Commentary: The value of close surveillance after lung cancer surgery: How close absence of evidence is not evidence of absence

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As “the other pandemic,” lung cancer kills more humans worldwide than the other 3 leading cancers combined (breast, colorectal, and prostate). Survival remains dismal, except in early stages when surgical resection is the standard of care, offering a 5-year survival up to 94% for stage I disease. After surgery, however, there are inherent risks of cancer recurrence, either the recurrent initial pulmonary cancer (RIPLC) or a new primary lung cancer (NPLC).

A retrospective study in 2013 described the results of computed tomography (CT) surveillance of 1294 patients who underwent lung cancer resection between 2004 and 2009. On follow-up, 27% redeveloped malignancy (RIPLC in 20% and NPLC in 7%). The risk of RIPLC was 6% to 10% per person year the first 4 years after surgery but decreased to 2% thereafter. The risk of NPLC was 3% to 6% per person year and remained constant over time. In another study, 20,032 patients in the SEER database who survived at least 5 years after lung resection had a 10-year risk of NPLC of 8.36%. To put this risk of recurrence in perspective, the number of lobectomies or pneumonectomies performed for lung cancer in 2012 in the United States was 86,700. By extrapolation, the expected number of RIPLCs (20%) is approximately 17,000 and that of NPLC (7%-8%) is approximately 7000 patients.

Notwithstanding this known risk of redeveloping cancer, few studies have shown any significant benefit from postresection imaging surveillance (PRIS). A meta-analysis in
2011 of 9 comparative studies including 1669 patients, comparing clinical follow-up with scheduled PRIS, showed nonsignificant improved survival in the PRIS group. However, others showed no improvement in overall or disease-free survival from scheduled PRIS compared with simple clinical or even absent follow-up. Likewise, no difference in outcome has been detected on the basis of frequency or modality (positron emission tomography, CT, or x-ray) of PRIS. Despite this, most professional societies recommend CT scan surveillance every 3 to 6 months for the first few years after resection followed by annual studies in perpetuity. These recommendations undoubtedly stem at least in part from lessons learned in lung cancer screening studies. However, it is important to note that surveillance is significantly different from screening. The National Lung Cancer Screening Trial was designed to look for positive findings of new primaries, for example, nodules that are noncalcified, that are greater than 4 mm, that are enlarging in size, or that have changes in attenuation. It did not specifically look for signs of recurrence of lung cancer, which usually include regional adenopathy and distant metastasis.

Heiden and colleagues presented a comprehensive treatise on the current guidelines for PRIS, reviewing the evidence or lack thereof behind them. The article determines that the current recommendations of scanning every 3 to 6 months may be too aggressive and suggests that a more “balanced” protocol of once a year may be sufficient. The article justifies this approach by the lack of effective therapy for most regional or distant recurrences and the lack of proof of any benefit from frequent surveillance.

Regional or distant RIPLC carries a grim prognosis, but there are more therapeutic options today than even a decade ago, including targeted therapy, immunotherapy, hypofractionated radiation, and catheter-based ablation. This makes it difficult to justify intentionally avoiding its early identification by less frequent scanning. It is also difficult to know whether delayed treatment of RIPLC may lead to shorter survival. Obviously, the additional benefit of early diagnosis of NPLC is undeniable. As we have learned from the NLST, CT scanning saves lives in individuals who meet high-risk criteria. Of course, no one is at a higher risk of lung cancer than a patient who has already had one.

Finally, attempting to conduct a long-term randomized study comparing different surveillance modalities and frequencies on a large number of participants and for a long enough period to show a statistical difference is unlikely to ever be attempted or funded. Therefore, although there may be absence of evidence for the value of close PRIS, most physicians instinctively know that this does not mean evidence of absence.

References