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.[1] Lung cancer has one of the poorest prognoses of all cancers, with a 5-year survival rate of less than 13%.[1] 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.[2]

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.[3] Radiologists frequently disagree on the interpretation of chest x-rays (interobserver variability). In one study, over 40% of these disagreements were considered potentially significant.[4] 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.[4] 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.[5] Current radiographic technologies require greater than 20 doublings of tumor size to reach the 1 cm^3 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.[6]

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.[7] Other studies have confirmed a low yield of performing chest x-rays on asymptomatic persons.[8,9]

Sputum cytology is an even less effective screening test, largely due to its low sensitivity compared to chest x-ray.[6] 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.[7] The majority of incident cases detected in subsequent screenings were detected by chest x-ray.[10] In other trials using dual screening, sensitivity of chest x-ray ranges from 40% to 50%, versus 10% to 20% for sputum cytology.[11] Mass screening to detect lung cancer with tests that lack a high sensitivity will be inefficient.[12]

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%.[1] Under optimal conditions, survival can be higher.[10,12,13] 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.[14] Similar findings were reported in the Philadelphia Pulmonary Neoplasm Research Project[15] and, more recently, in a case-control study.[16] 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.[17]

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.[18]

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.[7,10,19–23] Two trials comparing annual dual screening with annual radiographic screening tested the incremental benefit of adding sputum cytology to radiographic screening.[20,21] 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.[22] 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.[24] 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.[25]

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.[26–31]

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,[9] including false-positive results that lead to unnecessary expense and morbidity from follow-up procedures.[32] Current research and clinical trials of chemoprevention,[33] as well as research in early detection markers such as monoclonal antibodies,[6,34] 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.[11] 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 Kathlyne Anderson, MD, MOH, and Donald M. Berwick, MD, MPP.

REFERENCES

1. Wingo PA, Tong T, Bolden S. Cancer statistics, 1995. CA Cancer J Clin 1995;45:8–30.
2. Department of Health and Human Services. Reducing the health consequences of smoking: 25 years of progress. A report of the Surgeon General. Rockville, MD: DHHS, 1989. (Publication no. DHHS (PHS) 89-8411.)
3. Tape TG, Mushlin AL. The utility of routine chest radiographs. Ann Intern Med 1986;104:663–670.
4. Herman PG, Gerson DE, Hessel SJ, et al. Disagreements in chest roentgenogram interpretation. Chest 1975; 68:278–282.
5. Kuritzky L, Haddy RI, Curry RW Sr. Interpretation of chest roentgenograms by primary care physicians. South Med J 1987;80:1347–1351.
6. Mulshine JL, Tockman MS, Smart CR. Considerations in the development of lung cancer screening tools. J Natl Cancer Inst 1989;81:900–906.
7. The National Cancer Institute Cooperative Early Lung Cancer Detection Program. Summary and conclusions. Am Rev Respir Dis 1984;130:565–567.
8. Rucker L, Frye EB, Staten MA. Usefulness of screening chest roentgenograms in preoperative patients. JAMA 1983;250:3209–3211.
9. Hubbel FA, Greenfield S, Tyler JL, et al. The impact of routine admission chest x-ray films on patient care. N Engl J Med 1985;312:209–213.
10. Melamed MR, Flehinger BJ, Zamen MB, et al. Screening for early lung cancer: results of the Memorial Sloan-Kettering study in New York. Chest 1984;86:44–53.
11. Marfin AA, Schenker MB. Screening for lung cancer: effective tests awaiting effective treatment. In: Harber P, Balmes JR, eds. Occupational medicine state of the art review: prevention of pulmonary disease. Philadelphia: Hanley & Belfus, 1991:111–131.
12. Wright JL, Coppin C, Mullen BJ, et al. Surgical treatment of lung cancer: promise and problems of early diagnosis. Can J Surg 1986;29:205–208.
13. Moores DW, McKneally MF. Treatment of Stage 1 lung cancer (T1N0M0, T2N0M0). Surg Clin North Am 1987;67: 937–943.
14. Brett GZ. The value of lung cancer detection by six-monthly chest radiographs. Thorax 1968;23:414–420.
15. Weiss W. Survivorship among men with bronchogenic carcinoma: three studies in populations screened every six months. Arch Environ Health 1971;22:168–173.
16. Ebeling K, Nischan P. Screening for lung cancer: results from a case-control study. Int J Cancer 1987;40:141–144.
17. Sanderson DR. Lung cancer screening: the Mayo study. Chest 1986;89(suppl):324S.
18. Sobue T, Suzuki T, Naruke T, and the Japanese Lung-Cancer-Screening Research Group. A case-control study for evaluating lung-cancer screening in Japan. Int J Cancer 1992;50:230–237.
19. Berlin NI, Buncher CR, Fontana RS, et al. The National Cancer Institute Cooperative Early Lung Cancer Detection Program: results of the initial screen (prevalence): introduction. Am Rev Respir Dis 1984;130:545–549.
20. Flehinger BJ, Melamed MR, Zaman MB, et al. Early lung cancer detection: results of the initial (prevalence) radiologic and cytologic screening in the Memorial Sloan-Kettering study. Am Rev Respir Dis 1984;130:555–560.
21. Frost JK, Ball WC Jr, Levin ML, et al. Early lung cancer detection: results of the initial (prevalence) radiologic and cytologic screening in the John Hopkins study. Am Rev Respir Dis 1984;130:549–554.

22. Fontana RS, Sanderson DR, Taylor WF, et al. Early lung cancer detection: results of the initial (prevalence) radiologic and cytologic screening in the Mayo Clinic study. Am Rev Respir Dis 1984;130:561–565.
23. Tockman MS, Frost JK, Stitik FP, et al. Screening and detection of lung cancer. In: Aisner J, ed. Lung cancer. New York: Churchill Livingstone, 1985:25–40.
24. Kubik A, Parkin DM, Khlat M, et al. Lack of benefit from semi-annual screening for cancer of the lung: follow-up report of a randomized controlled trial on a population of high-risk males in Czechoslovakia. Int J Cancer 1990;45:26–33.
25. Kramer BS, Gohagan J, Prorok PC, Smart C. A National Cancer Institute sponsored screening trial for prostatic, lung, colorectal, and ovarian cancers. Cancer 1993;71:589–593.
26. American Cancer Society. Guidelines for the cancer-related checkup: an update. Atlanta: American Cancer Society, 1993.
27. American Academy of Family Physicians. Age charts for periodic health examination. Kansas City, MO: American Academy of Family Physicians, 1994. (Reprint no. 510.)
28. American College of Radiology. ACR standard for adult chest radiography, 2d ed. Reston, VA: American College of Radiology, 1993.
29. Tockman MS, Becklake MR, Clausen JL, et al. American Thoracic Society. Screening for adult respiratory disease. Am Rev Respir Dis 1983;128:768–774.
30. Eddy DM, ed. Screening for lung cancer. In: Common screening tests. Philadelphia: American College of Physicians, 1991:312–325.
31. Canadian Task Force on the Periodic Health Examination. Canadian guide to clinical preventive health care. Ottawa: Canada Communication Group, 1994:780–787.
32. Bailar JC 3d. Screening for lung cancer: where are we now? Am Rev Respir Dis 1984;130:541–542.
33. Benner SE, Lippman SM, Hong WK. Chemoprevention strategies for lung and upper aerodigestive tract cancer. Cancer Res 1992;52(suppl):2758S–2763S.
34. Tockman MS, Gupta PK, Myers JD, et al. Sensitive and specific monoclonal antibody recognition of human lung cancer antigen on preserved sputum cells: a new approach to early lung cancer detection. J Clin Oncol 1988;6:1685–1693.