Screening for Lung Cancer: For Patients at Increased Risk for Lung Cancer, It Works

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Screening for lung cancer is not currently recommended, even in persons at high risk for this condition. Most patients with lung cancer present with symptomatic disease that is usually at an incurable, advanced stage. The recently reported NLST (National Lung Screening Trial) showed a 20% decrease in deaths from lung cancer in high-risk persons undergoing screening with low-dose computed tomography of the chest compared with chest radiography.

The high-risk group included in the trial comprised asymptomatic persons aged 55 to 74 years, with smoking history of at least 30 pack-years. Screening with low-dose computed tomography detected more cases of early-stage lung cancer and fewer cases of advanced-stage cancer, confirming that screening has shifted the stage of cancer at diagnosis and provides more persons with the opportunity for curative treatment. Although computed tomography screening has risks and limitations, the 20% decrease in deaths is the single most dramatic decrease ever reported for deaths from lung cancer, with the possible exception of smoking cessation. Physicians should offer computed tomography screening for lung cancer to patients who fit the high-risk profile defined in the NLST.

A 62-year-old woman with a history of well-controlled hypertension presents for routine follow-up. She is asymptomatic and feels well. She has jogged 3 miles 3 times weekly for years, with no recent change in exercise tolerance. She has a 30–pack-year history of cigarette smoking but stopped 10 years ago. There is no personal or family history of cancer.

Physical examination is normal. She read a recent study that found a benefit to screening for lung cancer with computed tomography and inquires whether you think screening is appropriate for her. What should you recommend?

Would we recommend that a 62-year-old woman with a 30–pack-year history of smoking undergo screening for lung cancer with low-dose computed tomography (LDCT)? Yes, but we would also discuss the potential risks and limitations as well as the potential benefits of screening before scheduling the test. If the patient currently smoked, we would strongly recommend a smoking cessation consultation and schedule it before or concurrent with LDCT (1). Smoking cessation significantly reduces the risk for lung cancer over time (2).

Most persons with lung cancer present with symptomatic disease at an advanced stage (stage III or IV) and at that point have little chance of curative treatment (3). Only 15% of patients with lung cancer in the United States are diagnosed with early-stage (stage I or II) disease, which is usually discovered incidentally on chest imaging studies done for other reasons (3, 4). Five-year survival with localized (early-stage) disease is 50% but only 4% in those with distant (stage IV) disease (3).

The NLST (National Lung Screening Trial) was a randomized, controlled trial of LDCT versus chest radiography screening in persons at high risk for lung cancer (5). High-risk persons were defined as being 55 to 74 years of age; having a smoking history of at least 30 pack-years; and, in former smokers, having quit smoking in the past 15 years. Participants received baseline and annual screening for 2 additional years and were followed for a median of 6.5 years. The patient framing our discussion meets the eligibility criteria for the NLST.

In the CT group of the NLST, 63% of cases of lung cancer diagnosed from a positive finding on a screening test were stage I and 70% were stage I or II (early stage). In 92.5% of cases, stage I lung cancer was treated with surgery (5). Treatment of stage I lung cancer offers the best chance of cure, with a 5-year survival rate of 70% to 80% (6). In the NLST, the LDCT group had fewer cases of stage IV cancer than did the chest radiography group at the second and third rounds of screening. These data show that, compared with chest radiography, screening with LDCT can shift the diagnosis of cancer from advanced- to early-stage disease and provide a better opportunity for curative treatment.

Screening with LDCT showed a 20% decrease in lung cancer deaths compared with chest radiography. To date, screening with chest radiography has not been shown to be superior to no screening. Patients who choose CT screening must understand that screening will diminish but not eliminate their chance of death due to lung cancer.

In the CT screening group, 356 deaths from lung cancer occurred (247 per 100 000 person-years) compared with 443 deaths (309 per 100 000 person-years) in the chest radiography group. This 20% decrease in lung cancer deaths is arguably the single greatest advance in decreasing lung cancer deaths ever reported, with the possible exception of smoking cessation (2).

The NLST also demonstrated an all-cause mortality reduction of 6.7%, although this predominantly resulted from reducing deaths from lung cancer. Lung cancer caused 60% of the 121 excess deaths in the chest radiography group (5).

Screening for lung cancer has been shown to be a “teachable moment” for smoking cessation. Quit rates of smokers participating in screening trials have exceeded the
Each component contributed to the accuracy of the model. The risk model had good accuracy with an area under the receiver-operating characteristic curve for predicting lung cancer of 0.805. When the model was used in an external validation sample, the area under the receiver-operating characteristic curve was 0.784 for predicting the 9-year risk for lung cancer. This model does not work well for predicting risk in never-smokers.

Refinement of future models may include the presence or absence of genetic susceptibility variants for lung cancer (18–22). Extensive investigation is under way for serum biomarkers associated with lung cancer that are also likely to improve risk models (23–26). Measured pulmonary function data compared with a history of chronic obstructive pulmonary disease also will further augment risk prediction models (27–29).

In summary, we recommend LDCT screening for this patient at high risk for lung cancer to decrease her risk for death from this condition. Medicare and insurance companies presently do not reimburse patients for LDCT screening, but this decision is likely to change on the basis of the NLST results. The positive trial results strongly advocate that physicians discuss CT screening with patients who fit the risk profile of those in the NLST.

Screening should be done when desired by an informed patient only in a center with expertise in interpreting imaging studies, evaluating lung nodules, and diagnosing and treating lung cancer. We do not recommend that CT screening be done at the neighborhood shopping mall or medical facility without the appropriate expertise to pursue the results and maximize the benefits of this testing (30, 31).

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4% background quit rate per year in smokers. The 1-year quit rate for smokers in CT screening trials varies from 12% to 20% (7–9). To date, studies have not shown an increased smoking rate in persons with negative screening results and indicate that participants are not using negative findings to rationalize continuing or resuming smoking.

The lay media and opponents of screening have emphasized the risk for cancer from medical imaging studies but have routinely failed to quantify real risk. The radiation dose associated with CT screening of the chest is generally less than 2 mSv, whereas the dose of standard non–contrast-enhanced chest CT is 7 mSv (10).

Investigations of the NLST have estimated that the risk for radiation exposure from LDCT screening in 55-year-old smokers is 1 to 3 deaths from lung cancer per 10 000 persons screened and 0.3 new cases of breast cancer per 10 000 women screened. The cumulative mortality reduction in the NLST was 30 cases of lung cancer per 10 000 persons screened. The benefit–risk ratio clearly demonstrates benefit (5, 11, 12). The American College of Radiology and the Radiological Society of North America have rated the additional lifetime risk for fatal cancer from LDCT as “very low” (1 per 10 000 to 1 per 100 000 persons) (www.radiologyinfo.org).

If results from the initial LDCT are negative, should this 65-year-old former smoker have additional yearly LDCT screening, and if so, for how long? The NLST participants underwent 3 yearly CTs. The 3 rounds of screening did not demonstrate a substantial decrease in the cases of lung cancer per year (270, 168, and 211, respectively). An additional 367 cases of lung cancer were detected in the CT group in the 5-year follow-up after the initial 3 years of screening. The cumulative rate of new cases and deaths from lung cancer did not decrease during the 8 years of observation after participants were randomly assigned to the CT or chest radiography screening group (5). Therefore, the NLST data support yearly screening for at least 3 to 5 years; perhaps by that time, new information will be available to guide decisions on the length and frequency of screening.

We recommend LDCT screening for this high-risk patient on the basis of age and smoking history alone. In the future, we are likely to use a risk prediction algorithm to better assess individual likelihood of developing lung cancer.

Persons at higher risk are more likely to benefit from screening. Current risk prediction models are approximately 70% accurate (13–15). A risk model recently developed on the basis of the PLCO (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial) accounts for the age, education level, body mass index, family history of lung cancer in first-degree relatives, history of chronic obstructive pulmonary disease, recent history of chest radiography, smoking status (current or former), pack-years smoked, and smoking duration (16, 17).
In the Balance | Screening for Lung Cancer: It Works


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