Does screening for stage I lung cancer improve survival in a high-risk population?

Original article Henschke CI *et al.* (2006) Survival of patients with stage I lung cancer detected on CT screening. *N Engl J Med* 355: 1763–1771

SYNOPSIS

KEYWORDS cigarette smoking, lung cancer, spiral CT, surgery, survival

BACKGROUND

Over 80% of the cigarette smokers diagnosed with lung cancer following annual CT screening as part of the Early Lung Cancer Action Project (ELCAP) had clinical stage I disease, but the usefulness of screening of asymptomatic high-risk populations is still unclear.

OBJECTIVE

To assess whether early intervention following diagnosis of stage I lung cancer by annual spiral CT screening is effective in improving survival rates.

DESIGN AND INTERVENTION

Participants in this large collaborative study, performed from 1993 to 2005, were 40 years of age or older, and were asymptomatic but at risk for lung cancer because of a history of cigarette smoking, exposure to second-hand smoke, or occupational exposure to asbestos, beryllium, uranium or radon. Low-dose CT scanning was used for baseline screening, and 27,456 repeat screenings were performed 7–18 months later. The type of intervention in those patients diagnosed with lung cancer was left to the discretion of the physician and patient.

OUTCOME MEASURES

The main outcome measure was 10-year lung-cancer-specific survival rate.

RESULTS

The median age of the 31,567 participants at baseline was 61 years (range 40–85 years) and the smoking history for this group was a median of 30 pack-years (range 0–141 pack-years). Lung cancer was diagnosed as a result of baseline and annual screening in 405 and 74 participants, respectively. Radiotherapy and/or chemotherapy were administered following diagnosis of lung cancer in 57 patients, 411 underwent surgery, and 16 received no treatment. The estimated 10-year lung-cancer-specific survival rate for the entire group of 484 patients with disease of any stage and regardless of type of treatment was 80% (95% CI 74–85%). Among the 412 (85%) patients who had clinical stage I lung cancer, the estimated 10-year survival rate was 88% (95% CI 84–91%). In this group, 375 patients underwent surgical resection, 29 received chemotherapy and/or radiation but not resection, and 8 received no treatment. For the participants who underwent surgical resection, the diagnosis of clinical stage I cancer was confirmed by pathology review. The estimated 10-year survival rate was 92% (95% CI 88–95%) among the 302 participants with clinical stage I cancer who underwent surgery within 1 month after diagnosis, whereas all 8 participants who did not receive treatment died within 5 years of diagnosis. Among the patients who underwent resection, lymph-node metastases were identified in 28 (7%) patients, and more than one cancer in another 35 (9%) patients.

CONCLUSION

Annual low-dose CT scans can detect lung cancer at an early stage, when the disease is still curable.

COMMENTARY

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Pilot studies in heavy smokers have proved that low-dose spiral CT can detect early lung cancer, with very high detection and resection rates. The excellent survival rate of patients with CT-detected stage I lung cancer in the International (I-)ELCAP report is not a surprise, particularly considering that median follow-up was only 3 years and the end point was lung-cancer-specific rather than overall survival. What is remarkable is the high proportion of stage I lung cancers detected in this study: over 60% compared with 20% in historical clinical series. Whether this change will translate into significant reductions in mortality is unknown. We must remember the lesson of early randomized trials in which 4-monthly chest X-ray screening improved cancer stage distribution and patient survival after resection, but with no impact on overall lung cancer mortality and a failure to show the more-favorable long-term outcome for the screening arm expected from the initial stage shift.[1]

I-ELCAP data refer essentially to baseline examination and first CT repeat; outcome in the vast majority of subjects after 2 years is not evaluable. In the Mayo Clinic study, as well as in our pilot trial in Milan, in which 85% of volunteers have now completed their fifth year of CT screening, survival of stage I lung cancers was equivalent to survival in the I-ELCAP study reported here, but the proportion of stage I disease fell dramatically after the second year, and cumulative lung cancer mortality at 5 years was very close to that expected without screening.[2,3] A reasonable explanation for such a discrepancy is that radiological screening can detect early-stage, slow-growing or indolent disease, but is unable to prevent more-aggressive and early metastatic lung cancer.[4]

In contrast with other common neoplasms, lung cancer has a definite environmental etiology, and is just one component of a large spectrum of chronic tobacco-related diseases. Each of these diseases represents a major competing risk of death that could both reduce the benefit of early lung cancer detection and increase the cost and harms of screening programs. In fact, the chance of detecting lung cancer with spiral CT in a heavy smoker older than 50 years is about 1% per year, but the frequency of benign lesions is 50 times higher; furthermore, 15% of screened subjects require further diagnostic testing, which is more complex and potentially harmful than in breast or colon screening. In addition, if current smokers feel themselves protected by annual CT screening, while continuing to smoke, the ultimate effect of such scans could be a public health care disaster.

The I-ELCAP initiative had the fundamental merit of pioneering clinical research on early lung cancer detection worldwide, and setting gold standards for pulmonary imaging by spiral CT. The results of ongoing randomized trials must be seen, and the real impact of this intervention on lung cancer mortality assessed, before annual spiral CT scanning is recommended to current or former smokers. Combining radiological screening with genomic and proteomic research in the framework of randomized trials will provide a new opportunity to understand this heterogeneous and multifocal disease, define the biological bases of individual lung cancer risk, and improve the clinical management of lung cancer.

References

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Competing interests
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PRACTICE POINT
The efficacy of annual low-dose spiral CT scans must be proven by a reduction in lung cancer mortality in large-scale randomized trials before routine screening can be recommended to current or former smokers