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BRIEF REPORT

A retrospective analysis comparing the use of ProCore® with standard fine needle aspiration in endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)

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Abstract

Endobronchial ultrasound has become first line in the investigation of mediastinal lesions suspicious for malignancy in keeping with National Institute for Health and Care Excellence (NICE) guidelines; however, needle size and type required to maximise diagnostic sensitivity remains unclear. Previous meta-analyses have compared the use of ProCore with standard fine needle aspiration in the assessment of pancreatic masses with differences noted only in the number of passes required. We aim to assess whether a ProCore needle improves diagnostic sensitivity in EBUS-TBNA. Complete follow-up data regarding all 235 patients undergoing EBUS-TBNA in a district general hospital has been collected since the service's inception in 2012. Results were collated and retrospectively analysed allowing for calculation of test sensitivity and specificity. Comparison was then made between procedures where standard fine needle aspiration was performed and those using a ProCore needle. Overall sensitivity of EBUS-TBNA was shown to be 85% with a specificity of 100% in keeping with quoted figures from other centres. Standard fine needle aspiration produced a sensitivity of 77% (85/110) versus ProCore sensitivity of 92% (115/125) with a p value of 0.0016. Thirty percent (33/110) of patients undergoing standard fine needle aspiration required an appropriate crossover technique such as mediastinoscopy or CT-guided FNA in order to either obtain or confirm the diagnosis compared with 15% (19/125) of the ProCore group with a p value of 0.0064. Our retrospective analysis shows a statistically significant difference in the diagnostic sensitivity of sampling mediastinal lymphadenopathy using a ProCore needle compared with standard fine needle aspiration. It also shows that a significantly fewer number of patients required further procedures in order to obtain or confirm the diagnosis. This could potentially be confounded by the retrospective nature of the study design; however, due to the statistical significance demonstrated, further study is required.

Keywords EBUS · Endobronchial ultrasound · ProCore

Background

Endobronchial ultrasound (EBUS) has become first line investigation in the assessment of mediastinal lesions suspicious for malignancy and in the diagnosis and staging of lung cancer in keeping with National Institute for Health and Care Excellence (NICE) guidelines. [1] This is because of high sensitivity and diagnostic accuracy comparable with mediastinoscopy as well as reduced cost from a less invasive procedure. [2, 3] Specimen adequacy is paramount in ensuring an accurate diagnosis but also due to the increasing requirement for immunohistochemical analysis in non-small cell lung cancer (NSCLC). Needle size and type, along with number of passes required to maximise this diagnostic sensitivity and specimen adequacy remains unclear.

Several methods have attempted to improve diagnostic yield, such as the development of a larger 19-gauge needle. The ProCore® needle, however, is the same 22-gauge as standard needles used in routine practice and has been designed to provide a core of histological tissue in contrast to the cytological specimens from standard fine needle aspirations. [4] It differs from conventional needles as it includes a reverse bevel—a unique feature which aims to increase the collection of a core histological sample by shearing material from the lesion

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during retrograde motion. Currently, it is used primarily to obtain intra-abdominal or pancreatic tissue specimens via endoscopic ultrasound (EUS), and the largest meta-analysis comparing the use of ProCore® with standard fine needle aspiration in this setting included 576 patients [5]. Differences were noted only in the number of passes required but not in diagnostic sensitivity. These results were replicated in small pilot study of 65 patients designed to assess the value of ProCore® with EBUS in mediastinal lymph node sampling [6]; however, further study is clearly required.

Method

We aimed to assess whether a ProCore® needle improved diagnostic sensitivity in EBUS-TBNA (transbronchial needle aspiration) by retrospectively analysing results from all patients undergoing the procedure in a Northern Ireland district general hospital since the inception of an EBUS service in 2012.

The service was initially commenced in October 2012, before the ProCore® [Cook Echo-HD-22-C] was commercially available, using only a standard 22-guage needle [Cook Echo-HD-22-O]. Following the introduction of ProCore® (also 22-guage) 20 months later, patients were allocated to either group-based solely on needle availability. Node size, location, and pre-test diagnosis were not determining factors in needle selection. With increasing use of ProCore®, local pathology services deemed these specimens superior, and this became established as the preferred technique and needle type. Prospective audit data collected as part of a trust approved audit of the EBUS service allowed calculation of sensitivity and specificity supported ongoing use of ProCore®. No funding support or sponsorship was received in relation to this study.

All procedures were completed by one of the two consultant respiratory physicians trained in the procedure. Nodal stations were sampled with three passes of the respective needle. Pathology services are not available on site, and all specimens were forwarded to the trust's regional pathology laboratory.

Samples were aspirated directly into ThinPrep® CytoLyt® solution for transport to the laboratory. Following centrifugation, ThinPrep® slides were created and fixed in ethanol prior to staining using the Papanicolaou method. All remaining deposit was used to make a CytoBlock™ preparation for histological analysis using the plasma-thrombin clotting method. Ancillary testing such as immunohistochemistry was performed on the remaining block where necessary.

Complete follow up data regarding all 235 patients undergoing EBUS-TBNA in two distinct groups (110 versus 125) allowed results to be collated and retrospectively analysed and calculated of test sensitivity and specificity. Sensitivity was calculated per patient. Any suspected lung cancer cases were discussed at the lung cancer multidisciplinary meeting with any non-cancer cases discussed at a medical radiology multidisciplinary meeting. In those patients who did not have confirmatory testing, medical follow-up was for a minimum of 12 months. Comparison was then made between procedures where standard fine needle aspiration was performed and those using a ProCore® needle. p values were subsequently calculated using a Chi-squared test.

Results

A total of 235 patients underwent EBUS-TBNA over a 44-month period. One hundred ten of those were conducted using standard fine needle and 125 using ProCore®. There was no significant difference in the number of nodal sites sampled, as standard fine needle averaged 1.2 sites versus 1.4 for ProCore® giving a p value of 0.5. Samples were also obtained from a range of nodal stations; however, station 7 was sampled somewhat more frequently in the ProCore® group (see Table 1). Each node was sampled using three passes.

Overall sensitivity of EBUS-TBNA was shown to be 85% with a specificity of 100% in keeping with quoted figures from other centres. [2] Standard fine needle aspiration produced a sensitivity of 77% (85/110) versus ProCore® sensitivity of 92% (115/125) with a p value of 0.0016. This finding was consistent for each aetiological subgroup (see Table 2).

Thirty percent (33/110) of patients undergoing standard fine needle aspiration required an appropriate crossover technique such as mediastinoscopy or CT-guided FNA in order to either obtain or confirm the diagnosis compared with 15% (19/125) of the ProCore® group with a p value of 0.0064.

Table 1 Lymph node station sampling (expressed as percentage of patients in whom station was sampled)

	Standard FNA ($n = 110$)	ProCore® ($n = 125$)
2R	1.8% (2)	0% (0)
2L	0.9% (1)	0% (0)
4R	12.7% (14)	6.4% (8)
4L	2.7% (3)	0.8% (1)
7	45.5% (50)	62.4% (78)
10R	13.6% (15)	28.8% (36)
10 L	7.3% (8)	6.4% (8)
11R	25.5% (28)	20.8% (26)
11L	10% (11)	15.2% (19)
Average number of nodes sampled	1.218	1.408

Table 2 Sensitivity of standard FNA versus ProCore® by aetiology

Condition	Sensitivity		
	Standard FNA	ProCore®	Combined
Carcinoma	78.6% (44/56)	92% (69/75)	86.3% (113/131)
Sarcoidosis	59.1% (13/22)	86.2% (25/29)	74.5% (38/51)
Lymphoma	50% (2/4)	100% (2/2)	66.7% (4/6)
Other (TB, Reactive etc.)	92.9% (26/28)	100% (19/19)	95.7% (45/47)
Total	74.5% (82/110)	92% (115/125)	83.8% (197/235)

Discussion

Our retrospective analysis shows a statistically significant difference in the diagnostic sensitivity of sampling mediastinal lymphadenopathy using a ProCore® needle compared with standard fine needle aspiration. It also shows that a significantly fewer number of patients required further procedures in order to obtain or confirm the diagnosis.

Given the retrospective nature of the data, however, a number of potential confounding factors need to be considered.

One important area to consider is the possibility of chronological or performance bias given that ProCore® was only introduced after the service had become established. This does not appear to be the case however as the sensitivity from cases of standard fine needle aspiration did not increase over time, and in fact decreased following the introduction of ProCore® from 83% (72/87) to 57% (13/23). Subsequent direct comparison between all cases in both groups performed after the introduction of ProCore® also remains statistically significant in favour of ProCore® with a p value of less than 0.00001, excluding an apparent learning curve effect.

It is unclear whether our standard practice of only conducting three passes in sampling each nodal site could act as a potential confounding aspect. Current Chest Guidelines suggest that three passes per node is sufficient [6]. This is based largely on data published by Lee et al. which found that optimum sensitivity occurred at this point [7]. As previously mentioned, former studies demonstrated a reduction in the number of passes required with ProCore® [5]; however, the optimum number remains uncertain. Xing et al. quoted 2.3 passes required for ProCore® versus 4 for standard fine needle [8]; however, Witt et al. quoted 2.11 versus 2.94 [9]. It is therefore possible in our study, that a low number of passes could have unfairly favoured ProCore®; however, standardisation of procedure technique allows a valid comparison of needle types, and three passes per nodal station is in keeping with current guidelines [6].

Previous studies have also noted the ability to obtain histological samples using standard EBUS needles; however, the quoted sensitivity is lower than noted in our study [10], and a larger gauge of needle appears to be required [11].

Xing et al. is the only other published study directly comparing ProCore® with standard FNA in a cohort of patients undergoing EBUS. They also quoted a number of limitations to their study design, including the retrospective nature of the analysis, operator unfamiliarity with ProCore®, and a small study size as only 65 patients were included [8]. Our cohort is therefore the largest of its kind; and despite the retrospective nature of the study design allowing for a number of potential confounding factors as discussed above, the statistical significance demonstrated in contrast to previous studies raises the possibility of an increased sensitivity and diagnostic yield when using ProCore® compared with standard fine needle. This suggests that further study is required in the form of a prospective randomised control trial.

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