

# Wet- versus dry-suction techniques for endoscopic ultrasound-guided fine-needle aspiration of solid lesions: a multicenter randomized controlled trial

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## ABSTRACT

**Background** The optimal sampling techniques for endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) remain unclear and have not been standardized. The aim of this study was to compare the wet-suction and dry-suction techniques for sampling solid lesions in the pancreas, mediastinum, and abdomen.

**Methods** This was a multicenter, crossover, randomized controlled trial with randomized order of sampling techniques. The 296 consecutive patients underwent EUS-FNA with 22G needles and were randomized in a ratio of 1:1 into two separate groups that received the dry-suction and wet-suction techniques in a different order. The primary outcome was to compare the histological diagnostic accuracy of dry suction and wet suction for malignancy. The secondary outcomes were to compare the cytological diagnostic accuracy and specimen quality.

**Results** Among the 269 patients with pancreatic ( $n = 161$ ) and non-pancreatic ( $n = 108$ ) lesions analyzed, the wet-suction technique had a significantly better histological diagnostic accuracy (84.9% [95% confidence interval (CI) 79.9%–89.0%] vs. 73.2% [95%CI 67.1%–78.7%];  $P = 0.001$ ), higher specimen adequacy (94.8% vs. 78.8%;  $P < 0.001$ ), and less blood contamination ( $P < 0.001$ ) than the dry-suction technique. In addition, sampling non-pancreatic lesions with two passes of wet suction provided a histological diagnostic accuracy of 91.6%.

**Conclusions** The wet-suction technique in EUS-FNA generates better histological diagnostic accuracy and specimen quality than the dry-suction technique. Furthermore, sampling non-pancreatic lesions with two passes of EUS-FNA with wet suction may provide a definitive histological diagnosis when rapid on-site evaluation is not routinely available.

\* contributed equally

## Introduction

It has been well-established that endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) provides tissue diagnosis as the standard of care for pancreatic, mediastinal, and abdominal lesions, with the diagnostic accuracy ranging from 78% to 95% [1–3]. However, EUS-FNA has limited diagnostic value for lesions such as neuroendocrine neoplasm, lymphoma, and autoimmune pancreatitis, because of the lack of a sufficient specimen for further immunohistochemistry (IHC) staining or biomarker assessment for targeted treatment of these unresectable tumors [1, 4]. Although our previous study showed that the fine-needle biopsy (FNB) approach improved diagnostic accuracy [5], FNB needles may be more expensive and are not as widely used as FNA needles in some institutions.

To improve the diagnostic accuracy, suction techniques for EUS-FNA have been developed and are widely used among operators. These suction techniques require removing the stylet and subsequently placing a syringe to generate negative pressure on uptake of the specimens. The so-called “dry-suction technique” requires puncture of the lesion, removal of the stylet, and then placement of a pre-vacuum syringe. It has been reported to increase cellularity. However, applying dry suction enhances the chances of blood contamination and therefore hinders accurate cytological interpretation [6]. Later on, the “traditional wet-suction technique” was developed to overcome this issue. It requires removal of the stylet first, then pre-flushing of the needle with saline, and subsequently placement of a 10-mL syringe prefilled with 3-mL saline for aspiration [7]. It is reported that the technique may increase the cellularity and adequacy of specimens without adding blood contamination when sampling solid lesions [8].

More recently, the “wet-suction technique” was developed, with a modification that involves placing a 10-mL syringe without saline loaded to maximal suction, to combine the benefits of the wet technique for needle preparation and the dry technique for suction syringe preparation [7]. A pilot study of 15 patients highlighted that this wet-suction technique achieved a larger volume of aspirate compared with dry suction. Owing to the limited study sample size, there was insufficient evidence to prove whether the wet-suction technique could improve sample adequacy and the final diagnosis in comparison with dry suction [9].

Therefore, we designed this multicenter randomized controlled trial to clarify the effect of dry suction and wet suction on pathological specimens obtained using a standard 22G needle.

## Methods

### Study design

This was a prospective, multicenter, single-blind, crossover, randomized controlled, superiority trial. Rapid on-site evaluation (ROSE) was not available in our trial. EUS-FNA was performed by experienced endosonographers using 22G needles with either dry suction or wet suction as the first pass.

The study was conducted at four tertiary care centers in China, including Tongji Hospital, Union Hospital, Renmin Hospital of Wuhan University, and the Central Hospital of Wuhan. It was approved by the institutional review boards of all participating centers and registered online at clinicaltrials.gov (NCT02789371). It was performed in compliance with the Declaration of Helsinki.

### Patients

Patients between the ages of 18 and 85 years who presented for EUS-FNA of solid lesions identified on imaging were eligible for study participation. Patients with the following conditions were excluded: pregnancy; coagulopathy (platelet count < 50 000/mm<sup>3</sup>, international normalized ratio > 1.5); acute pancreatitis in the preceding 2 weeks; severe cardiorespiratory dysfunction precluding endoscopy; and failure to provide informed consent. All consecutive patients provided informed consent for participation in the study.

### Randomization and masking

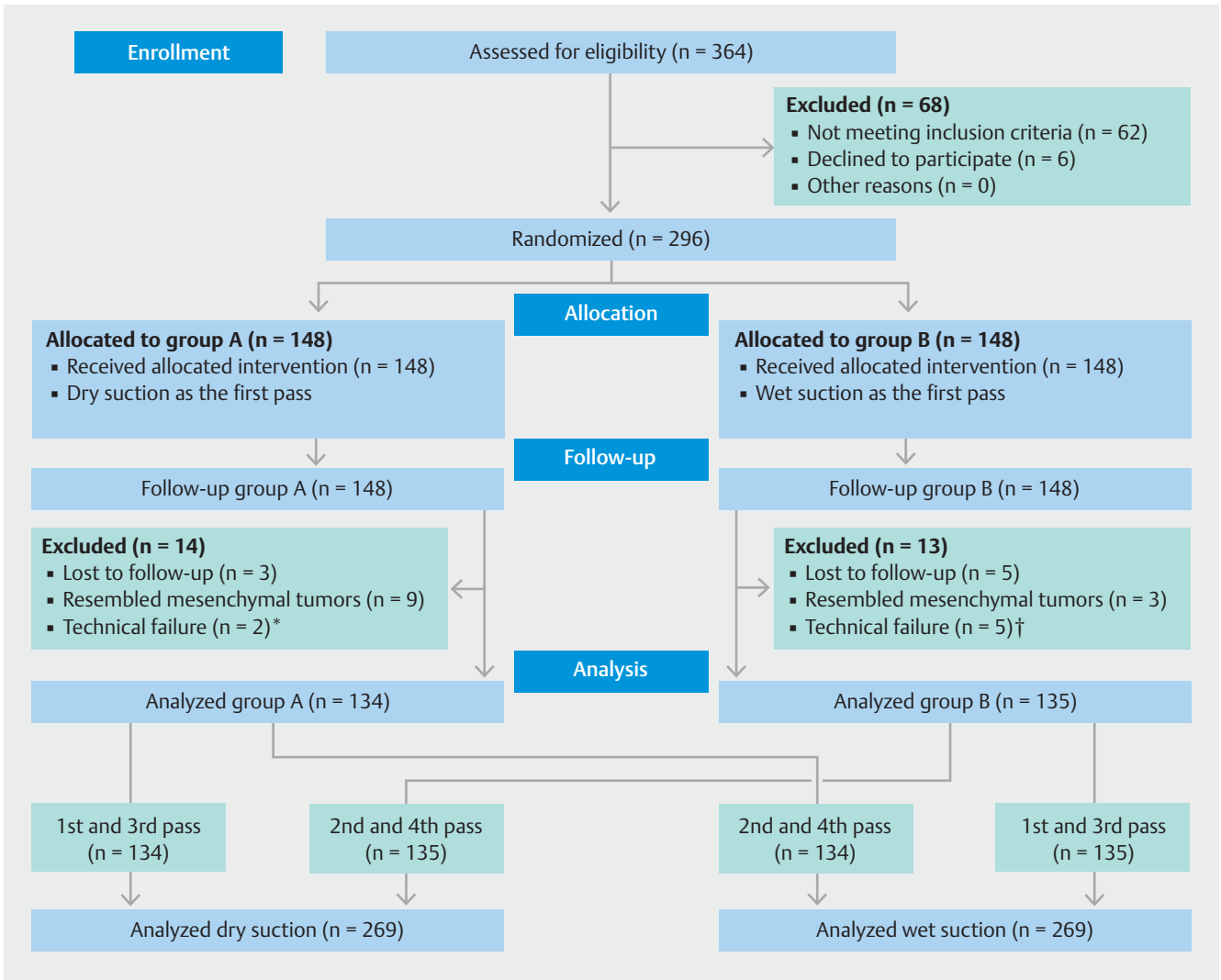
Computer-generated randomization assignments were centralized using the block randomization method (block size of 8) by a data manager who was not involved in the data analysis or patient enrollment. The allocation was placed in scratch cards to be scratched off after baseline assessment and study consent. The patients were randomly assigned to either Group A, using dry suction for the first pass, or Group B, using wet suction for the first pass, in a ratio of 1:1 (► **Fig. 1**). The assessors (cytopathologists) were blinded during the entire study.

### Procedures

All procedures were performed by experienced endosonographers at each center and using a linear Olympus echoendoscope (GF-UCT 260, GF-UCT 240; Olympus, Tokyo, Japan), a Fujifilm linear echoendoscope (EG-530UT2; Fujifilm, Tokyo, Japan) or a Pentax linear echoendoscope (EG3870UK, EG 3270UK; Pentax, Tokyo, Japan).

Four needle passes were taken from each lesion using a 22G needle (EchoTip Ultra, Cook Medical, Winston Salem, North Carolina, USA) with each of the two suction methods described below. For dry suction, after puncturing the lesion, the endoscopist removed the stylet and attached a 5-mL pre-vacuum syringe for aspiration. For wet suction (**Fig. 1s**, see online-only Supplementary Material), the stylet was removed and the needle was pre-flushed with 1–2 mL of saline using a 10-mL syringe, the endoscopist then punctured the lesion and replaced the 10-mL syringe with a 5-mL pre-vacuum syringe. Each pass consisted of 20 back-and-forth movements of the needle within the lesion, using the fanning technique whenever possible. Afterwards, the needle was withdrawn from the lesion.

Four passes were performed in the following order in Groups A and B, respectively: dry suction, wet suction, dry suction, wet suction, and wet suction, dry suction, wet suction, dry suction. If no macroscopically visible core tissue (whitish or yellowish pieces of tissue of at least 4 mm in the greatest axis measured) was obtained after four passes [10], the endosonographers would conduct a back-up procedure using a proper puncture



► **Fig. 1** Study flowchart. \* Two patients with technical failure in group A: incomplete operation process of four passes (n = 1), no samples obtained from the four passes (n = 1). † Five patients with technical failure in group B: incomplete operation process of four passes (n = 2), no samples obtained from the four passes (n = 2), randomized principles not followed (n = 1).

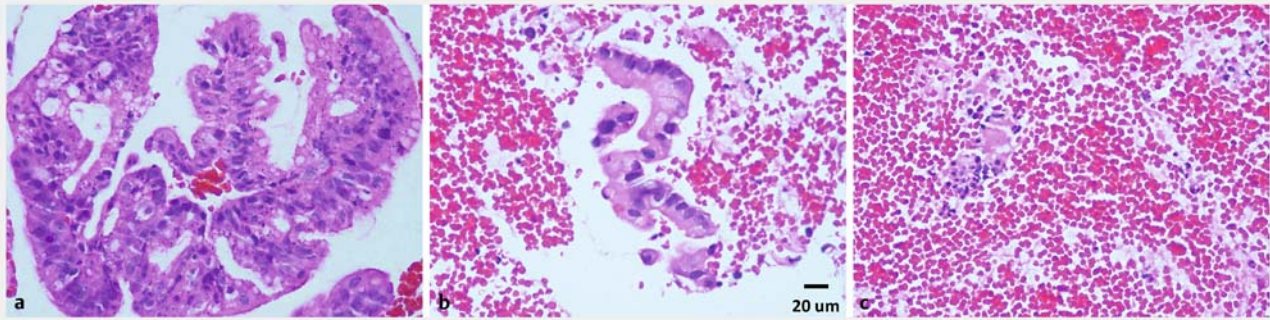
method to obtain an adequate specimen. We routinely observed complications and checked the patient's serum amylase for 3 days after sampling with FNA. All patients were then followed up with telephone calls for 4–7 days after the procedure to record adverse events.

### Pathological assessment

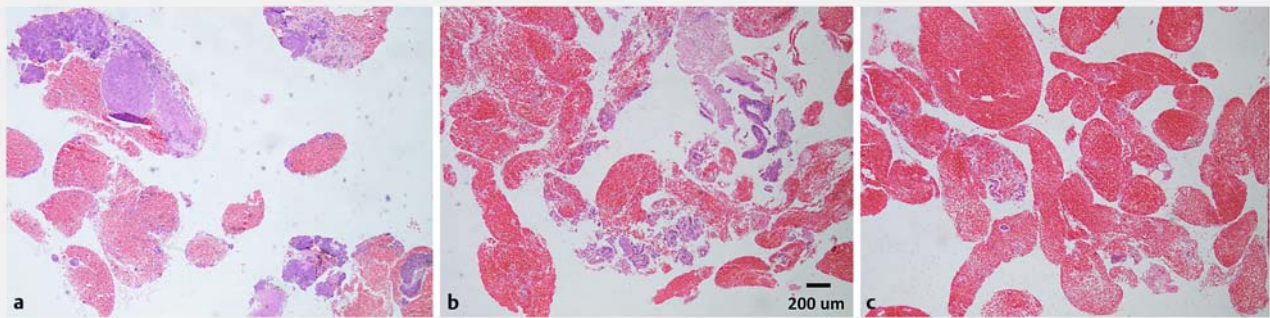
The aspirated samples from each pass were expelled onto separate slides with a stylet. Following this, 0.1-mL of sterile saline was flushed into the 22G FNA needle and followed with 5-mL of air. The macroscopically visible core was transferred into Ependorf tubes containing 10% formalin for histological examination. The remaining tissue was used in smears for cytological evaluation. The central cytopathologists from Tongji Hospital, Huazhong University of Science and Technology were blinded to the suction techniques and two independent experts assessed the specimens. If the two experts made different judg-

ments of any passes, they reviewed all clinical materials together to make a final decision [11].

The tissue integrity for histological analysis was scored from 0 to 3 as follows (► **Fig. 2**): score 3, sufficient material for adequate histological interpretation (an architecturally intact piece of tissue with a length of at least 550 µm under the microscope); score 2, samples allowing limited histological assessment (the tissue did not meet the criteria for architecturally intact histology but could still yield a diagnosis based on cell morphology); score 1, samples did not provide histological information (no architecturally intact tissue present to yield a diagnosis); score 0, sample with no material, based on the scoring system previously reported by Iwashita et al. [12], Fabbri et al. [13], and Cheng et al. [5]. Samples scoring 2 or 3 were classified as adequate specimens. The degree of blood contamination was categorized into four grades according to the blood cell percentage in quartiles (score 3, <25%; score 2, 25%–50%; score 1, >50%; score 0, no material) (► **Fig. 3**) [8, 14].



► **Fig. 2** The tissue integrity assessments of specimens (hematoxylin and eosin [H&E] stained, original magnification  $\times 400$ ). Examples of: **a** score 3, sufficient material for adequate histological interpretation; **b** score 2, samples allowing limited histological assessment; **c** score 1, samples not providing histological information.



► **Fig. 3** The blood contamination assessments of specimens (hematoxylin and eosin [H&E] stained, original magnification  $\times 40$ ). Examples of: **a** score 3, blood cells present in  $<25\%$  of the slide; **b** score 2, blood cells present in  $25\%–50\%$  of the slide; **c** score 1, blood cells present in  $>50\%$  of the slide.

Samples that were considered malignant or suspicious for malignancy were categorized as positive for malignancy, whereas samples that were considered benign or atypical were categorized as negative for malignancy. Pancreatic cancer, metastatic cancer, neuroendocrine neoplasm, solid pseudopapillary tumor, lymphoma, and malignant solitary fibrous tumor were defined as malignant diseases. Chronic pancreatitis, autoimmune pancreatitis, tuberculosis, other granulomatous diseases, reactive lymphadenopathy, ectopic spleen and adrenal hyperplasia were defined as non-malignant diseases. Those cases with histological characteristics resembling mesenchymal tumors but without IHC evaluation were excluded from the final analysis.

## Outcomes

The primary outcome of this study was to compare the histological diagnostic accuracy of EUS-FNA using wet- vs. dry-suction techniques for the diagnosis of malignancy in patients with solid lesions. The diagnostic accuracy was defined as the ratio between the sum of true positive values and true negative values divided by the total number of samples. We evaluated both of the two samples taken using the same method. If either one or two samples proved to be malignant, the sample was identified

as positive; otherwise, it was identified as negative. The overall diagnosis for the dry-suction technique was calculated from the first and third passes in group A and the second and fourth passes in group B. While the overall diagnosis for the wet-suction technique was calculated from the first and third passes in group B and the second and fourth passes in group A.

The secondary outcomes were to compare the cytological diagnostic accuracy for malignancy, and the specimen quality (the number of adequate specimens and blood contamination) in the samples obtained by EUS-FNA using dry suction vs. wet suction. The scores of specimen quality, namely tissue integrity and blood contamination, for each suction technique were calculated as the mean scores for the two samples obtained with this technique.

A final diagnosis of malignancy was defined by one or more of the following criteria: (i) pathological evidence of malignancy in a surgical resection specimen; (ii) progression or metastasis of lesions on imaging or with malignant symptoms, such as weight loss or anemia; (iii) cancer-related death within 48 weeks of follow-up. Lesions were considered benign if they did not meet one or more of the above criteria, and on the basis of the patient's well-being over 48 weeks of follow-up [15].

## Statistical analysis

The sample size was determined based on the primary objective of comparing diagnostic accuracy between dry suction (75%) [5, 16, 17] and wet suction (85%). The calculation yielded target sample sizes of 248 for dry suction and 248 for wet suction ( $\alpha=0.05$ ,  $\beta=0.2$ , power=0.8). As all lesions would be punctured with the two suction techniques following the crossover design, a total of 248 patients needed to be included. Assuming a 20% dropout or withdrawal rate, we calculated a final sample size of 296 patients.

Data were expressed as mean and standard deviation (or range) for continuous variables and as number and percentage for categorical variables. The diagnostic accuracy and the difference in this between the two groups were computed using a 2×2 table and described as a proportion (95% confidence interval [CI]) using McNemar's test. The tissue integrity and blood contamination scores in specimens were divided into four grades (from score 0 to score 3), and a chi-squared test or Fisher's exact test were used to compare them. Statistical significance was defined as  $P<0.05$  (two-tailed). All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina, USA).

## Results

### Patient characteristics

Between May 2016 and January 2018, 364 patients were screened for participation in this study, of whom 68 were excluded (► Fig. 1). A total of 296 patients constituted the study cohort and were randomized in a 1:1 ratio, while we excluded from the analysis 27 patients who had technical failure, suspicion of mesenchymal tumor, or were lost to follow-up during the trial.

The patient baseline and lesion characteristics are listed in ► Table 1. During the study period, 269 patients were involved in the analysis: 161 patients had lesions in the pancreas and 108 patients had lesions in non-pancreatic sites. Pancreatic cancer contributed most of the pancreatic lesions (97/161; 60.2%), while non-pancreatic lesions were mainly metastatic lymph nodes or other sites (60/108; 55.6%). A total of 56 patients underwent surgical resection and the median follow-up was 33 weeks.

### Diagnostic accuracy

EUS-FNA was performed on all 269 patients with at least four passes, including two passes of wet suction and two passes of dry suction. We observed that the overall histological diagnostic accuracy of the wet-suction technique for all lesions (84.9% [95%CI 79.9%–89.0%]) was significantly higher than the dry-suction technique (73.2% [95%CI 67.1%–78.7%]), with a group difference of 11.7% (95%CI 4.5%–18.8%) and  $P$  value of 0.001 (► Table 2). On subgroup analysis, similar trends were observed in both the pancreatic lesions (80.3% vs. 68.8%, group difference, 11.4%;  $P=0.02$ ), especially pancreatic cancer (71.1% vs. 56.5%, group difference, 14.7%;  $P=0.04$ ) (► Ta-

► **Table 1** Baseline characteristics of the 269 patients with solid lesions who were analyzed in this study.

Patients characteristics	
Sex, male/female, n	161/108
Age, mean (SD) [range], years	57.5 (11.1) [18–84]
Lesion size, mean (SD) [range], mm	35.0 (15.1) [10–105]
<ul style="list-style-type: none"> <li>&gt;20 mm, n (%)</li> </ul>	230 (85.5%)
<ul style="list-style-type: none"> <li>≤20 mm, n (%)</li> </ul>	39 (14.5%)
Final diagnosis	
Pancreatic lesions, n (%)	161 (59.9%)
<ul style="list-style-type: none"> <li>Pancreatic cancer</li> </ul>	97 (60.2%)
<ul style="list-style-type: none"> <li>Metastatic cancer</li> </ul>	10 (6.2%)
<ul style="list-style-type: none"> <li>Neuroendocrine neoplasm</li> </ul>	11 (6.8%)
<ul style="list-style-type: none"> <li>Solid pseudopapillary tumor</li> </ul>	4 (2.5%)
<ul style="list-style-type: none"> <li>Chronic pancreatitis</li> </ul>	29 (18.0%)
<ul style="list-style-type: none"> <li>Autoimmune pancreatitis</li> </ul>	7 (4.3%)
<ul style="list-style-type: none"> <li>Pancreatic tuberculosis</li> </ul>	3 (1.9%)
Non-pancreatic lesions, n (%)	108 (40.1%)
<ul style="list-style-type: none"> <li>Metastatic lymph-nodes or other sites</li> </ul>	60 (55.6%)
<ul style="list-style-type: none"> <li>Lymphoma</li> </ul>	16 (14.8%)
<ul style="list-style-type: none"> <li>Malignant solitary fibrous tumor</li> </ul>	2 (1.9%)
<ul style="list-style-type: none"> <li>Neuroendocrine neoplasm</li> </ul>	2 (1.9%)
<ul style="list-style-type: none"> <li>Tuberculosis</li> </ul>	10 (9.3%)
<ul style="list-style-type: none"> <li>Other granulomatous diseases</li> </ul>	3 (2.8%)
<ul style="list-style-type: none"> <li>Reactive lymphadenopathy</li> </ul>	13 (12.0%)
<ul style="list-style-type: none"> <li>Others*</li> </ul>	2 (1.9%)

SD, standard deviation.  
\* Others included ectopic spleen and adrenal hyperplasia.

ble 3), and non-pancreatic lesions (91.6% vs. 79.4%, group difference, 12.2%;  $P=0.01$ ).

The overall cytological diagnostic accuracy was higher with wet suction (84.8% vs. 81.0%); however, there was no statistically significant difference between the two techniques (3.7%;  $P=0.25$ ). When the data were further stratified by the lesion size, we observed that the wet-suction technique achieved a higher histological diagnosis rate for lesions larger than 20 mm (Table 1 s). Furthermore, sampling non-pancreatic lesions with two passes of wet suction achieved histological diagnostic accuracy rates of more than 90% (all lesions, 91.6%; >20 mm, 93.9%) (► Tables 2 and 1 s).

The application of dry suction or wet suction as the first pass was randomized to eliminate any selection bias. We further compared the histological diagnosis between samples acquired through dry suction vs. wet suction in each group. We observed that the histological diagnostic accuracy of wet suction (85.5%

► **Table 2** Comparison of the overall diagnostic accuracy between the dry-suction and wet-suction techniques.

	Dry suction <sup>1</sup> % (95%CI)	Wet suction <sup>2</sup> % (95%CI)	Group difference <sup>3</sup> % (95%CI)	P value
Cytological diagnostic accuracy				
All lesions (n = 269)	81.0 (75.8 to 85.6)	84.8 (79.9 to 88.8)	3.7 (−2.6 to 10.1)	0.25
▪ Pancreatic (n = 161)	78.3 (71.1 to 84.3)	84.5 (77.9 to 89.7)	6.2 (−2.3 to 14.7)	0.15
▪ Non-pancreatic (n = 108)	85.2 (77.1 to 91.3)	85.2 (77.1 to 91.3)	0.0 (−9.5 to 9.5)	>0.99
Histological diagnostic accuracy				
All lesions (n = 269)	73.2 (67.1 to 78.7)	84.9 (79.9 to 89.0)	11.7 (4.5 to 18.8)	<b>0.001</b>
▪ Pancreatic (n = 161)	68.8 (60.4 to 76.5)	80.3 (73.2 to 86.2)	11.4 (1.5 to 21.3)	<b>0.02</b>
▪ Non-pancreatic (n = 108)	79.4 (70.0 to 86.9)	91.6 (84.6 to 96.1)	12.2 (2.6 to 21.8)	<b>0.01</b>

CI, confidence interval.

P values in bold indicate significant differences between the dry-suction and wet-suction techniques.

<sup>1</sup> Dry suction = 1st and 3rd passes in group A; 2nd and 4th passes in group B.<sup>2</sup> Wet suction = 2nd and 4th passes in group A; 1st and 3rd passes in group B.<sup>3</sup> Group difference = wet suction – dry suction.► **Table 3** Comparison of the overall diagnostic accuracy between the dry-suction and wet-suction techniques for pancreatic cancer.

Diagnostic accuracy	Dry suction <sup>1</sup> % (95%CI)	Wet suction <sup>2</sup> % (95%CI)	Group difference <sup>3</sup> % (95%CI)	P value
Cytological (n = 97)	75.5 (65.8 to 83.6)	79.6 (70.3 to 87.1)	4.1 (−7.6 to 15.8)	0.49
Histological (n = 97)	56.5 (45.3 to 67.2)	71.1 (61.1 to 79.9)	14.7 (0.8 to 28.5)	0.04

CI, confidence interval.

<sup>1</sup> Dry suction = 1st and 3rd passes in group A; 2nd and 4th passes in group B.<sup>2</sup> Wet suction = 2nd and 4th passes in group A; 1st and 3rd passes in group B.<sup>3</sup> Group difference = wet suction – dry suction.

was significantly higher than dry suction (72.3%), when wet suction was performed as the first-pass (n = 135; group difference, 12.2%;  $P = 0.01$ ) (**Table 2s**). Meanwhile, when dry suction was performed as the first-pass (n = 134), the histological diagnostic accuracy from wet suction (84.2%) was still higher than dry suction (74.1%), with a group difference of 10.1%, even though this difference was not statistically significant ( $P = 0.06$ ). Together, these results suggest that applying wet suction in the first pass may be practically important in improving histological diagnosis.

### Histology assessment

Wet suction and dry suction were further compared for sampling solid lesions to provide the histological characteristics such as the number of adequate specimens and amount of blood contamination. As described previously, specimens with a tissue integrity score of 2 or 3 were classified as adequate. For the wet-suction technique, 94.8% of the specimens were regarded as adequate, which was significantly higher than for the dry-suction technique (78.8%;  $P < 0.001$ ) (► **Fig. 4**). Meanwhile, using wet suction resulted in a higher score distribution for blood contamination than the use of dry suction for all solid lesions ( $P < 0.001$ ) (► **Fig. 5**). Therefore, we demonstrated that

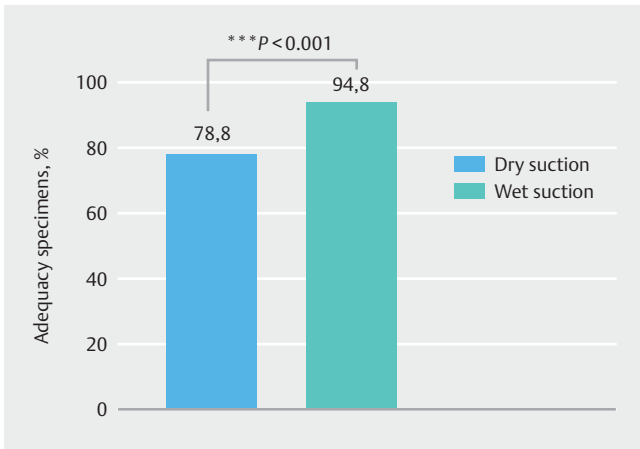
wet suction resulted in better specimen quality (more tissue adequacy and less blood contamination) than dry suction.

### Adverse events

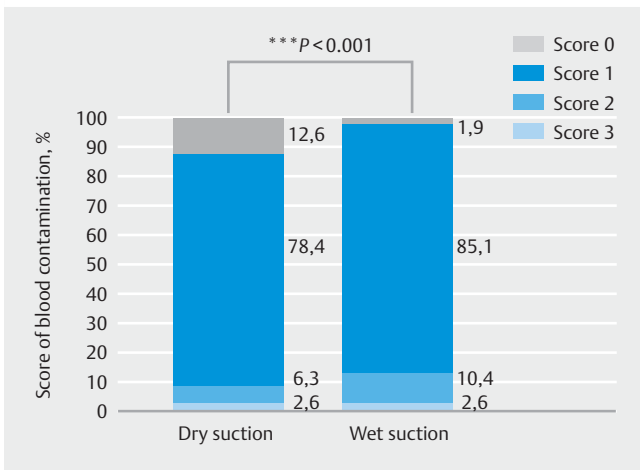
There were no major adverse events reported in this study. The rate of minor adverse events relating to the EUS-FNA procedure was 0.7%. Overall, after sampling, one patient developed an asymptomatic rise in amylase level and another patient developed mild bleeding. There were no reports of needle malfunction or significant clogging during this study.

### Discussion

EUS-FNA has become the first-line sampling procedure to obtain tissue and achieve definitive diagnosis for lesions within or adjacent to the gastrointestinal tract [18, 19]. Current guidelines do not endorse any particular FNA suction technique to improve the outcomes owing to the lack of evidence-based studies. Wet suction is a new suction technique that uses a column of fluid in the needle to generate the continuous negative pressure through a pre-vacuum syringe. Here, we conducted the first prospective, multicenter, randomized controlled clinical study so far to investigate the diagnostic accuracy of wet suction compared with dry suction.



► **Fig. 4** Comparison of the percentage of adequate specimens (scores 2 or 3) between the dry-suction and wet-suction techniques for all lesions.



► **Fig. 5** Comparison of the score distribution for blood contamination between the dry-suction and wet-suction techniques for all lesions (score 0, no specimen).

Recently, Berzosa et al. [9] conducted a pilot study of 15 patients and compared dry suction vs. wet suction for EUS-FNA of solid lesions, but failed to demonstrate a significant difference for specimen adequacy (67% vs. 87%) or diagnostic yields (90% vs. 100%), which was probably a result of the limited sample size. Given that wet suction provided a larger volume of aspirate compared with dry suction, Villa et al. [7] favored wet suction over dry suction. With sampling of 269 solid lesions, we demonstrated the significant superiority of wet suction (84.9%) over dry suction (73.2%;  $P=0.001$ ) in terms of overall histological diagnostic accuracy. Furthermore, we observed that wet suction resulted in better specimen adequacy (94.8% vs. 78.8%;  $P<0.001$ ) and lower blood contamination ( $P<0.001$ ) than dry suction for all solid lesions. Given more adequate specimens were obtained, with lower blood contamination displaying better conditions for tissue diagnosis [20], it is not surprising that the wet-suction technique achieved better histological diagnostic accuracy.

The rationale for a column of saline yielding a better tissue sample than air in the presence of negative pressure was explained nicely by a proof-of-concept study performed by Berzosa et al. [21]. They used a three-dimensional computational fluid dynamic model to monitor the effect on tissue aspiration. The wet (water-filled) technique led to faster aspiration of material into the distal end of the needle, and was therefore superior to the dry (air-filled) technique [7]. This is based on the principle that water is less compressible than air and water may coat the inner lining of the needle and thereby change the surface properties, leading to easier movement of the tissue aspirate into the needle [7,8]. One concern with regard to the use of suction is that of more blood contamination affecting the overall quality of the specimen [22]. However, interestingly, in this study we found that wet suction may overcome this issue by generating specimens with less bloodiness and better adequacy. It is possible that the presence of the saline solution eliminates the “empty space” in the needle lumen for the red blood cells to flow into, and thereby reduces the degree of bloodiness [8].

We previously suggested that, for non-pancreatic masses, either FNA or FNB applied with a slow pull and dry suction may not be sufficient to improve the histological diagnostic yield [5]. Nevertheless, our current study shows that, for non-pancreatic masses evaluated by two passes of FNA, the wet-suction technique was superior to the dry-suction technique in terms of histological diagnostic accuracy (91.6% vs. 79.4%;  $P=0.01$ ). Together, our two parallel studies suggest that, when sampling non-pancreatic masses, two passes of FNA through wet suction provide adequate tissue for histological analysis, with no requirement for FNB.

For pancreatic masses, significantly higher histological diagnostic accuracy was also observed with wet suction compared with dry suction (80.3% vs. 68.8%;  $P=0.02$ ). Because we know that more passes are needed in order to reach a definitive diagnosis for pancreatic masses than for non-pancreatic masses, this may explain our findings that two passes of each technique work better for non-pancreatic masses than for pancreatic lesions. Recently, Mitri et al. [23] retrospectively assessed 59 pancreatic solid lesions that underwent wet suction with FNB needles. The diagnostic accuracy of the FNB needles with wet suction (98.3%, 2.8 passes) was higher than that for FNB needles with dry suction and slow pull (92.7%, 2 passes dry suction and 2 passes slow pull) [5]. In our study, we found that the diagnostic accuracy of FNA needles with wet suction in pancreatic solid lesions was 80.3% (2 passes). In conclusion, these studies suggest that FNB needles with wet suction may be more beneficial in the diagnosis of pancreatic lesions.

The safety of EUS-FNA is well established, being marked by a very low rate of complications (~1%) [24]. Consistently, our study observed no major adverse events and a very low minor adverse event rate of 0.7%. The wet suction procedure is relatively safe as the saline-filled syringe used to pre-flush the needle is always kept in contact with the needle to ensure the column of saline remains within the needle. Once the lesion is punctured, the syringe is replaced with a 5-mL air-prefilled suction syringe in a quick and timely fashion. The use of suction

and a forward jabbing motion of the needle ensures the generation of negative pressure inside the target lesion and therefore prevents saline leaking into the lesion [8].

This study has several limitations, including the lack of ROSE, which is the real-time evaluation of sample adequacy and could promote a better diagnostic yield of EUS-FNA/B even for experienced operators [25]. However, in this study, all endosonographers and their assistants were trained prior to the trial in macroscopic on-site evaluation and assessment of sample sufficiency [10]. Another limitation of the current study is that either wet suction or dry suction was conducted only twice for each lesion and we hypothesize that if more passes of wet suction were performed, particularly for pancreatic masses, the overall diagnostic accuracy should be further improved. Therefore, future studies on the optimal numbers of passes for pancreatic lesions are warranted.

In conclusion, our study demonstrated that wet suction yields significantly better histological diagnostic accuracy and specimen quality than dry suction for all solid lesions, especially for masses larger than 20 mm. Although FNA needles are routinely used to achieve a cytological diagnosis, our study showed that using wet suction for FNA could also obtain sufficient histological specimens too. We further showed that the two passes of FNA with wet suction achieved a definitive histological diagnosis for non-pancreatic lesions, in a way that may be of benefit for those institutions where ROSE is unavailable.

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## Competing interests

The authors declare that they have no conflict of interest.

## Clinical trial

clinicaltrials.gov  
NCT02789371  
TRIAL REGISTRATION: ClinicalTrials.gov- Registration number (trial ID): NCT02789371- Type of study: Prospective, multicenter, single-blind, randomized controlled, superiority trial

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