Endobronchial ultrasound-guided transbronchial mediastinal cryobiopsy in the diagnosis of mediastinal lesions: safety, feasibility and diagnostic yield – experience in 50 cases

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Shareable abstract (@ERSpublications)
Transbronchial mediastinal cryobiopsy is a minimally invasive, rapid and safe technique that can be performed in a bronchoscopy suite under moderate sedation. It has a higher diagnostic yield than transbronchial needle aspiration. https://bit.ly/3vSKTxO

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Abstract

Background Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is the technique of choice in the study of mediastinal and hilar lesions; however, it can be affected by the insufficiency of intact biopsy samples, which might decrease its diagnostic yield for certain conditions, thus requiring re-biopsies or additional diagnostic procedures such as mediastinoscopy when the probability of malignancy remains high. Our objectives were to 1) attempt to reproduce this technique in the same conditions that we performed EBUS-TBNA, *i.e.* in the bronchoscopy suite and under moderate sedation; 2) describe the method used for its execution; 3) determine its feasibility by accessing different lymph node stations applying our method; and 4) analyse the diagnostic yield and its complications.

Methods This was a prospective study of 50 patients who underwent EBUS-TBNA and EBUS-guided transbronchial mediastinal cryobiopsy (TMC) in a single procedure using a 22-G TBNA needle and a 1.1-mm cryoprobe subsequently between January and August 2022. Patients with mediastinal lesions >1 cm were recruited, and EBUS-TBNA and TMC were performed in the same lymph node station.

Results The diagnostic yield was 82% and 96% for TBNA and TMC, respectively. Diagnostic yields were similar for sarcoidosis, while cryobiopsy was more sensitive than TBNA in lymphomas and metastatic lymph nodes. As for complications, there was no pneumothorax and in no case was there significant bleeding. There were no complications during the procedure or in the follow-up of these patients.

Conclusions TMC following our method is a minimally invasive, rapid and safe technique that can be performed in a bronchoscopy suite under moderate sedation, with a higher diagnostic yield than EBUS-TBNA, especially in cases of lymphoproliferative disorders and metastatic lymph nodes or when more biopsy sample is needed for molecular determinations.

Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is the technique of choice for mediastinal diagnosis and staging in nonsmall cell lung cancer (NSCLC) due to its high diagnostic yield and excellent safety profile, avoiding more invasive procedures, such as mediastinoscopy. In recent years, a proper molecular characterisation of tissue samples has become crucial for the management of thoracic malignancies, and more specifically lung cancer.

Although EBUS-TBNA provides an excellent diagnostic yield for primary pulmonary malignancies, it retrieves a limited amount of tissue that might be insufficient to allow for a confident diagnosis of rare tumours or benign mediastinal diseases, which frequently requires histopathological rather than cytological samples and evaluation of the overall background architecture [1, 2].

The ability of EBUS-TBNA to accurately diagnose and subtype lymphoma has been questioned because of lesser sampling of core tissue, and recent research has highlighted the value of histological specimens rather than TBNA-acquired cytology for diagnosing lymphoma [3]. In the case of mediastinal lymphadenopathy and a suspicion of lymphoma, a surgical biopsy is the preferred diagnostic approach; however, mediastinoscopy is a more invasive procedure with more associated complications when directed compared with endoscopic ultrasound techniques [4]. The role of EBUS-TBNA in a lymphoma diagnosis is, therefore, of uncertain value in cases of marginal zone and follicular lymphoma [5].

The pathological confirmation of the clinical suspicion of sarcoidosis is a common indication for bronchoscopy. As lymphadenopathy is, by far, the most common manifestation of the disease across all ethnic groups, EBUS-TBNA has become the first-choice diagnostic technique in most centres worldwide. Several groups have addressed the influence of technical aspects of EBUS on its diagnostic success in sarcoidosis, including needle gauge, availability of rapid on-site evaluation (ROSE) of cytological material, number of needle passes and number of sampled lymph nodes [6]. However, despite a considerable amount of clinical research, large individual studies [7, 8] and systematic reviews/meta-analyses [9, 10] have demonstrated that EBUS-TBNA still fails to detect granulomas in ∼20% of patients with sarcoidosis.

The cryoprobe was initially applied within the airways for debulking of endobronchial lesions through freezing and thawing [11]. Because of its capacity to harvest a relatively large amount of pulmonary tissue, cryobiopsy has been recently used for sampling of diffuse lung disease, a setting in which forceps biopsies are of limited value [12].

Aiming at obtaining larger intact samples containing more diagnostic information for mediastinal diseases, our group recently published a series of four consecutive patients who underwent both EBUS-TBNA and EBUS-guided transbronchial mediastinal cryobiopsy (EBUS-TMC) in a single procedure [13], concluding that, although EBUS-TBNA is the technique of choice at present for the diagnosis and staging of malignant mediastinal lesions, TMC might provide an additive value to current diagnostic approaches for mediastinal diseases, specifically in cases of uncommon tumours, suspicion of lymphoproliferative or granulomatous disorders, or when more biopsy sample is needed for molecular determinations. Hence, despite the considerable success of EBUS-TBNA, we believe there remains significant room for improvement in the diagnosis of mediastinal lesions.

Methods

Study design and patients

A prospective study was conducted in the Central University Hospital of Asturias (Oviedo, Spain) and in the HLA La Vega Hospital (Murcia, Spain) from January to August 2022 to evaluate the diagnostic yield, feasibility and safety of EBUS-TMC in patients with mediastinal lesions. The study was approved by the ethics committee from both hospitals following the principles of the Declaration of Helsinki and all patients provided written informed consent prior to bronchoscopy. EBUS-TBNA and TMC were performed in a single procedure using a 22-G needle and a 1.1-mm cryoprobe subsequently. Three cryobiopsies were performed per lymph node. All procedures were performed by the same two operators in each centre. A fluorodeoxyglucose positron emission tomography (FDG-PET) or a chest computed tomography (CT) scan was performed in all patients prior to bronchoscopy.

Patients with mediastinal lesions >1 cm were recruited consecutively from the start of the study, and EBUS-TBNA and TMC were performed in the same lymph node station. ROSE was not always performed. The pathologists received a sample identified as EBUS-TBNA and another as EBUS-TMC. The FDG-PET/CT standard uptake value (SUV), tissue sample size (diameter) obtained by both techniques and length of the procedures were recorded. Bleeding was collected into a mucus reservoir (Mocstrap; Proclinics, Barcelona, Spain), which has a scale in millilitres, and quantified according to the following classification: mild <10 mL, moderate 10–40 mL and severe >40 mL. In all patients, the protocol included complete blood count and coagulation. We excluded patients who presented with blood dyscrasias, severe respiratory failure, unstable heart diseases and pulmonary hypertension. In cases in which the final diagnosis was nonmalignant, a clinical-radiological follow-up was performed.

EBUS-TBNA procedure and TMC procedures

All procedures were performed in the bronchoscopy suite by a pulmonologist with multiyear experience in endoscopic procedures, developed in a department with a high number of yearly EBUS-TBNAs. All patients underwent EBUS under conscious sedation with midazolam and fentanyl after signing informed consent. A continuous record of oxyhaemoglobin saturation, blood pressure, heart rate, respiratory rate and ECG was made. For performing EBUS-TMC we use a 22-G needle (SonoTip TopGain; Medi-Globe, Rohrdorf, Germany) (figure 1a), the ERBECRYO 2 system (figure 1b) and a 1.1-mm cryoprobe (Erbecryo 20402-401; Erbe, Tubingen, Germany) (figure 1c). The 1.1-mm cryoprobe easily enters the working channel of the EBUS bronchoscope (EB19-J10U; Pentax Medical, Hamburg, Germany) (figure 1d). We proceed to describe step by step the complete procedure applying the Ariza–Pallarés method [13].

After identification of the suitable lymph node station at EBUS, we performed three passes of TBNAs (figure 2a and b). As it is an ultrasound-guided procedure, it is key to identify the trace left by the TBNA within the lymph node (figure 2c). After initial puncture with the TBNA needle (figure 2d), a 1.1-mm cryoprobe was introduced into the working channel of the EBUS bronchoscope. The cryoprobe is advanced towards the puncture site and inserted gently through the previous puncture site created by the 22-G needle. The EBUS image confirmed the cryoprobe position within the lymph node. The cryoprobe was cooled down with liquid carbon dioxide for 4 s, and then retracted with the bronchoscope and the frozen biopsy tissue attached to the tip of the probe (figure 3a–c). The cryobiopsy site was immediately examined and no bleeding was observed (figure 3d). Cryobiopsies were retrieved in saline and fixed in formalin. TMC samples of a sarcoidosis and a squamous lung cell carcinoma are shown in figure 4a–c and d–f, respectively All patients received post-procedural chest radiographs or pleural echography to confirm that a pneumothorax had not been produced and the patient was discharged 2 h after verifying that there had been no complications. Follow-up was conducted on all patients at 24 h *via* phone call and 2 weeks after the procedure to check that there were no delayed complications.

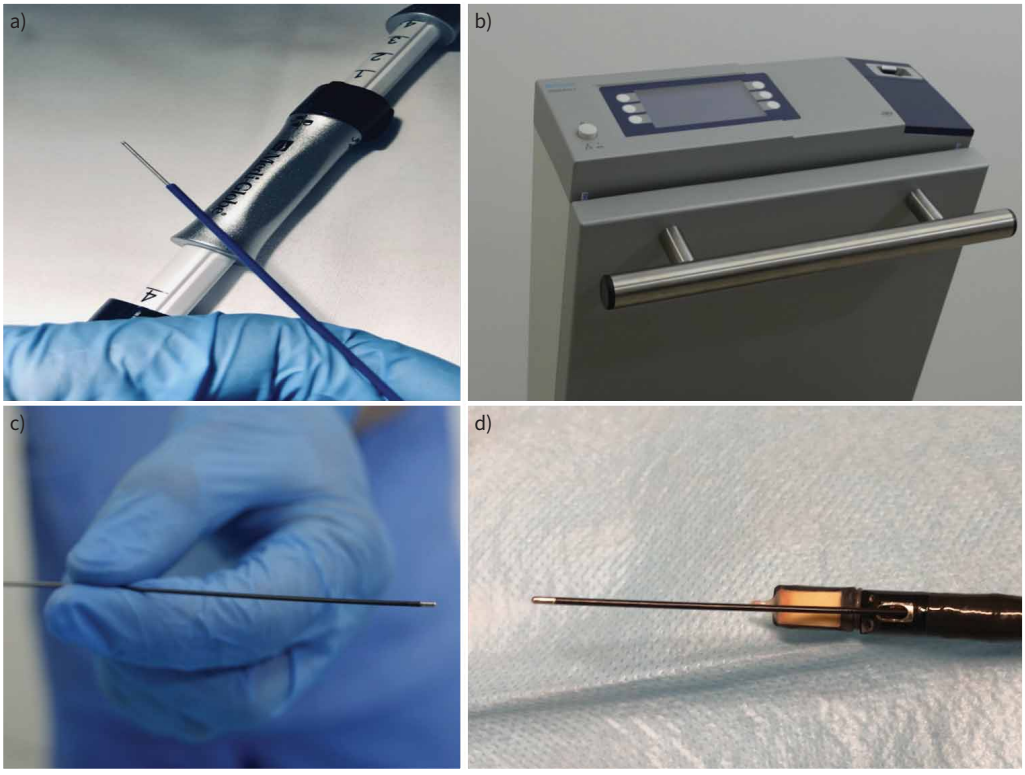

FIGURE 1 a) 22-G needle (SonoTip TopGain: three-point needle tip design with a crown cut). b) ERBECRYO 2 system. c) 1.1-mm cryoprobe (Erbecryo 20402-401). d) 1.1-mm cryoprobe through the working channel of the endobronchial ultrasound bronchoscope (EB19-J10U).

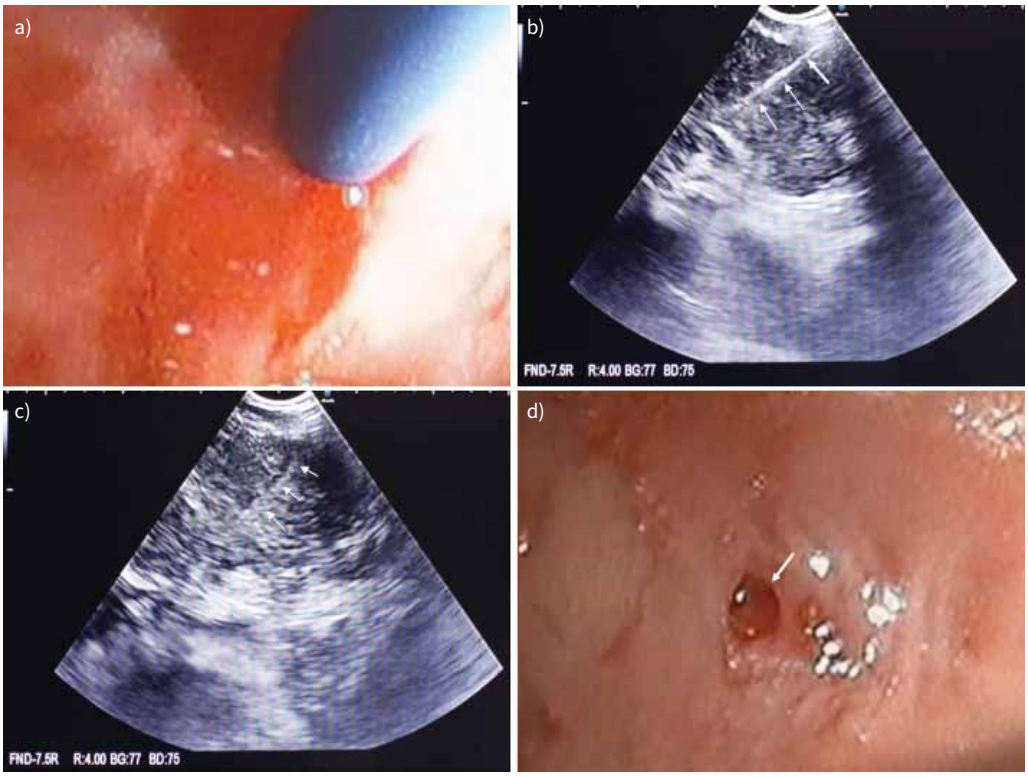

FIGURE 2 a) Performing endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in station 7 lymph node; TBNA needle sheath. b) EBUS image of the 22-G needle inside the lymph node (white arrows). c) Trace left inside the lymph node by the needle after three TBNAs (white arrows). d) Puncture site made by the TBNA needle (white arrow).

Results

During the study period, 50 patients (32 males and 18 females; 42 patients from Asturias Central University Hospital and eight patients from HLA La Vega Hospital) with mediastinal lesions were included for carrying out EBUS-TBNA and TMC in a single procedure. Baseline characteristics of these patients and the biopsied lymph node stations are shown in table 1. 50% of the patients were current smokers (mean±SD 37.5±13.14 pack-years) with a mean±SD age of 63±11.8 years (range 34–87 years) and a FDG-PET/CT scan was performed in 25 of them with a mean±SD SUV of 9.16±3.89. TMC was not performed in three lymph node stations (10L, 10R and 11Rs); the most biopsied stations were 7 and 4R, with a mean±SD diameter of 25.66±8.78 and 17.33±8.35 mm, respectively.

EBUS-TBNA and TMC diagnostic yields are reported in table 2. The diagnostic yield for TBNA was 82% and for TMC was 96%. The 50 patients (100%) had a definitive overall diagnosis based on the biopsies obtained from both techniques (48 from TMC). The two patients that had an insufficient diagnosis by TMC were diagnosed by TBNA (two lung adenocarcinomas; station 3p and 7, respectively). In nine cases, TBNA was not diagnostic; however, a definitive diagnosis was reached by cryobiopsy (four lung adenocarcinoma, two squamous cell lung carcinoma, one lymphoma, one prostate carcinoma and one anthracosis). In 10 patients, the sample obtained by TBNA was considered negative for malignancy; of this group of patients, TMC diagnosed one lymphoma and three anthracosis; and in the remaining six patients the diagnosis of nonmalignancy was maintained. No differences were found in diagnostic yield between both techniques for patients with sarcoidosis nor in the diagnosis of small cell lung carcinoma; however, TMC diagnosed six cases of lung adenocarcinoma and four cases of squamous cell lung carcinoma that had been previously classified by TBNA as insufficient sample (n=6), carcinoma of unknown origin (n=3) and unclassified nonsmall cell lung carcinoma (n=2). TMC established the diagnosis of lymphoma in all patients in whom this pathology was suspected (100%) and all cases were successfully subclassified; meanwhile, no definitive diagnosis of lymphoma was reached with TBNA. The diagnostic concordance between the two techniques was 56%. Sample size comparison between EBUS-TBNA and TMC is shown in table 3.

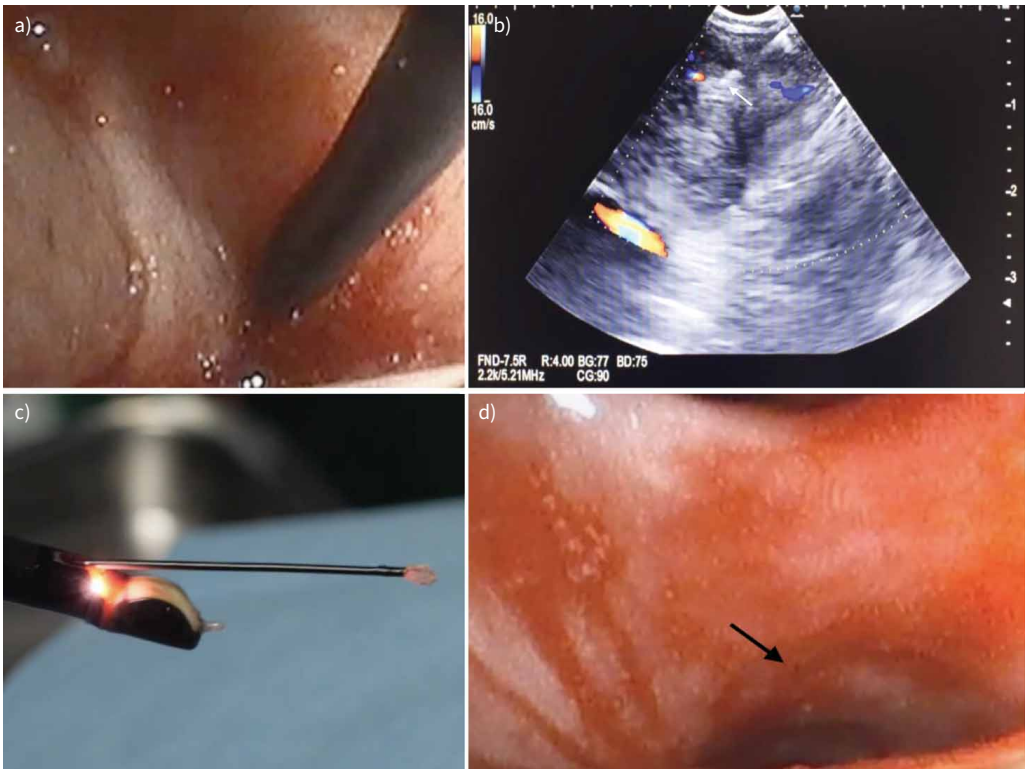

FIGURE 3 a) Tip of the cryoprobe approaching the puncture site. b) Endobronchial ultrasound-Doppler image showing the tip of the 1.1-mm cryoprobe within the lymph node (white arrow). c) Cryobiopsy sample attached to the tip of the probe. d) No bleeding observed after the cryobiopsy (black arrow).

There were no major complications in our series of patients during the procedure, nor 24 h later, nor at the 2-week follow-up. The most predominant adverse event was mild bleeding (<10 mL) and it was more frequent when performing TBNA than when TMC was performed (table 4). There was no pneumothorax, pneumomediastinum or mediastinitis in our study. The overall mean±SD procedure time was 33.96±5.86 min (range 21–42 min). The mean±SD TMC procedure time was 9.54±2.10 min (range 6–15 min). In patients with a nonmalignancy diagnosis, the clinical-radiological follow-up showed no changes.

Discussion

This study tested and analysed the diagnostic yield, feasibility and safety of TMC as a novel procedure for the diagnosis of mediastinal and hilar lesions. ZHANG *et al*. [14] conducted a randomised trial that included a total of 197 patients who underwent EBUS-TBNA and TMC in the same procedure to assess the diagnostic yield and safety of this technique. For TMC they performed a small incision in the tracheobronchial wall adjacent to the mediastinal lesion using a high-frequency needle-knife; the knife was then replaced by the cryoprobe and biopsies were performed by cooling down for 7 s. In their trial the overall diagnostic yield was 79.9% and 91.8% for TBNA and TMC, respectively, while TMC was more sensitive than TBNA in uncommon tumours (91.7% *versus* 25%) and benign disorders (80.9% *versus* 53.2%) [14]. In our study the overall diagnostic yield was 82% and 96% for TBNA and TMC, respectively.

An important difference in our report is the way we perform the procedure. We have shown that the high-frequency needle-knife is not essential; we eliminated this step of the process by directly introducing the 1.1-mm cryoprobe always guided by the ultrasound image through the puncture site created by the EBUS-TBNA needle, allowing us to perform the procedure in a faster way [13]. The overall mean±SD procedure time in our series was 33.96±5.86 min (range 21–42 min). In the ZHANG *et al*. [14] trial using the high-frequency needle-knife, the overall mean±SD procedure time was 31.9±9.1 min. In our study the mean±SD TMC procedure time was 9.54±2.10 (range 6–15 min); we believe these times seem acceptable in consideration of the benefits of a more intact and bigger biopsy sample, which avoids repetitions of EBUS-TBNA and invasive techniques such as mediastinoscopy.

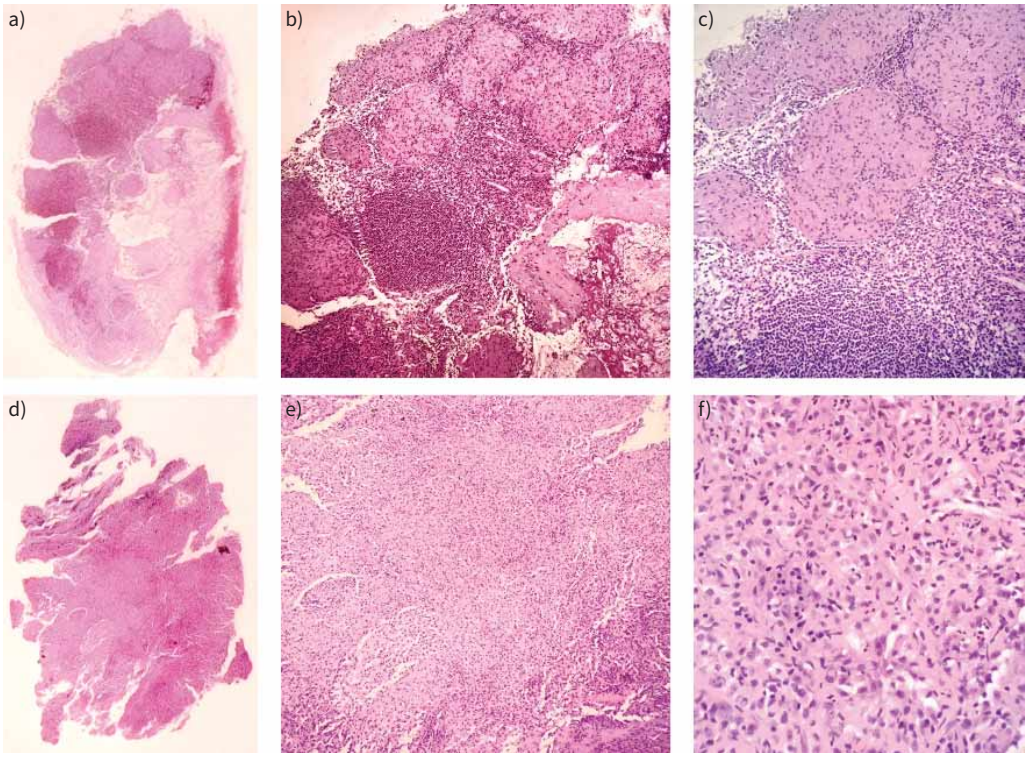

FIGURE 4 a–c) A 39-year-old male with multiple mediastinal and hilar enlarged lymph nodes. Transbronchial mediastinal cryobiopsy (TMC) sample of station 11L lymph node stained with haematoxylin–eosin stain showing a well-preserved lymph node architecture with presence of multiple nonnecrotising granulomas confirming the diagnosis of sarcoidosis. d–f) A 78-year-old male patient, nonsmoker, with a nodule in the right upper lobe, brain metastasis and enlarged mediastinal lymph node. TMC sample of station 7 lymph node, stained with haematoxylin–eosin in which almost exclusively a nonsmall cell neoplastic epithelial proliferation is observed, organised in solid nests, with clear cytoplasm, karyomegaly, nuclear hyperchromasia and reddish nucleolus. Immunohistochemistry for p40 was positive, confirming an advanced-stage lung squamous cell carcinoma, in which the abundant tumour sample of the TMC assured the realisation of molecular testing.

Since EBUS-TMC is a new technique, only 18 cases have been published in the literature to date without using the high-frequency needle-knife and without relevant complications [13–16]. One of the perceived limitations of the EBUS technique is the small size obtained by the 22-G needle. The small amount of material obtained makes it difficult for the pathologist to diagnose benign and haematological diseases. Previous studies have demonstrated that EBUS-guided mediastinal forceps biopsy compared with TBNA improves specimen quality and diagnostic yield, particularly in patients with sarcoidosis and lymphoma [2, 17–20]. However, one of the largest prospective trials of transbronchial forceps biopsy reported a lower diagnostic sensitivity of this technique compared with TBNA in malignant lymph nodes [19].

The diagnostic value of EBUS-TBNA, which provides groups of cells for a cytological evaluation instead of tissue for histological analysis in the majority of the cases, is less well established in patients with sarcoidosis or other benign diseases [21–23]. The reason for a suboptimal diagnostic hit rate seems to be the small specimen size by EBUS-TBNA that does not allow adequate pathological analysis because the general tissue architecture cannot be evaluated. Previous studies have reported that EBUS-TBNA can have a diagnostic yield in sarcoidosis of 54–93%, at least in experienced centres [22, 23]. A meta-analysis by Agarwal *et al.* [9] in 553 patients suggests an excellent overall diagnostic yield of EBUS-TBNA in this pathology. In our study, 12 patients were diagnosed with sarcoidosis, with a concordance between TBNA and TMC of 100%. Although multiple studies have shown potentially limited ability of EBUS-TBNA to diagnose sarcoidosis, we demonstrated no significant difference in diagnostic yield between both techniques regarding this condition. It is important to mention that our pathologists reported that the quality of the samples obtained by TMC was optimal for obtaining a definitive diagnosis with greater certainty.

TABLE 1 Baseline characteristics

Sex, n (%)	
Female	18 (36)
Male	32 (64)
Smoking status, n (%)	
Nonsmoker	12 (24)
Current smoker	25 (50)
Ex-smoker	13 (26)
FDG-PET/CT, n (%)	
No	25 (50)
Yes	25 (50)
TBNA lesion station, n (%)	
2R	1 (2)
4R	11 (22)
7	27 (54)
10R	1 (2)
11Rs	1 (2)
11Ri	7 (14)
4L	4 (8)
3p	3 (6)
11L	14 (28)
TMC lesion station, n (%)	
2R	1 (2)
4R	7 (14)
7	24 (48)
10R	0 (0)
11Rs	0 (0)
11Ri	7 (14)
4L	3 (6)
3p	3 (6)
11L	13 (26)
FDG-PET/CT SUV, mean±SD	9.16±3.89 (n=25)
EBUS lesion size (short axis), mm	
2R	16 (n=1)
4R	17.33±8.35 (n=12)
7	25.66±8.78 (n=27)
10R	18 (n=1)
11Rs	20 (n=1)
11Ri	22.71±4.11 (n=7)
4L	19.75±12.01 (n=4)
3p	20.5±9.19 (n=2)
11L	20.86±8.97 (n=15)

Data for lesion size are presented as mean±SD for n>1. FDG-PET: fluorodeoxyglucose positron emission tomography; CT: computed tomography; SUV: standard uptake value; TBNA: transbronchial needle aspiration; TMC: transbronchial mediastinal cryobiopsy; EBUS: endobronchial ultrasound.

Lymphoid neoplasia is diagnosed on the basis of the World Health Organization (WHO) classification system. The WHO recommends the use of multidimensional diagnostic modalities, including cytomorphological studies, immunophenotyping, cytogenetic analyses and molecular studies to accurately subtype lymphoma [24, 25]. Surgical excision and core biopsy are the current preferred sampling techniques for diagnosing lymphoma, but there is growing interest in using less invasive endoscopic techniques with lower complication rates [4]. In patients who present with intrathoracic adenopathy that is suspicious for lymphoma, EBUS-TBNA is in most cases the first diagnostic option, given the risks of surgical sampling [26]. The inherent disadvantages of EBUS-TBNA include lesser sampling of core tissue and an inferior negative predictive value [27]. The low-volume samples can be a major concern, particularly in diagnosing marginal zone and follicular lymphoma [5], in which studies have suggested a high level of discordance between cytological and histological specimens [28]. This has led many authors to conclude that EBUS-TBNA is not usually a clinically appropriate diagnostic tool if lymphoma is suspected [29]. Several studies have demonstrated that the use of mini-forceps guided by EBUS increases the diagnostic yield with respect to Hodgkin disease, non-Hodgkin lymphoma and sarcoidosis [2, 30]. However, these studies have been performed mainly in subcarinal nodes, and the blunt forceps did not

TABLE 2 Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and transbronchial mediastinal cryobiopsy (TMC) diagnostic yields

	EBUS-TBNA	EBUS-TMC
Diagnosis		
Insufficient	9 (18)	2 (4)
Nonmalignancy	10 (20)	6 (12)
Sarcoidosis	6 (12)	6 (12)
Lung adenocarcinoma	7 (14)	12 (24)
Squamous cell lung carcinoma	4 (8)	8 (16)
Small cell lung carcinoma	6 (12)	6 (12)
Breast carcinoma	1 (2)	1 (2)
Carcinoma of unknown origin	3 (6)	0 (0)
Nonsmall cell lung carcinoma	2 (4)	0 (0)
Not classified lymphoma	2 (4)	0 (0)
Prostate carcinoma	0 (0)	1 (2)
B-cell non-Hodgkin lymphoma	0 (0)	4 (8)
Anthracosis	0 (0)	4 (8)
Diagnoses by pathologies		
Lung cancer	22 (78)	26 (92.9)
Lymphoma	0 (0)	4 (100)
Benign conditions	6 (60)	10 (100)
Diagnostic yield	82	96
Sensitivity	60.7	92.9
Specificity	100	100
Negative predictive value	66.7	91.7
Positive predictive value	100	100
Concordance		
Yes	28 (56)[#]	

Data are presented as n (%) or %. [#]: p=0.239, κ= −0.078.

TABLE 3 Sample size comparison between endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and transbronchial mediastinal cryobiopsy (TMC)

	Sample size (cm)		p-value
	Mean±SD	Minimum–maximum	
TBNA	0.20±0.08	0.10–0.40	<0.001
TMC	0.46±0.13	0.20–0.80	

TABLE 4 Adverse events for endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and transbronchial mediastinal cryobiopsy (TMC)

	EBUS-TBNA	EBUS-TMC
Bleeding		
Mild <10 mL	8	2
Moderate 10–40 mL	2	0
Severe >40 mL	0	0
Pneumothorax	0	0
Pneumomediastinum	0	0
Mediastinitis	0	0
Death	0	0

Data are presented as n.

pass the perforated mucosa and penetrate the lymph node in all cases. In our study, TMC established the diagnosis of lymphoma in all patients in whom this pathology was suspected (100%) and all cases were successfully subclassified; meanwhile, with TBNA no definitive diagnosis of lymphoma was reached. Although there were only four cases of lymphoma in our study, the mediastinal cryobiopsy was able to avoid EBUS-TBNA repetition and the potential risks of mediastinoscopy in this group of patients.

EBUS-TBNA has an excellent yield in normal sized and enlarged mediastinal and hilar lymph nodes, with a sensitivity of 84–94% [21, 31, 32]. With specific regard to NSCLC, the number of potentially actionable oncogenic drivers is constantly increasing. While the first acknowledged driver was the epidermal growth factor receptor, novel biomarkers of therapeutic interest are emerging, this requiring increasing quantity of tumour tissue for testing multiple biomarkers at once. This is especially relevant considering the role that next-generation sequencing (NGS) is acquiring in current clinical practice; in this context, the tissue collected at diagnosis needs to be adequate both in terms of quantity and quality, in order to prevent repeated procedures [33]. Retrospective data on a small subset of cancer patients suggest that cryobiopsy performed on peripheral lesions might provide more adequate samples for NGS compared with EBUS-TBNA on mediastinal stations, allowing to analyse more genes [34]. In this study, the diagnostic yield of EBUS-TBNA was marginally lower than reported before in bigger studies. In our study, no differences were found in diagnostic yield between both techniques in the diagnosis of small cell lung carcinoma; however, TMC diagnosed six cases of lung adenocarcinoma and four cases of squamous cell lung carcinoma that had been previously classified by TBNA as insufficient sample (n=6), carcinoma of unknown origin (n=3) and unclassified nonsmall cell lung carcinoma (n=2). The two patients that had an insufficient diagnosis by TMC were diagnosed by TBNA (two lung adenocarcinomas). In all cases in which a definitive diagnosis of lung cancer was not obtained by TBNA, the cryobiopsy allowed optimal molecular testing to be performed.

We performed EBUS-TMC under conscious sedation and it was well tolerated by all patients, suggesting that moderate sedation is sufficient and safe for performing TMC. There were no relevant complications during the procedure, nor 24 h later, nor at the 2-week follow-up. The most predominant adverse event was minor bleeding and it was more frequent when performing TBNA. There was no pneumothorax, pneumomediastinum or mediastinitis in our study.

Several limitations need to be considered in the present study. In five cases we had to make five passes of TBNA prior to performing the cryobiopsy because it was not possible to penetrate the bronchial wall. This problem occurred in patients with suspected silicosis, where the bronchial wall is more rigid and cartilaginous. TMC was not performed in three lymph node stations (10L, 10R and 11Rs). In our series, we did not have the necessity to make a diagnosis at these lymph node stations, so its feasibility in these three stations is unknown. Two patients with lung cancer were not diagnosed by TMC, despite the acquisition of more material compared with TBNA. We believe that this may have been due to the fact that cryobiopsies were always conducted at the same site of the lesion and as such may have missed the affected tissue. Another probable limitation of the study is the lack of ROSE of the TBNA samples in all procedures, which could have improved the diagnostic yield of EBUS-TBNA, and also the fact that the pathologist was not blinded between the samples obtained by the two techniques.

A strength of our study is that it is the first report in which EBUS-TMC was performed in two centres without using the high-frequency needle-knife with this number of patients.

Conclusions

EBUS-TMC following our method is a minimally invasive, feasible and safe technique that can be performed in a bronchoscopy suite under moderate sedation by an interventional pulmonologist highly experienced in performing EBUS. This technique seems to offer a higher overall diagnostic yield compared with EBUS-TBNA, especially in the diagnosis of lymphoma, tumours of nonpulmonary origin and in those lung carcinomas in which molecular testing is needed for a personalised antineoplastic treatment.

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and L. Fernández-Fernández conducted histological analysis. M. Ariza-Prota is the guarantor of the paper, taking responsibility for the integrity of the work as a whole, from inception to published article.

Conflict of interest: No conflicts of interest exist for any of the authors.

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