Screening for Lung Cancer: An Expert Review

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ABSTRACT

The NCCN Guidelines for Lung Cancer Screening have evolved over time to reflect the latest evidence and expert consensus. These NCCN Guidelines have played a significant role in shaping clinical practice and policy, leading to increased payer coverage for lung cancer screening and decreasing lung cancer mortality. Continued research and advancements in early detection methods, along with the implementation of effective screening programs, will be crucial in the ongoing effort to reduce lung cancer mortality and improve the overall quality of life for patients affected by this disease.

The NCCN Guidelines for Lung Cancer Screening have played a significant role in shaping clinical practice and policy, leading to increased coverage for lung cancer screening, increased incidence of early-stage disease, decreased incidence of late-stage cancer, and decreased lung cancer mortality. However, significant barriers remain to the uptake of lung cancer screening. During the NCCN 2023 Annual Conference, Ella A. Kazerooni, MD, MS, Professor of Radiology and Internal Medicine, and Associate Chief Clinical Officer for the Diagnostic and Clinical Information Oversight Team, University of Michigan Rogel Cancer Center, and Vice Chair of the NCCN Lung Cancer Screening Panel; Jacob Sands, MD, Thoracic Medical Oncologist, Dana-Farber Cancer Institute, and Assistant Professor of Medicine, Harvard Medical School, and panel member of the NCCN Lung Cancer Screening Panel; and Douglas E. Wood, MD, Henry N. Harkins Professor, and Chair, Department of Surgery, University of Washington, and Chair of the NCCN Lung Cancer Screening Panel, reviewed current evidence for and preferred modalities of lung cancer screening and identified patients at high risk who would be appropriate for such screening. The presenters also discussed current challenges regarding the use of lung cancer screening and strategies to address them.

Lung Cancer Screening: Background and Overview

Dr. Sands underscored the critical role of early diagnosis in lung cancer, which is responsible for approximately 1 in 4 deaths related to cancer. According to Dr. Sands, lung cancer screening can significantly impact mortality rates. However, it is a team effort and not just a simple test, he emphasized.

The National Lung Screening Trial (NLST) was a landmark study involving >53,000 individuals and was a $250 million investment, which compared low-dose CT (LDCT) scans with annual chest x-rays (CXRs) for lung cancer screening.1 Inclusion criteria were age of 55 to 74 years and a smoking history of ≥30 pack years, with exclusion of individuals after 15 years of smoking cessation. Individuals were randomized to CXR or LDCT and underwent baseline imaging followed by 2 yearly follow-up screening scans. The NLST demonstrated that screening with LDCT resulted in a 20% reduction in lung cancer mortality and a 6.7% (P=.02) reduction in all-cause mortality, primarily due to the early detection of lung cancer.

The US Preventive Services Task Force (USPSTF) and the Centers for Medicare & Medicaid Services (CMS) both approved the use of lung cancer screening based on this trial, with coverage policies essentially following the inclusion criteria of the study. Patients should discontinue screening if they develop a health problem that substantially limits life expectancy.

The European NELSON trial involved >15,000 participants and examined the use of CT scans at baseline, 1 year, 3 years, and 5.5 years. The study found a >20% lung cancer-specific mortality benefit, with the benefit for women appearing to be even higher.2 This trial influenced the updated USPSTF guidelines, which currently recommend the initiation of screening at age 50 years for those with a ≥20 pack-year smoking history.

The Italian MILD trial, a smaller study with approximately 4,100 participants, showed a significant separation in survival curves after 5 years (hazard ratio, 0.42; 95% CI, 0.42–0.79).3 The trial compared screening (combined yearly and biennial) versus observation, demonstrated...
the importance of consistent screening for increasing the benefits of early detection.

In addition, Dr. Sands discussed the issue of false-positives and lung cancer diagnosis rates in screening. A study by McKee et al reported a 13% positive scan rate at baseline and about a 6% rate in following years. The lung cancer diagnosis rate was 2.3% at baseline and around 1% in subsequent years. According to Dr. Sands, there has been widespread misunderstanding about false-positive rates that is important to clarify for a better understanding of the benefits and risks associated with lung cancer screening.

Shared Decision-Making Aid
Dr. Sands also presented a shared decision-making aid, which can be used as an effective tool for primary care providers (PCPs) to help patients understand the benefits and risks of lung cancer screening. The decision aid highlights that, in a full-duration screening program, participants have an approximately 10% chance of developing lung cancers and a 1% chance of undergoing invasive testing for a false-positive test.5

The decision aid also emphasizes the higher proportion of early-stage diagnoses (stage I–II) within a screening program compared with non-screen-detected lung cancers. This decision aid, developed by a group of experts from Canada, the United States, and Europe, may be a valuable resource for PCPs and patients alike, according to Dr. Sands.

Lung Cancer Screening: Focus on NCCN Guidelines
As Dr. Wood reported, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Lung Cancer Screening have evolved significantly since 2010.

Since then, the NCCN Lung Cancer Screening Guidelines Panel has led the way for the evidence-based guidelines, publishing the first guidelines in 2011. In 2010–2011, a diverse panel of world experts used the evidence from the recently published NLST to make category 1 recommendations for lung cancer screening for a well-defined, high-risk population. But the NCCN panel recognized that the NLST had limited inclusion criteria and did not assess more diverse patients with high risk of lung cancer. Therefore, the panel extrapolated the NLST risk factors to an additional broader group of individuals to be considered for lung cancer screening with a lower 2A level of evidence. NCCN was widely criticized for the broadened criteria, but annually reviewed the data and stayed consistent with their forward-thinking recommendations. Of note, in 2021 and 2022, respectively, both USPSTF and CMS updated their guidelines in a way that nearly matched the broader recommendations that had been part of NCCN Guidelines for 9 years. Furthermore, NCCN Guidelines for Lung Cancer Screening positively influenced healthcare policy, particularly the approval of lung cancer screening by CMS in February 2015 and the updated inclusion criteria in 2022. The guidelines have also been used broadly by health systems and healthcare providers to guide their new lung cancer screening programs.

Two important, unique factors have made the NCCN Guidelines for Lung Cancer Screening particularly valuable and relevant. First, the guidelines provide extensive support and recommendations to assist healthcare providers in the management of screen-detected lung nodules. Second, annual updates have allowed the NCCN Guidelines to respond to rapidly changing data from other studies and gained from ongoing screening experience.

The update to the NCCN Guidelines in 2021 simplified and broadened the criteria for lung cancer screening. Current recommendations include screening for individuals aged ≥50 years and smoking exposure of ≥20 pack-years.6 Although these guidelines have played a crucial role in influencing decisions made by the USPSTF and CMS, there are 2 very important differences.

First, the USPSTF and CMS stipulate an upper age limit of 80 years for screening. In contrast, NCCN considers an upper age limit to be arbitrary and age-biased, and instead recommends function-based rather than age-based criteria for cessation of screening. NCCN recommends screening unless functional status and/or comorbidity would prohibit curative-intent treatment, including shared decision-making regarding an individual’s interest and willingness to undergo treatment. Some individuals aged <80 years may not be eligible for curative-intent treatment, and therefore should no longer be screened, whereas others may continue to have a fitness and health status making them eligible for treatment past age 80 years; they should still have the option of screening. NCCN considers this difference in recommendation more equitable and justified by evidence and the pragmatic delivery of healthcare.

Secondly, USPSTF and CMS limit access to individuals who formerly smoked to those who quit within the last 15 years. NCCN believes that a 15-year restriction for these individuals at high risk for lung cancer is not based on or justified by evidence. Further, this restriction creates an unintended consequence and a paradox of incentives for individuals who formerly smoked who are at high risk for lung cancer and wish to continue screening. This criterion may have the unintended consequence of encouraging individuals to resume smoking or to lie about their smoking history in order to remain eligible for screening. Neither result is what we want to encourage in patient engagement for early detection. Furthermore, studies that have looked at patients with lung cancer and reviewed their retrospective eligibility for lung cancer screening have identified this 15-year restriction as the most common
cause of excluding these individuals for screening eligibility. The NCCN Lung Cancer Screening Guideline Panel continues to lead, rather than follow, the effort to minimize disparities and stigma in the delivery of early detection for individuals at risk of lung cancer and are proud to see rapidly decreasing mortality from lung cancer over the past decade that equates to thousands of lives saved each year.

“Lung cancer is the leading cause of cancer death in the United States, with more people dying from lung cancer than the next 3 most common cancers combined [colorectal, breast, pancreas],” said Dr. Wood. “Early detection through screening is the best chance to improve survival for patients with lung cancer.”

The International Early Lung Cancer Action Program (I-ELCAP) demonstrated a 5-year survival rate of 84% for patients with lung cancer detected through screening compared with the standard lung cancer survival rate of 22%.6

Recent reductions in cancer mortality in the United States have been driven predominantly by lung cancer, with a decrease of overall cancer mortality by 2.2% in 2016–2017 and further declined by 2.4% in 2017–2018. The pace of decline in lung cancer mortality has increased from 3.1% per year in 2005–2014 to 5.3% per year in 2014–2020.7 According to Dr. Wood, the significant improvement in cancer mortality rates is attributed to advancements in smoking cessation, lung cancer screening, and treatment options, including targeted therapy and immunotherapy.

“Early diagnosis has the potential to save up to $26 billion a year, making it a more economically viable approach compared with other interventions,” said Dr. Wood.8 “Early detection can significantly reduce the burden of cancer on patients, their families, and the healthcare system.”

**Lung Cancer Screening: Benefits and Challenges**

According to Dr. Kazerooni, addressing the challenges of identifying eligible patients, optimizing electronic health records (EHRs), and engaging with communities are crucial for the success of lung cancer screening programs and ultimately improving lung cancer outcomes. Dr. Kazerooni outlined several key challenges faced in reaching high-risk populations.

One of the first challenges is that lung cancer screening programs need to be tailored to different healthcare environments and populations. Factors such as socioeconomic status, ethnic minorities, and rural communities play a significant role in determining the most locally optimal program structure. Healthcare providers should be realistic about their own local capabilities within the lung cancer screening care continuum, and ensure they are connected to specialized resources when patients require additional diagnostic testing and procedural care.

Identifying patients eligible for screening is not a simple task, because EHRs often have insufficient documentation of pack-year history, and many frontline staff are not well trained to understand either why pack-years are important during healthcare visits or how to collect the information accurately. Continuous education and support for PCPs, medical assistants, and other members of the primary care team are essential for accurate smoking history documentation. This is particularly important considering the relatively high turnover rate and low pay for medical assistants, who are often responsible for entering the pack-year history, noted Dr. Kazerooni.

Setting up primary care practices for success in lung cancer screening involves optimizing EHRs and engaging in community outreach to build trust and address stigma surrounding lung cancer. Each EHR system is different, commented Dr. Kazerooni, so it is crucial to adapt and develop strategies that work best for the specific primary care practice and lung cancer screening program.

Another challenge is that community engagement is vital for identifying patients eligible for screening, especially those who may not readily seek healthcare appointments, and those who may be underinsured or uninsured. Building trust with the community and helping people understand the lung cancer screening process are essential to overcome stigma and encourage individuals to consider screening, said Dr. Kazerooni.

Furthermore, stigma in lung cancer is real and pervasive, and prevents many patients from seeking care, staying with their care, or trusting their healthcare providers. Patients may feel nihilism, including being undeserving of care or skeptical about the potential benefits of screening due to the historically poor outcomes associated with the disease. Changing the narrative to one of hope and involving community health workers are key to reaching high-risk populations and addressing these concerns.

Because radiology plays a critical role in lung cancer screening, according to Dr. Kazerooni, radiologists should use LDCT scan techniques to minimize radiation exposure for patients, especially because these patients will be returning for annual screenings. Radiologists should also provide clear and consistent structured reports to help healthcare providers understand both the findings and the appropriate steps, whether it is return for annual screening, an interval low-dose CT scan, or referral to a specialist.

The last challenge that Dr. Kazerooni discussed is the importance of smoking cessation in reducing the risk of lung cancer and other health conditions. Healthcare systems should explore available resources to support smoking cessation as the number one way to reduce mortality from lung cancer.
Ultimately, Dr. Kazerooni emphasized, collaboration among PCPs, specialists, and key staff members is essential for creating a successful lung cancer screening program, with nurse care coordinators having a pivotal role in program success. This includes shared decision-making, tobacco cessation support, and effective management of positive screening results.

“Healthcare systems should invest in resources and education to support these initiatives and address barriers to their success,” Dr. Kazerooni concluded.

Disclosures: Dr. Sands has disclosed serving as a scientific advisor for AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Boehringer Ingelheim, Curadev Pharma, Daiichi-Sankyo Co., Jazz Pharmaceuticals Inc., Medtronic, Inc., PharmaMar, Sanofi, and Takeda Pharmaceuticals North America, Inc. The remaining presenters have disclosed no relevant financial relationships.

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References