Commentary: Targeted sampling during EBUS: Additional prerequisites for clinical implementation

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Central Message: Targeted sampling was non-inferior to systemic sampling for mediastinal staging in feasibility study.

Central Picture Legend: Kwon Joong Na, Young Tae Kim

Evaluating the mediastinal lymph nodes is crucial for staging and leads to accurate lung cancer treatment plans and prognosis predictions. As computed tomography (CT) and positron emission tomography (PET) have high false-positive rates and relatively low sensitivity and specificity, invasive mediastinal staging plays a vital role in the histologic confirmation of metastasis and ruling out false positives. Currently available lung cancer guidelines by the National Comprehensive Cancer Network, the European Society of Thoracic Surgeons, and the American College of Chest Physicians emphasize the invasive mediastinal staging in some groups of patients who has a high probability of node metastasis.\textsuperscript{1-3} Endoscopic modalities, either endobronchial ultrasound with transbronchial needle aspiration (EBUS-TBNA) or endoscopic ultrasound with fine-needle aspiration technique, have become more popular as they can be performed at lower morbidity, lower cost with acceptable sensitivity and specificity than surgical methods; moreover, they also have superior access to several lymph node stations to mediastinoscopy. Current guidelines recommend systemic sampling (SS) for at least three stations (4R, 4L, and 7) during EBUS-TBNA regardless of their appearances on images and ultrasonographic characteristics. However, several investigators had suggested diagnostic scores for predicting malignancies based on ultrasonographic features.\textsuperscript{4-6} They claimed that these
scoring systems by ultrasonographic assessment could be helpful for clinical decisions. Practically, however, SS is performed below 50% due to the small size of lymph nodes, technical challenges, inadequate samples, and inconclusive results.\textsuperscript{7}

In this edition of the Journal, Sullivan and colleagues\textsuperscript{8} reported a feasibility study evaluating the non-inferiority of targeted sampling (TS) compared to routine SS during EBUS-TBNA. They set progression criteria as recruitment rate (70% minimum), procedure length (no significant increase for TS), and incidence of missed nodal metastasis (below 6%). The recruitment rate was achieved early, and the length for TS was significantly shorter than SS (3.07 minutes vs. 19.07 minutes; \( p < 0.001 \)). In addition, after crossover analysis, 5.45\% of lymph nodes in the TS were upstaged from N0 to N2, but the incidence of missed metastasis was below the threshold.

As far as we know, this is the first randomized study comparing TS versus SS during EBUS-TBNA. Though it was a feasibility study, the result demonstrated the value of TS for invasive mediastinal staging. However, there are several requirements to be considered for worldwide clinical implementation. The ongoing main study with high statistical power may provide solid evidence for the TS in actual clinical practice. The rationale of TS in this study is based on identifying triple normal lymph nodes by CT, PET, and the Canadian Lymph Node Score they proposed in a previous study.\textsuperscript{7} Among them, the ultrasonographic examination has a high dependency on the examiner and the reliability of EBUS-TBNA might significantly affect the quality of TS. Thus, the presence of local expertise with EBUS-TBNA is a crucial prerequisite of the successful implementation of the study result.

Nevertheless, the study’s objective is valid and clinically vital, and therefore we hope the main trial be commenced successfully.
References
