Endoscopic ultrasound: a primer for pathologists

Bronte A Holt

Shyam Varadarajulu

Abstract

Endoscopic ultrasound-guided fine needle aspiration is a multi-step procedure that involves appropriate clinical indication and selection of needles, adapting evidence-based sampling techniques, and establishing reliable cytopathology support. Integrating cytopathology in the training curriculum and developing a more flexible platform of needles and echoendoscopes are likely to further advance the field of endosonography. This review aims to summarize the technical issues that are key to performing high quality endoscopic ultrasound-guided fine needle aspiration.

Keywords cytology; endoscopic ultrasound; endoscopy training; fine needle aspiration; fine needle biopsy

Introduction

Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) is an indispensible tool for tissue acquisition from within and adjacent to the gastrointestinal tract. The impact of EUS-FNA on the practice of pancreatic pathology is significant,[1] such that the National Comprehensive Cancer Network has incorporated EUS-FNA cytology in its diagnostic algorithm for pancreatic cancer.[2] The role of EUS-FNA will continue to expand as the accuracy of EUS tissue acquisition improves. Fields where EUS-FNA has increasing importance include mediastinal staging of non small cell lung cancer, where the combination of EUS with endobronchial ultrasound (EBUS)—FNA will likely replace surgical mediastinal staging,[3,4] and EUS-guided liver biopsy in patients with abnormal liver function tests undergoing EUS.[5,6]

Obtaining a high quality, diagnostic specimen is integral to performing EUS-FNA. In room confirmation of diagnostic adequacy is a defining feature that establishes EUS-FNA as a fundamental part of integrated, multidisciplinary patient care. The benefits include procedural efficiency, whereby diagnostic adequacy, rather than a predetermined number guides the number of FNA passes performed. Procedural time and risk of complications are reduced if a diagnosis is rapidly confirmed. Non-diagnostic initial FNA passes trigger a change in the sampling location or needle type, and avoid repeated non-contributory passes. Onsite diagnosis limits the need for repeated EUS, with its associated morbidity and cost. In addition, the preliminary diagnosis enables collection of additional samples for ancillary testing such as flow cytometry. Quality care is enhanced by providing an immediate preliminary diagnosis to patients and their families, and allows timely referral for further testing and specialist consultation.

The outcomes of EUS-FNA are affected by factors such as needle selection, maneuvers to procure quality tissue and the presence of an onsite cytopathologist. This review aims to summarize the technical issues that are key to performing high quality EUS-FNA.

Effect of GI tract location on EUS-FNA

The degree of technical difficulty of EUS-FNA varies according to the location of the targeted lesion. Generally, transesophageal and transgastric FNAs are technically easier than transduodenal FNA as the position of the scope is relatively straight when accessing the majority of lesions via the esophagus or stomach. An exception is access from the gastric fundus, where near complete retroflexion of the echoendoscope may be required. The technical difficulty of passing the FNA needle through the scope's working channel, moving the needle back and forth through the targeted tissue, and maintaining scope stability is increased with acute angulation of the tip of the scope, significant torsion through the scope shaft, and maximal elevator use. This is predominantly an issue in the duodenum. A 25G needle is suitable for sampling the majority of lesions accessed from the second part of the duodenum, and a flexible 19G needle may be beneficial if histology is required.[7]

EUS-FNA needle selection

EUS-FNA can be performed using a 25G, 22G or a 19G needle. The choice of needle is guided by a number of considerations. The needle should provide an adequate tissue sample to establish a definitive diagnosis, have the degree of flexibility required for lesion access, a low risk of complications, and the ability to obtain core tissue when necessary.

Seven randomized trials and two meta-analyses[8–16] have evaluated different needles for EUS-FNA (Table 1). The 22G and 25G needles were compared in five randomized trials,[8–10,13,14] and established the needles had a similar overall diagnostic accuracy and a trend in favor of the 25G needle for transduodenal sampling. Two meta-analyses have compared the 25G and 22G needles for EUS-FNA of solid pancreatic masses, and found a higher diagnostic sensitivity[15] and accuracy[16] with the 25G needle.

The 19G and 22G needles were prospectively compared in a randomized trial in 117 patients with pancreatic and peripancreatic masses.[11] The 19G needle resulted in superior diagnostic accuracy and tissue acquisition, however there was a high rate of technical failure for lesions in the head of pancreas. Histological samples obtained with the standard 19G FNA needle were prospectively assessed in a single-arm study of 120 patients with pancreatic lesions.[17] The procedure was technically successful in 119 patients (98.9%) and adequate histological sample was obtained in 116 (97.5%). The results only apply to lesions of

Abbreviations: EUS, endoscopic ultrasound; FNA, fine needle aspiration; EBUS, endobronchial ultrasound; FNB, fine needle biopsy; ROSE, rapid on-site evaluation; CNB, core needle biopsy; ERCP, endoscopic retrograde cholangiopancreatography.

Bronte A Holt *MBBS MBBS BMEDSC FRACP PHD Department of Gastroenterology-Hepatology, St. Vincent's Hospital, Melbourne, Australia. Conflicts of interest: none declared.*

Shyam Varadarajulu *MD Center for Interventional Endoscopy, Florida Hospital, Orlando, FL, USA. Conflicts of interest: Shyam Varadarajulu is a consultant for Boston Scientific and Olympus.*

Comparison of different needles for EUS-FNA of solid mass lesions: Randomized trials and meta-analyses

Author/study type [ref]	Number patients	Lesion type	Needle size	Diagnostic accuracy/pooled sensitivity in meta-analysis	Remarks
Camellini et al./RT[8]	127	All lesions	22 vs. 25G	77.8 vs. 78.1%, P = NS	25G needle better for uncinate masses and 22G needle better for subepithelial masses.
Fabbri et al./RT[9]	50	Pancreatic masses	22 vs. 25G	86 vs. 94%, P = NS	Trend towards better yield with 25G needle
Siddiqui et al./RT[10]	131	All lesions	22 vs. 25G	87.5 vs. 95.5%, P = NS	NA
Song et al./RT[11]	117	Pancreatic/peri-pancreatic masses	22 vs. 19G	8.9 vs. 94.5%, P = 0.01	Technical success for FNA of pancreatic head masses was significantly less with the 19G needle. 19G needle yielded significantly better cellular material.
Ramesh et al./RT[12]	72	Pancreatic masses	22 vs. 19G	94.4 vs. 88.9%, P = 0.69	19G needle yielded significantly more core biopsies but specimens were bloodier.
Vilmann et al./RT[13]	135	Mixed lesions	22 vs. 25G	89 vs. 90%, P = NS	25G needle more difficult to visualize.
Lee et al./RT[14]	188	Pancreatic masses	22 vs. 25G	89.4 vs. 88.3%, P = NS	25G needle had lower complication rate
Madhoun et al./MA[15]	1292	Pancreatic masses	22 vs. 25G	85 (95% CI: 82–88%) vs. 93% (95% CI: 91–96%), P = 0.0003	NA
Affolter et al./MA[16]	1452	Pancreatic/peri-pancreatic masses	19 vs. 22 vs. 25G	P = 0.97	25G needle had higher diagnostic adequacy compared to 22G needle. Sample size for 19G needle too small for analysis.

RT = randomized trial; MA = meta-analysis; NA = not applicable; NS = not significant.

Table 1

the pancreatic body and tail, as patients with pancreatic head or uncinate masses were excluded. A recent multicenter randomized trial compared a flexible 19G needle made of nitinol (Flex 19; Boston Scientific, Natick, MA, USA) to a 25G needle for FNA of solid pancreatic masses.[12] Diagnostic accuracy and technical failure rates were similar between needles, however the 19G needle yielded histological core tissue in significantly more patients than the 25G needle (86.1 vs. 33.3%, $P < 0.001$).

The 19G Trucut biopsy needle (Cook Medical, Winston–Salem, NC, USA) was developed to attain core histologic tissue,[18] however is has limited ability to sample from the duodenum due to the needle's rigidity.[19] A 19G fine needle biopsy (FNB) device (ProCore; Cook Medical, Winston–Salem, NC, USA) with reverse bevel technology was subsequently developed. This needle successfully obtained histological samples in a majority of patients with a diagnostic accuracy of >90%[20] however, some technical challenges were encountered with transduodenal passes. 22G and 25G ProCore needles are also available, which facilitate transduodenal sampling. Three recent randomized trials comparing the 22G or 25G ProCore needles to standard FNA needles in pancreatic masses and peri-pancreatic lymphadenopathy[21–23] have concluded there is no significant difference in establishing a correct diagnosis between needles. In a study using the 25G ProCore needle, a cytological diagnosis was established in 96% of 50 patients and histological core tissue was procured in 32% of patients.[22] A study in 144 patients using the 22G ProCore needle vs. a standard 22G FNA needle showed similar diagnostic accuracy between needles, and fewer passes were required to obtain sufficient tissue with the ProCore needle (1.2 ± 0.5 passes with ProCore vs. 2.5 ± 0.9 passes with standard needle, $P < 0.001$).[23]

FNA technique

Fanning

FNA sampling from the center of a malignant mass is more likely to provide non-diagnostic tissue compared to the tumor periphery due to central degeneration.[24] In addition, repeated sampling along the same trajectory through a lesion is more likely to result in bloodier specimens. Two studies have explored whether aspirating a lesion at the peripheries or across multiple trajectories (the 'fanning' technique) improves the diagnostic yield.[25,26] In a randomized trial of 54 patients with solid pancreatic masses, the fanning technique resulted in a significantly higher first pass diagnosis compared with the standard FNA technique (85.7 vs. 57.7%, P = 0.02).[26] The fanning