NCCN Lung Screening Guideline Is 'A Lot of Work' to Follow

Nick Mulcahy

March 19, 2012 (Hollywood, Florida) — The new guideline on lung cancer screening was presented to an audience for the first time here at the National Comprehensive Cancer Network (NCCN) 17th Annual Conference.

In November of last year, the NCCN became the first professional organization to update their recommendations for screening and strongly recommend the use of low-dose helical computed tomography (CT) screening for select individuals at high risk for lung cancer.

The guideline was subsequently published in the February issue of the *Journal of the National Comprehensive Cancer Network* (2012;10:240-265).

In the past, the NCCN did not recommend lung cancer screening as a routine practice for any set of at-risk patients, Douglas Wood, MD, from the Seattle Cancer Care Alliance, University of Washington, told meeting attendees.

The impetus for the new guidance was the landmark National Lung Screening Trial (NLST), which found a 20% reduction in deaths from lung cancer among current and former heavy smokers screened with helical low-dose CT, compared with those screened with chest radiograph.

That translates into 1 lung-cancer-related death prevented for every 320 high-risk individuals screened in the study, said Dr. Wood.

In her presentation, Ella Kazerooni, MD, from the University of Michigan Comprehensive Cancer Center in Ann Arbor, noted that the NLST asked a basic question: "Does early detection reduce lung-cancer-specific mortality?"

The answer is an emphatic yes, copresenter Mary Reid, PhD, associate professor of oncology at Roswell Park Cancer Institute in Buffalo, New York, told *Medscape Medical News* before the meeting.

"This is really big," said Dr. Reid about the potential of lung cancer screening to reduce mortality. If there are 150,000 lung cancer deaths a year in the United States, then a fully implemented and participatory screening program could save 30,000 lives a year, she pointed out.

Before the meeting, Dr. Reid said that she expected "skepticism" from clinicians in the audience about the recommendation to screen high-risk smokers and former smokers, but she and her 2 copresenters were well received.

However, the audience members did not ask any highly specific questions about the practicalities of incorporating the NCCN recommended screening into clinical practice.

Implementing lung cancer screening "will require big changes in how these patients are managed," Dr. Reid said.

Dr. Reid and her colleagues at Roswell Park have more experience with lung cancer screening than most. They have run a program since 1998 and have screened more than 700 patients.

"We have a lot of CTs that require surveillance," she said, referring to the fact that nodules have been found in many individuals. However, the great majority of nodules are false positives. In the NLST, 96% of all nodules found by CT were not cancer. Nonetheless, the "burden" of following up with patients with nodules is "not trivial," Dr. Reid told the NCCN audience.
After her presentation, Dr. Reid told Medscape Medical News that 2 clinicians at Roswell Park devote 1 day a week to work with the lung cancer screening patients. The center also has a designated radiologist to read CT scans and a designated pathologist to assess tissue samples.

"The process of following this guideline will require a lot of work," Dr. Reid summarized in an earlier interview.

She noted that "over half of primary care physicians" have ordered lung cancer screenings of some kind. However, once a nodule is found, primary care physicians want these patients followed by a specialist, she said.

**Who to Screen?**

In the new guideline, regular annual CT scans are recommended for 2 target groups of high-risk smokers and former smokers.

The one group of high-risk individuals consists of adults 55 to 74 years of age with a 30-pack-year or more history of smoking tobacco (i.e., smoking 1 pack a day for 30 years), even if they stopped smoking in the previous 15 years.

This is the same as the inclusion criteria for the NLST.

This is a category 1 recommendation, which is based on high-level evidence (i.e., NLST, a randomized controlled trial) and uniform NCCN consensus that the intervention is appropriate.

"The evidence is really strong," said Dr. Reid.

The other group of high-risk individuals recommended for annual screening are those who are slightly less-heavy smokers (a 20-pack-year or more history of smoking) but who have an additional risk factor, such as cancer history, lung disease history, family history of lung cancer, radon exposure, or occupational exposure.

This is a category 2B recommendation for CT screening. It is based on lower-level evidence and NCCN consensus, but not uniform consensus (as in category 2A), which signifies that there was some debate about this recommendation.

**False-Positive Results and a Follow-Up Algorithm**

In the NLST, participants were screened once a year for 3 years, and were followed for 3.5 additional years with no screening.

There were 247 deaths from lung cancer per 100,000 person-years in the low-dose CT group, and 309 deaths per 100,000 person-years in the radiography group, which is a relative reduction in mortality from lung cancer with low-dose CT screening of 20% (95% confidence interval, 6.8 to 26.7).

The rate of positive screening tests was more than 3 times higher with low-dose CT than with radiography (24.2% vs 6.9%) in all 3 rounds in the NLST. All told, 40% of the NLST participants had at least 1 false-positive result during the 3 years.

As noted above, most of the positive tests were false; 96.4% of the positive screening results in the low-dose CT group and 94.5% in the radiography group were false-positive results.

In their published paper (N Engl J Med. 2011;365:395-409), the NLST researchers explained that "the vast majority of false-positive results were probably due to the presence of benign intrapulmonary lymph nodes or noncalcified granulomas."

The new guideline spells out how clinicians should proceed with a variety of screening findings.
Some nodules require no follow-up, such as those with a benign pattern of calcification, fat in the nodule as in hamartoma, and features that suggest inflammation or infection.

For all solid or part-solid nodules in need of follow-up, there are recommendations for further CT screenings; the frequency depends on the size of the nodule. A similar size-dependent follow-up applies to nodules that are of ground glass opacity, ground glass and nonsolid, and new nodules that occur during follow-up.

**Cost Issues**

The NCCN guideline list the risks and benefits of lung cancer screening.

The benefits, in addition to decreased mortality, include improved quality of life through a reduction in disease-related morbidity and reduction in anxiety and psychosocial burden.

The risks include the "futile" detection of small aggressive tumors or indolent disease, complications from diagnostic work-up (the rate of which, however, was low in NLST, at 1.4%), false-positive results, radiation exposure, and cost.

Cost remains a huge issue with regard to the future implementation of screening in the United States. However, a representative of the Lung Cancer Alliance told the audience that the health insurer WellPoint has decided to cover the cost of the screening.

When the NLST results were published, the researchers, led by Christine Berg, MD, from the National Cancer Institute, wrote that more evidence is needed to support lung cancer screening. "The current NLST data alone are...insufficient to fully inform such important decisions [on lung cancer screening recommendations]."

The researchers estimated the immensity of the potential impact of a nation-wide screening policy in the United States. Although there are only 7 million adults in the United States who meet the entry criteria for the NLST, there are an estimated 94 million adults who are current or former smokers, and thus potential screens, they said.

An expert in preventive medicine expressed deep reservations about cost. Whatever the target population, "a national screening program of annual low-dose CT would be very expensive," wrote Harold Sox, MD, from Dartmouth Medical School in West Lebanon, New Hampshire, in an editorial that accompanies the published NLST study (N Engl J Med. 2011; 365:455-457). "I agree with the authors that policy makers should wait for more information before endorsing lung cancer screening programs," he wrote, citing cost as his principal objection.

Cost-effectiveness studies are underway but are not yet complete, Dr. Wood told the NCCN audience.


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