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Original Article

The diagnostic yield of specimens obtained from endoscopic ultrasound guided fine needle biopsy of solid masses with the Acquire™ needle

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A B S T R A C T

Background: Recent developments in the design of needle tips used for fine needle biopsy via endoscopic ultrasound (EUS) allows for the procurement of core tissue for histological assessment in addition to cytology. Core tissue provides tissue architecture as well as the ability to perform molecular profiling investigations. We present a single centre study of experience with a new EUS needle with a Franseen tip (Acquire™; Boston Scientific, Natick, MA, USA). The aim of the study was to assess the diagnostic yield of biopsies from solid lesions throughout the gastrointestinal tract.

Methods: We performed a retrospective study of consecutive patients undergoing EUS biopsy between January 2017 and November 2018. Cystic lesions with no solid component were excluded or if samples were not sent for both cytology and histology. Rapid onsite evaluation (ROSE) was performed and the core tissue obtained was sent for histology.

Results: Forty-six patients underwent EUS biopsy of solid lesions with specimens sent for both cytology and histology. Lesions included solid pancreatic masses ($n = 31$), lymph node ($n = 3$), gastric subepithelial lesion ($n = 3$), other ($n = 9$). The mean number of passes per lesion was 1.9 (range 1–4). In 43/46 (93%) of cases, a core specimen was obtained. Tissue obtained by EUS biopsy was adequate for evaluation by ROSE in 39/46 cases (85%). Histological diagnosis was confirmed in 41/46 (89%) cases compared to 31/46 (67%) cases with cytology ($P = 0.011$). Subgroup analysis of pancreatic lesions showed histological diagnosis was superior to cytology (90% vs 61%, $P = 0.007$). There were no adverse events.

Conclusion: Histological analysis of specimens obtained via EUS biopsy was superior to cytology, particularly in assessment of solid pancreatic lesions.

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Keywords: Endoscopic ultrasound; Fine needle biopsy; Solid lesions

Introduction

Endoscopic ultrasound (EUS) has emerged as an important modality in the diagnosis and treatment of gastrointestinal diseases, especially in imaging of the pancreatobiliary system. The current method of obtaining biopsies through EUS is by fine needle aspiration (FNA). It is a minimally invasive and relatively safe procedure for obtaining tissue/cell samples inside gastrointestinal tract and surrounding organs such as the pancreas and local lymph nodes.^{1,2} This procedure is done by inserting a long needle through the accessory channel of an echoendoscope and is targeted into the organ of interest; cells are aspirated into a syringe with negative pressure attached to the opposite end of the needle.^{3,4}

Recent developments in needle types have allowed the procurement of tissue with preserved architecture, suitable for histological evaluation. A Franseen tip (Acquire™; Boston Scientific, Natick, MA, USA) end cutting needle with a crown shaped distal tip with three symmetrical bevelled cutting edges has recently become available. This design of the needle tip with multiple cutting surfaces provides more depth of insertion into the lesion to enable acquisition of more tissue specimens and maximize tissue capture.⁵ This also enhances stability and better control of the needle.⁶ Procurement of core tissue is preferred since it improves diagnostic accuracy and allows for more comprehensive molecular profiling investigations.^{7,8}

The aim of the study was to assess the diagnostic yield of and histologic examination of biopsies performed with the new needle

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from solid lesions throughout the gastrointestinal tract comparing cytologic and histologic analysis. The secondary aim was to assess the adequacy rate of specimens obtained for analysis.

Methods

We performed a retrospective single centre study of patients undergoing EUS-fine needle biopsy (FNB) with the needle between January 2017 and November 2018. Ethics approval was granted via the Sydney Local Health District Ethics Committee (Approval number: X18-0445 & LNR/18/RPAH/638). Biopsies were performed using the 22 gauge Acquire™ needle via linear echoendoscope. All EUS procedures were performed by experienced endosonographers with multiple years of experience at performing high-volume EUS.

All procedures were performed using a linear array echoendoscope (Olympus America Corp., Center Valley, PA, USA) with patients in the left lateral decubitus position after administration of propofol or with the patient under general anesthesia. The technique used for tissue acquisition was as follows: no stylet used for the FNA, only 10 mL suction. Ten to fifteen to-and-fro movements were performed through the mass lesion. The same technique was used exclusively in this study for the sake of uniformity.⁹ Number of passes was at the discretion of the endoscopist. The primary outcome of the study was to assess the diagnostic yield of biopsies sent for cytology and histology from solid lesions throughout the gastrointestinal tract. A secondary outcome was to assess the adequacy rate of adequacy of specimens.

Patients were included if they were > 18 years of age and had a solid lesion identified that warranted biopsy. Patients were excluded if they were < 18 years of age, pregnant, or were undergoing EUS-guided biopsy of a cystic lesion. Diagnostic yield was defined as the percentage of patients biopsied in which a definitive diagnosis was made. Adequacy rate was defined as the percentage

of patients biopsied in which the specimen was suitable for analysis but not necessarily able to make a definitive diagnosis.

Specimen processing

The specimen was expelled onto a slide using the stylet. If core tissue was apparent, it was expelled into a jar of formalin (Fig. 1). Any fluid material and core specimens were also expelled into Hank's solution (ScienCell, Carlsbad, CA, USA).

Routine air-dried Diff-Quik stained smears were prepared at the time of aspiration for rapid onsite evaluation (ROSE) by experienced cytotechnologists. Wet-fixed (95% ethanol) smears were also prepared for later Papanicolaou staining and cytologic diagnosis. Aspirate material was placed in Hank's solution for cell block preparation, which involved centrifugation of specimens at 2,000 Hz for 5 minutes followed by resuspension in human plasma and diluted thromboplastin/fibrinogen in a 1:3 mL ratio with distilled water. Cell blocks were then fixed in 3–5 mL of 10% neutral buffered formalin and placed in tissue cassettes for paraffin processing, microtomy and haematoxylin and eosin (H&E) staining. Standard 10% formalin fixation, paraffin embedding and H&E staining were used in processing the specimens for histologic examination. Immunohistochemistry studies were undertaken for evaluation of morphologically challenging lesions when required.

Statistical analysis

Continuous variables were expressed in median (interquartile range) as appropriate. Differences between subgroups were analysed using chi square test for categorical parameters. Statistical analysis was performed by Statistical Package for Social Science (SPSS ver. 22.0; IBM Corp., Armonk, NY, USA). A result was considered statistically significant if $P < 0.05$.

Fig. 1. Examples of tissue obtained from pancreas sampling obtained with Acquire™ needle. (A, B) Macroscopic image of sample acquired from core biopsy. (C–E) Cytology sample (Papanicolaou stain). Core sample showing pancreatic adenocarcinoma. Tumour thrombus evident in the venule (H&E stain).

Results

Over the study period, forty-six patients (52% male) underwent EUS biopsy of solid lesions. The patient characteristics are

Table 1 Patient Demographics ($n = 46$)

Variable	Value
Sex	
Male	24 (52)
Female	22 (48)
Median age, IQR (yr)	67.5 (57–73.5)
Mean number of passes, range	1.9 (1–4)
Indication for biopsy	
Pancreatic mass ($n = 31$)	
Head/uncinate process	27 (87)
Body/tail	4 (13)
Gastric mass	3
Lymph node	3
Other (duodenal lesion, mediastinal lesion, bile duct mass, retroperitoneal lesion)	9

Values are presented as number (%) or number only unless otherwise indicated.

IQR, interquartile range.

Fig. 2. Adequacy of specimen taken for assessment.

outlined in Table 1. The median age was 67.5 years. Lesions biopsied included solid pancreatic masses ($n = 31$) of which 27 (87%) were from the head or uncinate of pancreas, lymphadenopathy ($n = 3$), gastric subepithelial lesions ($n = 3$), other (including duodenal, mediastinal, and retroperitoneal lesions) ($n = 9$). The mean number of passes per lesion was 1.9 (range 1–4). In 43/46 (93%) of cases, a core specimen was obtained. Tissue obtained by EUS biopsy was adequate for evaluation by ROSE in 39/46 cases (85%) (Fig. 2, Table 2).

The primary outcome of tissue diagnosis could be achieved in 41/46 (89%) cases from the histology specimen alone compared to 31/46 (67%) cases with cytology ($P = 0.011$) (Fig. 3). Subgroup analysis of pancreatic lesions showed histological diagnosis was superior to cytology (90% vs 61%, $P = 0.007$) (Fig. 3, Table 3). In 7 cases, adenocarcinoma was missed on cytology but present in the histology sample.

In the 5 cases where histology did not yield a diagnosis, 3 of the 5 cytology was also non-diagnostic. In one case the diagnosis confirmed on cytology was sarcoidosis and the other pancreatic cancer in which the core sample displayed necrosis with some atypical cells. In the 3 cases that were found to not have a diagnosis one patient underwent a distal pancreatectomy for a subsequently diagnosed neuroendocrine tumour, and two patients were lost to follow-up with no subsequent procedures for a pancreatic and gastric subepithelial lesion. There were no adverse events noted throughout the study period.

Table 2 Primary Outcome Group (Both Cytology and Histology Sent) ($n = 46$)

Variable	Cytology	Histology	P-value
Diagnostic yield	31 (67)	41 (89)	0.011
Adequate sample	39 (85)	43 (93)	0.18

Values are presented as number (%).

Table 3 Subgroup Analysis

Variable	Cytology	Histology	P-value
Pancreatic lesions ($n = 31$)	19 (61)	28 (90)	0.007
Non-pancreatic lesions ($n = 15$)	12 (80)	13 (87)	0.624

Values are presented as number (%).

Fig. 3. (A) Diagnostic yield in all lesions ($n = 46$) (percentage of the samples in which a histological diagnosis was obtained). (B) Diagnostic yield of pancreatic lesions ($n = 31$) (percentage of the samples in which a histological diagnosis was obtained).

Discussion

In the era of personalised treatments for malignancy, characterisation of tumour biology has become critical in determining tailor made treatments to improve outcomes, particularly when the prognosis from many upper gastrointestinal malignancies is poor.^{10,11} Procuring adequate core tissue samples for histology provides the ability to perform molecular investigations to further characterise tissue biology and aid in personalising treatment for patients. In obtaining accurate diagnosis, there is a preference by pathologists for histology rather than cytology specimens as the volume of neoplastic cells in aspirates alone is often insufficient for tumour marker analysis.^{1,2} ROSE has been previously thought to be a possible solution to increasing diagnostic yield from EUS specimens. ROSE, as opposed to histological analysis, requires the availability of an onsite cytopathologist, is not widely available and is often inaccessible after regular working hours. In addition, Wani et al¹² in a randomised controlled trial in biopsy of pancreatic masses did not demonstrate a significant difference of ROSE in diagnostic yield of malignancy, proportion of adequate specimens or accuracy.

This study demonstrates that the Acquire™ needle was able to obtain samples suitable for core tissue analysis with the diagnostic yield close to 90%. Limited number of previous studies have shown the feasibility and safety of the Acquire™ needle with performance advantages over other available needles such as EchoTip ProCore (Wilson-Cook Medical Inc., Winston Salem, NC, USA) and SharkCore (Beacon Endoscopic, Newton, MA, USA).^{13–15} Adler et al¹⁶ demonstrated a similar rate of histologic diagnosis with a mean number of passes of 3 compared to 2 in our study. In a study by Bang et al,⁶ the technical success rate of using the Acquire™ needle for EUS-FNB was 96.7% but an adverse event rate of 3.3%. Another study by Adler et al¹⁷ showed that tissue samples obtained through the Acquire™ needle was sufficient for histological diagnosis in 96% of cases and tissue cores were obtained in 71% of cases. The study by Al-Haddad et al⁵ revealed the diagnostic yield of the Acquire™ needle for ROSE was 94% and the diagnostic yield for histological assessment was 100%. This suggests our results are comparable to other studies and that tissue acquisition with the Acquire™ needle presents a promising solution to the issue of optimal handling of specimens obtained via EUS-FNB.

Histologic assessment was found to be significantly superior to cytological analysis, particularly when assessing pancreatic lesions. This finding adds to the body of evidence suggesting that the technique is not only safe but has a high rate of technical success in obtaining a suitable specimen and clinical success establishing a tissue diagnosis. Importantly, the alternative method of specimen processing (depositing in formalin) is a practical advantage for centers where ROSE is not available. Furthermore, single modality processing with formalin alone may have a cost benefit compared to ROSE where the presence of a technician is required.

The cytology diagnostic rate is lower than rates published in other studies and this may reflect that the Acquire™ needle is designed primarily for core tissue sampling. The finding of 7 malignancies that were missed on cytology suggests the value and importance of the ability of histology as a method of assessment for this indication. This provides evidence that the lack of availability of ROSE does not necessarily impair diagnostic accuracy.^{18–20}

The limitations of the study mainly relate to those inherent to retrospective studies in general. We are unable to assess the sensitivity and specificity as well as predictive values of the technique as not all patients with either positive or negative result under-

went resection. Finally, the study was performed at an academic centre with experienced endosonographers with a high throughput of gastrointestinal pathology, with expert gastrointestinal pathologists, experienced in cytology and histopathology, and this also may affect the generalisability of these results to non-tertiary centres or those without access to ROSE.

In summary, histologic analysis of specimens obtained with an Acquire™ needle is superior to cytologic analysis. Centers where ROSE is not available may deposit their specimens directly into formalin with an expected high diagnostic yield rate. This finding whilst promising, requires validation in a larger sample size and for the growing list of indications of EUS-FNB in the gastrointestinal tract.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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