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Preoperative mediastinal LN staging provides information to predict prognosis and it is a valuable tool to guide the most appropriate treatment in each patient, a matter of great importance in the current era of immunotherapy and targeted therapies [1]. Focusing on those tumors with an intermediate suspicion of N2-3 disease and normal mediastinum by CT/PET, i.e., cN1 tumors and cN0 tumors >3 cm, the rate of unsuspected mediastinal nodal disease ranges from 20% to 42% [2-5] for cN1 tumors, and 6% to 22% [5-7] for those cN0 and >3cm.

The debate continues about which is the best mediastinal staging algorithm for this subgroup of tumors. The American College of Chest Physicians guidelines favors endosonography over surgical procedures as the best first test (level of evidence IIb) [8]. The ESTS guidelines describe that the choice between mediastinoscopy with biopsies, or with pre-surgical lymphadenectomies or endoscopic staging by EBUS-TBNA/EUS-FNA depends on local expertise (level of evidence V) [9]. However, the accuracy of endosonography methods for cN0-1 tumors is low. Two metaanalyses of EBUS-TBNA in cN0-1 NSCLC reported a pooled sensitivity of 49% (95% CI, 41-56) and 49.5% (95% CI, 36.4-62.6), respectively [10,11]. In the results of subgroup analysis conducted by dividing studies into those with only radiological N0 versus N0-1, pooled sensitivities of EBUS-TBNA were similar between the two groups (47% vs. 50%) [10,11].

Transcervical lymphadenectomies represent the most reliable methods for mediastinal staging with sensitivity ranging from 0.85 to 1, and negative predictive value ranging from 0.93 to 0.99 [3,12-14]. Both achieve complete clearance of all mediastinal nodal stations explored (including LNs and surrounding adipose tissue), allowing the identification of nodal disease that is not identified on CT, PET, EBUS-TBNA or mediastinoscopy. Therefore, the ideal indication for these techniques is the staging of tumors without suspicion of N2-3 by PET/CT.

Recently we have analyzed prospectively the performance of VAMLA in a cohort of patients with cN0-1 NSCLC demonstrating a high sensitivity (0.98) and negative predictive value (0.99), and a high rate of unsuspected N2-3 disease (18.8%) in the whole series. The unsuspected N2-3 rates according to presurgical nodal and tumor categories determined by PET/CT were: 3.6% (4/111) in cT1N0; 16.3% (18/110) in cT2N0; 10,25% (4/39) in cT3N0; 32% (7/22) in cT4N0; 42% (39/93) in cN1 [15].

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