

Computed Tomographic Screening for Lung Cancer: The Mayo Clinic Experience



Erin A. Gillaspie, MD, Mark S. Allen, MD*

KEYWORDS

• Lung cancer • Screening • Low-dose CT • Prevention

KEY POINTS

- Screening with low-dose computed tomography (LDCT) reduces lung cancer mortality.
- Results from screening for lung cancer need to be carefully managed to avoid unnecessary surgery.
- Screening using LDCT is superior to screening with chest roentgenograms.

BACKGROUND

Lung cancer has long stood as the most lethal cancer faced by the medical profession. An estimated 1.6 million patients worldwide are expected to die this year of lung cancer, which accounts for 19% of all cancer deaths.¹

The most important risk factor for the development of lung cancer remains smoking. Despite the plethora of evidence proving the detriments of smoking, approximately 18% of the adult US population continues to smoke.² The relative risk of developing lung cancer is 25 times higher in a smoker than in a nonsmoker.³ Still, there are other risks to consider including family history, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, environmental radon exposure, passive smoking, asbestos exposure, and certain occupational exposures.

Lung cancer presentation varies from indolent and subtle symptoms to persistent cough, hemoptysis, chest pain, or recurrent pneumonia or bronchitis. Too often, the presentation of lung cancer with symptoms leads to the finding of an advanced-stage cancer that is unlikely to be cured.

Screening examinations for lung cancer have significantly lagged behind those for other types

of cancers including colon, breast, and prostate cancer, all of which have a significantly better survival.

BENEFITS OF EARLY DETECTION

The stage at presentation determines the overall survival. Approximately 46% of patients with lung cancer present at an advanced stage with limited treatment options.⁴ A screening tool that could provide an earlier diagnosis would potentially shift a significant number of patients into a stage with more treatment options.

For the past 5 decades, the Mayo Clinic has participated in efforts to establish a protocol for the earlier detection of lung cancer.

CHEST RADIOGRAPH AS A SCREENING TOOL: THE MAYO LUNG PROJECT

Study Design

The Mayo Lung Project (MLP) was a randomized controlled study conducted between 1971 and 1983. The study accrued 10,933 male outpatients who were known smokers and not suspected of having lung cancer. These patients underwent a baseline screening with chest radiograph (CXR)

Disclosures: the authors have nothing to disclose.

Mayo Clinic, Rochester, MN 55905, USA

* Corresponding author. Department of Surgery, 200 First Street, SouthWest, Rochester, MN 55905.

E-mail address: Allen.mark@mayo.edu

Thorac Surg Clin 25 (2015) 121–127

<http://dx.doi.org/10.1016/j.thorsurg.2014.11.001>

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and sputum cytology (prevalence study). Patients with a negative result of CXR and a life expectancy of greater than 5 years were invited to participate in a randomized controlled trial of lung cancer incidence. Ultimately, 9211 men were randomly assigned to receive either the standard of care at Mayo for the 1970's, which was annual CXR and sputum cytology, or to belong to the intervention arm in which participants underwent CXR and sputum cytology every 4 months for 6 years (incidence studies). There was 75% compliance in the intervention arm of the study. Follow-up of the MLP concluded in 1983.⁵

Results from the Study

The prevalence CXRs revealed 91 previously undiagnosed lung carcinomas (8.3 per 1000 screened). Of these, half were early-stage cancers and were amenable to resection. Overall, the 5-year survival for these patients was 40%.

Over the next 6 years, an additional 206 (5.5 per 1000 person-years) cases of lung carcinoma were diagnosed in the intervention arm compared with 160 (4.3 per 1000 person-years) in the control group. The additional cases diagnosed in the intervention arm were early-stage cancers.⁶

Mortality

The incidence of lung cancer and the stage at which it was diagnosed differed between the 2 arms of the study. The median survival for patients who were diagnosed with lung cancer in the intervention arm was 1.3 years versus 0.9 years in the usual care arm.

For resected, early-stage disease (T1 or T2 lesions), the median survival was 16 years for the intervention arm compared with only 5 years in the usual care arm. Treatment was the same in each group, with 81% and 80% of patients in the intervention and usual care groups, respectively, going on to have resection. In advanced-stage lung cancer, survival rates were same in both arms of the study.

Despite these differences in survival, the values never reached statistical significant ($P = .16$). Therefore, it was concluded that more frequent examinations with CXR and sputum cytology did not seem to confer a survival benefit and therefore these should not be used as screening tools.⁶

Extended Follow-up for the Mayo Lung Project

In 1996, the National Death Index (NDI) was used to provide extended follow-up on any remaining MLP patients who were still alive at the conclusion

of the study in 1983. Medical records and the NDI database were reviewed for clinical status, and if deceased, the date and cause.

Of the 6523 patients remaining at the end of the study, 2961 patients had available data for review. After 13 years, death totals for the study were 303 patients in the usual care arm and 337 in the intervention arm. The median follow-up was 20 years. Lung cancer mortality rate was calculated to be 4.4 per 1000 person-years in the intervention arm and 3.9 deaths per 1000 person-years in the usual care arm. There was no statistical difference. All-cause mortality also did not differ by study arm.

The data were adjusted for lung cancer risk modifiers including age, smoking, exposure to nontobacco lung carcinogens, and history of pulmonary illnesses, and the mortality rates did not differ significantly between the 2 study arms.⁷

Case Survival

No reduction in lung cancer mortality was seen in the intervention arm of the MLP. However, a case survival difference was observed at 1, 5, 10, and 15 years. One year after the diagnosis of lung cancer, survival was 61.7% for patients participating in the intervention arm compared with 50.1% in the usual care arm. Similar trends were seen in continued follow-up at 5, 10, and 15 years.

The extended follow-up and reevaluation of data still could not conclude that CXR was an appropriate modality for screening for lung cancer despite trends to improved survival.⁷

Comparable Trials

Similar studies were conducted to evaluate the effectiveness of CXR in screening for lung cancer. The Prostate, Lung, Colorectal and Ovarian (PLCO) randomized trial, for example, offered annual CXR to patients for 4 years versus no screening. Groups were well matched. Annual screening with CXR did not reduce lung cancer mortality compared with usual care.⁸

Computed Tomographic Scan as a Screening Tool

The computed tomographic (CT) scan was first used clinically in the 1970s. During that time, scans required high radiation dosages and long image acquisition times. These requirements made CT an impractical modality for screening.

As CT scanning technology improved with superior image quality, thinner slices, and faster acquisition of imaging, many groups began to study the CT scan as a screening tool for lung cancer. Detractors of CT screening cited radiation exposure as a prohibitive risk. The

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