Surveillance and the second primary lung cancer: Enhancing our understanding beyond Martini and Melamed

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Computed tomographic (CT) imaging surveillance after lung cancer resection is an important part of survivorship care and allows for the early detection of recurrence or second primary lung cancer. Traditionally, determination of second primary lung cancer has been based on features including histologic type, location, time interval between presentation and initial cancer diagnosis according to criteria published by Martini and Melamed¹ in 1975. Understanding of the differences in outcomes between synchronous primary lung cancer and metachronous primary lung cancer, however, remains suboptimal.

In their study in this issue of the *Journal* focusing on patients undergoing CT surveillance after lung cancer resection, Wang and colleagues² compared imaging characteristics, histology, and long-term outcomes of patients with either synchronous primary lung cancer or metachronous primary lung cancer. They observed that synchronous and metachronous primary lung cancers differed in characteristics of imaging density, growth rate, and interval between identification and diagnosis. Despite these differences, more than 80% of synchronous and metachronous primary lung cancers alike were diagnosed at clinical stage I. This translated to a relatively high percentage of patients (>75%) receiving curative intent therapy by either surgery or stereotactic body radiation therapy. Despite the second primary lung cancer, long-term survival remained high. Five-year second lung cancer survival was 73%, with no significant differences observed between patients with synchronous and metachronous primary lung cancers.

What do the findings derived from this study by Wang and colleagues² tell us? First, CT surveillance in patients undergoing resection of non-small cell lung cancer is critical and can potentially make an impact on long-term survival. As noted by Wang and colleagues,² all patients but one had the second primary lung cancer identified at the

Melanie P. Subramanian, MD (left), and Varun Puri, MD, MSCI (right).

Central Message

CT surveillance plays an important role in identifying key features of second primary lung cancer. When second primary lung cancer is detected early, patients can have good long-term survival.

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asymptomatic stage. Presence of symptoms at the time of diagnosis of recurrence or second primary lung cancer has previously been demonstrated to be associated with detection at later stage and worse overall survival.^{3,4} Whether findings from this study can be generalized to the lung cancer population at large, however, is difficult to say. Wang and colleagues² examined patterns of second primary lung cancer in patients undergoing CT scans at fixed 6-month intervals during the first 2 years. In actual practice, surveillance is much more heterogeneous in both imaging modality and frequency, and adherence to established imaging surveillance guidelines has been documented to be as low as 60%.⁵

Currently, histologic subtyping and molecular profiling serve as important adjuncts to traditional Martini and Melamed criteria (known as modified Martini and Melamed criteria) and enhance our understanding of tumor heterogeneity in second primary lung cancers.⁶ In a study of genomic profiles of 15 synchronous primary lung tumors removed from 6 patients, Liu and associates⁷ found that tumors from the same patient were no more similar to each other than were tumors of different patients. Testing of tumors for mutations genes such as *EGFR*, *KRAS*, or *TP53* has become routine when there is concern of synchronous or metachronous primary lung cancer.⁸ Further advances in surveillance, histologic subtyping, and mutational

analysis can inform the decision-making process and optimize long term outcomes of patients with second primary lung cancer.

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