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Commentary: Postrecurrence survival in patients with lung cancer after curative surgery warrants systematic investigation to optimize management strategies

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CENTRAL MESSAGE

Postresection survival in patients with lung cancer may be improved by genomic classification of tumors to separate new primary cancer from recurrence, and systematic postresection surveillance.

In this issue of the *Journal*, the Kyushu Lung Surgery Study Group (KLSS) reported a prospective observational study from 14 institutions on lung cancer recurrence after radical resection and postrecurrence survival (PRS).[1] They analyzed 498 cases of lung cancer recurrence and reported that prognostic factors for PRS included performance status, age, presence of symptoms, interval between surgery and recurrence, number of recurrence foci, and epidermal growth factor receptor status. They concluded that the PRS differed significantly depending on the patient's background characteristics and the initial treatment of disease recurrence.

The 5-year survival after curative intent surgery for non–small cell lung cancer (NSCLC) is 30% to 75% depending on the stage.[2] Between 4.6% and 24% of patients with NSCLC develop locoregional recurrence after resection, with 80% of these occurring within the first 2 years.[3-6] The literature on lung cancer PRS is underexplored, and the KLSS paper is the first reported multicenter prospective observational study.

One limitation of the KLSS study is that disease recurrence was not based on histologic or genetic diagnosis in all cases. Differentiation of recurrence versus a second primary lung cancer in the absence of histologic diagnosis was based on the classic Martini and Melamed[7] criteria. However, it has been shown that in patients with lung cancer who met these criteria for intrapulmonary or hematogenous metastases, using whole-genome sequencing or whole-exosome sequencing to determine the genetic makeup of the tumors, there is a marked absence of shared mutations in individual patient tumors, underscoring the importance of molecular diagnosis.[8,9]

Distinguishing a metachronous second primary lung cancer from recurrence or metastatic disease is important because the prognosis and treatment are very different. In recurrent disease following resection of NSCLC, survival at 2 years for metachronous disease was 51.8%, whereas for local recurrence this was 24.3%, and only 8.9% for non-regional metastases.[10]

Another limitation of this study is the lack of fixed protocols for postresection surveillance and therapeutic strategies. Inevitably, some of the reported findings may be influenced by selection bias. A recent meta-analysis showed that in patients who underwent curative intent resection for NSCLC, using a systematic follow-up strategy significantly increased the likelihood of detection of disease recurrence or second primary lung cancer. These patients are more likely to be asymptomatic and more likely to be candidates for retreatment with curative

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intent, suggesting potential survival benefit. However meta-analysis was not possible when the authors tried to determine whether a greater proportion of curative intent retreatment leads to increased survival, because results could not be combined across studies. Indeed, in the IFCT-0302 trial, the first randomized study of follow-up in resected NSCLC, the addition of computed tomography surveillance failed to show a survival benefit, and the results of a longer follow-up are awaited to assess the potential long-term overall survival benefit of computed tomography surveillance.[11,12]

Despite these limitations, the descriptive study by the KLSS group adds important real-world data to an area of clinical practice where there is uncertainty regarding the optimal management of recurrent NSCLC.

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