Response to: Histological type, invasive mediastinal staging, and prognosis in patients with lung cancer

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With the increase in early-stage lung cancer with strong clinical suspicion, the decision to perform invasive mediastinal nodal staging (IMNS) should be considered from a more practical point of view. The NCCN guidelines recommend upfront surgery with intraoperative tissue confirmation without preoperative tissue biopsy.[1] Hence, in our propensity matching analysis, although retrospective in nature, we aimed to emulate randomized controlled trials without hindsight bias by including only the information known at the time of deciding on the implementation of IMNS in the propensity score.[2,3] Consistently, international guidelines have not considered histologic subtype in the application criteria of IMNS.[4] Indeed, in our cohort, 2522 of 4545 (55%) patients did not undergo preoperative tissue biopsy.

We evaluated the IMNS in the diagnosis of N2 disease according to the histologic subtype. In patients with adenocarcinoma in the IMNS group (N = 501), pathologic N2 disease was identified in 86 patients (17.2%), of which only 34 patients were diagnosed with N2 disease through IMNS. Meanwhile, in patients with squamous cell carcinoma in the IMNS group (N = 304), 24 (7.9%) were found to have pathologic N2 disease, and of these, only 5 (1.6%) were identified through IMNS (Table 1).

Despite age, sex, smoking history, and histologic subtype affecting the frequency of unforeseen N2, IMNS has significant limitations in diagnosing unforeseen N2 regardless of the cell type. Hence, we believe that the histologic type is not a mandatory factor in the decision-making process for IMNS, considering the very low accuracy of IMNS in radiologic N0 case, regardless of the histologic type.[5] However, we believe it is critical to meticulously perform systematic lymph node dissection and, accordingly, appropriate adjuvant treatment should be administered as necessary.

Histologic subtype	IMNS		Non-IMNS		P-value	SMD
	(N = 866)		(N = 866)			
Adenocarcinoma	501 (57.85%)		541 (62.47%)		0.056	−0.0945
N stage	Clinical	Pathologic	Clinical	Pathologic		
N0	455 (90.8%)	358 (71.5%)	534 (98.7%)	423 (78.2%)		
N1	12 (2.4%)	57 (11.4%)	7 (1.3%)	58 (10.7%)		
N2	34 (6.8%)	86 (17.2%)	0	60 (11.1%)		
Squamous cell carcinoma	304 (35.1%)		236 (27.25%)		<0.001	0.1701
N stage	Clinical	Pathologic	Clinical	Pathologic		
N0	280 (92.1%)	199 (65.5%)	225 (95.3%)	167 (70.8%)		
N1	19 (6.3%)	81 (26.6%)	11 (4.7%)	52 (22%)		
N2	5 (1.6%)	24 (7.9%)	0	17 (7.2%)		

IMNS, invasive mediastinal nodal staging; SMD, standardized mean differences. Statistical analyses were conducted using the chi-squared test.

Table 1: **Histologic subtype and N stage in matched pairs.**

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