Macroscopic on-site quality evaluation of biopsy specimens to improve the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration using a 22-gauge needle for solid lesions: A single-center retrospective study

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Received November 10, 2022; Accepted May 3, 2023

DOI: 10.3892/etm.2023.12037

Abstract. The present study aimed to evaluate the clinical value of macroscopic on-site evaluation (MOSE) of solid masses by endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) using a standard 22-gauge needle and to explore the cut-off length of macroscopic visible core (MVC) required to obtain an accurate histopathological diagnosis. In total, 119 patients who satisfied the inclusion and exclusion criteria and underwent EUS-FNA were divided into conventional FNA and FNA combined with MOSE groups. In the MOSE group, the presence of MVC was examined and its total length measured, after which the pathological results of FNA were compared with the final diagnosis. The diagnostic sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of FNA in the two groups were calculated and the effect of MOSE on the FNA result was analyzed. The MOSE group had a higher diagnostic sensitivity (75.0% vs. 89.8%; P=0.038) and accuracy (74.5% vs. 90.6%; P=0.026). MVC was observed in 98.4% (63/64) of patients in the MOSE group. The median length of MVC was 15 mm. The optimal cut-off length of MVC for obtaining an accurate histological diagnosis was 13 mm, with a sensitivity of 90.2%. No statistically significant significance was observed in the specificity, PPV and NPV between the groups. Thus, MOSE helps to improve the diagnostic ability of FNA for solid masses and may be a useful alternative to assess the adequacy of puncture specimens in units where rapid on-site evaluation cannot be performed.

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Key words: endosonography, endoscopic ultrasound-guided fine needle aspiration, macroscopic on-site evaluation, macroscopic visible core

Introduction

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA), a minimally invasive interventional diagnostic technique, involves the insertion of a puncture needle into the target lesion for aspiration biopsy under real-time EUS guidance to obtain cells or tissues for pathological analysis. EUS-FNA has now become the preferred method for obtaining diagnostic samples of lesions of the gastrointestinal tract and its adjacent organs (1-3) and is routinely used for pancreatic lesions, subepithelial lesions, abdominal lymph nodes, the liver, spleen, adrenal glands, mediastinum and pelvis. EUS-FNA operates through the natural cavity of the body, shortening the distance between the probe and the lesion. It passes through the less normal tissue during puncture, thus reducing the side injuries caused by the puncture, with an overall complication rate of less than 1% (4,5).

Wiersema *et al* (6) first described the important role of on-site cytopathologists in assessing the adequacy of puncture specimens and several subsequent studies (7-9) have demonstrated that rapid on-site evaluation (ROSE) is an effective method for improving the diagnostic ability of EUS-FNA. ROSE can assess whether cell sampling is adequate or representative in real time. However, owing to the increased human and financial burden associated with ROSE, it is not routinely performed in all healthcare facilities (2,10). To improve the positivity rate of FNA, Iwashita *et al* (11), in 2015, introduced the concept of macroscopic on-site evaluation (MOSE), which helps to determine the presence of a macroscopic visible core (MVC), a white or yellowish strip of tissue, in histological specimens obtained by visual inspection during puncture. The MVC is a more accurate predictor of the presence of a histologic core in a puncture specimen. A histologic core is a tissue mass that is structurally intact and sufficient for histologic evaluation and its presence often indicates good sample adequacy (12).

Most previous studies related to MOSE (13-19) selected 19G standard FNA needles and 22G fine needle biopsy (FNB) needles. EUS-FNB with MOSE shows comparable accuracy to that of EUS-FNB with three needle passes. MOSE reliably assesses sample adequacy and reduces the number of needle passes required to obtain a diagnosis with a 22G Franseen needle (20), whereas 22G FNA needles are currently the most used in clinical practice. It is uncertain whether the results of these studies are applicable to 22G standard FNA needles and further studies are needed to determine whether 22G standard FNA needles can improve clinical diagnostic efficacy through MOSE in the absence of ROSE.

Materials and methods

Patients. The present retrospective study included patients who underwent EUS-FNA for solid lesions between October 2015 and June 2021 at the Affiliated Hospital of Nantong University. EUS-FNA was performed using the PENTAX linear-array echoendoscope (PENTAX EPK-i5000 and PENTAX EG-3270UK; PENTAX Medical) under anesthesia. Patients in whom the first puncture had been performed by the same endoscopist using a standard 22G FNA needle and those with relatively complete clinical data, detailed records of FNA operations and traceable follow-up information were included. Patients operated with 19G or 25G FNA needles or FNB needles; those with severe cardiac, cerebral and pulmonary disorders and hence could not tolerate the operation; those with severe psychiatric disorders who could not cooperate with the clinical team members; those with untreated bleeding tendencies, including a platelet count $<50x10^9$/l, an international normalized ratio >1.5, or those on anticoagulation or antiplatelet drugs; and those with incomplete follow-up data and unknown clinical outcomes were excluded from the present study. All patients provided written informed consent prior to enrolment. The present study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethical Committee of Affiliated Hospital of Nantong University (approval no. 2019-K055).

Endoscopic procedures. EUS was performed using the PENTAX linear scanning video echoendoscope (PENTAX EPK-i5000 and PENTAX EG-3270UK; PENTAX Medical) and a 22G needle (Expect™; Boston Scientific Corp.) was used as the EUS-FNA needle in all cases. All solid lesions were classified as pancreatic and non-pancreatic. EUS-FNA was performed by a single endoscopist who had experience in performing the operation under sedation with intravenous propofol, without any specific experience in cytopathology. No on-site cytologic pathologist was present during the puncture. The puncture site was determined under real-time EUS guidance by avoiding blood vessels, pancreatic ducts, bile ducts and other important organs. The puncture needle, which was pressed against the wall of the GI tract, was linearly hyperechoic on EUS and the 'comet tail' sign produced by the metal could be observed. The puncture needle was inserted into the target lesion, the core was removed, a negative-pressure syringe was attached and the needle was lifted and inserted into the lesion more than 20 times (Fig. S1). The endoscopist decided the number of punctures and chose the appropriate puncture method, such as using the needle core, adjusting the negative pressure and the fan puncture technique, according to the characteristics of the lesion, the situation while obtaining the specimen and his or her own experience. After each puncture, the negative pressure was released, the puncture needle was withdrawn and the specimen was pushed into the culture dish.

MOSE technique. The specimen was carefully examined by the endoscopist for the presence of MVC, which was defined as whitish or yellowish pieces of tissue with an apparent bulk, not including paste-like or liquid-like material (Fig. 1). The FNA procedure would be terminated if the endoscopist observed MVC in the obtained specimen. MVCs scattered throughout the sample were collected and aligned using an injection needle, after which the total length of the MVC was measured using a ruler. If the endoscopist could not detect the MVC, additional punctures were performed while ensuring procedural safety.

Final diagnosis. On the basis of the patient's preoperative laboratory tests, imaging data and clinical presentation, the final diagnosis was established based on the following points: i) Pathological findings after surgical resection; ii) positive FNA malignancy without surgical intervention and a clinical course consistent with the FNA diagnosis; and iii) negative FNA or puncture pathology showing benign lesions without worsening or spontaneous lesions on imaging review after at least 6 months of regression observed on follow-up.

Main outcome measures. The primary objectives of the present study were to evaluate the ability of different lengths of MVC to obtain an accurate histological diagnosis and to determine the optimal cut-off value for MVC length and to study the effect of the application of MOSE on the diagnostic efficacy of FNA. The secondary objectives were to analyze the factors affecting the accuracy of histological diagnosis and to compare any differences between the two groups in terms of operative time, number of punctures and the incidence of puncture-related complications.

Cases in which the nature of the lesion could be determined by puncture, including cytological or (and) histological pathological findings that clearly defined the histological diagnosis of the lesion as benign or malignant, tumor cells or cancer cells seen by puncture, were considered as FNA positive and otherwise, as FNA negative (Fig. S2). The accuracy of FNA was defined as the sum of cases with true positive and true negative results divided by the total number of cases. The operative time was defined as the difference in time from the insertion to the exit of the endoscope.

Statistical methods. SPSS 23.0 software (IBM Corp.) was used for statistical analysis and the results of the normality test for continuous variables showed that they did not obey normal distribution; hence, median (quartiles) was used for descriptive statistics and frequency or percentage was used for descriptive statistics for categorical variables. The Mann-Whitney U test was used for intergroup comparisons of continuous variables and the χ^2 test or Fisher exact probability method was used to compare the variables between the groups. The accuracy of the area under the curve (AUC) of the receiver-operating

Figure 1. Macroscopic visible core at macroscopic on-site evaluation (magnification, x10).

characteristic (ROC) curve was assessed by plotting the curve of the length of the MVC for histopathological diagnosis, using the Youden index to calculate the optimal cut-off value of MVC length required to obtain an accurate histological diagnosis. Factors that may be associated with an accurate histological diagnosis were investigated using univariate and multivariate logistic regression analysis. P<0.05 was considered to indicate a statistically significant difference.

Results

Patient and lesion characteristics. A total of 141 patients underwent FNA for occupying lesions during the study period, of whom 22 were excluded according to the inclusion and exclusion criteria, including 15 patients in whom puncture was performed using other types of puncture needles (including 19G and 25G FNA needles and FNB needles), 6 patients with cystic lesions and 1 patient who was excluded owing to his absence. Finally, 119 patients, namely 55 in the conventional FNA group and 64 in the FNA combined with MOSE group, were included (Fig. 2).

The patient and lesion characteristics of the two groups are listed in Table I. There were no statistically significant differences in sex, age, lesion site (divided into pancreatic and non-pancreatic lesions), or lesion size between the two groups. In the conventional FNA group, 33 patients had pancreatic lesions and 22 had non-pancreatic lesions. Among patients with non-pancreatic lesions, five had gastric lesions; five had hepatogastric interstitial lesions; four had lymph node enlargement; three had hepatic lesions; and one patient each had esophageal, rectal, hepatopancreatic interstitial, retroperitoneal and adrenal lesions. In the FNA combined with MOSE group, 47 patients had pancreatic lesions and 17 had non-pancreatic lesions. Among patients with non-pancreatic lesions, seven had gastric lesions; two had lymph node enlargement; two had mediastinal lesions; two had hepatic lesions; and one patient each had rectal, adrenal, parapancreatic and splenogastric interstitial lesions.

Outcomes. The success rate of FNA was 100% in both groups, with 1-5 punctures performed per lesion. The differences in the number of punctures (a median of 3 in the conventional FNA group and 3 in the FNA combined with MOSE group; P=0.151), operative time (a median of 17 min in the conventional FNA group and 19 min in the FNA combined with MOSE group; P=0.448), puncture route (P=0.353) and complication rates (5.4% vs. 1.5%; P=0.506) in both groups were not statistically significant. Three puncture-related complications occurred in the conventional FNA group, namely two cases of hyperamylasemia and one case of transient fever and one case of self-limiting bleeding at the puncture site in the FNA combined with MOSE group, all of which improved after symptomatic treatment, without serious puncture-related complications (Table II).

The final diagnosis of the patient was used as the criterion to determine the FNA results and to evaluate whether the application of MOSE had any effect on the diagnostic ability of FNA and the results are shown in Table III. Compared with the conventional FNA group, the diagnostic sensitivity (75.0% vs. 89.8%, P=0.038) and accuracy (74.5% vs. 90.6%, P=0.026) were higher in the FNA combined with MOSE group and the differences between the groups were statistically significant, whereas the differences in the specificity (66.7% vs. 100.0%), PPV (97.5% vs. 100.0%) and NPV (13.3% vs. 45.5%) were not statistically significant (P<0.05).

The final diagnosis of the patients was established by combining the FNA results, surgical pathology findings and follow-up observations. Tables IV and V show the specific pathological types and the corresponding number of patients in each of the two groups according to the primary site of the pancreatic and non-pancreatic lesions. A total of 39 patients in the conventional FNA group could be diagnosed based on FNA results and/or post-surgical pathology. Only tumor cells or cancer cells were seen by FNA puncture in eight patients; however, the specific pathology was not known. FNA did not show any abnormalities and on follow-up, two patients remained in good general condition without receiving any special treatment; hence, they were considered as true negatives. In the FNA combined with MOSE group, a specific histopathological diagnosis could be established in 55 patients in combination with FNA results or (and) surgical pathology, as shown in Table V. FNA cytology showed positive results in four patients; however, the histopathology was unknown because no surgical operation was performed. The results were confirmed as true positive on follow-up; five patients had FNA-negative results, which were confirmed at follow-up.

MVC was observed in 63 of 64 (98.4%) patients in the FNA combined with MOSE group, with a median MVC length of 15 (interquartile range, 13-19) mm. Analysis of the relationship between histological diagnosis and MVC length showed that MVC length was greater in the group of patients in whom an accurate histological diagnosis was obtained compared with those in whom an accurate histological diagnosis was not obtained (median: 12 mm vs.

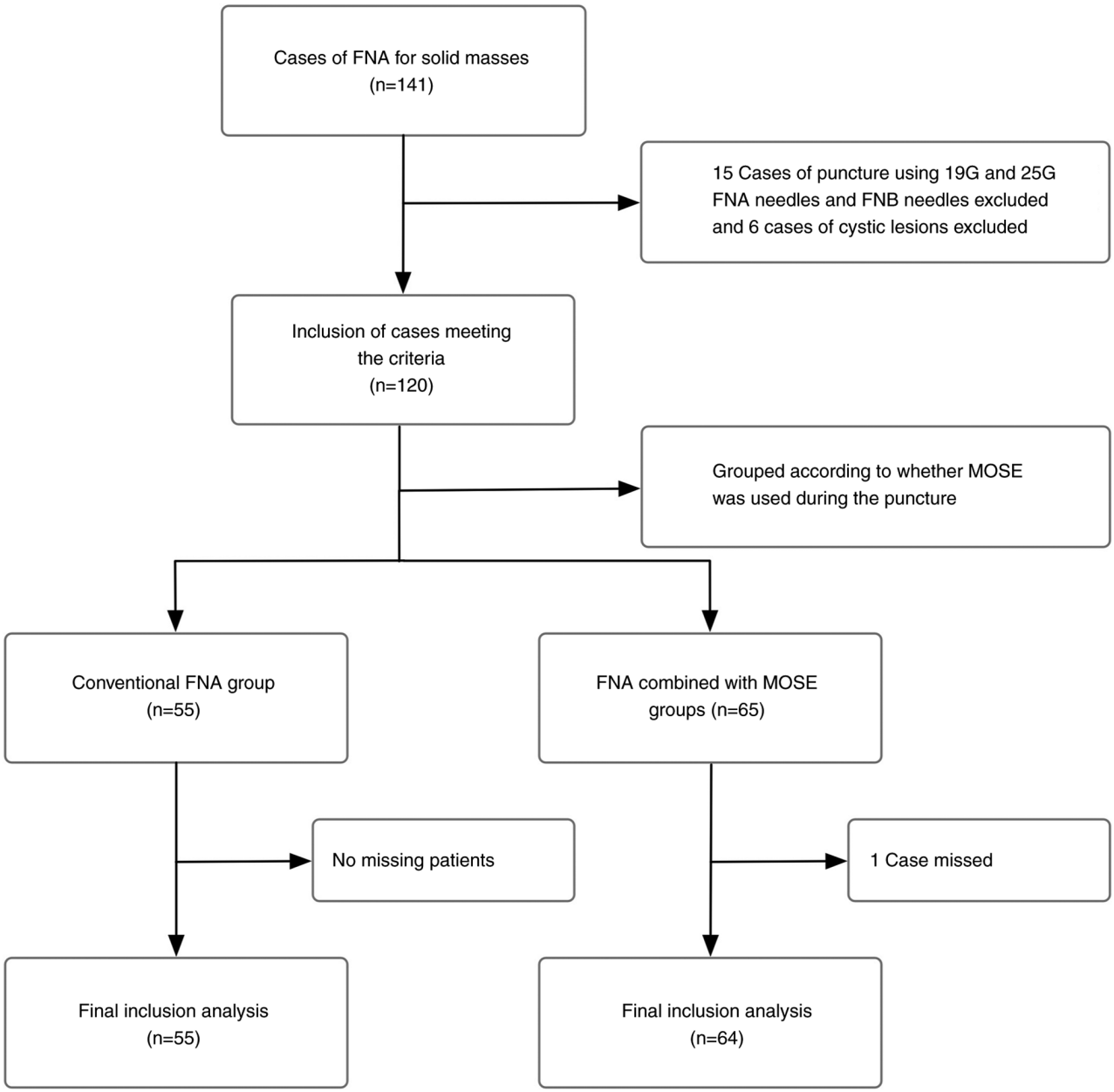

Figure 2. Diagram of study flow. FNA, fine needle aspiration; MOSE, macroscopic on-site evaluation.

17 mm, P<0.001; Fig. 3). ROC curves were plotted regarding the MVC length for histological diagnosis (Fig. 4) and the optimal MVC cutoff length required to obtain an accurate histological diagnosis was determined using the Youden index. The results showed that the optimal MVC length cutoff value was 13 mm and the AUC was 0.775 (95% CI 0.651-0.898), which corresponds to a diagnosis at this MVC length cutoff value, at a sensitivity of 90.2%.

Factors that may be associated with obtaining an accurate histological diagnosis were investigated using univariate and multifactorial logistic regression analysis, which included sex, age, lesion site (divided into pancreatic and non-pancreatic lesions), lesion size, number of punctures and MVC length. The data from the statistical analysis are shown in Table VI. Univariate logistic regression analysis showed that histological diagnostic accuracy was associated with the number of punctures (P=0.042) and MVC length (P=0.001). Multifactorial logistic regression analysis showed that only MVC length 13 mm (odds ratio=9.426, 95% CI 1.923-46.204; P=0.006) was associated with a correct histopathological diagnosis.

Discussion

ROSE is a more reliable method to improve the diagnostic efficacy of FNA and the role of ROSE in FNA has been confirmed by several studies (8,21-23). The presence of an on-site cytopathologist helps to improve sample adequacy and diagnostic positivity, while also avoiding unnecessary repetitive FNA procedures. In addition, fewer punctures may reduce the rate of potential procedure-related complications and improve procedural safety. However, ROSE is not routinely performed in many hospitals and a global survey showed that ROSE is available in only 55% of Asian institutions (24). Moreover, ROSE requires additional time for slide

Table I. Comparison of patient and lesion characteristics between the two groups.

Characteristic	Conventional FNA group (n=55)	FNA united MOSE group (n=64)	P-value
Sex, n			0.800
Male	34	41	
Female	21	23	
Median age (range), years	65 (60-72)	66 (58-71)	0.769
Location of lesions, n			0.119
Pancreatic lesions	33	47	
Non-pancreatic lesions	22	17	
Median lesion size (range), mm	33 (28-45)	34 (25-40)	0.602

FNA, fine needle aspiration; MOSE, macroscopic on-site evaluation.

Table II. Comparison of puncture-related parameters between the two groups.

Puncture-related parameter	Conventional FNA group (n=55)	FNA combined MOSE group (n=64)	P-value
Median number of punctures (range)	3 (2-3)	3 (2-4)	0.151
Median operation time (range), min	17 (13-24)	19 (14-23)	0.448
Puncture paths, n			0.353
Trans-duodenal	17	25	
Trans-esophageal, stomach or rectal	38	39	
Complications associated with puncture, n	3	1	0.506

FNA, fine needle aspiration; MOSE, macroscopic on-site evaluation.

Table III. Comparison of the diagnostic ability of FNA between the two groups.

Diagnostic ability	Conventional FNA group	FNA combined MOSE group	P-value
Sensitivity, %	75.0 (60.8-85.5)	89.8 (78.5-95.8)	0.038
Specificity, %	66.7 (12.5-98.2)	100.0 (46.3-100.0)	0.375
PPV, %	97.5 (85.3-99.9)	100.0 (91.6-100.0)	0.430
NPV, %	13.3 (2.3-41.6)	45.5 (18.1-75.4)	0.095
Accuracy, %	75.0 (60.8-85.5)	90.6 (80.7-96.0)	0.026

P<0.05 was considered to indicate a statistically significant difference. FNA, fine needle aspiration; MOSE, macroscopic on-site evaluation; PPV, positive predictive value; NPV, negative predictive value.

staining and pathological analysis, increasing the procedural duration (25,26).

Iwashita *et al* (11) reported on direct MOSE performed by an endoscopist on the acquired specimens. They found that the diagnostic rate was significantly higher when the MVC was 4 mm and that MVC >4 mm could be used as an indicator of specimen adequacy, which serves as an important reference indicator when performing FNA in many endoscopy centers where ROSE cannot be performed. However, as the present study used a 19G FNA needle, this criterion may not be applicable to other needle types. A similar study using a 22G FNB needle (Acquire™) reported that MVC length predicted correct pathologic diagnosis and that the diagnostic accuracy of the FNB needle was positively correlated with MVC length, with a length of 10 mm independently influencing correct diagnosis (16). A recent prospective multicenter study using the same FNB needle (Acquire™) showed that MVC length was positively correlated with the number of samples with a score of 5 (cytology, 1-2; histology, 3-5). The optimal cut-off value of MVC length for sample score 5 was 15 mm and the histological diagnostic accuracy and sensitivity of specimens with MVC >15 mm was greater than that of specimens with MVC <15 mm. MVC length is also positively correlated with the sensitivity of histological diagnosis (12). In a systematic

Table IV. Final pathological results of conventional FNA group.

Lesion site and pathological results	n
Pancreatic lesions	
Adenocarcinoma	16
Neuroendocrine tumor	4
Mucinous tumor	1
Parenchymal pseudopapillary tumor	1
Non-pancreatic lesions	
Gastrointestinal mesenchymal tumor	5
Lymphoma	3
Tuberculosis	2
Esophageal adenocarcinoma	1
Gastric squamous carcinoma	1
Gastric adenocarcinoma	1
Liver Cancer	1
Mucinous smooth muscle sarcoma	1
Metastatic cancer	1
Hepatic adenoma	1

Table V. Final pathological results of FNA combined with MOSE group.

Lesion site and pathological results	n
Pancreatic lesions	
Adenocarcinoma	27
Neuroendocrine tumor	5
Acute pancreatitis	2
Chronic pancreatitis	2
Autoimmune pancreatitis	1
Parenchymal pseudopapillary tumor	1
Metastatic cancer	1
Non-pancreatic lesions	
Gastrointestinal mesenchymal tumor	4
Lymphoma	3
Metastatic cancer	3
Gastric squamous carcinoma	2
Mediastinal nerve sheath tumor	1
Gastric adenocarcinoma	1
Gastric Induced cell carcinoma	1
Abscess	1

FNA, fine needle aspiration; MOSE, macroscopic on-site evaluation.

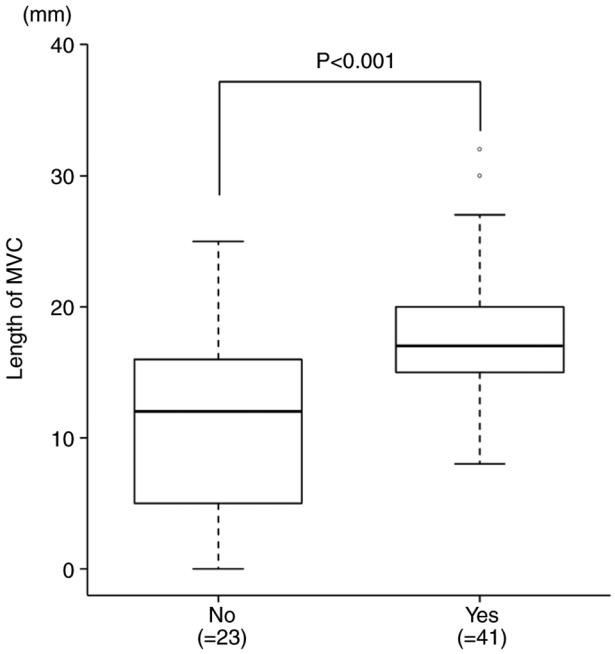

Figure 3. Comparison of the lengths of the two groups of MVC for an accurate histological diagnosis. MVC, macroscopic visible core.

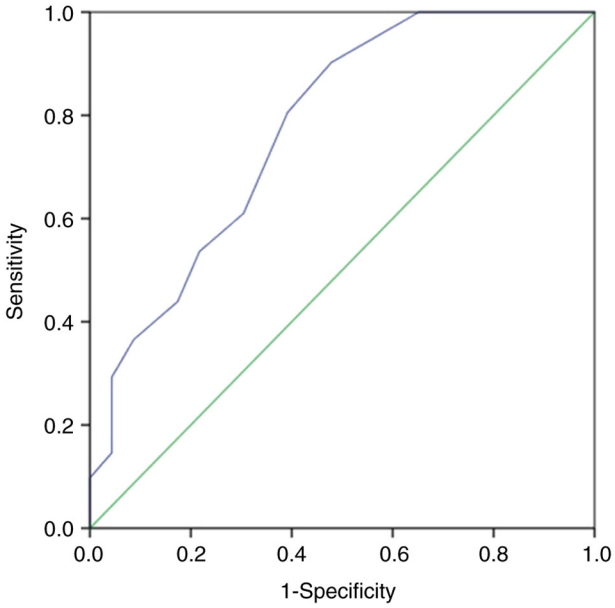

Figure 4. ROC curve on the length of MVC for histological diagnosis. ROC, receiver-operating characteristic; MVC, macroscopic visible core.

review and meta-analysis, excellent pooled diagnostic accuracy parameters were observed in EUS-guided tissue acquisition by FNB using the MOSE method (27).

The European Society of Gastrointestinal Endoscopy recommends 3-4 punctures when performing FNA on target lesions when ROSE cannot be performed (2). Previous related studies (11,15,16) have shown that obtaining an MVC above the truncation length may be a useful indicator for terminating the puncture, which may be helpful for institutions unable to perform ROSE. Using this cut-off length to guide the puncture process is expected to improve the rate of diagnosis by FNA, reduce the number of punctures and subsequently reduce the occurrence of potential needle tract metastases, which may benefit patients with surgically resectable caudal pancreatic body tumors.

A standardized MOSE procedure has not yet been established and evidence regarding its guidance for the puncture procedure is limited and controversial (2,11,17,28). By performing MOSE on specimens obtained with a 22G FNA

Table VI. Univariate and multivariate logistic regression analysis associated with accurate histological diagnosis.

	Univariate		Multivariate	
Characteristic	OR (95% CI)	P-value	OR (95% CI)	P-value
Sex				
Male	0.355 (0.110-1.140)	0.082	0.435 (0.094-2.010)	0.286
Female	1.000		1.000	
Age, years	1.027 (0.984-1.073)	0.223	1.044 (0.982-1.110)	0.165
Location of lesions				
Pancreatic lesions	0.453 (0.128-1.603)	0.220	0.423 (0.083-2.147)	0.299
Non-Pancreatic lesions	1.000		1.000	
Size of lesions	1.042 (0.999-1.087)	0.056	1.053 (0.992-1.118)	0.092
Number of punctures	1.778 (1.022-3.094)	0.042	1.688 (0.867-3.287)	0.123
Length of MVC, mm				
≥13	10.091 (2.705-37.648)	0.001	9.426 (1.923-46.204)	0.006
<13	1.000		1.000	

P<0.05 was considered to indicate a statistically significant difference.

needle, the present study aimed to investigate the effect of MOSE on the results of FNA guided by a standard 22G needle and to determine the optimal cut-off value of MVC length required to perform an accurate histological diagnosis, with the aim of using this length to guide the subsequent FNA procedure and improve the FNA positivity rate and safety.

The present study showed that FNA combined with MOSE was superior to conventional FNA for the diagnosis of solid masses, with statistical differences in diagnostic sensitivity and accuracy, suggesting that MOSE can be used to improve the diagnostic efficiency of FNA when ROSE cannot be performed. MVC length may predict the correct histologic diagnosis of FNA; an MVC length >13 mm may provide accurate histological pathology results, corresponding to a sensitivity of 90.2% at this truncation length, following which the FNA operation can be terminated. Univariate and multivariate logistic regression analyses also showed that MVC length ≥13 mm influenced accurate histopathological diagnosis and puncturing with this cut-off length as a reference was expected to improve the FNA positivity rate and reduce the number of punctures required for diagnosis.

The MOSE procedure involves several steps such as visual observation, collection and measurement of MVC length, which may prolong the operation time; however, the results of the present study showed that the operative time in the FNA combined with MOSE group was not significantly different from that in the conventional FNA group, indicating that MOSE did not significantly increase the operative time.

The advantage of the present study is that it selected the most widely used 22G standard FNA needle for puncture, whereas most previous related studies used 19G standard FNA needles and 22G FNB puncture needles. Although these needles are of higher caliber and more likely to obtain the core tissue, their stiffness and poor flexibility reduce the feasibility of FNA and limit the endoscopic position, angle and forceps lifter function, increasing the potential risk of complications (29). Compared with FNA needles, FNB needles are characterized by their lateral beveled orifice or barb (5), a special design that improves tissue access; however, owing to the characteristics of the FNB tip shape and the stiffness of the needle body, this procedure is more difficult than that using standard FNA needles, which is more commonly performed by less experienced endoscopists (17). 22G standard FNA needles are more flexible and visualization is improved under ultrasound for obtaining adequate cytology or histology samples without increasing the risk of operation-related complications (5). The effect of MOSE on the diagnostic role of the 22G standard FNA needle has not been fully elucidated and studies on the relationship between MVC length obtained with the 22G FNA needle and histological diagnosis are lacking.

In the present study, MVC was observed in 98.4% (63/64) of patients in the FNA combined with MOSE group, while pathological diagnostic information was available in only 89.1% (57/64) of patients. This indicated that the MVC did not contain valuable diagnostic components in six patients and the white or yellowish samples in these cases could have been necrotic material or fibrous components. Thus, MOSE is not completely accurate for visual inspection and it may mistake non-diagnostic components for meaningful pathological tissue, leading to the occurrence of false-negative diagnosis. Moreover, unlike ROSE, it cannot assess the presence of tumor cells; hence, obtaining a large number of samples and a longer MVC does not necessarily lead to a correct diagnosis. In this context, the assessment in the present study of the relationship between MVC length and histological diagnostic accuracy is of greater clinical value, especially for pancreatic lesions, where pancreatic adenocarcinoma often contains a large fibrous component and less substantial tissue or cellular components (30), which may be mistaken for core tissue during visual assessment. A study by Iwashita *et al* (11) also showed that pancreatic lesions are important risk factors for false-negative puncture. The use of computer analysis software to quantify the characteristics

of core tissue (including chromaticity, transparency and hardness) and to elucidate the criteria for good-quality core tissue may reduce the number of false-negative cases to some extent, compared to visual assessment (15).

The present study has several limitations. First, it was a single-center retrospective study with a small sample size, which may lead to a bias in the FNA diagnostic results and patient selection. For example, the small number of GIST cases made it difficult to group by lesion type. Therefore, the present study attempted to minimize the selection bias through quality score matching, such as number of functions, operation time and function route. (Tables I and II). Further validation in multicenter studies with larger sample sizes may be needed, considering the differences in equipment and technical level between the various procedures. Second, the present study only performed a preliminary study with the 22G FNA needle and the results may vary when other types of puncture needles are used for tissue sampling. In addition, the amount of tissue obtained by aspiration with the 22G FNA needle is relatively small compared with the tissue obtained using large-bore puncture needles. Further, it is often difficult to identify MVC in samples containing large amounts of blood-based components, which may require a body vision microscope for the collection and measurement of MVC. Finally, the diagnostic expertise of different pathologists may vary and all FNA specimens may not be judged by the same pathologist; use of blinded methods can only minimize the relevant variability.

Based on the current evidence, FNB using Franseen or Fork-tip needles is a clinically preferred scheme for solid lesions (31). However, in cases where FNB cannot be performed, FNA combined with MOSE may be used. When using 22G FNA for puncture sampling of solid masses, an MVC length of >13 mm may help to achieve an accurate histologic diagnosis and this truncation length may be used to guide the puncture procedure and improve the diagnostic yield. MOSE helps to improve the diagnostic ability of FNA for solid masses and may be a useful alternative to assess the adequacy of puncture specimens in units where ROSE cannot be performed.

Acknowledgements

Not applicable.

Funding

The present study was supported by Jiangsu Provincial Geriatric Health Research Project (grant no. LKM2022023), the Science and Technology Program of Nantong (grant nos. JC12022001 and JC22022040), Nantong University Hospital Postdoctoral Research Program (grant no. BSH202214), Nantong Commission of Health Research Fund Project (grant no. MA2021004) and the Natural Science Foundation of Jiangsu Province Youth Fund Project (grant no. BK20200965).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

CG and MW drafted the manuscript and conceived the study. JY and ZL were responsible for the collection and analysis of case data and literature. JZ helped to design the study and revised the manuscript. ZM and CL performed the statistical analysis, and confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All the patients provided written, informed consent and the study was approved by the Ethical Committee of Affiliated Hospital of Nantong University (approval no. 2019-K055).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interest.

References

1. Dumonceau JM, Deprez PH, Jenssen C, Iglesias-Garcia J, Larghi A, Vanbiervliet G, Aithal GP, Arcidiacono PG, Bastos P, Carrara S, *et al*: Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European society of gastrointestinal endoscopy (ESGE) clinical guideline-updated january. Endoscopy 49: 695-714, 2017.
2. Polkowski M, Jenssen C, Kaye P, Carrara S, Deprez P, Gines A, Fernández-Esparrach G, Eisendrath P, Aithal GP, Arcidiacono P, *et al*: Technical aspects of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European society of gastrointestinal endoscopy (ESGE) Technical guideline-march 2017. Endoscopy 49: 989-1006, 2017.
3. ASGE Standards of Practice Committee, Eloubeidi MA, Decker GA, Chandrasekhara V, Chathadi KV, Early DS, Evans JA, Fanelli RD, Fisher DA, Foley K, *et al*: The role of endoscopy in the evaluation and management of patients with solid pancreatic neoplasia. Gastrointest Endosc 83: 17-28, 2016.
4. Wang KX, Ben QW, Jin ZD, Du YQ, Zou DW, Liao Z and Li ZS: Assessment of morbidity and mortality associated with EUS-guided FNA: A systematic review. Gastrointest Endosc 73: 283-290, 2011.
5. Tan Y, Tang X, Huang J and Li R: Efficacy, feasibility, and safety of endoscopic ultrasound-guided fine-needle biopsy for the diagnosis of gastrointestinal subepithelial lesions: A systematic review and meta-analysis. J Clin Gastroenterol 56: e283-e292, 2022.
6. Wiersema MJ, Wiersema LM, Khusro Q, Cramer HM and Tao LC: Combined endosonography and fine-needle aspiration cytology in the evaluation of gastrointestinal lesions. Gastrointest Endosc 40: 199-206, 1994.
7. Klapman JB, Logrono R, Dye CE and Waxman I: Clinical impact of on-site cytopathology interpretation on endoscopic ultrasound-guided fine needle aspiration. Am J Gastroenterol 98: 1289-1294, 2003.
8. Iglesias-Garcia J, Dominguez-Munoz JE, Abdulkader I, Larino-Noia J, Eugenyeva E, Lozano-Leon A and Forteza-Vila J: Influence of on-site cytopathology evaluation on the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of solid pancreatic masses. Am J Gastroenterol 106: 1705-1710, 2011.
9. Hébert-Magee S, Bae S, Varadarajulu S, Ramesh J, Frost AR, Eloubeidi MA and Eltoum IA: The presence of a cytopathologist increases the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration cytology for pancreatic adenocarcinoma: A meta-analysis. Cytopathology 24: 159-171, 2013.

10. Masutani H, Okuwaki K, Kida M, Yoshida T, Imaizumi H, Yamauchi H, Iwai T, Kaneko T, Hasegawa R, Miyata E, *et al*: On-site stereomicroscope quality evaluations to estimate white core cutoff lengths using EUS-FNA biopsy sampling with 22-gauge needles. Gastrointest Endosc 90: 947-956, 2019.
11. Iwashita T, Yasuda I, Mukai T, Doi S, Nakashima M, Uemura S, Mabuchi M, Shimizu M, Hatano Y, Hara A and Moriwaki H: Macroscopic on-site quality evaluation of biopsy specimens to improve the diagnostic accuracy during EUS-guided FNA using a 19-gauge needle for solid lesions: A single-center prospective pilot study (MOSE study). Gastrointest Endosc 81: 177-185, 2015.
12. Kaneko J, Ishiwatari H, Sasaki K, Yasuda I, Takahashi K, Imura J, Iwashita T, Uemura S, Hatano Y, Miyazaki T, *et al*: Macroscopic visible core length can predict the histological sample quantity in endoscopic ultrasound-guided tissue acquisition: Multicenter prospective study. Dig Endosc 34: 622-631, 2022.
13. So H, Seo DW, Hwang JS, Ko SW, Oh D, Song TJ, Park DH, Lee SK and Kim MH: Macroscopic on-site evaluation after EUS-guided fine needle biopsy may replace rapid on-site evaluation. Endosc Ultrasound 10: 111-115, 2021.
14. Chong CCN, Lakhtakia S, Nguyen N, Hara K, Chan WK, Puri R, Almadi MA, Ang TL, Kwek A, Yasuda I, *et al*: Endoscopic ultrasound-guided tissue acquisition with or without macroscopic on-site evaluation: Randomized controlled trial. Endoscopy 52: 856-863, 2020.
15. Okuwaki K, Masutani H, Kida M, Yamauchi H, Iwai T, Miyata E, Hasegawa R, Kaneko T, Imaizumi H, Watanabe M, *et al*: Diagnostic efficacy of white core cutoff lengths obtained by EUS-guided fine-needle biopsy using a novel 22G franseen biopsy needle and sample isolation processing by stereomicroscopy for subepithelial lesions. Endosc Ultrasound 9: 187-192, 2020.
16. Kaneko J, Ishiwatari H, Sasaki K, Satoh T, Sato J, Matsubayashi H, Yabuuchi Y, Kishida Y, Yoshida M, Ito S, *et al*: Macroscopic on-site evaluation of biopsy specimens for accurate pathological diagnosis during EUS-guided fine needle biopsy using 22-G Franseen needle. Endosc Ultrasound 9: 385-391, 2020.
17. Ishiwatari H, Sato J, Fujie S, Sasaki K, Kaneko J, Satoh T, Matsubayashi H, Kishida Y, Yoshida M, Ito S, *et al*: Gross visual inspection by endosonographers during endoscopic ultrasound-guided fine needle aspiration. Pancreatology 19: 191-195, 2019.
18. Stigliano S, Balassone V, Biasutto D, Covotta F, Signoretti M and Di Matteo FM: Accuracy of visual on-site evaluation (Vose) in predicting the adequacy of Eus-guided fine needle biopsy: A single center prospective study. Pancreatology 21: 312-317, 2021
19. Mangiavillano B, Frazzoni L, Togliani T, Fabbri C, Tarantino I, De Luca L, Staiano T, Binda C, Signoretti M, Eusebi LH, *et al*: Macroscopic on-site evaluation (MOSE) of specimens from solid lesions acquired during EUS-FNB: multicenter study and comparison between needle gauges. Endosc Int Open 9: E901-E906, 2021.
20. Mangiavillano B, Crinò SF, Facciorusso A, Di Matteo F, Barbera C, Larghi A, Rizzatti G, Carrara S, Spadaccini M, Auriemma F, *et al*: Endoscopic ultrasound-guided fine-needle biopsy with or without macroscopic on-site evaluation: A randomized controlled noninferiority trial. Endoscopy 55: 129-137, 2022.
21. Collins BT, Murad FM, Wang JF and Bernadt CT: Rapid on-site evaluation for endoscopic ultrasound-guided fine-needle biopsy of the pancreas decreases the incidence of repeat biopsy procedures. Cancer Cytopathol 121: 518-524, 2013.
22. Wani S, Mullady D, Early DS, Rastogi A, Collins B, Wang JF, Marshall C, Sams SB, Yen R, Rizeq M, *et al*: The clinical impact of immediate on-site cytopathology evaluation during endoscopic ultrasound-guided fine needle aspiration of pancreatic masses: A prospective multicenter randomized controlled trial. Am J Gastroenterol 110: 1429-1439, 2015.
23. Matynia AP, Schmidt RL, Barraza G, Layfield LJ, Siddiqui AA and Adler DG: Impact of rapid on-site evaluation on the adequacy of endoscopic-ultrasound guided fine-needle aspiration of solid pancreatic lesions: A systematic review and meta-analysis. J Gastroenterol Hepatol 29: 697-705, 2014.
24. van Riet PA, Cahen DL, Poley JW and Bruno MJ: Mapping international practice patterns in EUS-guided tissue sampling: outcome of a global survey. Endosc Int Open 4: E360-E370, 2016.
25. Khan MA, Grimm IS, Ali B, Nollan R, Tombazzi C, Ismail MK and Baron TH: A meta-analysis of endoscopic ultrasound-fine-needle aspiration compared to endoscopic ultrasound-fine-needle biopsy: Diagnostic yield and the value of onsite cytopathological assessment. Endosc Int Open 5: E363-E375, 2017.
26. Hayashi T, Ishiwatari H, Yoshida M, Ono M, Sato T, Miyanishi K, Sato Y, Kobune M, Takimoto R, Mitsuhashi T, *et al*: Rapid on-site evaluation by endosonographer during endoscopic ultrasound-guided fine needle aspiration for pancreatic solid masses. J Gastroenterol Hepatol 28: 656-663, 2013.
27. Mohan BP, Madhu D, Reddy N, Chara BS, Khan SR, Garg G, Kassab LL, Muthusamy AK, Singh A, Chandan S, *et al*: Diagnostic accuracy of endoscopic ultrasound (EUS) guided fine needle biopsy (FNB) by macroscopic on-site evaluation (MOSE): A systematic review and meta-analysis. Gastrointest Endosc 96: 909-917.e11: 2022.
28. Nguyen YP, Maple JT, Zhang Q, Ylagan LR, Zhai J, Kohlmeier C, Jonnalagadda S, Early DS, Edmundowicz SA and Azar RR: Reliability of gross visual assessment of specimen adequacy during EUS-guided FNA of pancreatic masses. Gastrointest Endosc 69: 1264-1270, 2009.
29. Vilmann P, Săftoiu A, Hollerbach S, Skov BG, Linnemann D, Popescu CF, Wellmann A, Gorunescu F, Clementsen P, Freund U, *et al*: Multicenter randomized controlled trial comparing the performance of 22 gauge versus 25 gauge EUS-FNA needles in solid masses. Scand J Gastroenterol 48: 877-883, 2013.
30. Dougan SK: The pancreatic cancer microenvironment. Cancer J 23: 321-325, 2017.
31. Gkolfakis P, Crinò SF, Tziatzios G, Ramai D, Papaefthymiou A, Papanikolaou IS, Triantafyllou K, Arvanitakis M, Lisotti A, Fusaroli P, *et al*: Comparative diagnostic performance of end-cutting fine-needle biopsy needles for endoscopic ultrasound tissue sampling of solid pancreatic masses: A network meta-analysis. Gastrointestinal Endoscopy 95: 1067-1077.e15, 2022.