

# 11. Screening for Lung Cancer

## RECOMMENDATION

Routine screening for lung cancer with chest radiography or sputum cytology in asymptomatic persons is not recommended. All patients should be counseled against tobacco use (see Chapter 54).

### Burden of Suffering

Cancer of the lung is the leading cause of death from cancer in both men and women in the U.S. An estimated 172,000 new cases will be diagnosed in 1995, with an estimated 153,000 deaths.<sup>1</sup> Lung cancer has one of the poorest prognoses of all cancers, with a 5-year survival rate of less than 13%.<sup>1</sup> Important risk factors for lung cancer include tobacco use and certain environmental carcinogen exposures. Tobacco is associated with 87% of all cases of cancer of the lung, trachea, and bronchus.<sup>2</sup>

### Accuracy of Screening Tests

The chest radiograph (x-ray) and sputum cytomorphologic examination (cytology) lack sufficient accuracy to be used in routine screening of asymptomatic persons. The accuracy of the chest x-ray is limited by the capabilities of the technology and observer variation among radiologists. Suboptimal technique, insufficient exposure, and poor positioning and cooperation of the patient can obscure pulmonary nodules or introduce artifacts.<sup>3</sup> Radiologists frequently disagree on the interpretation of chest x-rays (interobserver variability). In one study, over 40% of these disagreements were considered potentially significant.<sup>4</sup> Most errors are false-negative interpretations, and pulmonary and hilar masses are among the most commonly missed diagnoses. From 10% to 20% of the incorrect radiologic diagnoses or indeterminate results require follow-up testing for clarification.<sup>4</sup> Interpretation of chest x-rays by primary care physicians is less accurate than interpretation by radiologists. Discrepancies were identified in 58% of chest x-rays read by both family physicians and radiologists.<sup>5</sup> Current radiographic technologies require greater than 20 doublings of tumor size to reach the 1 cm<sup>3</sup> needed for the lower limit of chest imaging sensitivity. By the time lung cancer is suspected on chest x-ray, micrometastatic dissemination has often occurred, limiting the effectiveness of early detection.<sup>6</sup>

Furthermore, the yield of screening chest radiography is low, largely due to the low prevalence of lung cancer in asymptomatic individuals, even those at high risk. Of the initial 31,360 screening x-rays of asymptomatic smokers in the National Cancer Institute (NCI) Cooperative Early Lung Cancer Detection Program, 256 (0.82%) were interpreted as “suspicious for cancer,” and only 121 (0.39% of those screened) were diagnosed with lung cancer.<sup>7</sup> Other studies have confirmed a low yield of performing chest x-rays on asymptomatic persons.<sup>8,9</sup>

Sputum cytology is an even less effective screening test, largely due to its low sensitivity compared to chest x-ray.<sup>6</sup> Of the 160 lung cancers detected by dual screening in the NCI study, 123 (77%) would have been detected by chest x-ray alone and 67 (42%) would have been detected by cytologic examination alone.<sup>7</sup> The majority of incident cases detected in subsequent screenings were detected by chest x-ray.<sup>10</sup> In other trials using dual screening, sensitivity of chest x-ray ranges from 40% to 50%, versus 10% to 20% for sputum cytology.<sup>11</sup> Mass screening to detect lung cancer with tests that lack a high sensitivity will be inefficient.<sup>12</sup>

#### Effectiveness of Early Detection

Lung cancer is usually asymptomatic until it has reached an advanced stage, when the treatment outcome is poor. Five-year survival for all stages is 11–14%; for Stage I it is 42–47%.<sup>1</sup> Under optimal conditions, survival can be higher.<sup>10,12,13</sup> Early detection of Stage I cases through screening might be expected to improve survival, but the small amount of available evidence does not show that screening reduces lung cancer mortality.

The efficacy of chest radiographic screening for lung cancer was first investigated in the 1960s. A controlled prospective study involving over 55,000 persons found that those receiving chest x-rays every 6 months had a larger proportion of resectable tumors, but mortality for lung cancer remained the same when compared with controls who received examinations only at the beginning and end of the trial.<sup>14</sup> Similar findings were reported in the Philadelphia Pulmonary Neoplasm Research Project<sup>15</sup> and, more recently, in a case-control study.<sup>16</sup> In addition, the results of one of the three centers participating in the NCI Cooperative Early Lung Cancer Detection Program provide indirect evidence of the limited efficacy of radiographic screening. In this study, persons receiving chest x-rays and sputum cytology every 4 months had the same lung cancer mortality as persons advised to obtain annual testing.<sup>17</sup>

No prospective randomized study with adequate follow-up time has compared radiographic screening with no screening. A case-control study in Japan compared the screening histories of 273 fatal cases of lung cancer to 1,269 controls, and although the data suggest a trend toward a decreased

risk of lung cancer mortality in those screened with chest x-rays (with or without sputum cytologic tests), the difference was not statistically significant.<sup>18</sup>

Three large clinical trials published by the NCI Cooperative Early Lung Cancer Detection Program examined the efficacy of dual screening (chest x-ray and sputum cytology) in over 30,000 male smokers aged 45 or older.<sup>7,10,19–23</sup> Two trials comparing annual dual screening with annual radiographic screening tested the incremental benefit of adding sputum cytology to radiographic screening.<sup>20,21</sup> The third trial, which compared dual screening every 4 months with advice to receive the same tests annually, examined the benefit of frequent dual screening compared to usual medical care.<sup>22</sup> In each study, lung cancer mortality did not differ between experimental and control groups. Although early-stage, resectable tumors were more common and 5-year survival significantly higher in groups receiving regular dual screening, lead-time and length biases may have been responsible for these findings. A randomized prospective trial of dual screening in Czechoslovakia produced similar results.<sup>24</sup> The investigators found no substantial difference in the number or causes of death between study groups.

The NCI is currently conducting the multicenter PLCO (prostate, lung, colorectal, and ovarian cancers) Trial, which will compare annual chest radiographic testing with usual care in both men and women.<sup>25</sup>

#### Recommendations of Other Groups

No organizations currently recommend routine screening of either the general population or of smokers for lung cancer with either chest x-rays or sputum cytology.<sup>26–31</sup>

#### Discussion

Lung cancer is the leading cause of cancer mortality. Although screening may increase early detection of resectable early cancers, controlled trials provide no significant evidence that lung cancer screening reduces mortality from this disease. To the weakness of the evidence for screening must be added the substantial costs of routine testing,<sup>9</sup> including false-positive results that lead to unnecessary expense and morbidity from follow-up procedures.<sup>32</sup> Current research and clinical trials of chemoprevention,<sup>33</sup> as well as research in early detection markers such as monoclonal antibodies,<sup>6,34</sup> may improve efficacy in prevention or early identification of lung cancer. Primary prevention—mainly through discouraging tobacco use—is a more effective strategy than screening to reduce lung cancer morbidity and mortality.<sup>11</sup> Unless ongoing trials find a benefit of periodic chest x-rays, the cost, inconvenience, and potential harms of screening cannot be justified.

## CLINICAL INTERVENTION

Routine screening of asymptomatic persons for lung cancer with chest radiography or sputum cytology is not recommended ("D" recommendation). All patients should be counseled against tobacco use (see Chapter 54).

The draft update of this chapter was prepared for the U.S. Preventive Services Task Force by Kathyline Anderson, MD, MOH, and Donald M. Berwick, MD, MPP.

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