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A Prospective, Randomized Trial Comparing Suction to No Suction in The Diagnostic Yield of EUS-Guided Fine Needle Sampling of Solid Lesions

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1. Abstract

1.1. Background and Objectives: Endoscopic ultrasound (EUS) guided fine needle sampling has been proven as an effective modality for the evaluation of potentially malignant lesions. Technological advances and high-quality research have enhanced this diagnostic tool. Several studies have examined the use of suction, but the yield of this method is not yet certain. We performed a prospective, randomized trial to determine if the use of suction alters the diagnostic yield.

1.2. Patients and Methods: 136 patients with solid lesions amenable to EUS-guided fine needle sampling were randomized to receive either suction with 10mL syringe on the first two passes followed by no suction on the second two of four successive passes for each lesion, or the reverse order. The slides were prepared by and underwent gross evaluation by a trained registered nurse, subsequently evaluated by a blinded, on-site cytotechnologist, and a final diagnosis was made in the pathology lab.

1.3. Results: Most lesions sampled were pancreatic (58%) followed by lymph nodes (26%), others (9%), gastric masses (5%) and lung and mediastinum (2%). When using suction, samples were shown to be significantly bloodier for all lesions ($p<0.001$) and pancreatic lesions ($p<0.001$) on gross evaluation, and there was no statistically significant difference for cellularity between the two methods. Additionally, across all solid lesions sampled, there were no statistically significant differences with respect to diagnostic yield ($p=0.64$).

1.4. Conclusion: This prospective, randomized trial evaluating the use of suction revealed no statistically significant difference in the diagnostic yield for all solid lesions. A statistically significant difference was noted in the gross appearance of samples that favored the use of no suction; however, the clinical relevance of this remains uncertain.

2. Introduction

Endoscopic ultrasound (EUS) with fine needle sampling gained momentum in the early to mid-1990's as a viable alternative to Computed Tomography (CT), ultrasound, and/or direct intraoperative fine needle sampling for gastrointestinal tumors [1-4] EUS guided fine needle sampling currently has a good sensitivity and excellent specificity for the diagnosis of extraluminal abdominal and mediastinal malignancies. [5-7] A myriad of studies examining a variety of aspects of this modality such as needle insertion site (i.e. tumor center versus edge), the presence of on-site cytology services, and stylet use continue to increase its yield and diagnostic accuracy. [8-10]

Multiple studies have compared suction (negative pressure applied to the sampling needle) with no suction during fine needle sampling performed on superficial body masses, the thyroid, and breast tissue. [11-17] These studies demonstrated bloodier, more traumatic specimens and loss of appropriate architecture and cellular arrangement with the use of suction. [11-14, 16] Although most studies showed specimen inferiority with the use of suction, none of the studies proved that the lack of suction was associated with diagnostic superiority. Additionally, several studies have prospectively examined the optimal technique of EUS guided fine needle sampling with respect to the use of suction. Unfortunately, these four studies were limited by the number of subjects enrolled and/or the type of lesions included. [18-21] Data from these studies indicated that suction was generally superior for pancreatic lesions, but consensus on other le-

sions had not been determined. More recently, European Society of Gastrointestinal Endoscopy (ESGE) guidelines published in March, 2017 encouraged the use of suction for EUS guided sampling of solid masses and lymph nodes. [22] This endorsement (high quality of evidence, strong recommendation) was based on the analysis of three randomized controlled trials (RCT) that showed suction improves sensitivity and accuracy for malignancy compared to no suction. [19, 20, 23] Given conflicting data, we performed a prospective, randomized, blinded trial of all solid lesions undergoing EUS-guided fine needle sampling to determine whether suction improved the diagnostic yield.

3. Patients and Methods

This was a prospective, randomized clinical trial performed at a tertiary care medical center. The study protocol was reviewed and approved by a local Institutional Review Board (IRB). All patients who presented to an academic medical center over a 12-month period for EUS-guided fine needle sampling of a solid lesion discovered on CT and/or magnetic resonance imaging were considered for inclusion in this study. All patients were appropriately consented and underwent conscious sedation or monitored anesthesia care. The location of the mass was confirmed by radial scanning EUS (GFUM160; Olympus America Corp, Melville, NY). EUS-guided fine needle sampling was then performed with standard technique by using a linear-array echoendoscope (GF-UCT140P-AL5; Olympus) and a 22-gauge disposable needle (EchoTip® Ultra; Wilson-Cook Medical, Inc., Winston-Salem, NC). The needle device was inserted through the channel of the echoendoscope and was advanced in the target lesion under real-time EUS imaging. All solid lesions were punctured with a stylet in place in the needle. After withdrawal of the stylet, the needle was moved to and fro within the lesion for 30 seconds and then the needle was withdrawn.

The technique to be used first, suction or no suction, was assigned by using a pre-printed randomization scheme obtained from a sealed envelope, see (Figure 1). For the suction technique, a 10 mL syringe was attached to the proximal end of the needle device and was used to apply 10 mL negative pressure. All lesions underwent four passes, two with suction and two without suction, using a 22-gauge needle (Cook Medical, Winston-Salem, NC). [24] If a definitive diagnosis was not obtained by the fourth pass, additional passes were permitted with the choice of technique(s) and number of passes at the discretion of the endoscopist. Each fine needle sample was expressed by using a 10 mL air-filled syringe onto a separate glass slide by a trained EUS nurse and a direct smear was made by an on-site cytopathologist. [9] Separate results for the gross evaluation and cytology analysis were recorded for each pass. A sterile saline solution was used to flush any residual contents into a balanced salt solution (Hank's solution) and subsequently the needle and stylet were thoroughly cleaned with sterile gauze and sterile saline solution in an effort to minimize any cross-contamination between passes. One half of all slides were air-dried and a Romanowsky stain was used. The others were ethanol fixed and Papanicolaou stained. In all sessions, one or more members of the cytology team of the pathology department were present to assess overall specimen adequacy for subsequent routine diagnosis. Passes from the lesion were consolidated for a single cytospin-cell-block analysis. [25]

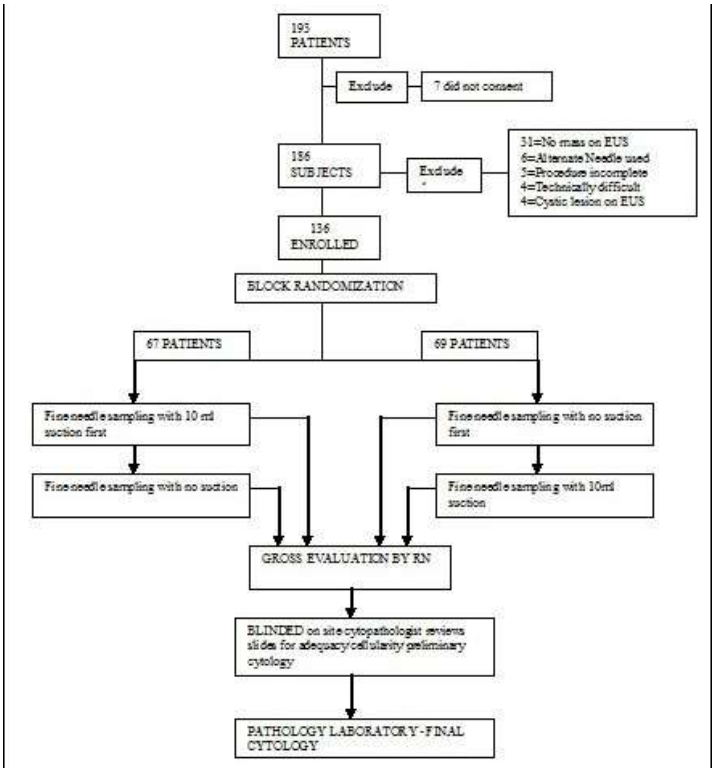

Figure 1: Study Protocol

The primary outcome for our study was diagnostic yield of EUS sampling. Diagnostic yield was defined as the acquisition of an adequate number of cells on a slide for the pathologist to render a diagnosis. An onsite cytotechnologist assessed the specimen adequacy. Thereafter, a single cytopathologist, who was blinded to the technique for fine needle sampling, characterized each individual needle pass for a diagnosis of the lesion (positive, negative, suspicious, insufficient) and cellularity (low or high). A single, experienced EUS nurse characterized each specimen for quality (serous, serosanguinous or grossly bloody). The nurse was not blinded to the method of fine needle sampling. Cellularity and specimen quality were secondary outcomes.

The diagnosis arrived at for each needle pass was compared with the final diagnosis of that specimen. The diagnosis was considered correct if the individual pass diagnosis matched the final diagnosis. Specimens were classified as diagnostic or non-diagnostic. Diagnostic specimens included samples described as positive, negative or suspicious. Insufficient specimens were considered non-diagnostic.

Statistical analyses of the first four passes for each lesion were performed with Stata Version 7 statistical software. If the lesion required more or less than four passes, these were performed based on clinical assessment only and any missing passes were treated as missing at random. The Type I error was set at 0.05. Odds ratios and 95% confidence intervals were evaluated. A subgroup analysis to determine the association between sampling location and correct cytology diagnosis was performed for pancreatic lesions and lymph nodes. In addition, suction first or no suction first while performing EUS sampling was also noted to ensure that performing either procedure first did not influence the diagnostic yield.

4. Results

A total of 193 patients were eligible for our study; 57 patients were excluded for the following reasons: no lesion detected by EUS (31), alternate needle used (6), four needle passes not obtained (5), cystic lesion detected (4), technical difficulty (4), and consent not approved (7). Therefore, a total of 136 patients were included in the final analysis (Figure 1). These 136 patients with solid masses detected by EUS underwent fine needle sampling using suction and no suction. Average patient age was 65 years and 55% were male. Our study included all lesions that could be sampled using EUS and fine needle technology (Table 1). Pancreatic mass was the most common solid lesion sampled followed by lymph nodes and gastric tumors.

Table 1: Lesion Location

Lesion Location	N (%)
Pancreas	78 (58%)
Lymph Nodes	36 (26%)
Gastric Mass	7 (5%)
Lung & Mediastinum	3 (2%)
Others	12 (9%)

The diagnostic yield was unaffected by the fine needle sampling technique used - whether it was suction or no suction (Figure 2). This finding was present in all lesions (p=0.44), the pancreas (p=0.48) and in the lymph nodes (p=0.65). The use of suction produced bloodier gross specimens in pancreatic lesions (p<0.001) and all lesions combined (p<0.001), and was almost statistically significant in lymph nodes (p=0.06) when compared to specimens without suction (Table 2). We did not find any statistical difference in obtaining highly cellular specimens either with or without use of suction (Table 2). Finally, suction or no suction technique used first did not alter the diagnostic yield (p=0.64).

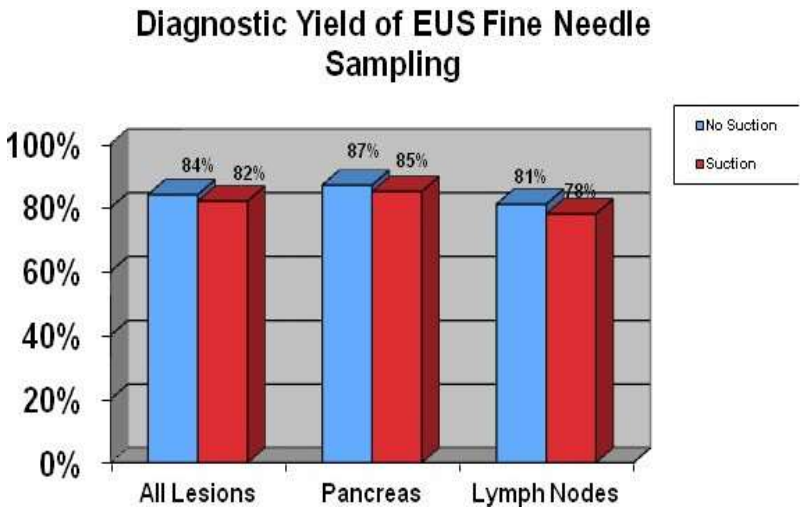

Figure 2: Diagnostic Yield

Table 2: Slide Characteristics

	No Suction	Suction	P value
Bloody Gross Appearance			
All Lesions	43%	65%	<0.001
Pancreas	33%	55%	<0.001
Lymph Nodes	63%	80%	0.06
High Cellularity			
All Lesions	60%	55%	0.38
Pancreas	57%	57%	1
Lymph Nodes	71%	66%	0.76

5. Discussion

Improving diagnostic yield remains a challenge for all endosonographers, and the use of suction during EUS-guided fine needle sampling is debatable and often user dependent. A multitude of studies have examined the use of suction in EUS-guided fine needle sampling, and four studies have specifically utilized a prospective, randomized study design. [18-21] These four studies showed that the use of suction is, in general, advantageous; however, each study had caveats with limiting factors such as the site of fine needle sampling and sample size. This study is one of the largest to date in terms of number of patients enrolled and encompasses all solid lesions

amenable to EUS-guided fine needle sampling. [26] Our study evaluated data based on a study design that allowed for comparison of sample quality and diagnostic accuracy for each lesion. Additionally, in obtaining the sample data, we utilized established principles such as rapid on-site evaluation (ROSE) and method of expulsion of sample [27].

There are several limitations in our study. While the number of subjects included was the largest to date, it was not the largest sample size for each particular lesion. Additionally, there was no inter-observer comparison for the cytopathologist reviewing the adequacy of each slide and the nurse assessing specimen quality was not blinded. Our study could not make a true assessment of sensitivity and specificity due to incomplete clinical follow up on all patients.

A 2012 meta-analysis revealed that EUS-FNA is an accurate diagnostic test, specifically for solid pancreatic neoplasms. [28] As Tarantino et al and Lee et al show, the use of suction in these lesions can be helpful; however, even among these two prospective randomized trials, reports are conflicting regarding the diagnostic advantage of the use of suction for solid pancreatic lesions. In a retrospective analysis performed by Storch et al, a similar analysis of solid lesions revealed the use of suction did not improve the diagnostic accuracy of EUS-guided fine needle sampling. [29] Our study, in contrast with the 2017 ESGE guidelines, adds to the body of evidence suggesting that the use of suction produces a bloodier gross appearance and, importantly, has no significant impact on the diagnostic yield of EUS-guided fine needle sampling. Based on the findings of our study, our group routinely performs all initial passes without suction, and we recommend against the use of suction when sampling potentially malignant solid lesions.

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