Lung Cancer Screening Most Beneficial for Those at Highest Risk, Analysis Suggests

Screening can save lives, but recent studies suggest that only 2 percent to 4 percent of eligible people are being screened for lung cancer

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A new analysis of data from a demonstration project led by the Veterans Health Administration (VHA) may help to better define who is most likely to benefit from lung cancer screening.

Using a risk model, researchers found that people identified as having the highest risk of lung cancer were most likely to have lung cancer detected with low-dose computed tomography (CT).

People with the lowest risk of lung cancer were less likely to have lung cancer detected, and their ratio of benefits to harms from screening was not as favorable, lead investigator Tanner Caverly, MD, MPH, of the University of Michigan, and his colleagues reported January 22 in JAMA Internal Medicine.

In an editorial that accompanied the new analysis, Michael Incze, MD, and Rita Redberg, MD, of the University of California, San Francisco, wrote about the importance of re-evaluating the lung cancer screening process.

“The future of [lung cancer screening] depends on our ability to re=examine and refine our approach to patient selection and clearly communicate risks and benefits of screening,” they wrote.

Revisiting a Lung Cancer Screening Demonstration Project

In the VHA’s demonstration project, approximately 2,100 patients considered to be at high risk for developing lung cancer because of their age and smoking history were screened with low-dose CT over 3 years at eight VHA centers around the country. The project found a much higher false-positive rate (58.2 percent) following low-dose CT screening than did the NCI-funded National Lung Screening Trial (NLST) (26.3 percent).

Updated results from NLST, which enrolled more than 53,000 participants, show an approximately

16 percent reduction in lung cancer deaths among patients at high risk—that is, current and former heavy smokers aged 55 to 74 years—who were screened with low-dose CT. This finding led the US Preventive Services Task Force (USPSTF) in 2013 to recommend that people at high risk for lung cancer (based largely on the NLST enrollment criteria) undergo annual screening with low-dose CT.

The VHA's demonstration project was launched soon after the USPSTF recommendation to better understand how a comprehensive screening program for lung cancer would operate in the VHA and outside the confines of a clinical trial, said Linda Kinsinger, MD, MPH, of the VHA, who led an earlier analysis of the demonstration project.

The high false-positive rate seen in the study got a lot of attention, explained Caverly, so he and his colleagues thought it important to look more closely at the harm-to-benefit ratio of screening for people at different levels of lung cancer risk.

The harms can include detecting benign growths that can lead to unnecessary invasive procedures and emotional stress, as well as radiation exposure from unnecessary follow-up CT scans. Because of the high false-positive rates, there is also concern about the cost-effectiveness of screening. This is why Caverly and his team wanted to see which patients might benefit the most.

"It seemed that, if we were going to analyze this data in a little more depth, we might find that the [benefit-to-harm] balance was really concerning for some people and not as concerning for other people," he said.

A Risk-Based Approach to Lung Cancer Screening

To conduct the analysis, Caverly and his team used a previously developed lung cancer risk model to divide patients in the VHA project into five groups from lowest to highest risk, based on such factors as age and smoking status.

They found that for those in the highest-risk groups, fewer people needed to be screened to diagnose one case of lung cancer than for those in the lowest-risk groups. For example, for every 1,000 patients in the highest-risk group who underwent screening, nearly 30 lung cancer diagnoses were made, compared with approximately 5 diagnoses in the lowest-risk group.

However, all the groups had similar rates of false-positive results—the overall rate was 56.2 percent across all five groups.

With this analysis, Caverly and his team have "made the important contribution of applying a validated risk stratification tool to a real-world cohort to improve screening criteria," Drs. Incze and Redberg wrote.

However, they also pointed out that, even in the highest-risk group, low-dose CT screening was associated with "alarmingly high rates of false-positive results" and that most participants in the

project were “exposed to an unfavorable benefit-to-risk ratio.”

Moving toward More Personalized Screening

“The simple message from this analysis is that the balance of benefits and harms varied substantially across individuals,” said Caverly. “Interpreting what that variation means is harder.”

Based on the new analysis, many people still need to be screened to prevent one lung cancer death. But, Caverly cautioned, “it’s important to note that the analysis was only based on first-time screenings.” If repeat screenings had been included, he continued, the number of people needed to screen to prevent one death would have been much lower.

Other recent studies have also looked at the impact of risk-based lung cancer screening. For example, a cost-effectiveness analysis published February 6 in Annals of Internal Medicine that used data from NLST participants also found that people at the highest risk of lung cancer were most likely to benefit from low-dose CT screening. Using a model to identify risk categories, the study found that more lung cancer-related deaths were averted over 7 years in the highest-risk group than in the lowest-risk group.

However, higher-risk participants in the study “were older, had greater smoking exposure, and were more likely to have a preexisting diagnosis of chronic obstructive pulmonary disease,” wrote study investigator David Kent, MD, of Tufts Medical Center, and his colleagues. As a result, the extent of the screening benefit in this group “was greatly attenuated” because these individuals were more likely to die of other causes and have lower quality-of-life measures.

“Clearly more work is needed” to minimize the harms of lung cancer screening, wrote Drs. Incze and Redberg, “while preserving benefit for those whose lives could be saved by the early detection of lung cancer.”

In an editorial accompanying the Annals of Internal Medicine study, Angela Green, MD, and Peter Bach, MD, of Memorial Sloan Kettering Cancer Center, agreed that screening can save lives and noted that using risk models “might increase the efficiency of lung cancer screening.”

But, they added, recent studies suggest that, at the moment, only 2 percent to 4 percent of eligible people are being screened for lung cancer.

So identifying “exactly who should be screened may only be academic,” they wrote, “because screening rates are low.”

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