Lung Cancer Screening: The Last 10 Years

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For decades, experts advocated early detection of common cancers to improve chances for long-term survival and cure. Breast, colon, and prostate cancers all have established screening programs that are covered by insurers, embraced by physicians and the public, (generally) endorsed by professional societies and policy-makers, and, though not always without controversy, touted as critical public health measures as the health care system in the United States strives to prevent rather than treat disease. Yet, in the midst of this enthusiasm for early diagnosis, lung cancer has floundered with no approved, endorsed, or supported screening modality, despite the fact that it causes more cancer-related deaths than breast, colon, and prostate cancers combined.

Of course, lung cancer screening has been behind screening for other types of cancer for good reasons: concerns about the adverse unintended consequences of screening, including radiation exposure, false-positive diagnoses with unnecessary testing and surgery, and the potential lack of true patient benefit due to lead-time and overdiagnosis bias. Yet many people have asked troubling questions about the prolonged lack of support for lung cancer early diagnosis, and some suggest that patients with lung cancer may suffer from public and policy-maker bias that their disease may be “self-inflicted.” Further, the demographics of patients with lung cancer (older, lower socioeconomic status) may undermine advocacy for diagnosis and treatment advances.

This concern appears to be supported by a comparison of national research funding. Breast cancer receives more than 3 times as much NIH research funding as lung cancer. And the adverse consequences of screening are not unique to lung cancer. The risk of false-positive results and a significant incidence of additional testing and invasive procedures are shared with breast cancer screening, and the problem of overdiagnosis bias in prostate cancer screening far outpaces the same concern in patients at risk for lung cancer. So one may become cynical about the historical lack of support for lung cancer screening and wonder whether politics, rather than insufficient evidence, is the reason for withholding the opportunity for early diagnosis from patients at risk for lung cancer.

We are at the beginning of a new and exciting era for patients with lung cancer. The NCI provided funding for the National Lung Screening Trial (NLST), a randomized trial comparing low-dose CT (LDCT) with chest radiography for patients at risk for lung cancer. More than 53,000 patients were randomized, and LDCT resulted in a 20% reduction in lung cancer mortality and a 7% reduction in all-cause mortality.1 Clearly, this is a major advance for patients at risk for lung cancer and will mean a major policy change by payers, policy-makers, guidelines groups, and patient advocates. This enthusiasm, however, although deserved, must be tempered with caution. Another view of the NLST data reveals that 320 individuals must undergo screening for each lung cancer death avoided; many patients will be exposed to the emotional and physical risks of lung cancer screening to achieve the desired benefit. A careful, measured approach is important for the institution of lung cancer screening nationwide.

The NLST enrolled only patients at high risk of lung cancer. Although it would be naïve and narrow-minded to not recognize that additional patients outside the NLST criteria may have a substantial risk for lung cancer, we must be very cautious in extrapolating the NLST results to other patient populations. We must also recognize the unintended consequences of screening these patients. Second, the NLST centers included only programs with substantial experience and resources in radiology, pulmonary medicine, thoracic surgery, and pathology, along with a disciplined and multidisciplinary approach to nodule management.
In the NLST, 96% of lung nodules found were ultimately determined to be false-positives, and 24% of patients had at least one positive result during the study. A highly organized and disciplined approach to management is the only way to mitigate potential harm to patients caused by excessive and unnecessary testing and the morbidity of invasive procedures. The margin between net benefit and net harm in lung cancer screening is likely small, and the benefit to patients could easily be lost if a higher percentage of patients with false-positive findings undergo unnecessary workup and invasive testing.

Successful implementation of lung cancer screening will require:

• Pragmatic and thoughtful guidelines that define patients eligible for screening (not limited to NLST criteria but reasonably narrow in scope);
• Experienced radiologists to interpret screening studies and minimize false-positive results;
• A predetermined protocol for the management of screen-detected nodules;
• Diagnostic and therapeutic surgical procedures performed by board certified thoracic surgeons to optimize staging and minimize morbidity; and
• Experienced multidisciplinary oncology management with thoracic surgery and medical and radiation oncology to optimize oncology treatment and outcomes.

The development of lung cancer screening guidelines is underway, with the first published by NCCN in October 2011. The NCCN has a robust history and experience in the development of cancer guidelines, and assembled a panel of 26 professionals representing thoracic surgery, radiology, pulmonary medicine, medical oncology, epidemiology, pathology, internal medicine, and patient advocacy who worked together for 24 months to produce the first lung cancer screening guidelines developed after the NLST. Most notable in the NCCN Guidelines is the extrapolation of high-risk patients beyond the inclusion criteria of the NLST to include patients aged 50 to 54 years (NLST included only ages 55–74 years) and patients with a greater than 20 pack-year smoking history (NLST required >30 pack-years) if they had another lung cancer risk factor (chronic obstructive pulmonary disease, pulmonary fibrosis, radon or occupational exposure, cancer history, or family history). NCCN also recommended a highly systematized protocol to the follow up, workup, and invasive testing of positive findings, similar to those recommended by the Fleischner Society and others.

The biggest challenge in lung cancer screening is the thoughtful management of screen-detected nodules, most of which are benign. Several variations in the management of screen-detected lung nodules exist among recommendations proposed by the Fleischner Society, International Early Lung Cancer Action Program (I-ELCAP), NLST, Nederlands Leuvens Longkanker Screenings Onderzoek (NELSON) Trial, and specific recommendations regarding nonsolid nodules by Godoy et al. NCCN Lung Screening Panel has amalgamated these recommendations into a pragmatic algorithm for nodule management. NCCN recommendations are less aggressive than the I-ELCAP for the workup of baseline, new solid, and part-solid nodules less than 6 mm. NCCN recommendations are also slightly different in recommending a contrast-enhanced CT or PET scan in the evaluation of solid or part-solid nodules greater than 8 mm. Finally, NCCN defined nodule growth as either an increase in mean diameter of 2 mm or more for nodules smaller than 15 mm or in the solid portion of a part-solid nodule, or an increase of 15% or greater in mean diameter for nodules larger than 15 mm.

This definition of nodule growth is simplified compared with I-ELCAP, and should result in fewer false-positive results than seen in the NLST. Notably, surveys of compliance with the Fleischner Society guidelines have shown only 35% to 60% compliance by members of the Radiologic Society of North America and 27% compliance by members of the Society of Thoracic Radiology, with an overall trend toward overmanagement. The successful application of screening programs will
require an algorithmic and disciplined approach to nodule workup and follow up to minimize the serious potential harms from excessive and invasive testing in patients undergoing screening.

Once a nodule has been identified, the involvement of an experienced thoracic surgeon will help the multidisciplinary team refine a strategy for further workup, including biopsy or resection. The Lung Cancer Early Detection and Prevention Clinic at the University of Washington incorporates a “nodule board,” consisting of experts in thoracic radiology, pulmonary medicine, and thoracic surgery. This group reviews clinical details and imaging and develops a management plan based on a treatment algorithm and informed by the combined expertise of the involved specialists.

The NCCN Non–Small Cell Lung Cancer Panel now recommends assessment and management of presumed or proven lung cancer by “board certified thoracic surgeons who perform lung cancer surgery as a prominent part of their practice.” This recommendation is based on data showing that as much as 50% of lung cancer surgery in the United States continues to be performed by general surgeons and that surgical outcomes (morbidity and mortality) and oncology outcomes (correct staging, extent of resection, cancer survival) are better when performed by specialists in thoracic surgery. Non-specialist surgery confers multiple potential adverse consequences, which are even more profound for recipients of lung cancer screening: unnecessary surgery in cases in which follow up or other diagnostic testing may have been preferred, inadequate staging before or during lung cancer surgery, underuse of minimally invasive surgery for both diagnostic and resection procedures, and lack of advanced techniques (segmentectomy, sleeve resection) to minimize the extent of pulmonary resection.

Specialist thoracic surgeons working in a multidisciplinary lung cancer team are best equipped to maximize the benefit of early detection. They are an important part of avoiding the adverse consequences of unnecessary procedures or substandard cancer outcomes that could potentially result in more harm than good from lung cancer screening programs applied without adherence to guidelines and necessary professional expertise.

References