Lung Cancer Screening

Recommendation Statement

U.S. Preventive Services Task Force

This statement summarizes the current U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer and the supporting scientific evidence, and updates the 1996 recommendations contained in the *Guide to Clinical Preventive Services, Second Edition: Periodic Updates*.[1] In 1996, the USPSTF recommended against screening for lung cancer (a "D" recommendation). The Task Force now uses an explicit process in which the balance of benefits and harms is determined exclusively by the quality and magnitude of the evidence. As a result, current letter grades are based on different criteria than those in 1996. Explanations of the ratings and of the strength of overall evidence are given in Appendix A and in Appendix B, respectively. The complete information on which this statement is based, including evidence tables and references, is available in the summary of the evidence[2] and in the Systematic Evidence Review[3] on this topic, available through the USPSTF Web site (www.preventiveservices.ahrq.gov) and through the National Guideline Clearinghouse™ (www.guideline.gov). The summary of the evidence and the recommendation statement are also available through the Agency for Healthcare Research and Quality (AHRQ) Publications Clearinghouse in print through subscription to the *Guide to Clinical Preventive Services, Third Edition: Periodic Updates*. To order, contact the Clearinghouse at 1-800-358-9295, or e-mail ahrqpubs@ahrq.gov.

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Summary of Recommendation

The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for or against screening asymptomatic persons for lung cancer with either low dose computerized tomography (LDCT), chest x-ray (CXR), sputum cytology, or a combination of these tests. **I recommendation.**

The USPSTF found fair evidence that screening with LDCT, CXR, or sputum cytology can detect lung cancer at an earlier stage than lung cancer would be detected in an unscreened population; however, the USPSTF found poor evidence that any screening strategy for lung cancer decreases mortality. Because of the invasive nature of diagnostic testing and the possibility of a high number of false-positive tests in certain populations, there is potential for significant harms from screening. Therefore, the USPSTF could not determine the balance between the benefits and harms of screening for lung cancer.

Clinical Considerations

- The benefit of screening for lung cancer has not been established in any group, including asymptomatic high-risk populations such as older smokers. The balance of harms and benefits becomes increasingly unfavorable for persons at lower risk, such as nonsmokers.
- The sensitivity of LDCT for detecting lung cancer is 4 times greater than the sensitivity of CXR. However, LDCT is also associated with a greater number of false-positive results, more radiation exposure, and increased costs compared with CXR.

Corresponding Author: Ned Calonge, MD, MPH, Chair, U.S. Preventive Services Task Force, c/o Program Director, USPSTF, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, e-mail: uspstf@ahrq.gov.

- Because of the high rate of false-positive results, many patients will undergo invasive diagnostic procedures as a result of lung cancer screening. Although the morbidity and mortality rates from these procedures in asymptomatic individuals are not available, mortality rates due to complications from surgical interventions in symptomatic patients reportedly range from 1.3% to 11.6%; morbidity rates range from 8.8% to 44%, with higher rates associated with larger resections.
- Other potential harms of screening are potential anxiety and concern as a result of false-positive tests, as well as possible false reassurance because of false-negative results. However, these harms have not been adequately studied.

Discussion

Lung cancer is the second leading cancer in the United States and the leading cause of cancer-related death among men and women. In 2003, approximately 157,200 lung cancer-associated deaths were predicted in the United States.[4] Incidence of lung cancer increases with age.[5] Although cigarette smoking is the major risk factor for lung cancer,[6] other risk factors include family history, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, environmental radon exposure, passive smoking, asbestos exposure, and certain occupational exposures.[3] For a given amount of tobacco exposure, some studies suggest that women are at higher risk for developing lung cancer than men.[7] Women tend to develop adenocarcinoma of the lung disproportionately to men,[8] and adenocarcinoma tends to occur peripherally, making it more readily visible on radiography. Lung cancer has a poor prognosis; even with advances in therapy, average 5-year survival rates are less than 15% for all those with lung cancer.[4] Five-year survival ranges from 70% for patients with Stage I disease to less than 5% for those with Stage IV disease.[9]

The USPSTF examined the evidence for the accuracy of screening tests for lung cancer (CXR, with or without sputum cytology, and LDCT) in the general population as well as in the high-risk population. The sensitivity and specificity of CXR for diagnosing lung cancer are 26% and 93%, respectively, with a positive predictive value of an abnormal CXR of 10% (estimates based on LDCT as the gold standard).[10] The false-positive rate of LDCT (defined as number of patients with abnormal LDCT requiring further evaluation who do not have cancer) ranges from 5% to 41%.[3] Most abnormalities found on LDCT are resolved on high-resolution CT. This wide range of false-positive results is likely to be because of underlying differences, such as prevalence of pulmonary fungal infections, in the populations studied. Most of the patients (63% to 90%) with abnormalities found on high-resolution CTs are subsequently found to have cancer.[3]

Two fair-quality randomized controlled trials (RCTs) screened high-risk males using annual CXR with or without sputum cytology every 4 months and have shown no lung cancer mortality benefit from adding cytology to annual CXR.[11,12] Two fair quality RCTs among high-risk men comparing intensive screening with less intensive screening (CXR plus sputum cytology every 4 months versus CXR plus sputum cytology every year,[13] or CXR every 6 months versus CXR every 3 years) also showed no lung cancer mortality benefit from more frequent screening.[14] Five fair-quality case-control studies from Japan show lung cancer mortality benefit with CXR screening among high-risk men (with smoking exposure) and low- to high-risk women (with and without direct smoking exposure).[15–19] Interpretation of these studies is limited by lack of control for occupational exposures and family history, and possible bias from the screening of healthy persons.[3] Another limitation of the lung cancer screening-specific RCTs was the use of prevalence screening at the beginning of the studies. Consequently, there were no completely unscreened control groups.

Six recent cohort studies of LDCT have shown that LDCT is significantly more sensitive than CXR for identifying lung cancer and also identifies a significantly higher proportion of small (early-stage, resectable) lung cancers than CXR.[20–26] However, the effectiveness of LDCT in decreasing lung cancer mortality cannot be evaluated from these studies because of the absence of randomization and the

lack of an unscreened control group for which mortality was an outcome.

An important concern in lung cancer screening is over-diagnosis (and potential over-treatment). Data from the Mayo Lung Project showed increased rates of early tumors in the CXR/sputum cytology-screened group compared with the control group, without a change in numbers of advanced tumors or subsequent mortality rates, suggesting diagnosis of a pool of indolent tumors.[27] The false-positive rate with LDCT ranges from 5% to 41% in prevalence screening and 3% to 12% in incidence screening, with most abnormalities resolved on high-resolution computerized tomography. Harms include cost and risk associated with further evaluation and the potential anxiety and concern of false-positive test results. In addition, the rate of false-negative CXRs is estimated to be as high as 75%, which can lead to false reassurance LDCT, which also has been shown to have false-negative results (eg, nodules identified retrospectively).[21] More studies are needed to quantify the harms of over- and under-diagnosis.

Overall, mortality rates from invasive procedures in symptomatic patients range from 1.3% to 11.6%, with lower mortality among patients undergoing smaller resections.[2,3] Comorbidity and the volume of surgery have also been shown to affect surgical risks. The morbidity reported among several series of thoracotomy ranges between 8.8% and 44%, depending on the extent of the resection, the number of procedures performed by the center, and the comorbidities of the patient.[2,3]

Although no RCT of screening for lung cancer with mortality outcomes in the general population has yet been completed, at least 3 such RCTs are currently in progress.[3] In addition, new technologies are being studied for potential use in lung cancer screening, including immunogenetic-based tests, molecular analysis of sputum, automated image sputum cytology, and fluorescence bronchoscopy. In the absence of results from an RCT screening of the general population with mortality outcomes, the USPSTF concludes there is insufficient evidence to recommend for or against screening for lung cancer.

Recommendations of Others

Lung cancer screening recommendations from the American Cancer Society can be accessed at www.cancer.org/docroot/PUB/content/PUB_3_8X_American_Cancer_Society_Guidelines_for_the_Early_Detection_of_Cancer_update_2001.asp. The policy of the American Academy of Family Physicians can be accessed at www.aafp.org/x24974.xml. Recommendations from the Canadian Task Force on Preventive Health Care can be accessed at www.ctfphc.org. Relevant guidelines from other organizations on lung cancer screening can be accessed at the National Guideline Clearinghouse at www.guideline.gov.

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Appendix A
U.S. Preventive Services Task Force—Recommendations and Ratings

The Task Force grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A. The USPSTF strongly recommends that clinicians provide [the service] to eligible patients. *The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.*

B. The USPSTF recommends that clinicians provide [the service] to eligible patients. *The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.*

C. The USPSTF makes no recommendation for or against routine provision of [the service]. *The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D. The USPSTF recommends against routinely providing [the service] to asymptomatic patients. *The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.*

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. *Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.*

Appendix B
U.S. Preventive Services Task Force—Strength of Overall Evidence

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

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