

# Mediastinal lymph node resection in stage IA non-small cell lung cancer with small nodule: is it mandatory?

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Lung cancer, one of the most popular cancers in the world, is still the leading cause of cancer related death. Until recently, the only proven screening tool for early detection of lung cancer was low-dose computed tomography (LDCT) (1). These days, the detection of small sized nodule or ground-glass opacity (GGO) has increased due to the wide spread of CT screening and enhanced technology.

When treating non-small cell lung cancer (NSCLC), if possible, surgical resection produces the best outcome when compared with other modalities. Since the report by the Lung Cancer Study Group in 1995, lobectomy with mediastinal lymph node sampling (MLNS) or dissection (MLND) has been the standard surgical procedure in patients with resectable NSCLC (2). However, in stage IA lung cancer with small sized nodule, it is challenging to perform a lobectomy with MLNS or MLND. Recent evidence has suggested that sublobar resection, usually a segmentectomy, can be performed in patients with small, peripheral, and node-negative early stage NSCLC without jeopardizing surgical outcomes (3,4). But it has been controversial whether to perform MLNS or MLND during lung resection in these cases.

Although MLNS or MLND during lung resection in stage IA lung cancer with small sized nodule may seem controversial, Okada *et al.* reported that 20 (7%) patients were found to have lymph node metastasis (N1=11 and N2=9) intraoperatively in the prospective non-randomized

trial of sublobar resection of 305 patients with clinical T1 (tumor size <2 cm) N0 NSCLC (5). Furthermore, N2 disease was shown to occur even in pT1 NSCLC. As shown by Defranchi *et al.*, 59 patients (6.1%) were found to have N2 disease at thoracotomy in a study of 968 patients with pT1 NSCLC (6). Similarly in a randomized study of patients with small clinical stage I (<2 cm, T1) NSCLC, Sugi and colleagues found no difference in the survival rate between the MLND and the sampling group, yet the percentage of unsuspected N2 disease identified in the MLND and the sampling group were 12% and 14%, respectively (7). Miller *et al.* investigated the incidence of lymph node metastasis in 100 patients that underwent the resection of NSCLC, which were 1 cm or less, and found that 7 (7%) had lymph node metastasis (N1=5 and N2=2) (8). These findings suggest that systemic lymph node dissection (SLND) should be recommended in clinical stage (c-stage) IA lung cancer with a solid-component tumor.

GGO, now considered as a different pathology than pure solid tumors, presents a different clinical pattern. In previous reports, the incidence of mediastinal lymph node metastasis was extremely low in c-stage I NSCLC cases with GGO-predominant tumor (9,10). Tsutani *et al.* reported that solid tumors exhibited more malignant behavior and had a poorer prognosis compared to subsolid tumors (11). On the contrary, GGO-dominant tumors rarely exhibited pathologic invasiveness, including lymphatic, vascular, or

pleural invasion and lymph node metastasis. In a study with 239 patients with clinical T1N0M0 stage IA lung adenocarcinoma that had GGO components greater than 50%, only two lymph node metastases were found among 84 patients (2.4%) with GGO-dominant T1b tumors, and none were found among the 155 patients with GGO-dominant T1a tumors. The frequency of mediastinal LN metastasis in GGO-dominant tumors was remarkably less compared to that of solid tumors in most cases (12). Haruki *et al.*'s study, which focused on the incidence of lymph node metastasis that occurred in 1,923 consecutive patients who underwent pulmonary resection for lung cancer, revealed significant results. The result showed that the total incidence of mediastinal lymph node metastasis was 9.1%. Surprisingly, there were no cases of hilar and mediastinal lymph node metastasis in GGO-predominant tumors, while there were many cases of unexpected hilar and mediastinal lymph node metastasis in solid-predominant tumors. The study suggested that lobe-specific selective lymph node dissection (LSLND) may be acceptable in GGO-predominant cases. Moreover, hilar and mediastinal LND may even be unnecessary in GGO-predominant lung cancer (13). In a retrospective registry study from Japan with 5,392 patients with c-stage I or II NSCLC, LSLND and SLND were performed in 1,268 patients (23.5%) and 4,124 patients (76.5%), respectively. LSLND did not have a negative prognostic impact and instead was associated with a favorable survival. This suggested that LSLND could be an alternative to SLND for selected patients with c-stage I or II NSCLC (14). In a retrospective study with c-stage IA lung cancer from the database of the diagnosed cases of NSCLC identified as a result of CT screening in the I-ELCAP cohort, the frequency of N2 metastases increased with increasing tumor size. The long-term survival rate in patients with a subsolid tumor was 100%. Among the 404 patients with a solid nodule, 311 with and 93 without MDLD, the survival rate was 87% versus 94%, respectively. Of the 311 patients with a solid tumor who underwent MDLD, 15 (4.8%) had N1 lymph node metastases only and 17 (5.4%) had N2 lymph node metastases. However, among the 151 patients with a subsolid tumor who underwent MDLD, only one patient (0.7%) had mediastinal lymph node metastasis (15).

It may be acceptable to perform lobe-specific selective LND for c-stage IA GGO-predominant tumor instead of systemic LND, or to completely omit mediastinal LND itself in such cases. Systemic LND should be recommended in c-stage IA solid-predominant tumors.

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## Footnote

*Conflicts of Interest:* The author has no conflicts of interest to declare.

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