Transbronchial Needle Aspiration

R. Trisolini1, M. Patelli1, L. Ceron2, S. Gasparini3

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Transbronchial needle aspiration (TBNA) is a low cost, minimally invasive bronchoscopic procedure which has been successfully used in the diagnosis of neoplastic, inflammatory, infectious, and developmental disorders [1].

Although it has been developed and predominantly used to sample mediastinal lesions, the technique is extremely versatile, as it can also be used to sample submucosal, peribronchial, and peripheral pulmonary lesions [1].

Technique

Conventional TBNA of hilar and mediastinal lesions was originally thought as a “blind” procedure since target lymph nodes cannot be visualized directly by the operator and the site for aspiration/biopsy is chosen based on the knowledge of a few endobronchial landmarks and prior contrast enhanced CT evaluation [2, 3]. In the last decade, the development of new technologies, especially endobronchial ultrasounds (EBUS) and CT-fluoroscopy, has led to the concept of integration with TBNA to improve the diagnostic yield [4-11]. Initial studies assessing the value of ultrasound-guided TBNA (EBUS-TBNA) compared with conventional TBNA demonstrated the superiority of EBUS-TBNA only for small lymph nodes (<1 cm) or for “difficult-to-reach” lymph node mediastinal areas (2R, 2L, 4L), but these studies were performed with a radial ultrasonic probe which did not allow for a real-time guidance of fine-needle aspiration [7-9]. More recently, a dedicated bronchoscope equipped with a linear array transducer that allows for real-time guidance of TBNA (real-time EBUS-TBNA) has been developed and has been associated with excellent results in the mediastinal staging of lung cancer and sarcoidosis [10]. Even though no other study carried out direct standard vs real-time EBUS-TBNA comparisons, several trials published in the last decade and aimed at evaluating the role of real-time EBUS-TBNA in patients with enlarged hilar/mediastinal adenopathy, obtained average sensitivity and accuracy values close to 90%, certainly superior to those reported for conventional TBNA in most studies [10, 11].

Recommendation

- EBUS-guided TBNA is superior to conventional TBNA mainly in some specific settings, such as difficult mediastinal LN areas (mainly 2, 3, 4L) and small LN size (<1 cm) (Grade A).

Specimen handling and preparation methods for cytologic material

As for the handling of TBNA specimens, in those cases in which a histologic core of tissue has been obtained, it is removed gently from the needle’s tip and placed in formalin solution before being sent for staining and pathologic analysis [1, 12]. Cytologic material can be managed in two different ways: 1) “smear” ("direct") technique: the aspirate’s content material is collected on clean glass slides that are quickly air- or alcohol-fixed before being sent for staining and pathologic analysis. 2) “flush technique”: the aspirate’s content is deposited in 2 mL 95% alcohol which undergoes cytocentrifugation, cell pellet resuspension and staining [1]. Diacon and Coll. recently compared the two preparation methods and concluded that the "direct" technique is associated with a higher yield than the “flush” technique even after stratification for anatomical site and tumour type [13].

It should be noted, however, that alternative or adjunctive preparation methods can be required based on clinicoradiological data or pathologist’s preference. In patients with suspected mediastinal infection (especially mycobacterial infection) or lymphoma, the aspirate’s content should also be deposited in saline solution for culture or flow cytometric analysis, respectively.

* Due to the mounting scientific evidence concerning EBUS-TBNA published after 2006, the reference list and some recommendations regarding the present topic have been updated in February 2011 after critical literature review and expert consensus.
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time of initial diagnostic bronchoscopy along with 
other sampling bronchoscopy procedures aimed at 
typing the primary tumour, TBNA may be the only 
positive test in a considerable percentage of cases.

After two decades of use, strengths and limits of 
TBNA in the mediastinal staging of NSCLC are 
quite well known and have been thoroughly de-
scribed in two recent extensive literature reviews. In 
2007, Detterbeck et al. performed a systematic re-
view on 17 studies where TBNA was used to stage 
the mediastinum of 1339 patients with NSCLC 
[14]. The overall sensitivity and specificity were 
78% and 99%, respectively. The main limit of TB-
NA was its high false negative rate (approximately 
30%), which suggests that a negative transbronchial 
aspirate result must not negate further evaluation 
with more invasive sampling techniques mainly if 
the clinical-radiological suspect of lymph node 
metastasis is high. A more recent meta-analysis on 
the results of TBNA in the mediastinal staging of 
lung cancer selected, based on rigorous criteria, 13 
study out of 525 initially taken into account [15]. 
The analysis basically confirmed the very high 
specificity of the method, but also clearly demon-
strated that its yield as well as its positive predictive 
value largely depend on the prevalence of lymph 
ode metastasis in the population being studied. In 
particular, the diagnostic yield of TBNA proved 
high in studies with high prevalence of N2-N3 in-
volve, and the general implication was that the 
mediastinal nodes were markedly enlarged in these 
study populations. On the contrary, TBNA yield 
was much lower than previously thought in popula-
tions with low prevalence of lymph node meta-
asis. This data suggests that the primary role for TB-
NA in the mediastinal staging of NSCLC should be 
that of confirming a neoplastic lymph node involve-
ment which looks likely based on the imaging tech-
niques results, by virtue of its high specificity and 
sensitivity in this specific setting.

Several studies have evaluated a number of fac-
tors to explain the differences seen among the re-
ported diagnostic yields of the procedure in the me-
diastinal staging of NSCLC, and identified several 
predictors of a positive TBNA aspirate such as: 
high prevalence of lymph node metastasis in the 
study population [14, 15], increasing lymph node 
size [8, 16], right paratracheal and subcarinal loca-
tions [8, 12, 16], use of a histology needle [17], in-
creasing number of needle passes up to 7 [18], ex-
prience of the operator [19-20], and small-cell car-
cinoma histologic type [8, 16, 21-24]. Rapid on-site 
cytopathologic examination (ROSE) was initially 
thought to increase both the percentage of adequate 
samples and diagnostic yield of TBNA [25-27], but 
more recent data suggests that the main utility of 
ROSE in the setting of mediastinal TBNA is its ca-
pacity to defer additional biopsy and reduce the 
complication rate of bronchoscopy without com-
promising its diagnostic success [28-29].

**Recommendation**

- **Cytologic material obtained with TBNA should be prepared with the smear (direct) technique (Grade B).**

**Indications**

**a) Mediastinal lesions**

Any lesion involving the middle mediastinum 
and in close contact with the airway wall is poten-
tially suitable for TBNA sampling.

**Bronchogenic carcinoma**

TBNA, mainly if performed at the time of ini-
tial diagnostic bronchoscopy, can offer the unique 
opportunity to prevent patients with lymph node 
extension of primary tumour from being submitted to 
unnecessary surgical mediastinal exploration. In 
those cases in which TBNA is performed at the 
time of initial diagnostic bronchoscopy along with 
other sampling bronchoscopy procedures aimed at 
typing the primary tumour, TBNA may be the only 
positive test in a considerable percentage of cases.

**Recommendation**

- **TBNA or EBUS-TBNA should be performed in every patient with radiological suspicion of lung cancer and mediastinal involvement, provided that the mediastinal staging is crucial for the therapeutic choice (Grade B).**

**Hylar and/or mediastinal lymphadenopathy**

Several studies investigated the usefulness of 
TBNA in an unselected group of patients with hylar 
and or mediastinal lymphadenopathy. Such a study 
population is likely to include patients with several 
different diseases (neoplastic, infectious, inflamma-
tory), and it allows to evaluate the performance of 
TBNA in patients who are selected almost exclu-
sively based on their imaging findings. The vast ma-
ajority of these studies concluded that TBNA is safe 
and effective in this setting and almost uniformly re-
ported a diagnostic yield superior to 60% [30-33].

**Recommendation**

- **TBNA or EBUS-TBNA should be the initial diagnostic procedure in patients with hylar and/or mediasti-
nal lymphadenopathy, provided that the enlarged nodes are in close con-
tact with the airway wall (Grade B).**

**Granulomatous disorders**

TBNA has been used with satisfactory results in 
patients with clinical suspicion of sarcoidosis or 
mycobacterial infection.

Conventional TBNA has been shown to in-
crease the diagnostic yield of bronchoscopy in the 
setting of sarcoidosis when performed along with 
the other sampling procedures (bronchoaveolar 
lavage, bronchial and transbronchial biopsy) [34-
The diagnostic yield of TBNA was particularly high (>70%) in stage I, whereas less satisfactory and widely variable results have been reported for the method in stage II [34-38]. More recently, a uniformly higher diagnostic yield has been obtained, both in stage I and in stage II, with ultrasound-guided TBNA [39, 40], and this superiority has been confirmed in a randomised trail comparing EBUS-guided versus conventional TBNA [41].

In the last decade, some groups of investigators reported their experience with the use of TBNA and EBUS-TBNA in the diagnosis of mediastinal/hilar lymph node involvement due to mycobacterial disease both in the setting of immunocompetent and immunocompromised patients [42-44].

Bilaceroglu et al. obtained very good results by using a 19-gauge histology needle for diagnosing isolated mediastinal/hilar tuberculosis in a large series of immunocompetent patients [42]. Sensitivity and specificity of the method were 83% and 100% respectively and TBNA was the only means of diagnosis in 68% of patients. Positive culture on TBNA specimens was obtained in 27% of cases. As already observed in the diagnosis and staging of lung cancer, TBNA procedures performed in the right paratracheal and subcarinal areas yielded the best results (91% and 100%, respectively), and the main limit of the method was the unsatisfactory negative predictive value (38%). Hassan et al. obtained excellent results (sensitivity 95%, accuracy 79%) by using EBUS-TBNA in a small series (24 patients) of patients with isolated thoracic tuberculous adenopathy [43]. The only possible problem limiting the generalisation of the results of both these studies is the fact that the authors included a cohort of patients with a high pre-test probability of tuberculosis, selected based on strong tuberculin skin test, high prevalence of symptoms, and originating from a country with a high prevalence of tuberculosis [42, 43].

Harkin et al. reported their experience with TBNA in the diagnosis of mediastinal/hilar adenopathy in patients infected with the acquired immunodeficiency virus [44]. By using a 19-gauge histology needle, the authors were able to diagnose 80% of patients with tuberculosis and 100% of patients with mediastinal lymph node disease due to mycobacteria other than tuberculosis. TBNA was the only means of diagnosis in 48% of cases. Curiously, a positive culture of TBNA specimens was obtained in 61% of cases, a much higher percentage than that usually observed in immunocompetent patients in the same setting [44].

Recommendation

- TBNA or EBUS-TBNA should integrate the standard bronchoscopic sampling procedures in patients with hiliar or mediastinal lymphadenopathy due to suspect sarcoidosis or mycobacterial infection, mainly if endobronchial or parenchymal signs of disease are lacking (Grade B).

b) Central lesions

Lung cancer may present in the central airway with four different patterns of involvement: 1) exophytic mass lesion; 2) submucosal infiltration; 3) peribronchial pattern with extrinsic compression; 4) peribronchial pattern without signs of extrinsic compression.

Importantly, exophytic lesions cause significant mucosal abnormality, whereas submucosal infiltration and, especially, peribronchial lesions may leave the mucosal surface almost intact. Dasgupta and coll. prospectively investigated the diagnostic yield of standard bronchoscopic sampling procedures (bronchial washing, bronchial brushing, endobronchial biopsy) with that obtained with standard procedures plus TBNA [45]. Of the 55 patients with central lung cancer included in the study, 32 had an exophytic mass whereas the remaining 23 patients had either a submucosal pattern or extrinsic compression [45]. The highest yield from any individual bronchoscopic procedure was obtained by TBNA. The combined use of standard bronchoscopic sampling procedures plus TBNA offered a statistically significant advantage as compared to standard procedures alone in patients with submucosal pattern or extrinsic compression (96% vs 65%, p=0.016). The ability of TBNA to penetrate either the submucosal layer or the bronchial wall into the tumour mass is the likely explanation for the above results. In patients with exophytic mass lesion, the combination of standard procedures plus TBNA was also associated with an increase of the diagnostic yield, yet not reaching statistical significance. The extra value of TBNA in exophytic lesions might be explained by its ability to bypass surface necrosis and sample from deep inside the lesion. Moreover, in the specific setting of small cell lung cancer crush artefacts produced during forceps biopsy may be responsible for a non-diagnostic result [45]. The results obtained by Dasgupta et al. have been confirmed in several other studies with similar design [46-48].

More recently, EBUS-TBNA has shown its ability to localise and sample central malignant lesions growing with a peribronchial pattern, yet not compressing the airways [49, 50]. Tournoy et al. performed EBUS-TBNA in 60 patients with peribronchial central lesion, most of whom had had a prior, non diagnostic bronchoscopy. They obtained an 82% sensitivity and could cancel transthoracic needle aspiration in 47% of patients and surgery in 30% of patients [49]. These studies suggest that EBUS-TBNA should be the first-step technique in the diagnostic approach to peribronchial central lung lesions not compressing the airways.

Recommendations

- In the diagnostic approach to a “central” malignant lesion there is indication to TBNA use when the pattern of airway involvement is either submucosal or peribronchial (extrinsic compression) (Grade B).
c) Peripheral lesions

Bronchoscopy in patients with peripheral lung lesions may have both staging and diagnostic purposes. The inspection of the airways allows, in fact, to complete the definition of the “T descriptor” of the TNM staging system, and to rule out the existence of synchronous lesions. As for the diagnosis, the yield of standard bronchoscopic sampling procedures (bronchial washing, bronchial brushing, transbronchial biopsy) in this setting depends on several variables such as size of the lesion, presence/absence of the bronchus sign, use of imaging techniques to guide the sampling [49].

In a recent, systematic literature review, Schreiber analysed the 5 studies (793 patients included) in which TBNA had been performed, under fluoroscopy, along with other bronchoscopic sampling procedures, and he demonstrated that the method was associated with a higher yield (67%) than bronchoalveolar lavage (42%), bronchial brushing (52%), and transbronchial biopsy (46%) [51]. Katis et al. prospectively investigated the diagnostic yield of standard bronchoscopic sampling procedures (bronchial washing, transbronchial biopsy) with that obtained with standard procedures plus TBNA [52]. The yield of TBNA under fluoroscopic guidance was superior to that of bronchial washing (62% vs 24%, p<0.005), bronchial brushing (62% vs 27%, p<0.005), and transbronchial biopsy (62% vs 38%, p<0.005). The combined use of standard bronchoscopic sampling procedures and TBNA offered a statistically significant advantage as compared to standard procedures alone (70% vs 46%, p<0.05).

Interestingly, similar results have been recently reported by Chao et al., who evaluated for the first time, the added value of TBNA guided by endobronchial ultrasound in patients with peripheral pulmonary lesions. The authors, in fact, demonstrated that the sensitivity of TBNA (72%) was higher than that of both transbronchial lung biopsy (50%, p=0.004) and bronchial washing (13.5%, p<0.001).

In conclusion, there is strong evidence in the literature that TBNA improves the diagnostic yield of bronchoscopy in patients with peripheral lesions, whatever the imaging guide [53-56].

Recommendation

- In the diagnostic approach to a “peripheral” lesion there is indication to the use of TBNA, whatever the imaging guide, along with other standard bronchoscopic sampling procedures (Grade B).

Summary of Recommendations

- EBUS-guided TBNA is superior to conventional TBNA mainly in some specific settings, such as difficult mediastinal LN areas (mainly 2, 3, 4L) and small LN size (<1 cm) (Grade A).
- Cytologic material obtained with TBNA should be prepared with the smear (direct) technique (Grade B).
- TBNA or EBUS-TBNA should be performed in every patient with radiological suspicion of lung cancer and mediastinal involvement, provided that the mediastinal staging is crucial for the therapeutic choice (Grade B).
- TBNA or EBUS-TBNA should be the initial diagnostic procedure in patients with hylar and/or mediastinal lymphadenopathy, provided that the enlarged nodes are in close contact with the airway wall (Grade B).
- TBNA or EBUS-TBNA should integrate the standard bronchoscopic sampling procedures in patients with hylar or mediastinal lymphadenopathy due to suspect sarcoidosis or mycobacterial infection, mainly if endobronchial or parenchimal signs of disease are lacking (Grade B).
- In the diagnostic approach to a “central” malignant lesion there is indication to TBNA use when the pattern of airway involvement is either submucosal or peribronchial (extrinsic compression) (Grade B).
- In the diagnostic approach to a “central” malignant lesion there is indication to the use of EBUS-TBNA when the pattern of airway involvement is peribronchial, especially if there is no sign of extrinsic compression (Grade B).
- In the diagnostic approach to a “peripheral” lesion there is indication to the use of TBNA, whatever the imaging guide, along with other standard bronchoscopic sampling procedures (Grade B).

References


