To screen or not to screen: lung and breast cancer

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Guidelines for lung cancer screening[1-4]

Although the incidence of lung cancer in the United States has been falling in recent years because of a decrease in cigarette smoking, the disease is still the third most common cancer, and the leading cause of cancer death. In March 2014, the US Preventive Services Task Force (USPSTF) updated its 2004 recommendations for lung cancer screening by commissioning a systematic evidence review of low-dose computed tomography (CT) by focusing on new evidence from randomized clinical trials published since 2004. In addition, a modeling study provided information about the optimum screening age, screening interval, and the risk–benefit ratio for screening.

Which of the following is *not* included in the current recommendations of the USPSTF for lung cancer screening?

a) Screen asymptomatic adults aged 55-80 years.
b) Do not screen those who are unwilling to have surgery or who have serious comorbid conditions.
c) Initiate screening in those with a 30 pack-year history and who currently smoke, or have done so within the past 15 years.
d) Supplement the low-dose CT screening with sputum cytology.
e) Discontinue screening after cessation of smoking for more than 15 years.

Harms from screening include all *except*:

a) Radiation exposure
b) Over-diagnosis
c) False positives
d) Decrease in smoking cessation

Key points

The USPSTF commissioned a review of 8,215 abstracts in Medline. The review resulted in the identification of 7 randomized, controlled trials, but found only 4 that met criteria for effectiveness of screening, which included the National Lung Screening Trial in the US, 2 Italian trials, and a Danish screening trial. Chest X-rays and sputum cytology were not found to have adequate sensitivity or specificity. The screening population projected to have a benefit is 30 pack-year smokers aged 55-80 years and who currently smoke or have quit within the last 15 years. Those who have significant comorbid conditions that would preclude surgery should be excluded from screening. Harms from screening include radiation exposure, over-diagnosis, and false positives that might lead to unnecessary procedures. However, smoking cessation was not affected by screening.

Answers d, d

(See online supplemental material, Understanding Task Force Recommendations, for patients.)

Probability of cancer in a pulmonary nodule[5]

Two cohorts from Canadian screening and prevention trials were analyzed to determine what factors might predict the likelihood of pulmonary nodules detected by low-dose CT scans being malignant. The 2 data sets included 102 malignant nodules discovered in 1,871 subjects with 7,008 nodules, and another 42 malignant nodules in 1,090 subjects with 5,021 nodules. A statistical analysis of various clinical variables resulted in the development of a predictive model.

According to the data analysis in this paper, the probability of detecting cancer in a pulmonary nodule detected on an initial screening CT is lower in:

a) Upper-lobe nodules
b) Lower rather than higher nodule counts
c) Perifissural nodules
d) Older individuals
e) Women

Key points

The NLCT showed that low-dose CT screening of high-risk individuals reduced lung cancer mortal-

JCSO 2014;12:228-230. ©2014 Frontline Medical Communications. DOI 10.12788/jcso.0053.

ity by 20%. However, this type of screening introduced the problems of assessing asymptomatic pulmonary nodules discovered on CT, false positives, and the risk of invasive diagnostic procedures. This study addresses these issues and provides models and calculators for the probability of nodules being malignant rather than benign. Statistical analysis of the 2 data sets produced positive predictors of cancer that included older age, female sex, family history of lung cancer, chronic obstructive pulmonary disease (COPD), larger nodule size, upper-lobe nodules, fewer rather than many nodules, and spiculaton. Perifissural nodules were never malignant.

Answer c

(See online supplemental material, Nodule risk calculators, and NEJM Quick Take on the evaluation of CT-discovered pulmonary nodules http://bit.ly/1nM68e1

The National Lung Screening Trial research team, recent papers[6-9]

The NLST researchers randomized 53,454 individuals who were at high risk for lung cancer to 3 annual screenings with either low-dose CT or chest X-ray.

The original paper in 2011 and subsequent 3 papers published in 2013 showed the following results, *except*:

a) Rate of death from any cause was reduced by 6.7% in the CT group.
b) The proportion of stage I lung cancers in the initial screen was higher than that seen in other screening studies.
c) The greatest number of deaths from lung cancer were prevented in high-risk individuals
d) By the 3rd annual screening, participants in the CT group had twice as many stage I lung cancers compared with those in the chest X-ray group.

Key points

The original report of the NLST revealed a reduction of 20% in mortality from lung cancer, and an overall reduction of 6.7% in death from any cause in high risk individuals who were screened with low-dose CT rather than chest X-ray. The proportion of lung cancers discovered with the initial screen that were stage I was only 55%, far lower than in most other studies, but the percentage of stage I patients was higher with subsequent screens (63% and 69% with the subsequent 2 screens). CT screening prevented deaths mostly in high-risk participants, and prevented little mortality in those at low risk.

Answer b

(See online supplemental material, lung cancer risk calculator)

The mammogram screening dilemma, 2014[10-13]

Two recently published studies of mammogram once again stirred up the debate about the value of screening mammography. A Canadian study published in February 2014 summarized the results of a randomized screening trial of 89,835 women begun in 1980 with follow-up for a mean of 22 years. The results indicated that annual mammography did not reduce breast cancer mortality. In April, Harvard physicians published a review of 54 years' worth of randomized clinical trials, meta-analyses, and observational studies. Their review showed a modest benefit in terms of breast cancer mortality, but at a huge cost of false positives and over-diagnoses.

Specific results of the Canadian study of mammogram screening included all *except*:

a) No reduction in breast cancer mortality in women aged 40-59 years.
b) An over-diagnosis incidence of 22% of cancers discovered.
c) Adjuvant therapy was not available for all women.
d) Mortality was the same in women who had been screened with physical examination alone.

The Harvard study results included:

a) A cumulative risk of a false-positive result of 61% after 10 years of screening.
b) An over-diagnosis incidence of 19%.
c) A 19% reduction in breast cancer mortality.
d) Reduction in breast cancer mortality was similar in all age groups.

Key points

The USPSTF 2009 guidelines for breast cancer screening sparked a controversy with its recommendation against routinely screening women younger than 50 years, biennial screening from age 50-74 years, and concern about false positives and over-diagnosis. The recent 2 studies add to the controversy.

The Canadian study casts doubt on the overall value of mammogram in terms of overall survival, although adjuvant therapy was available for all, so that delayed diagnosis may have had less of an impact because of the treatment effect. Over-diagnosis (about 20%) was a significant problem in both studies, and false positives were particularly high in the Harvard study (61%). Reduction in breast cancer mortality was twice as high in women in their 60s compared with those in their 40s, probably owing to the more virulent type of breast cancer seen in young women.

Overall, the Canadian study suggested futility in screening younger women, whereas the Harvard study recommended individualization based on risk profiles and the

need for other screening tools.

Answers c, d

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