EBUS-TBNA: A high-yield diagnostic procedure for benign and malignant aetiologies

EBUS in combination with EBUS-TBNA has become an essential tool for diagnosing and staging patients with suspected non-small-cell lung cancer (NSCLC), with a diagnostic accuracy superior to more traditional invasive modalities such as mediastinoscopy, and a much better safety profile. It is also employed for sampling mediastinal masses and lymphadenopathy of unclear aetiology (commonly in patients with bilateral hilar adenopathy to distinguish sarcoidosis from TB and lymphoma). But how does this modality perform in a high-burden TB and HIV setting such as sub-Saharan Africa (SSA), where the pre-test probability for NSLC is much lower, and where the incidence of infective (in particular, tuberculous) or lymphoproliferative causes of mediastinal lymphadenopathy or masses may be overrepresented compared with international reports?

In this issue of *AJTCCM* Eknewir *et al.*[1] retrospectively describe their experience from 201 EBUS-TBNA procedures performed over a 2-year period in a large tertiary public sector hospital in Cape Town, South Africa. Unsurprisingly, the authors found that malignant aetiologies (and NSLC, in particular) predominated among positive results, but tuberculosis was also diagnosed in 7% of the cohort. The pooled diagnostic performance of EBUS-TBNA (irrespective of indication, or malignant v. benign diagnosis) – sensitivity, specificity, positive predictive value and negative predictive value of 95.1%, 100%, 100% and 94%, respectively – was at least equal to that reported in a meta-analysis of 14 prospective studies (of which only 2 had a larger sample size than this study and only 1 was from a developing country).[2] All in all, and in these experienced authors' hands, EBUS-TBNA in a SSA setting had the same excellent diagnostic yield as international reports despite a heterogenous case mix of granulomatous (TB and sarcoidosis) and malignant aetiologies.

A few points are worthy of note. Firstly, the volume of EBUS-TBNA procedures performed in the study period was significant even by international standards. The interventional bronchoscopy service at their institution (Tygerberg Hospital) is well established and has experienced operators and rapid on-site cytology available. As the authors note, this very high diagnostic accuracy has not been emulated in a previous report from a lower-volume centre from a public sector hospital in the same city.[3] Secondly, 43% of the study cohort were ultimately diagnosed as having reactive lymphadenopathy ('true negatives'), but information is lacking on the number of additional procedures (PET scans, mediastinoscopies or other invasive thoracic or even extra-thoracic image-guided sampling procedures)[4] required to confirm this, and importantly, on the duration of follow-up to assess progression. The reported diagnostic accuracy of a test is highly dependent on its reference gold standard, and in particular, the rigour with which false negatives are investigated. Without more information on the thoroughness with which diagnoses in these patients with negative EBUS biopsies were pursued, it is unclear with what certainty we can say that these reactive nodes were really true negatives. Although the sensitivity of EBUS-TBNA can reach 99% for diagnosis and staging of thoracic malignancy, it has a significantly high false-negative rate,[5] and we are not told how many patients in the cohort underwent mediastinoscopy or video-associated thoracic surgery. Also, in a population with a high background prevalence of HIV infection, the incidence of HIV-related lymphoma (particularly non-Hodgkin's lymphoma) is likely to be higher, but the diagnostic sensitivity for full evaluation of lymphoma with EBUS-TBNA (even with immunohistochemistry and flow cytometry) is lower than for lung cancer, largely because of the difficulties of confirming the lymphoma subtype from a small specimen.[6] Inferences about the accuracy of the calculated specificity and negative predictive value naturally follow. Lastly, it is not clear whether the inclusion criteria for the study only included EBUS-TBNA for the evaluation of mediastinal and hilar lymphadenopathy, or also for non-lymph-node thoracic lesions (tracheobronchial wall-adjacent large centrally located lesions) – the yield from the latter type of lesion could be expected to be higher than that of an isolated enlarged mediastinal lymph node with no other pulmonary pathology.[7] Specific information about the biopsies themselves (number of passes and calibre of biopsy needle) may also be relevant.

Limitations notwithstanding, this study is an important addition to the local experience on EBUS-TBNA, and the clinical take-home point is that it should be the first-choice investigation for sampling large, centrally located masses and lymphadenopathy in the mediastinum as well as hilar lymph nodes, with excellent 'rule in' accuracy for both malignant and benign disease. The 'rule out' value is dependent on the clinical context and the presence of associated pathology amenable to non-invasive sampling, but the overwhelming majority of surgical diagnostic procedures may be avoided if EBUS-TBNA is employed upfront. Compared to the surgical alternatives, EBUS-TBNA is minimally invasive, generally very safe, and can be performed on an outpatient basis using local anaesthesia and conscious sedation.

G L Calligaro, BSc Hons (Phys), MB ChB, Dip PEC, MMed, FCP Cert (Pulm)
Centre for Lung Infection and Immunity, Division of Pulmonology, Department of Medicine, Groote Schuur Hospital, University of Cape Town Lung Institute, Cape Town, South Africa
greg.calligaro@uct.ac.za

1. Eknewir S, John TJ, Bennji SM, Koegelenberg CFN. The utility of endobronchial ultrasound-guided transbronchial needle aspiration in a community with a high HIV and tuberculosis burden. Afr J Thoracic Crit Care Med 2022;28(1):25-27. https://doi.org/10.7196/AJTCCM.2022.v28i1.156
2. Chandra S, Nehra M, Agarwal D, Mohan A. Diagnostic accuracy of endobronchial ultrasound-guided transbronchial needle biopsy in mediastinal lymphadenopathy: A systematic review and meta-analysis. Resp Care 2012;57(3):384-391. https://doi.org/10.4187/respcare.01274
3. Esmail A, Mottay L, Calligaro G, Laher Z, Symons G, Dheda K. To explore the diagnostic value of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in diagnosing mediastinal lesions in a high-burden TB setting – Cape Town experience. S Afr Resp J 2015;21(2):36-37.
4. Batum Ö, Katgı N, Özdemir Ö, Yılmaz U. Diagnostic efficacy of EBUS-TBNA in benign diseases in a population with a high prevalence of tuberculosis. Diagn Cytopathol 2021;49(3):374-380. https://doi.org/10.1002/dc.24661
5. Tian Q, Chen LA, Wang RT, Yang Z, An Y. The reasons of false negative results of endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of intrapulmonary and mediastinal malignancy. Thorac Cancer 2013;4(2):186-190. https://doi.org/10.1111/1759-7714.12010
6. Steinfort DP, Conron M, Tsui A, et al. Endobronchial ultrasound-guided transbronchial needle aspiration for the evaluation of suspected lymphoma. J Thoracic Oncol 2010;5(6):804-809. https://doi.org/10.1097/jto.0b013e3181d873be
7. Yang H, Zhao H, Garfield DH, Teng J, Han B, Sun J. Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of non-lymph node thoracic lesions. Ann Thorac Med 2013;8(1):14-21. https://doi.org/10.4103/1817-1737.105714

Afr J Thoracic Crit Care Med 2022;28(1):7-8. https://doi.org/10.7196/AJTCCM.2022.v28i1.218