Dr Pass. But if you are going to give potentially curative treatment and the patient has recurrence, then you want to see how long that patient is going to live and if he/she is going to die quicker because of later disease, as with symptomatic patients. That may be what you really want to find.

Dr Crabtree. So you're asking me if we went from the time of diagnosis of the recurrence?

Dr Pass. Yes, exactly, how long they live from the time of the diagnosis in each group.

Dr Crabtree. We did a separate analysis on that, which I didn't present, and the survival from the time of diagnosis of recurrence was still similar. Again, it could be a sample size issue.

Dr Pass. The biology of a second primary is a lot different than patients with local or systemic recurrence. You say you broke down the data with regard to CT and CXR for second primaries. Did you do that for patients who had a locoregional or systemic recurrence only?

Dr Crabtree. The truth is, as the Toronto group presented last year, I don't think it matters whether we call it a recurrence or a new primary, as long as the goal of treatment was curative. We did look at recurrences separately, however. The time to diagnosis of recurrences was similar between the cohorts (1.3 vs 1.4 years) and shorter compared with the time to diagnosis of new primary lesions. Also, overall survival was similar for recurrences, although we did not break them down further into systemic versus locoregional.

Dr Joshua Sonett (*New York, NY*). Given the number of patients who were needed for the NLST, I was impressed that you picked up any difference with the asymptomatic and the earlier diagnosis with such a small cohort. Given that, I wouldn't expect you to find a survival difference with such a small cohort.

I have 2 questions. If you are designing a prospective study, how many patients do you think you would need? Think of the large volume with the NLST. Two, given the results of the NLST, which put these patients basically in the high-risk group where we think they are going to have a survival advantage with a CT scan every year, how would you randomize them to not getting a CT scan?

Dr Crabtree. To answer your first question, I think one of the reasons we were able to detect a difference is because we had such a long accrual time and a follow-up time. For a randomized trial, I did a couple of models to look at that. If we use the International Association for the Study of Lung Cancer data, if we looked at specifically IA lung cancers and did a 3-year accrual and 5 years of follow-up, with a 90% power to detect a 20% difference, with approximately 10% attrition rate, we would need approximately 2000 patients in each group. If we specifically did the same parameters for just IIIA disease, then we would need approximately 700 patients in each group with that follow-up time. What was the second question, Dr Sonett?

Dr Sonett. How do you reconcile just getting CXRs when these patients are in the high-risk group for the NLST for surveillance?

Dr Crabtree. This was a retrospective study.

Dr Sonett. No, if you did a prospective study.

Dr Crabtree. If we did, I think we would have a discussion and would likely be looking at examining different types of CT scan, whether it be low-dose or contrast CT or even, again, the consideration of PET-CT for more advanced-stage disease. I suspect it would be hard to find enough surgeons who would agree on performing a CXR in a randomized study.

EDITORIAL COMMENTARY

Lung cancer survivors need lung cancer screening

Raja M. Flores, MD

See related article on pages 45-53.

Surveillance of patients with lung cancer after curative resection is essentially just screening for lung cancer. The success of screening relies on identifying early disease

and implementing curative surgery. A critical element of successful screening is the proper identification of a high-risk group. What better group than those who have already had lung cancer? A computed tomography (CT) screening program evaluating 20 year-old nonsmokers for lung cancer would clearly result in failure because the incidence of disease in this patient population is close to zero. The National Lung Screening Trial (NLST) clearly identified a group of smokers at a high enough risk of developing lung cancer to demonstrate a mortality reduction when CT screening was followed by early surgical intervention.¹ The trial included 33 different sites across the nation and cost more than US\$250 million to conduct. The outcome of the trial proved that treatment of smaller, earlier stage tumors resulted in a better cure rate than larger, later stage tumors. We do not need to spend resources on another randomized

From the Department of Thoracic Surgery, Mount Sinai Health System, Icahn School of Medicine at Mount Sinai, New York, NY.

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Address for reprints: Raja M. Flores, MD, Department of Thoracic Surgery, Mount Sinai Health System, One Gustave L. Levy Place, Box 1023, New York, NY 10029 (E-mail: raja.flores@mountsinai.org).

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controlled trial to study surveillance. We need a common sense approach to extrapolate lessons from screening studies of smokers and apply them to screen patients who have had lung cancer.

Despite widespread emphasis on practicing evidence-based medicine, the reality is that most medical and surgical practice is based on common sense and not clinical trials. A thoracic surgeon does not need a randomized controlled trial to know when to ligate bleeding arteries, secure an airway, or relieve a tension pneumothorax. In fact, the foundation of lung cancer treatment, surgical resection, is not based on a clinical trial.

Crabtree and colleagues² have performed an interesting study evaluating surveillance after curative resection for lung cancer. Despite the inherent limitations and biases of this retrospective study, it brings to light many important practical issues and highlights the single most important question in its title: does early detection lead to improved survival?

This question was recently unequivocally answered with a 'yes' with regard to lung cancer screening by the NLST. Crabtree and colleagues² show that lung cancer CT screening results in earlier detection of second primary cancers than chest radiography (CXR). The major weakness in their report is that they do not report the comparative stages of the second primaries in the CXR and CT groups as demonstrated by the NLST in Table 1. This stage shift from later to earlier stage tumors during the 2-year screening period was central to yielding the survival difference demonstrated in the CT versus CXR arms in the NLST trial.² The NLST trial detected more than 1000 cancers in 53,000 screened patients to demonstrate a statistically significant difference in survival of 20% between the CT scan and CXR arms. This difference was large enough to halt the trial prematurely at about 6 years. This survival difference was primarily the result of performing surgery on smaller, earlier stage tumors. Compare this number of patients with 554 in the Crabtree study, which yielded 36 new primary lung cancers. Clearly, the Crabtree study is severely underpowered, which the authors have explicitly acknowledged. But stage shift is the key to successful screening as demonstrated by both the NLST and I-ELCAP (International Early Lung Cancer Action Project) studies.^{3,4} The power of a study to prove or disprove survival differences is irrelevant if stage shift cannot be achieved. If stage shift is demonstrated, improved curability will follow.

Many areas of surveillance require further investigation. Patients who have had curative surgery for lung

TABLE 1. Stage shift from the National Lung Screening Trial before and after the 2-year screening period

Stage	% Stage during 2-year screening period (n = 649)	% Stage after 2-year screening period (n = 367)
I + II	70	37
III + IV	30	63

cancer are at the highest risk of developing a new lung cancer. The current staging system is based on enormous databases and views second primaries as distinct tumors benefitting from curative resection. The role of tumor biology, recurrent disease, and potential harms of surveillance require close examination of gathered data, but we do not need a randomized controlled trial to study these topics. We can extrapolate about tumor biology, for example, by observing that small cell lung cancer is much more curable in a screening setting than in the general population.^{3,4} The role of histologic differences and genetic influences on tumor recurrence should be evaluated in the laboratory. We can learn about the risk of unnecessary intervention in surveillance programs from previous studies of lung cancer screening risks.⁴ We do not need to prove survival differences again. We just need fine tuning.

We must not reinvent the wheel and spend valuable resources on questions that have already been answered or are answerable based on data available right now. We should try to extrapolate all we can from the highly powered NLST trial, I-ELCAP, and other screening studies by applying common sense. The problem: "Common sense ain't too common."

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