The utility and safety of linear endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in the paediatric population

To the Editor:

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in adults is an essential tool for investigating mediastinal and hilar lymphadenopathy. It is now integral to the diagnostic and staging algorithm for lung cancer [1], as well as the diagnosis of other malignancies, lymphoma and non-malignant granulomatous conditions, such as sarcoidosis and tuberculosis. The comparable diagnostic yield, along with decreased complications, has reduced the requirement for previously standard surgical biopsy sampling [2, 3].

There remains a paucity of data on convex probe (linear) EBUS in paediatric populations [4, 5] and no large European case series. The pathology in paediatric patients is distinct from adults due to the absence of lung cancer and logistical challenges, such as patient tolerance and scope diameter. We hypothesised that EBUS can be performed safely in the paediatric population and provide diagnostic material, obviating the need for more invasive procedures in most cases. The purpose of our study was to review the utility, safety and outcomes of paediatric EBUS in our centres.

A retrospective review of prospectively maintained bronchosopy and cytology databases was performed at two UK centres, Manchester Royal Infirmary and Guys and St Thomas's Trust, between May 2008 and November 2018. Cases aged ⩽18 years at time of procedure were included.

Procedures were performed by operators with experience of ⩾200 EBUS procedures in adults. EBUS-TBNA was performed using a standard EBUS bronchoscope (BF-UC180F-OL8, Olympus, Tokyo, Japan or EB-530US, Fujifilm, Japan). Lymph nodes were sampled using 22-guage needles employing a two-person technique, with a dedicated bronchoscopist but separate needle handler and labelled using the International Association for the Study of Lung Cancer lymph node map. Rapid on-site evaluation (ROSE) was used for all procedures, with consultant cytopathologist feedback on adequacy of lymph node sampling and preliminary diagnosis including presence of granuloma. All material was sent for microbiological analysis, including acid-fast bacilli (AFB).

Medical and anaesthetic records were reviewed for patient's demographics, ethnicity, indication for the procedure, final diagnosis, sedation, ventilation and any additional procedures or complications. Procedure, cytology and microbiology reports were reviewed to determine nodes sampled, nodal size, number of passes, immediate complications, as well as sample adequacy, cytology diagnosis, AFB stains and tuberculosis (TB) culture. Cases were considered to have a final diagnosis of TB if either culture positive or "clinically confirmed TB" if culture negative with granuloma on cytology and clinical response to TB treatment. Major complications were defined as death, bleeding requiring transfusion, advanced intervention or vasopressors, need for reversal agents, pneumothorax, mediastinitis or need for level 2–3 care.

All cases undergoing the procedure under general anaesthesia utilised a laryngeal mask airway size 4 or 5 performed with paediatric anaesthetists in paediatric theatres. Conscious sedation cases used a combination of opioid and benzodiazepines.

Cite this article as: Al-Najjar H, Breen R, Santis G, *et al*. The utility and safety of linear endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in the paediatric population. *Eur Respir J* 2020; 55: 1902277 [https://doi.org/10.1183/13993003.02277-2019].

40 patients aged ⩽18 years undergoing EBUS-TBNA for mediastinal or hilar abnormalities were identified. Basic demographics of the patients are displayed in table 1. The indication in 85% (n=34) of procedures was isolated mediastinal or hilar adenopathy with a strong suspicion of new or recurrent tuberculosis, with the remaining 15% (n=6) for suspected lymphoma. The procedure was performed under general anaesthesia in 30% (n=12), all in Royal Manchester Children's Hospital, with the remainder under conscious sedation. There were no deaths or major complications (as defined by British Thoracic Society bronchoscopy guidelines criteria [6]) related to the procedures.

In total 70 nodal stations were sampled. Table 1 includes lymph node stations sampled. The final diagnosis breakdown in the 40 patients was TB (either cultured or clinically confirmed) in 67.5% (n=27), reactive lymphadenopathy in 17.5% (n=7), exclusion of TB recurrence in 7.5% (n=3), haematological malignancy in 5% (n=2) and neurofibroma with granulomatous reaction in 2.5% (n=1). Of those initially suspected of having TB, the final diagnosis was TB in 76.5% (n=26); however, of those with suspected lymphoma the final diagnosis was lymphoma in 33% (n=2), TB in 17% (n=1) and reactive lymphadenopathy in 50% (n=3)

The cytology displayed granuloma in 15% (n=6), necrotic granuloma in 52.5% (n=21) and no granuloma in 32.5% (n=13). Overall, 63% (n=17) of TB cases were culture positive (all fully sensitive), with the

TABLE 1 Demographics and baseline characteristics (total n=40)

Gender	
Male	20 (50.0%)
Female	20 (50.0%)
Age years	17 (15–18) (12–18)
Age	
12 years	3 (7.5%)
13 years	2 (5.0%)
14 years	3 (7.5%)
15 years	6 (15.0%)
16 years	5 (12.5%)
17 years	10 (25.0%)
18 years	11 (27.5%)
Ethnicity	
Asian	15 (37.5%)
Caucasian	8 (20.0%)
Black African	12 (30.0%)
Black Caribbean	4 (10.0%)
Arab	1 (2.5%)
Initial indication	
TB suspected	32 (80.0%)
TB recurrence suspected	2 (5.0%)
Lymphoma suspected	6 (15.0%)
Number of nodes	
1	16 (40.0%)
2	19 (47.5%)
3	4 (10.0%)
4	1 (2.5%)
Nodes[#]	
10L	1/70 (1.4%)
10R	6/70 (8.6%)
11L	5 (7.1%)
11R	3 (4.3%)
12R	1 (1.4%)
2R	2 (2.9%)
4L	2 (2.9%)
4R	25 (35.7%)
7	25 (35.7%)
Node size[¶]	1.38 (1.00–2.08) (0.55–3.50)

Data are presented as n (%) or median (interquartile range) (range). Categorical variables were assessed using Chi-square test and continuous variables using t-test or Mann–Witney U-test (depending on their distribution) with p-values. [#]: total of all nodes; there is more than one node/patient, hence n=70; [¶]: all 70 nodes.

remaining cases negative. Culture-positive TB cases were more likely to display necrosis with granuloma on cytology than granuloma alone (82% *versus* 67%) and the nodes also tended to be larger in size (2.05 *versus* 1.72 cm; p=0.23) but neither reached statistical significance. Cytology had a sensitivity of 96% (95% CI 81–100%) for TB in our cases and a negative predictive value of 88% (95% CI 47–100%). Culture compared with cytology had a positive predictive value of 63% (CI 42–81%). 37% of culture-negative cases were identified on the basis of cytology alone and treated successfully. None of our cases required further surgical mediastinal sampling to ascertain the diagnosis.

Ours is the first exclusively European multicentre series reporting on linear EBUS safety and efficacy in the paediatric population. We encountered no major complications with an adequacy rate of 100% (assisted by ROSE). Our diagnostic yield is similar to previously reported studies in adult populations for both TB and lymphoma [7, 8]. Final diagnosis was changed from initial clinical suspicion by sampling in 23.5% of those suspected of having TB and 67% of those with suspected lymphoma. Whilst all our cases cultured fully sensitive TB, our latest national figures showed 1.2% multidrug resistant TB and 11.4% with resistance to any first-line drug [9].

We identified two large (n>20) multicentre studies in the literature. Gilbert *et al.* [10] reported a multicentre North American study on 21 paediatric patients undergoing EBUS-TBNA showing 95% adequacy with 48% of cases providing diagnostic material and obviating the need for invasive surgical biopsy in 62%. Like our study, they reported no major complications. In India, Dhooria *et al.* [11] included 55 paediatric EBUS-TBNA patients, most with suspected TB. They reported 92% adequacy with diagnostic material in 57%, no major complications and 78% positive culture rate.

We believe the results are encouraging and may herald the wider use of EBUS-TBNA at tertiary centres in the paediatric population, hence avoiding invasive surgical procedures such as mediastinoscopy with their inherent risks. Both our centres are high-volume tertiary referral centres for EBUS. A limitation to the availability of paediatric EBUS is the smaller numbers of patients involved, which may make it difficult for paediatric pulmonologists to retain skills required to practice. Procedures at our institutes were performed by experienced adult pulmonologists liaising with paediatric colleagues.

Another issue for younger children requiring general anaesthetic is scope and airway size. EBUS scopes have an external diameter of 6.7 to 6.9 mm, larger than paediatric bronchoscopes (2 to 4 mm) and the tracheal diameter of younger children [12]. Adequate ventilation around the scope is needed as well as the ability to manoeuvre the EBUS scope.

Being retrospective, all shortcomings and limitations associated with retrospective studies are particular to ours, although both centres collected data prospectively. Also, both centres are tertiary paediatric centres with cytopathologists performing ROSE and high-volume EBUS through-put, making it difficult to extrapolate safety and efficacy figures widely. Future pathways may task certain centres with providing this day case, less invasive alternative to mediastinoscopy or thoracotomy, thus providing cost benefit as well as a safer risk profile [13].

In conclusion, our multicentre study shows EBUS-TBNA is safe and technically feasible in older children, when utilising an experienced paediatric/adult pulmonology and anaesthetic team. Furthermore, in the presence of ROSE performed by a cytopathologist, the adequacy rates and diagnostic yield are comparable to invasive surgical procedures with less risk.

Haider Al-Najjar[1], Ronan Breen[2], George Santis[2] and Omendra Narayan[3]
[1]Respiratory Dept, Manchester University NHS Foundation Trust, Manchester, UK. [2]Thoracic Medicine Dept, Guy's and St Thomas' NHS Foundation Trust, London, UK. [3]Paediatric Respiratory Dept, Royal Manchester Children's Hospital, Manchester, UK.

Correspondence: Haider Al-Najjar, Respiratory Dept, Manchester University NHS Foundation Trust, Oxford Road, Manchester M13 9WL, UK. E-mail: Haider.al-najjar@mft.nhs.uk

Received: 25 Nov 2019 | Accepted after revision: 7 Jan 2020

Conflict of interest: None declared.

References

1 NICE. *Lung Cancer Guidelines*. 2019. http://guidance.nice.org.uk/ng122. Date last accessed: 14 October, 2019.
2 Navani N, Lawrence DR, Kolvekar S, *et al.* Endobronchial ultrasound-guided transbronchial needle aspiration prevents mediastinoscopies in the diagnosis of isolated mediastinal lymphadenopathy: a prospective trial. *Am J Respir Crit Care Med* 2012; 186: 255–260.
3 Annema JT, van Meerbeeck JP, Rintoul RC, *et al.* Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial. *JAMA* 2010; 304: 2245–2252.
4 Steinfort DP, Wurzel D, Irving LB, *et al.* Endobronchial ultrasound in pediatric pulmonology. *Pediatr Pulmonol* 2009; 44: 303–308.

5 Goussard P, Gie R, Kling S, *et al.* The diagnostic value and safety of transbronchial needle aspiration biopsy in children with mediastinal lymphadenopathy. *Pediatr Pulmonol* 2010; 45: 1173–1179.
6 Du Rand IA, Blaikley J, Booton R, *et al.* British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. *Thorax* 2013; 68: i1–i44.
7 Moonim MT, Breen R, Fields PA, *et al.* Diagnosis and subtyping of de novo and relapsed mediastinal lymphomas by endobronchial ultrasound needle aspiration. *Am J Respir Crit Care Med* 2013; 188: 1216–1223.
8 Navani N, Molyneaux PL, Breen RA, *et al.* Utility of endobronchial ultrasound-guided transbronchial needle aspiration in patients with tuberculous intrathoracic lymphadenopathy: a multicentre study. *Thorax* 2011; 66: 889–893.
9 Public Health England. Tuberculosis in England Report. 2019. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/821334/Tuberculosis_in_England-annual_report_2019.pdf. Date last accessed: 19 December, 2019.
10 Gilbert CR, Chen A, Akulian JA, *et al.* The use of convex probe endobronchial ultrasound-guided transbronchial needle aspiration in a pediatric population: a multicenter study. *Pediatr Pulmonol* 2014; 49: 807–815.
11 Dhooria S, Madan K, Pattabhiraman V, *et al.* A multicenter study on the utility and safety of EBUS-TBNA and EUS-B-FNA in children. *Pediatr Pulmonol* 2016; 51: 1031–1039.
12 Masters IB, Ware RS, Zimmerman PV, *et al.* Airway sizes and proportions in children quantified by a video-bronchoscopic technique. *BMC Pulmon Med* 2006; 6: 5.
13 Sharples LD, Jackson C, Wheaton E, *et al.* Clinical effectiveness and cost-effectiveness of endobronchial and endoscopic ultrasound relative to surgical staging in potentially resectable lung cancer: results from the ASTER randomised control trial. *Health Technol Assess* 2012; 16: 1–75.