SHORT COMMUNICATION

Technical tips, diagnostic yield and safety of endobronchial ultrasound-guided transbronchial mediastinal cryobiopsy

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SUMMARY

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is commonly used to diagnose and stage lung cancer. In clinical practice, cytology specimens from EBUS-TBNA may be low in cellularity, especially with necrotic lesions. Endobronchial ultrasound-guided transbronchial mediastinal cryobiopsy (EBUS-TBMC) has recently become the preferred method for obtaining histology biopsy. This retrospective cohort study analysed the first 30 patients who have undergone EBUS-TBMC in a tertiary centre in Malaysia. EBUS-TBMC demonstrated a high diagnostic yield and good safety profile. All the samples obtained were adequate for the detection of driver alteration by next-generation sequencing.

INTRODUCTION

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is an established technique for diagnosing and staging of lung cancer.[1,2] In clinical practice, cytology specimens from EBUS-TBNA may be low in cellularity,[3] especially with necrotic lesions. This hinders further ancillary diagnostic techniques such as immunohistochemistry, flow cytometry, molecular analysis and detection of driver alteration by next-generation sequencing (NGS) in non-small-cell lung carcinoma (NSCLC). Endobronchial ultrasound-guided transbronchial mediastinal cryobiopsy (EBUS-TBMC) is a new technique that has recently gained popularity for obtaining histology specimens. The EBUS-TBMC procedure involves a flexible cryoprobe that is precisely inserted into the same needle track (NT) created from EBUS-TBNA. A cryobiopsy can be extracted from the lesion through rapid freezing of the cryoprobe. After withdrawing the probe en-bloc with the EBUS-bronchoscope, the cryoprobe tip is submerged in saline to thaw and release the specimen.[4]

MATERIALS AND METHODS

We conducted a retrospective cohort analysis on patients who have undergone EBUS-TBMC following EBUS-TBNA at a single tertiary centre between July to December 2022. The data required for this study was traced using the hospital's electronic medical records. The EBUS-TBNA and EBUS-TBMC were performed by a European Respiratory Society-accredited EBUS-bronchoscopist. The procedure was conducted under conscious sedation or general anaesthesia, following established guidelines.[5] During EBUS-TBNA, four passes were performed for each lesion. Samples were processed in cytology smears and cell blocks. For EBUS-TBMC, a 1.1-mm flexible cryoprobe (Erbecryo 20402-401, Tubingen, Germany) was used. The frozen biopsy tissues were fixed in formalin. The choice of needle size (19, 21 or 22-gauge) and the number of cryo-activations per biopsy was determined by the operator's discretion. A positive diagnostic yield is considered when a definitive histology diagnosis is obtained from the cryobiopsy specimen.

RESULTS

Data from 30 patients were analysed. Twenty-eight patients underwent EBUS-TBNA followed by EBUS-TBMC, while two patients had EBUS-TBMC only. EBUS-TBMC was performed on 36 lesions. Insertion of the cryoprobe was unsuccessful for two lesions. EBUS-TBMC was performed on a single lesion in 83.4% (25 patients) of cases. 80% of the procedures were conducted under conscious sedation. On average, three EBUS-TBMC were conducted per patient (interquartile range [IQR]: 3-4), with a cryo-activation time of 6 seconds (IQR: 6-8). 83.3% (30 biopsies) targeted lymph nodes, while the remaining 16.7% (six biopsies) targeted masses.

The median cumulative tissue size retrieved from EBUS-TBMC was 6 mm (IQR: 5-8). 86.1% (31 lesions) had a positive histology yield, contributing to an overall diagnostic yield of 83.3% (25 cases). The patients' baseline characteristics and a comparison between the diagnostic yields of EBUS-TBNA and EBUS-TBMC are shown in Table I, respectively. In terms of safety, mild bleeding after EBUS-TBMC occurred in six cases (16.7%). No incidences of pneumothorax, pneumomediastinum, mediastinitis or other complications were observed.

DISCUSSION

To perform EBUS-TBMC, the main challenge is the insertion of the cryoprobe into the target lesion. As the tip of the probe is blunt, creating a good NT during EBUS-TBNA is important. It is crucial to avoid the bronchial cartilages, and the needle agitations should follow a consistent trajectory with every needle pass. The hyperechoic sonographic feature from each needle pass serves as a guide for the bronchoscopist to locate

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Table I: Baseline Characteristics and Diagnostic yield of EBUS-TBNA versus EBUS-TBMC

Baseline characteristics			
Variable	Number (%)		
Total number of patients	30		
Number of patients undergone EBUS-TBNA	28		
Number of patients undergone EBUS-TBMC	30		
Sex			
Male	19 (63.3)		
Female	11 (36.7)		
Type of sedation			
Conscious sedation	24 (80.0)		
General anaesthesia	6 (20.0)		
Number of lesions attempted EBUS-TBMC/patient			
1	25(83.4)		
2	4(13.3)		
3	1(3.3)		
Number of EBUS-TBMC/lesion			
2	7 (19.4)		
3	12 (33.3)		
4	11 (30.6)		
5	4 (11.1)		
6	2 (5.6)		
EBUS-TBMC activation time			
<7 (3-6sec)	21 (58.3)		
≥7 (7-10 sec)	15 (41.7)		
Type of lesions			
Lymph nodes	30 (83.3)		
Mass	6 (16.7)		
Lymph nodes (station)			
4R	9 (30.0)		
11/10R	2 (6.7)		
7	16 (53.4)		
11/10L	1 (3.3)		
4L	1 (3.3)		
Others	1 (3.3)		
Mass			
Paratracheal mass	2 (33.3)		
Posterior tracheal lesion	2 (33.3)		
Hilar mass	2 (33.3)		
Overall diagnostic yield	25 (83.3)		
Diagnostic yield of EBUS-TBNA vs. EBUS-TBMC			
	TBNA (n = 28)	TBMC (n = 30)	p value
Overall diagnostic yield	20 (71.4)	25 (83.3)	0.28
NSCLC	15 (75.0)	15 (60.0)	0.29
Others	5 (25.0)	10 (40.0)	

EBUS-TBNA: Endobronchial ultrasound guided transbronchial needle aspiration; EBUS-TBMC: Endobronchial ultrasound-guided transbronchial mediastinal cryobiopsy

the NT. If the hyperechoic sonographic feature is not well seen, the bronchoscopist must rely on precise recognition of the surrounding anatomical landmarks to trace and identify the NT. A pictorial narrative of the EBUS-TBMC procedure is shown in Figure 1. The use of a high-frequency needle knife to create a NT is not necessary, although it may potentially reduce the overall procedural time.[6] In terms of location, performing EBUS-TBMC on lesions situated at the hilar and posterior trachea can be challenging. This is due to the limitations of the EBUS scope in reaching lesions at an acute angle and the absence of a rotator function at the insertion tube of the EBUS scope.

Incoperating EBUS-TBMC to EBUS-TBNA but may have added value in the diagnosis of benign mediastinal lesions, lymphomas, and other rare malignancies.[6-9] In our study, EBUS-TBMC recorded an overall non-significant higher diagnostic yield when compared to EBUS-TBNA. A more important clinical implication lies in the ability of EBUS-TBMC to provide sufficient tissue for complete molecular profiling in the treatment of NSCLC.[9] EBUS-TBMC demonstrated similar diagnostic yield to EBUS-TBNA in 15 cases of NSCLC and the histology specimens from EBUS-TBMC were preferred over cytology cell blocks for NGS testing in all patients. Other conditions diagnosed by EBUS-TBMC (missed by EBUS-TBNA) included two cases of sarcoidosis, one case of mediastinal lymphoma, a sarcoid-like reaction, and a tuberculous mediastinal lymphadenopathy. However, intra-lesion necrosis, heterogeneity or fibrotic lymph nodes may still limit tissue availability, resulting in a potential reduction in diagnostic yield.[10] This is evident in our study where EBUS-TBMC was not able to establish a diagnosis in three cases

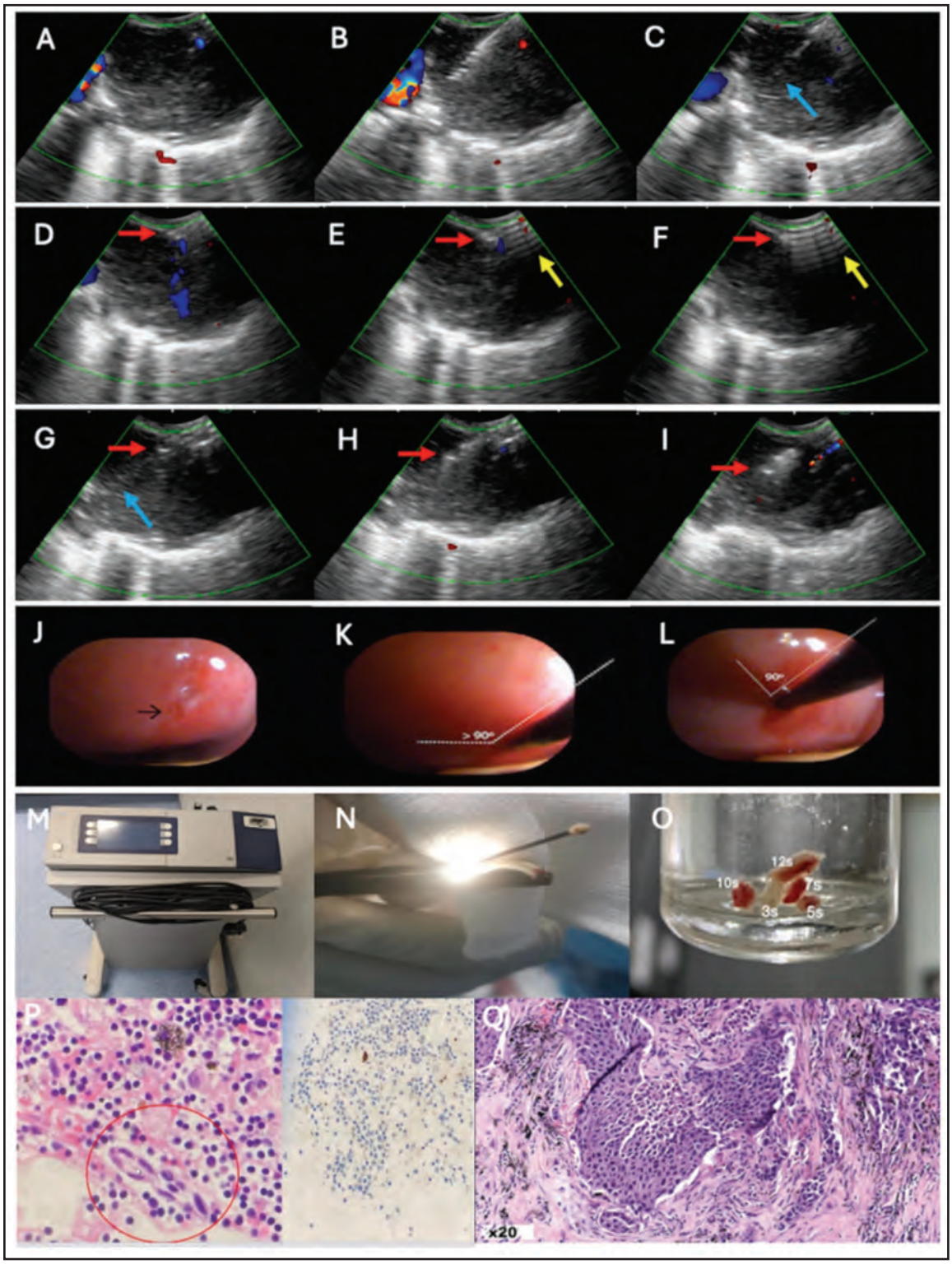

Fig. 1: Pictorial narrative of the EBUS-TBMC procedure.
(A) A lymph node seen on EBUS with colour doppler, (B) An EBUS-TBNA needle is inserted into the lymph node, (C) A faint hyperechoic needle track (blue arrow) after EBUS-TBNA passes, (D,E,F) Failed insertion of the cryoprobe (red arrow) into the needle track. Ultrasound artifact from the cryoprobe is seen (yellow arrow), (G,H,I) Successful insertion of the cryoprobe (red arrow) into the needle track (blue arrow), (J) Entry point after a 22 gauge TBNA needle puncture (black arrow) on endoscopic view, (K) Avoiding entry of cryoprobe at obtuse angle, (L) Maintain perpendicular entry of cryoprobe, (M) A cryosurgery unit, (N) Frozen biopsy at the tip of the cryoprobe, (O) Histology specimen obtained at different cryo-activation time, (P) A small cluster of atypical cells seen on cytology cell block obtained from EBUS-TBNA (red circle) (x 40 magnification), (Q) Histology sample from EBUS-TBMC shows stroma infiltrated by malignant cells which form solid nests. Both squamoid and glandular differentiation are seen. Findings are consistent with poorly differentiated adenosquamous carcinoma (x20 magnification)

involving lesions with extensive necrosis. Poor tolerance to procedure and imprecise biopsy location resulted in negative diagnostic yield in the remaining two cases.

EBUS-TBMC has manageable and self-limiting complications.[6-9] Rare incidents of minor bleeding, pneumothorax and pneumomediastinum have been reported.[6] We did not encounter any complications apart from six cases of minor bleeding from the NT which was self-limiting.

While EBUS-TBMC appears promising, one significant drawback is the cost of the single-used flexible cryoprobe. Maturu et al.,[8] proposed a diagnostic algorithm, utilizing EBUS-TBNC selectively when rapid on-site evaluation (ROSE) yielded inconclusive results. This approach led to an additional diagnostic yield of 43.7%[8] Hence, the bronchoscopist needs to necessitate careful consideration and justification of its use.

CONCLUSION

EBUS-TBMC potentially offers a higher diagnostic yield than EBUS-TBNA. It has the advantage of minimising the need for repeat biopsies and delay in diagnosis, which could translate into overall cost savings. Further prospective studies are needed to validate these findings before permanently adopting this new procedure into our clinical practice.

AUTHORSHIP STATEMENT

Conception and design: Chun Ian Soo and Nai-Chien Huan; Provision of study materials: All authors; Collection and acquisition of data: Chun Ian Soo; Data analysis and interpretation: Chun Ian Soo; Manuscript writing: All authors; Final approval of manuscript: All authors.

CONFLICT OF INTEREST

The authors declare no conflict of interest relevant to this article. This study has been approved by the Medical Research Ethics Committee, Universiti Malaya Medical Centre (MECID. No: 2024418-13645)

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