Controversies in Lung Cancer Screening

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Abstract

There remains an extensive debate over lung cancer screening, with lobbying for and against screening for very compelling reasons. The National Lung Screening Trial, International Early Lung Cancer Program, and other major screening studies favor screening with low-dose CT scans and have shown a reduction in lung cancer–specific mortality. The increasing incidence of lung cancer and the dismal survival rate for advanced disease despite improved multimodality therapy have sparked an interest in the implementation of national lung cancer screening. Concerns over imaging workflow, radiation dose, management of small nodules, overdiagnosis bias, lead-time and length-time bias, emerging new technologies, and cost-effectiveness continue to be debated. The authors address each of these issues as they relate to radiologic practice.

Key Words: Lung cancer, lung cancer screening, low-dose CT, CT scan, overdiagnosis bias, tumor volume doubling time

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INTRODUCTION

Lung cancer is the second most common cancer in the United States, accounting for 14% of all newly diagnosed cancers [1]. It is estimated that in 2013, there will be about 228,190 new cases of lung cancer (118,080 in men and 110,110 in women) and 159,480 deaths from lung cancer (87,260 in men and 72,220 in women), accounting for about 27% of all cancer-related deaths in the United States [1,2]. Untreated early-stage lung cancer continues to have dismal 5-year to 10-year mortality, with 80% to 100% of victims succumbing to the disease. Surgically treated early-stage lung cancer, on the other hand, has been associated with improved survival and potential cure, with a reported 10-year survival of 88% in the International Early Lung Cancer Action Project study [3-5]. At present, more than 50% to 60% of lung cancer cases are diagnosed in advanced stages, without screening, thus incurring significant treatment-related costs with little or no survival benefit. Collectively, these observations make a strong case for screening and early diagnosis. Recently the US Preventive Task Force issued a grade B (indicating high certainty for moderate benefit or moderate certainty for moderate to substantial benefit) for CT screening for lung cancer for individuals at high risk. This recommendation, if approved in final form, will pave the way for Medicare and insurance coverage [6].

Lung cancer screening (LCS) is best defined as an evidence-based "process," not just a single CT scan or a series of scans over a specified time period. Further bolstering this evidence-based process is the National Lung Screening Trial, a randomized multicenter study comparing low-dose CT (LDCT) with chest radiography in the screening of older current and former heavy smokers. The National Lung Screening Trial reported 20% improved lung cancer–specific mortality through the use of LDCT in an at-risk population [7]. The International Early Lung Cancer Action Project also demonstrated striking improvement in early-stage detection of lung cancer with LDCT screening [8,9]. Despite these large clinical trials demonstrating improved patient outcomes, opponents continue to question the cost-effectiveness of LCS [10-13], with lingering questions about who should be screened, when, where, and with what frequency. In this article, we discuss the continuing controversies in LCS as they relate to radiologic practices, including imaging workflow, radiation dose, management of small nodules, over diagnosis bias, lead-time and length-time bias, new emerging technologies, and cost-effectiveness.

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IMAGING WORKFLOW

From a radiologist's perspective, the most important issue is the anticipated increase in workload and evaluation of large-volume imaging data sets affecting daily workflow if LCS is to be implemented. Several larger academic centers previously were sites for the National Lung Screening Trial and the International Early Lung Cancer Action Project and may be equipped with the infrastructure needed for handling LCS. However, it is debated that the population at highest risk is best evaluated at the community center level. Regardless of where screening is implemented, it is anticipated that there will be an increase in imaging scans, thus contributing to the daily workload of radiologists and potentially requiring the hiring of additional full-time faculty support staff members and patient navigators. At this time, the following workflow issues remain unresolved: (1) the expected increase in the number of scans per day, (2) the rate and slope of increase, and (3) how to incorporate the additional examinations into the daily workflow. There are other hurdles, such as issues with imaging protocols, reliable and reproducible nodule measurement tools, and the use of volumetric measurements to assess tumor-doubling times [14-19]. Technological innovations and standardization of LDCT protocols have enabled the generation of data sets that can be compared across scanners and institutions, thus making the implementation of LCS a feasible option. Improved computer-aided detection software and postprocessing techniques further help with workflow issues by quantifying information and serving as aides to interpreting radiologists [17]. However, the increasing trend to have thin-section data included in the routine imaging protocols both for interpretation and postprocessing often results in vast data sets that far outstrip radiologists' ability to view, digest, and interpret modern medical images using traditional methods and may require a paradigm shift to perhaps a more quantitative process [20].

For screening to be made available to the populations most at risk, community practices may be the most optimal sites to offer LCS, rather than large tertiary or academic centers. To equip community radiologists with the armamentarium necessary for successful screening programs, an extensive educational and training endeavor needs to be launched. Academic centers should serve as a backbone for the community and lead the educational and training effort and serve as extenders of resources and infrastructure. This would require a detailed survey of the multidisciplinary team of physicians at the community centers by the affiliated tertiary or academic center, the creation of educational material, and training and accreditation. Additional support for consults and referrals will improve compliance with the process and outcomes.

When we compare LCS with breast cancer screening, one of the greatest shortcomings is the lack of consensus and uniformity on descriptive terminology in reporting CT scans despite the availability of the Fleischner Society lexicon and the pulmonary nodule guidelines. There remains a need to develop standardized and structured reporting for LDCT consistent with these guidelines [21]. The ultimate solution may be the development and standardization of a "LUNG-RADS" lexicon to address the clinical significance of screening findings similar to the BI-RADS® lexicon for breast cancer screening.

RADIATION DOSE

Controversies regarding patient radiation dose have steadily decreased since the release of the American Association of Physicists in Medicine statement that CT scans are an important diagnostic tool when used appropriately and also in large measure because of technological advances such as iterative reconstruction that allow a significant decrease in the radiation dose from each CT scan [21]. However, the recent promulgation of screening guidelines calling for $\geq$20 years of annual LDCT for high-risk individuals has rekindled this controversy, with a debate on whether cumulative radiation dose may also need to be considered in the risk-benefit calculation. Currently concerns exist regarding the overuse of CT scans for diagnostic purposes and a need to document the cumulative radiation dose per patient and the logistics of obtaining and propagating this information as patients move among practices and geographic locations. In response, radiologists should continue to have a full commitment to keeping ionizing radiation dose as low as reasonably achievable, in keeping with the Image Wisely® and Image Gently® initiatives. At the level of the individual LDCT study, this demands strict adherence to a scanning range limited to the thorax only and the optimization of imaging protocols. On a population basis, this requires continuing data analyses to stratify the risk for lung cancer. Risk assessment and data collection must be made central to the practice of LCS. The potential risk for radiation-induced cancer from the accumulation of repeat scans and additional imaging tests continues to be undefined and remains a controversy.

MANAGEMENT OF SMALL NODULES

Negative CT results are the best-case scenario for patients and radiologists, but this is unrealistic in the high-risk