Lung Cancer Screening for All? Not Yet, Panel Says

A reanalysis of a large randomized screening trial, the publication of results from five case–control studies, and the emergence of low-dose computed tomography (CT) as a potential screening tool has prompted the U.S. Preventive Services Task Force to update its recommendations for lung cancer screening: There is not enough information available from clinical trials and studies to recommend for or against screening for lung cancer in people who do not have symptoms of the disease, the task force concluded.

In 1985 and again in 1996, the task force recommended against screening for lung cancer largely because of negative results from three randomized trials of chest x-ray conducted in the 1970s. But the largest of these studies—the Mayo Lung Project—has some limitations that have more recently come under scrutiny. The trial compared male smokers who received chest x-ray and sputum cytology every 4 months with those who received usual care. However, all participants received a chest x-ray at the beginning of the study, and those in the usual-care group who had lung cancer were not included in the overall study analysis.

The quality and limitations of the Mayo lung study played a major role in shifting the recommendation, said Paul Frame, M.D., a member of the task force and a physician at Tri-County Family Medicine in Cohocton, N.Y. “There was a feeling that we weren’t quite as confident that the Mayo study was the be-all-end-all trial,” Frame said. Also a factor were five recently published case–control studies from Japan that compared case patients who were screened for lung cancer by chest x-ray with or without sputum cytology with patients in a control group who were not screened. Four of those studies found a statistically significant decrease in lung cancer death among those screened for the disease. However, the results of the case–control studies—a study design that is considered weaker than randomized clinical trials and that is subject to additional sources of bias—were not enough to trump the results of the six randomized trials the task force included in its analysis.

Whereas there are several clinical trials and studies—albeit of varying quality—of chest x-ray as a lung cancer screening tool, there are far fewer studies of a much newer technology, low-dose CT or spiral CT. Lung cancer survival is directly related to the stage of the cancer at diagnosis, so there has been strong interest for decades in finding a way to stop the disease early. Cohort studies published in the last few years have found that low-dose CT can detect lung cancer at an early stage. However, whether that translates into a benefit for the patient by extending the patient’s life remains to be seen.

“The big caution with low-dose CT screening is that we know that somewhere in the neighborhood of 20% to 30% [of people screened] are going to have an abnormality, so if you elect to have this screen, you have about a 1 in 4 chance of having an abnormality that needs further workup,” Frame said. “Only 1 out of 10 of those will turn out to be cancer.”

He added that some of the cohort studies of low-dose CT had very specific protocols about the size of nodules that should undergo biopsy and had the added quality control of multiple radiologists reading the films from the test. “That kind of rigorous caution may or may not happen in the non-trial, real-world setting,” Frame said.

Cohort studies also do not have control groups, so they cannot be analyzed for the factor the task force and other experts are most interested in—whether lung cancer screening ultimately results in fewer deaths from the disease.
“The challenge is to wait until we have evidence before incorporating spiral CT screening into routine clinical practice,” said Pamela Marcus, Ph.D., an epidemiologist at the National Cancer Institute. “If there are people out there who want it, then they have to be informed by their physicians that it’s never been shown to reduce lung cancer mortality.”

Marcus is involved with the National Lung Screening Trial (NLST), which includes more than 50,000 people who will be randomly assigned to be screened with either chest x-ray or spiral CT once a year for 3 years. The trial finished accrual in January, and the health of its participants will be monitored until 2009.

“You can’t get definitive evidence overnight,” Marcus said. “There’s too much at stake for just applying [CT screening] without having evidence that it works. … There are always going to be downsides to screening. We’ve come to accept some of the downsides and some of the adverse events if it means that it will save lives. But we certainly don’t want to accept those adverse events if it won’t save lives.”

Meanwhile, the task force’s change in recommendation is an acknowledgement that there are still open questions regarding lung cancer screening, and particularly low-dose CT.

“What [the change in recommendation] does is [change] it from a level of, ‘we think we know the answer and the answer is, and you shouldn’t do it,’ to, ‘we’re not sure what the answer is and we need more data,’” Frame said.

The task force’s evidence review was published in the May 4 issue of the Annals of Internal Medicine.

—Kate Travis