



Commentary: Expanding the Surgical Indications in Lung Cancer

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Non-small cell lung cancer (NSCLC) with distant metastasis has been regarded as a contraindication for surgical resection, but many papers have reported survival benefits of primary tumor resection in patients with single distant metastasis, such as brain or adrenal metastasis [1]. The Current National Comprehensive Cancer Network guidelines also recommend surgical treatment with therapeutic intent for patients with stage IV NSCLC who have metastasis to the brain or adrenal glands [2]. In addition to single distant metastasis, recent clinical trials have also shown that local consolidative therapy for primary and metastatic lesions (mainly stereotactic body radiotherapy [SBRTx]) could prolong survival in patients with oligometastatic disease [3].

Yoo et al. [4] analyzed 117 patients with oligometastatic NSCLC who underwent complete resection of the primary tumors and concluded that surgical resection of primary lung cancer is a viable treatment option for selected patients with oligometastatic NSCLC in the context of multimodal therapy. Although the authors stated that they analyzed oligometastatic NSCLC patients, only 16 patients (13.6%) showed multiple metastatic lesions (2 or more), whereas 101 patients (86.4%) had single metastatic disease. The survival outcomes of this cohort, therefore, mainly reflect the survival outcomes of single distant metastasis, which have already been published in many papers and are not novel findings. However, an interesting and unique aspect of this paper is that survival was statistically significantly better in patients with positive biomarker tests, such as epidermal growth factor receptor, anaplastic

lymphoma kinase, or ROS1, than in patients with negative biomarker tests. Patients with targetable mutations have additional treatment options, such as tyrosine kinase inhibitors (TKIs) in addition to conventional cytotoxic chemotherapy, and it has already been reported that targeted therapy significantly improved survival in advanced NSCLC [5]. Given that the initial progression of TKI-treated NSCLCs occurs predominantly at the original disease sites [6], the resection of primary lung lesions potentially delays the progression of TKI-treated NSCLCs and improves survival [7].

Even though the authors recommended surgical treatment in patients with oligometastatic NSCLC when targeted therapy is deemed possible, it is difficult to assume that these strategies might be the only viable option for patients with targetable mutations. In recent years, dramatic advances in immunotherapy have taken place. Combination therapy, including surgical resection of primary lung lesions, systemic immunotherapy, and local control for metastatic lesions, also could be a treatment option for advanced NSCLC. Given the complexity of deciding the indications of this maximal treatment, decisions must be made through multi-disciplinary discussions among radiation oncologists, oncologists, pathologists, and thoracic surgeons.

The classical indication of surgical resection in NSCLC is stage I and II disease, and partly in stage III disease. The interest in using local aggressive therapy for oligometastatic NSCLC patients has recently increased, mainly focusing on SBRTx. Surgery should not be excluded in pa-



tients with oligometastatic disease. Surgery has advantages over SBRTx in these clinical situations, such as better local control, improved staging, and tissue acquisition for molecular analysis. Beyond the classical indications, thoracic surgeons must consider performing surgical resection in stage IV and oligometastatic disease in combination with novel systemic therapies. In my opinion, this will be a new way forward for thoracic surgeons in the era of targeted therapy and immunotherapy.

Article information

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References

1. Euhus CJ, Ripley TR, Medina CG. *The role of surgery for oligometastatic non-small cell lung cancer*. *Cancers (Basel)* 2022;14:2524. <https://doi.org/10.3390/cancers14102524>
2. Ettinger DS, Wood DE, Aisner DL, et al. *Non-small cell lung cancer, version 3.2022, NCCN clinical practice guidelines in oncology*. *J Natl Compr Canc Netw* 2022;20:497-530. <https://doi.org/10.6004/jncn.2022.0025>
3. Gomez DR, Blumenschein GR Jr, Lee JJ, et al. *Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study*. *Lancet Oncol* 2016;17:1672-82. [https://doi.org/10.1016/S1470-2045\(16\)30532-0](https://doi.org/10.1016/S1470-2045(16)30532-0)
4. Yoo S, Cho WC, Lee GD, et al. *Long-term surgical outcomes in oligometastatic non-small cell lung cancer: a single-center study*. *J Chest Surg* 2023;56:25-32. <https://doi.org/10.5090/jcs.22.101>
5. Tan AC, Tan DS. *Targeted therapies for lung cancer patients with oncogenic driver molecular alterations*. *J Clin Oncol* 2022;40:611-25. <https://doi.org/10.1200/JCO.21.01626>
6. Al-Halabi H, Sayegh K, Digamurthy SR, et al. *Pattern of failure analysis in metastatic EGFR-mutant lung cancer treated with tyrosine kinase inhibitors to identify candidates for consolidation stereotactic body radiation therapy*. *J Thorac Oncol* 2015;10:1601-7. <https://doi.org/10.1097/JTO.0000000000000648>
7. Park BJ, Shim HS, Lee CY, et al. *Genetic analysis and operative outcomes in patients with oncogene-driven advanced NSCLC treated with cytoreductive surgery as a component of local consolidative therapy*. *Cancers (Basel)* 2021;13:2549. <https://doi.org/10.3390/cancers13112549>