suction technique (SST), slow-pull technique (SPT), and wet suction technique (WEST) of EUS-FNA are designed to improve the diagnostic yields of solid and solid-cystic lesions. We conducted a multicenter, prospective, randomized crossover trial to compare SST, SPT, and WEST on specimen quality and diagnostic accuracy using a 22G needle. Methods: Patients with solid or solid-cystic lesions referred for EUS-FNA at four tertiary hospitals from December 2017 to August 2019 were considered eligible. All lesions were sampled using a 22G needle by the three techniques performed consecutively in a randomized order. The primary outcome was quality of the specimen acquired by each technique regarding blood contamination, tissue integrity and cellularity for diagnosis, graded on a predefined scale. The secondary outcomes were the diagnostic yield of EUS-FNA and the incidence of adverse events. ClinicalTrial.gov registration number: NCT03567863. Results: A total of 300 patients (mean age, 60.6 years, 188 men) were enrolled. WEST was superior (mean score 4.02 ± 1.51) over SST (3.67 ± 1.57, P = 0.018), but comparable to SPT (3.83 ± 1.55, P = 0.370) in overall specimen quality evaluation. WEST produced better tissue integrity (1.42 ± 0.74) and higher cellularity (1.32 ± 0.80) than SST and SPT. SPT (1.43 ± 0.69)

How to cite this article: Chen TY, Cao JW, Jin C, Ji Y, Zhong L, Wang LM, et al. Comparison of specimen quality among the standard suction, slow-pull, and wet suction techniques for EUS-FNA: A multicenter, prospective, randomized controlled trial. Endosc Ultrasound 2022;11:393-400.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com
INTRODUCTION

EUS-FNA has become the most effective and valuable modality for the diagnosis of a variety of solid and solid-cystic lesions.[1] Although the adoption of EUS-fine needle biopsy (EUS-FNB) is becoming popular in western countries in the last decade,[2-7] in most countries, EUS-FNA remains to be one of the main ways of obtaining specimens for diagnosing various abdominal, pelvic, and mediastinal lesions due to its widespread availability and low cost. The reported accuracy and diagnostic yield of EUS-FNA have varied significantly in the literature.[8-11]

In recent years, in addition to the standard suction technique (SST), new techniques of EUS-FNA have been developed, including the slow-pull technique (SPT) and the wet suction technique (WEST). SST was designed to increase the quantity of the aspirated tissue by using negative pressure during EUS-FNA. However, negative pressure increases not only the amount of tissue acquired but also the amount of blood contamination and disruption of tissue integrity.[12] SPT, in comparison, uses minimal negative pressure to siphon the tissue, and thus in theory avoids excessive blood contamination.[13,14] Both SPT and SST have been well studied.[8,13,15] WEST, on the other hand, is still a novel and promising method with limited knowledge of its effectiveness.[10,21] The technique involves flushing the EUS-FNA needle with a saline solution to replace the column of air within the lumen of the needle before aspiration. The saline solution column keeps the needle from getting clogged while avoiding the inherent inconvenience of a metal stylet.[12]

While WEST has showed potential, relevant studies were limited, and the sample sizes were too small to confirm its true clinical value.[12,17,20] To date, there has been no study comparing head-to-head the three techniques.

Therefore, we conducted this study to compare the three techniques in a prospective, randomized crossover trial. Our study aimed to examine the effects of SST, SPT, and WEST on specimen quality and diagnostic accuracy in solid and solid-cystic lesions using a 22G needle to find the best technique.

METHODS

Study design and oversight

This multicenter, prospective, randomized crossover trial was conducted in four tertiary care hospitals in China, including Zhongshan Hospital (Fudan University, Shanghai), Huashan Hospital (Fudan University, Shanghai), Qilu Hospital (Shandong University, Jinan) and Renmin Hospital of Wuhan University (Wuhan University, Wuhan) from December 2017 to August 2019. The study was carried out in accordance with the Helsinki Declaration and was approved by the institutional review boards at all participating centers. All patients provided written informed consent before enrollment. The study was registered in the ClinicalTrial.gov database (NCT03567863). The trial steering committee designed the study and supervised the fidelity of the study protocol. The trial coordinating center managed the data collection and biostatistical analysis. All authors had full access to the study data and approved the final manuscript.

Patients

All patients who were referred to the endoscopy center for EUS-FNA in all four hospitals during the study period were screened. Patients were eligible for enrollment if they are at least 18 years old and had at least one imaging study (computed tomography [CT], magnetic resonance imaging, or positron emission tomography-CT) confirming the presence of and adequately characterizing a solid or solid-cystic lesion in the mediastinum, abdomen, or pelvis. The exclusion criteria were pregnancy, sepsis, cystic lesions, coagulopathy (international normalized ratio >1.5) or thrombocytopenia (platelets <50,000/mm$^3$), and refusal to participate in the study.

Randomization

Randomization, stratified according to the hospital, was done using a computer-generated sequence. The
randomization assignments establishing the order of the three techniques were placed in sealed envelopes and opened during the procedure when the patient matched the inclusion criteria. All three techniques were used on each patient. For Group A, the order was SST-SPT-WEST, and for Group B, Group C, Group D, Group E, Group F, the orders were SST-WEST-SPT, WEST-SST-SPT, SPT-SST-WEST, SPT-WEST-SST, respectively. The sequence was assigned regardless of lesion location or characteristics (solid/solid-cystic). The endosonographers were aware of the study-group assignments, but the patients, study coordinators, and pathologists were blinded.

**Intervention Equipment**

The endosonographers performed the procedures using a Fujifilm linear echoendoscope (EG-580UT; Fujifilm, Tokyo, Japan) with a SU9000 (Fujifilm, Tokyo, Japan) ultrasonic processor or an Olympus linear echoendoscope (GF-UCT 260, GF-UCT 240; Olympus, Tokyo, Japan) with an EU-ME2 (Olympus, Tokyo, Japan) ultrasound processor based on availability in each center. The procedures were performed using a 22G needle (EchoTip Ultra HD; Cook Endoscopy, Winston-Salem, NC).

**EUS-FNA procedures**

All procedures were performed by one of the four experienced endosonographers at each center (Z.Y., J.C., Z.N., C.J.). Each had experience of over 1000 EUS-FNA procedures. All patients received monitored anesthesia care with propofol. The EUS exam was performed before FNA in each case to locate the lesion. Once targeting the lesion, a total of 3 needle passes were performed according to the randomization sequence. Macroscopic on-site evaluation (MOSE) was used to assess on-site specimen adequacy. Each specimen was examined by MOSE no matter which technique it was to determine whether extra passes were needed. Additional passes were added if the endosonographer considered all three specimens inadequate.

For the SST, after the needle was advanced into the lesion, the stylet was removed, and a 10-mL syringe was attached in a “locked” position to the needle with maximal suction. Once the lesion was punctured, suction was applied. The slow-pull technique (SPT) required the assisting nurse to withdraw the stylet slowly and continuously throughout the FNA process once the needle was advanced into the lesion. For the wet suction technique (WEST), the stylet was removed before the puncture. The needle was then flushed with 5-mL saline solution to replace the column of air. A 10 mL syringe with maximal suction was applied after the needle punctured into the lesion.

With each technique, every pass required approximately 20-30 back and forth movements of the needle. Upon the completion of specimen collection, the suction was turned off, and the needle was withdrawn.

All samples were sent to a designated pathologist at each center, who had no information of the technique with which the specimens were collected.

**Histopathological assessment**

All aspirate specimens were reviewed and graded by an experienced pathologist (who had experience of over 500 EUS-FNA diagnoses) at each center. Each slide of the aspirate specimen was graded in three aspects: (1) blood contamination (0 = blood clots present, 1 = red blood cells contaminated and 2 = free of blood); (2) tissue integrity (0 = no architecturally intact tissue present, 1 = 1-2 architecturally intact tissue present, 2 = ≥3 architecturally intact tissue present); (3) cellularity (0 = <10/high power field [HPF], 1 = <50/HPF, 2 = >50/HPF). The grading system was modified from a previously validated scale, aiming for a comprehensive evaluation of the quality of the specimen. All three scores were added for a final score [Table 1 and Figure 1].

**Study outcomes**

The primary outcome was defined as the recorded quality of the specimens obtained by EUS-FNA with each aspiration technique. The specimen quality was assessed based on the grading system determined by blood contamination, tissue integrity, and cellularity, as mentioned above. The secondary outcomes included the diagnostic accuracy of each EUS-FNA technique and the incidence of an adverse event. The diagnostic accuracy was defined as the proportion of correct
Chen, et al.: Comparison of specimen quality of EUS-FNA

Follow-up was scheduled in the outpatient clinic for all patients on weeks 1, 12, 24, and months 12 to confirm the diagnostic yield of the EUS-FNA results. The gold standard of malignancy was: (1) surgical pathology showing malignancy when available; (2) if surgical pathology was not available, a positive EUS-FNA result or a characteristic clinical course indicative of malignancy was considered positive; (3) if surgery was not performed, a negative EUS-FNA result and no disease progression on clinical follow-up was considered negative.

**Statistical analysis**

Based on prior publications,[12] we hypothesized that the WEST was superior to SST and SPT. A sample size of 285 participants gave us an 80% power at a significance level (alpha) of 0.05 to detect a mean of paired differences of 0.1 with an estimated standard deviation of 0.6 with respect to the grading system. The sample size was expanded to 300 to compensate for possible sample loss. Intention-to-treat analysis was performed for patients who had at least one pass.

All categorical variables were described as counts and percentages, whereas the continuous variables were expressed as mean ± standard deviation. Quantitative descriptive analyses were computed for all variables as appropriate. Frequencies or means were calculated for demographic and clinical characteristics and compared between technique groups. To compare specimen quality, which was quantified by the grading system, a two-way analysis of variance followed by a two-tailed paired t-test was used. A two-tailed P value of <0.05 was considered statistically significant. Bonferroni’s correction was applied to adjust for multiple testing. All analyses were performed with SPSS version 25 (SPSS Inc., Chicago, IL, USA).

**RESULTS**

**Patient characteristics**

Between December 2017 to August 2019, a total of 300 patients underwent randomization, 52 in Group A, 53 in Group B, 55 in Group C, 38 in Group D, 51 in Group E, and 51 in Group F. Two patients (1 in Group C, 1 in Group E) dropped out of the trial due to presence of a vessel in the puncture path [Figure 2]. The baseline patient demographic and clinical characteristics are listed in Table 2. The six groups (A-F) were well matched in terms of baseline characteristics in the intention-to-treat population [Supplement Table 1]. Of the remaining 298 patients, 145 patients were from Zhongshan Hospital, 41 from Hua1shan Hospital, 67 from Qilu Hospital, and 45 from Renmin Hospital of Wuhan University. The mean age of all patients was 60.6 ± 10.6 years old, ranging from 23 to 87. Male patients made up 63.1% (188/298) of all participants. The median lesion size was 36mm with a mean of 38.2 ± 16.1mm, ranging from 6 to 163 mm. Related previous surgery was defined as a history of any surgical procedure involving the target of EUS-FNA or interfering with the FNA pathway.

Malignancies counted for 267 cases (89.6%) and benign lesions added up to 31 cases (10.4%). Pancreatic adenocarcinoma accounted for most malignancies (196/267, 73.0%) and chronic pancreatitis was the most common (15/31, 48.4%) benign lesion [Table 2].

**Specimen quality**

We scored blood contamination of EUS-FNA specimens as 0, 1, and 2 for blood clots present,
red blood cells contaminated, and free of blood, respectively. SPT was superior (mean score of 1.43 ± 0.69) to SST (1.27 ± 0.72, \(P = 0.004\)) and WEST (1.28 ± 0.71, \(P = 0.006\)) [Table 3 and Figure 3]. Tissue integrity and cellularity were both graded on a scale of 0 to 2. WEST offered the best tissue integrity with a mean score of 1.42 ± 0.74 and highest cellularity with a mean score of 1.32 ± 0.80 as compared to SST (tissue integrity 1.23 ± 0.78, \(P = 0.002\); cellularity 1.18 ± 0.84, \(P = 0.030\)) and SPT (tissue integrity 1.22 ± 0.77, \(P = 0.001\); cellularity 1.17 ± 0.82, \(P = 0.024\)) [Table 3 and Figure 3]. The overall specimen quality, as defined by the sum of the three scores, was the best for WEST (mean score 4.02 ± 1.51), followed by SPT (3.83 ± 1.55, \(P = 0.370\)) and SST (3.67 ± 1.57, \(P = 0.018\)) [Table 3 and Figure 4].

**Subgroup analysis**

A post-hoc analysis was made regarding lesion size as well as pancreatic and non-pancreatic lesions. All lesions were divided into four groups according to quartile of lesion size (≤26mm, >26mm to ≤36mm, >36mm to ≤46mm, and >46mm). There was no tendency for the final score of specimen quality in SPT to be higher than the other two techniques with larger lesion sizes, without reaching statistical significance (\(P = 0.479\)) [Supplement Table 2].

The final score of specimen quality between pancreatic lesions and non-pancreatic lesions with the three techniques were evaluated. There was no significant difference between pancreatic lesions and non-pancreatic lesions (\(P = 0.309\)) [Supplement Table 2].
Diagnostic accuracy

WEST achieved a diagnostic accuracy of 74.7% (222/297), which was higher than SST (64.4%, 192/298, P = 0.007) and SPT (65.0%, 193/297, P = 0.012) [Figure 4]. The diagnostic accuracy of EUS-FNA with all three passes was 93.3% (278/298).

Safety and adverse events

Only one patient (1/298, 0.3%) with a pancreatic lesion in the uncinate process experienced pulsatile bleeding after the first EUS-FNA pass with SST and was managed with metal clips successfully. The following two passes were suspended due to the risk of re-bleeding. EUS-FNA specimen and follow-up result confirmed the lesion was chronic pancreatitis. No other patients had severe bleeding nor other significant EUS-FNA related adverse events during and one week after the procedure.

DISCUSSION

The wet suction technique was first reported in 2015,[12] and only a few studies evaluated its performance. The 2017 ESGE EUS-FNA technical guideline[24] mentioned this technique, with only limited evidence supporting its use.

The quality of the sample was chosen as the major outcome in this study as this is a direct indicator of the technical performance of the FNA. A more clinically relevant outcome will be the diagnostic yield. However, diagnostic yield can be affected by multiple factors other than the effectiveness of the sampling method, such as methods used for pathology processing, experience of the pathologist, and also the case mix (e.g., percentage of malignancy). Using sample quality as the major outcome measurement, in addition to the direct head to head randomized trial design, took these confounding factors out of the equation, and thus provides valuable information on the effectiveness of the different techniques.

The results of our study suggested that in terms of the overall specimen quality, the wet suction technique is comparable to the slow-pull technique and is superior to the SST. In clinical practice, we noticed that inserting the stylet into the needle to release the aspirate was difficult with the SST, probably due to the high viscosity of the clots.[25] When a clot forms, the ability to aspirate will decrease, which leads to lower cellularity, tissue integrity, and diagnostic yield. This may be one of the reasons why the SST received a lower score in our study compared to the slow-pull technique, which aspirates little blood, or the wet suction technique, where the saline-solution column prevents clot formation.

There was a tendency for the slow-pull technique to perform better in larger lesions (mean final score 4.14 ± 1.58 vs. 3.93 ± 1.55 in wet suction technique and 3.85 ± 1.60 in SST for lesions larger than 46mm).
Lee’s study suggested a tumor size >40 mm is associated with increased diagnostic accuracy,[26] and El Haddad’s study suggests that more tissue is acquired using the slow-pull technique.[27] Our results backed up both findings from these studies. One theory behind these findings begins with the assumption that large lesions run out of blood supply leading to central necrosis. With higher negative pressure, it is more likely to aspirate fragile material like necrosis. However, since the slow-pull technique only provides minimal negative pressure, chances of acquiring visible tissue are higher than mere necrosis. Therefore, the aspirate of large lesions using the slow-pull technique may result in more viable tissue compared to other techniques. Moreover, we noticed that some of the studies which reported relatively low diagnostic efficacies were conducted using a 20G needle,[19] which might weaken the siphoning effect. Accordingly, we propose that in large lesions with necrosis, a combination of wet suction and slow-pull techniques may be a better option for EUS-FNA.

The safety of EUS-FNA with the three techniques has been well established in previous studies. The most common reported adverse events were acute pancreatitis, pain, fever, and bleeding, with an incidence rate of 0.56% to 2.54%.[28,29] In our study, one patient with a pancreatic uncinate process lesion experienced pulsatile bleeding after the first EUS-FNA pass using the SST and was managed successfully with metal clips. The incidence rate of bleeding was 0.3%, confirming the safety of EUS-FNA.

This study has a few limitations. The majority of lesions were pancreatic adenocarcinomas; therefore, there may not be sufficient power to detect a possible difference for non pancreatic lesions. In a future study, a larger sample size of nonpancreatic lesions may provide new insights.

CONCLUSIONS

In conclusion, the slow-pull technique acquired specimens with the least blood contamination. In terms of overall specimen quality, using a 22G EUS-FNA needle, the wet suction technique was superior to the SST and comparable to the slow-pull technique. In terms of tissue integrity, cellularity and diagnostic accuracy, the wet suction technique was superior to both the standard suction and the slow pull techniques.

Acknowledgments

We are indebted to associate research fellow Xuejuan Jin of the Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital, Fudan University, for her assistance with the statistical analysis and Dr. Lin Liu of the Department of Pathology, Renmin Hospital of Wuhan University and Dr. Peng Su of the Department of Pathology, Qilu Hospital of Shandong University, for reviewing and diagnosing the specimens. We thank all staff from the Endoscopy Center of Zhongshan Hospital for their helpful support and contributions.
Financial support and sponsorship
This work was financially supported in part by grant of the Shanghai Municipal Health Bureau (2019Y0138).

Conflicts of interest
There are no conflicts of interest.

Supplementary Materials
Supplementary information is linked to the online version of the paper on the Endoscopic Ultrasound website.

REFERENCES
1. Facciorusso A, Wani S, Triantafyllou K, et al. Comparative accuracy of needle sizes and designs for EUS tissue sampling of solid pancreatic masses: A network meta-analysis. Gastrointest Endosc 2019;90:893–903.e7.
2. Asokkumar R, Yung Ka C, Loh T, et al. Comparison of tissue and molecular yield between Fine-Needle Biopsy (FNB) and Fine-Needle Aspiration (FNA): A randomized study. Endosc Int Open 2019;7:E959-63.
3. Trindade AJ, Benias PC, Alshelleh M, et al. Fine-needle biopsy is superior to fine-needle aspiration of suspected gastrointestinal stromal tumors: A large multicenter study. Endosc Int Open 2019;7:E931-6.
4. Jovani M, Abidi WM, Lee LS. Novel fork-tip needles versus standard needles for EUS-guided tissue acquisition from solid masses of the upper GI tract: A matched cohort study. Scand J Gastroenterol 2017;52:784-7.
5. Bang JY, Hebert-Magee S, Navaaneethan U, et al. Randomized trial comparing the Franseen and Fork-tip needles for EUS-guided fine-needle biopsy sampling of solid pancreatic mass lesions. Gastrointest Endosc 2018;87:1432-8.
6. Naveed M, Siddiqui AA, Kowalski TE, et al. A Multicenter comparative trial of a novel EUS-guided core biopsy needle (SharkCore™) with the 22-gauge needle in patients with solid pancreatic mass lesions. Endosc Ultrasound 2018;7:34-40.
7. Ishikawa T, Mohamed R, Heitman SJ, et al. Diagnostic yield of small histological cores obtained with a new EUS-guided fine needle biopsy system. Surg Endosc 2017;31:5143-9.
8. Kim T, Katamura 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.
9. Turner BG, Cizginer S, Agarwal D, et al. Diagnosis of pancreatic neoplasia with EUS and FNA: A report of accuracy. Gastrointest Endosc 2010;71:91-8.
10. Weston BR, Bhutani MS. Optimizing diagnostic yield for eus-guided sampling of solid pancreatic lesions: A technical review. Gastroenterol Hepatol (N Y) 2013;9:352-63.
11. Ishikawa T, Mohamed R, Heitman SJ, et al. Diagnostic yield of small histological cores obtained with a new EUS-guided fine needle biopsy system. Surg Endosc 2017;31:5143-9.
12. Altam R, Arain MA, Bloechl SJ, Trikudanathan G, Munigala S, Bakman Y, et al. “Wet Suction Technique (WEST)”: A novel way to enhance the quality of EUS-FNA aspirate. Results of a prospective, single-blind, randomized, controlled trial using a 22-gauge needle for EUS-FNA of solid lesions. Gastrointest Endosc 2015;81:1401-7.
13. Saxena P, El Zein M, 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.
14. 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.
15. 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.
16. Weston BR, Ross WA, Bhutani MS, et al. Prospective randomized comparison of a 22G core needle using standard versus capillary suction for EUS-guided sampling of solid pancreatic masses. Endosc Int Open 2017;5:E505-12.
17. Mok SR, Diehl DL, Johal AS, et al. A prospective pilot comparison of wet and dry heparinized suction for EUS-guided liver biopsy (with videos). Gastrointest Endosc 2018;88:919-25.
18. Cheng S, Brunaldi VO, Minata MK, et al. Suction versus slow-pull for endoscopic ultrasound-guided fine-needle aspiration of pancreatic tumors: A prospective randomized trial. HPB (Oxford) 2020;22:779-86.
19. Di Mitri R, Mocciano 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.
20. Sugimoto M, Takagi T, Suzuki R, et al. Can the wet suction technique change the efficacy of endoscopic ultrasound-guided fine-needle aspiration for diagnosing autoimmune pancreatitis type 1? A prospective single-arm study. World J Clin Cases 2020;8:88-96.
21. Villa NA, Berzosa M, Wallace MB, et al. Endoscopic ultrasound-guided fine needle aspiration: The wet suction technique. Endosc Ultrasound 2016;5:17-20.
22. Leung Ki EL, Lemaistre AL, Fumes F, et al. Macrosopic onsite evaluation using endoscopic ultrasound fine needle biopsy as an alternative to rapid onsite evaluation. Endosc Int Open 2019;7:E189-94.
23. Wei E, Lakhtakia S, Gupta R, et al. Endoscopic ultrasound guided fine-needle aspiration of lymph nodes and solid masses: Factors influencing the cellularity and adequacy of the aspirate. J Clin Gastroenterol 2012;46:487-93.
24. Polkowski M, Jansen C, Kaye P, et al. Technical aspects of Endoscopic Ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESEG) Technical Guideline – March 2017. Endoscopy 2017;49:989-1006.
25. Lee KY, Cho HD, Hwangbo Y, et al. Efficacy of 3 fine-needle biopsy techniques for suspected pancreatic malignancies in the absence of an on-site cytopathologist. Gastrointest Endosc 2019;89:825-31.e1.
26. Litvinov RI, Weisel JW. Fibrin mechanical properties and their structural origins. Matrix Biol 2017;60-61:110-23.
27. 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.
28. Eloubeidi MA, Tamhane A, Varadarajulu S, et al. Frequency of major complications after EUS-guided FNA of solid pancreatic masses: A prospective evaluation. Gastrointest Endosc 2006;63:622-9.
29. 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.
### Supplement Table 1. Baseline patient characteristics

|                      | Group A     | Group B     | Group C     | Group D     | Group E     | Group F     | Total       | P       |
|----------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|---------|
| **Age, mean±SD, y/o**| 59.6±9.3    | 61.1±9.6    | 58.4±10.3   | 61.1±12.7   | 60.2±12.1   | 63.4±9.6    | 60.6±10.6 (23-87) | 0.244   |
| **Sex, n (%)**       |             |             |             |             |             |             |             |         |
| Male                 | 34 (65.4)   | 34 (64.2)   | 40 (74.1)   | 21 (55.3)   | 26 (52.0)   | 33 (64.7)   | 188 (63.1)  | 0.249   |
| Female               | 18 (34.6)   | 19 (35.8)   | 14 (25.9)   | 17 (44.7)   | 24 (48.0)   | 18 (35.3)   | 110 (36.9)  |         |
| **Size of the lesion, mm** |             |             |             |             |             |             |             |         |
| Mean±SD (range)      | 42.5±21.8 (16-163) | 36.4±11.6 (12-68) | 38.6±17.5 (12-100) | 36.7±14.2 (6-80) | 37.9±12.0 (18-67) | 36.7±16.2 (6-80) | 38.2±16.0 (6-163) | 0.395   |
| **Lesion location, n (%)** |             |             |             |             |             |             |             |         |
| Pancreas             | 35 (67.3)   | 45 (84.9)   | 37 (68.5)   | 32 (84.2)   | 34 (68.0)   | 43 (84.3)   | 226 (75.8)  | 0.417   |
| Lymph nodes          | 7 (13.5)    | 2 (3.8)     | 7 (13.0)    | 3 (7.9)     | 6 (12.0)    | 3 (5.9)     | 28 (9.4)    |         |
| Upper GI tract       | 4 (7.7)     | 5 (9.4)     | 6 (11.1)    | 3 (7.9)     | 5 (10.0)    | 3 (5.9)     | 26 (8.7)    |         |
| Abdominal mass       | 3 (5.8)     | 0            | 3 (5.6)     | 0            | 2 (4.0)     | 1 (2.0)     | 9 (3.0)     |         |
| Mediastinal mass     | 1 (1.9)     | 1 (1.9)     | 1 (1.9)     | 0            | 0            | 1 (2.0)     | 4 (1.3)     |         |
| Liver, rectum, and common bile duct | 2 (3.8) | 0            | 0            | 3 (6.0)     | 0            | 5 (1.7)     |         |         |
| **Pathological type (%)** |             |             |             |             |             |             |             |         |
| Malignancies         | 45 (86.5)   | 51 (96.2)   | 47 (87.0)   | 35 (92.1)   | 45 (90.0)   | 44 (86.3)   | 267 (89.6)  | 0.511   |
| Benign lesions       | 7 (13.5)    | 2 (3.8)     | 7 (13.0)    | 3 (7.9)     | 5 (10.0)    | 7 (13.7)    | 31 (10.4)   |         |

SD: Standard deviation, GI: gastrointestinal

### Supplement Table 2. Subgroup analysis of lesion size and lesion origins

| Lesion size | Suction | P     | Suction | P     | Suction | P     | Suction | P     |
|-------------|---------|-------|---------|-------|---------|-------|---------|-------|
| ≤36 mm      | 3.6±1.4 | 0.479 | 3.6±1.5 | 0.479 | 3.6±1.5 | 0.479 |         |       |
| >36 mm      | 3.6±1.5 | 0.511 | 3.6±1.5 | 0.511 |         |       |         |       |

**Lesion origins**

- Pancreatic lesions
  - ≤36 mm: 3.6±1.4
  - >36 mm: 3.6±1.5
- Nonpancreatic lesions
  - ≤36 mm: 3.6±1.4
  - >36 mm: 3.6±1.5