Commentary: Know Your Nodes

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Central Message: Targeted sampling of lymph nodes in suspected early non-small cell lung cancer may offer a more efficient alternative to systematic sampling, but care must be taken to minimize the risk of understaging.

Central Picture Legend:
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Main Text

In this issue of *JTCVS*, Sullivan and colleagues\(^1\) present the results of their prospective, multicenter trial evaluating the non-inferiority of preoperative targeted lymph node sampling (TS) versus systematic mediastinal lymph node sampling (SS) via endobronchial ultrasound (EBUS) among patients with suspected early-stage non-small cell lung cancer (NSCLC) in high-volume endosonography centers. Specifically, these data demonstrate that when radiographic and endosonographic nodal characteristics align appropriately for central lesions or those greater than 2 cm but with clinical N0 or N1 disease, the absolute risk increase of missed preoperative mediastinal nodal metastases (MNM) or upstaging is just 1.56% higher with TS than that achieved with SS. Although these cancers may be found to have pathologic N2-3 disease after resection of the primary tumor and lymph node dissection, the nodal sites responsible for upstaging are rarely accessible in the preoperative setting via EBUS.\(^2\) As such, the bulk of these patients’ tumors carry a very low likelihood of N2-3 disease. The authors then discuss that use of TS rather than SS was associated with shorter EBUS procedural time and lower rates of
nondiagnostic histopathologic samples, supporting an efficient and expeditious diagnosis and presumably moving patients along to optimal treatment.

But, what about those who would be upstaged with SS? Is there a way to more precisely identify those with MNM among those who would otherwise qualify for TS? Additionally, although identifying higher risk lesions for metastasis is helpful in improving overall accuracy, adoption of TS by designated radiographic and endosonographic criteria would likely inappropriately stage a minority of patients who have occult N2 (or higher) disease. The negative implications of this error will potentially be heightened in the future with improved systemic therapies, but currently there are conflicting data regarding the overall survival benefit of neoadjuvant therapy for N2 disease. This is reflected in the practice pattern variation across nations, with the European tradition long pursuing upfront surgery followed by adjuvant systemic therapy. Aside from identifying and excluding higher-risk lesions and considering that a fraction of patients will be understaged with TS, it is also critical to remember that any EBUS-guided biopsy carries operator-dependent false negative rates that will be incurred whether the TS or SS approach is used.

Ultimately, these data suggest that TS is a reasonable option for patients with lesions meeting the criteria designated by Sullivan and colleagues. Caution must be used when applying these data to practice, with care that it enlists the help of an expert endoscopist. Additionally, we as clinicians must continue to evaluate patient and tumor characteristics to identify potential predictors of MNM. While overall survival benefits are currently debatable, N2 disease typically results in pursuit of neoadjuvant therapy prior to resection in the US. We expect this practice pattern to continue, underscoring the need for accurate staging in this patient population.
References


