Lung Cancer Screening: Recommendation Statement

U.S. PREVENTIVE SERVICES TASK FORCE

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This is one in a series excerpted from the Recommendation Statements released by the U.S. Preventive Services Task Force (USPSTF). These statements address preventive health services for use in primary care clinical settings, including screening tests, counseling, and chemoprevention. The complete statement is available in HTML and PDF formats through the AFP *Web site at http://www.aafp.org/afp/20050315/us.html. This statement is part of* AFP*'s CME. See "Clinical Quiz" on page xxxx.*

This statement summarizes the current U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer and the supporting scientific evidence, and it updates the 1996 recommendations contained in the *Guide to Clinical Preventive Services, 2d ed*.[1] In 1996, the USPSTF recommended against screening for lung cancer ("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 *Tables 1 and 2*, 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 (http://www.preventiveservices.ahrq.gov) and through the National Guideline Clearinghouse (http://www.guideline.gov). The summary of the evidence and the recommendation statement also are available in print through the Agency for Healthcare Research and Quality Publications Clearinghouse through subscription to the *Guide to Clinical Preventive Services, 3d ed.: Periodic Updates.* To order, contact the Clearinghouse (telephone: 800-358-9295; e-mail: ahrqpubs@ahrq.gov).

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Summary of Recommendation

The USPSTF concludes that the evidence is insufficient to recommend for or against screening asymptomatic persons for lung cancer with either low-dose computed tomography (LDCT), chest radiographs, sputum cytology, or a combination of these tests. **I recommendation.**

The USPSTF found fair evidence that screening with LDCT, chest radiographs, 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 four times greater than the sensitivity of chest radiographs. However, LDCT also is associated with a greater number of false-positive results, more radiation exposure, and increased costs compared with chest radiographs.

• 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 patients are not available, mortality rates from complications of surgical interventions in symptomatic patients reportedly range from 1.3 to 11.6 percent; morbidity rates range from 8.8 to 44 percent, 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 in 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 five-year survival rates are less than 15 percent in all patients with lung cancer.[4] Five-year survival ranges from 70 percent in patients with stage I disease to less than 5 percent in patients with stage IV disease.[9]

The USPSTF examined the evidence for the accuracy of screening tests for lung cancer (i.e., LDCT, chest radiographs with or without sputum cytology) in the general population as well as the high-risk population. The sensitivity and specificity of chest radiographs for diagnosing lung cancer are 26 and 93 percent, respectively, with a positive predictive value of 10 percent for an abnormal chest radiograph (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 percent.[3] Most abnormalities found on LDCT are resolved on high-resolution computed tomography. 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 percent) with abnormalities found on high-resolution computed tomography subsequently are found to have cancer.[3]

Two fair-quality randomized controlled trials (RCTs) screened high-risk males using annual chest radiographs with or without sputum cytology every four months and showed no lung cancer mortality benefit from adding cytology to annual chest radiographs.[11,12] Two fair-quality RCTs of high-risk men comparing intensive screening with less-intensive screening (chest radiographs plus sputum cytology every four months versus chest radiographs plus sputum cytology every year,[13] or chest radiographs every six months versus chest radiographs every three 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 chest radiograph screening in 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 have shown that LDCT is significantly more sensitive than chest radiographs for identifying lung cancer and also identifies a significantly higher proportion of small (early-stage, resectable) lung cancers.[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 overdiagnosis (and potential overtreatment). Data from the Mayo Lung Project[27] showed increased rates of early tumors in the chest radiograph/sputum cytology-screened group compared with the control group, without a change in the number of advanced tumors or subsequent mortality rates, suggesting diagnosis of a pool of indolent tumors. The false-positive rate with LDCT ranges from 5 to 41 percent in prevalence screening and 3 to 12 percent in incidence screening, with most abnormalities resolved on high-resolution computed tomography. Harms include cost and risk associated with further evaluation and the potential anxiety arising from false-positive test results. In addition, the rate of false-negative chest radiographs is estimated to be as high as 75 percent, which can lead to false reassurance LDCT, which also has been shown to have false-negative results (e.g., nodules identified retrospectively).[21] More studies are needed to quantify the harms of over- and underdiagnosis.

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

Although no RCT of screening for lung cancer with mortality outcomes in the general population has been completed, at least three such RCTs are 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 online at http://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 online at http://www.aafp.org/x24974.xml.

Recommendations from the Canadian Task Force on Preventive Health Care can be accessed online at http://www.ctfphc.org.

Relevant guidelines on lung cancer screening from other organizations can be accessed online at the National Guideline Clearinghouse at http://www.guideline.gov.

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REFERENCES