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Understanding Updates in Lung Cancer Screening

Dr. Sands:

Some describe lung cancer screening as the single most important initiative to reduce cancer mortality. Welcome to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands, and joining me to discuss updates and lung screening is Dr. Andrea McKee, Chair Emeritus in Radiation Oncology and Director of the Lung Screening Program at Lahey Hospital and Medical Center, along with being President of the Rescue Lung Society. Dr. McKee, welcome to the program.

Dr. McKee:

Oh, thank you so much. It's a pleasure to be here, Jacob.

Dr. Sands:

Let's start with the data for lung screening. Everything in medicine is discussed as risk versus benefit. So what are the benefits to doing screening scans?

Dr. McKee:

Well, first and foremost is the benefit to detect early-stage lung cancer. I mean, that's what we have seen actually for a while in terms of the data. We had data from the I-ELCAP group that demonstrated that we could detect early-stage lung cancer, the majority of the time for patients who undergo annual low-dose CT of the chest. What was disputed and argued for a while was whether or not that translated into a mortality benefit. And it was ultimately the National Lung Screening Trial, that was published back in 2011 in the *New England Journal of Medicine*, that really ended the debate about whether or not there was a mortality benefit to CT lung screening. So the National Lung Screening Trial was one of the largest cancer prevention trials that has been conducted in this country. About 55,000 patients who were randomized to an annual chest x ray versus an annual low dose CT of the chest over three screens. So it was two years, three screens; one at baseline and then one at the first year and one at the end of the second year. And what that study demonstrated actually at an early timepoint, the NCI actually halted the study to reveal that the 20 percent mortality benefit was reached before the full six-year follow-up. And so the trial was published and everyone in the chest x ray was offered the opportunity to undergo low-dose CT screening, given the 20 percent mortality benefit that was seen in that study.

And then, of course, we were in this kind of difficult time where we had the evidence that CT lung screening saves lives, but we didn't actually have the ability to do it in clinical practice because there was no way that a physician could order a CT of the chest with an indication for screening, that the patient is at high risk for lung cancer and should undergo a screening CT. That code didn't exist, so insurance companies couldn't pay for it. And CMS didn't have a way to pay for it. And so it was a difficult time and it took several years for us to go through the process of first the USPSTF recommending the exam. And that came out in 2013 when the USPSTF recommended that patients between the ages of 55 and 80 undergo an annual low-dose CT of the chest if they had at least a 30-pack-year history of tobacco use and were currently smoking or quit within the past 15 years.

And then within about a year, CMS issued their own recommendation coverage for the exam. Since 2015, centers have been looking to offer this service to high-risk patients.

So since that time now we have new data. We have a large European study, as well as another relatively large European study. None of them are as large as the NLST. But the NELSON study had about 17,000 patients, and it was a randomization of annual low-dose CT of the chest versus no screening, which was really interesting. And it did somewhat predictably show an even larger benefit to CT lung screening. So we believe the 20 percent mortality benefit is actually the floor, and when you conduct low-dose CT screening over further years from the time someone enters the program at the age of 55 through the age of 80, the mortality benefit is even greater than that 20 percent.

Dr. Sands:

Yeah, you know, a lot of times I hear that discussion about mortality, and you've highlighted that the lung cancer specific mortality within the NLST reached that 20 percent benefit. I think a lot of people forget that it also showed an overall mortality benefit within NLST. And some of these smaller, but still multi-thousand-patient studies did not show that overall sort of survival mortality benefit although, of course, none of these trials were really designed to look at overall survival. But often I hear people kind of forgetting that the NLST did show that overall survival benefit despite being stopped early.

Dr. McKee:

Absolutely. There are other benefits in addition to the lung cancer specific mortality benefit, which is the reason for the exam, but we are also seeing within our program, we're seeing higher quit rates for tobacco users, current smokers. We have about a 50/50 mix of patients who currently smoke and former smokers in our program. And amongst the current smokers, we have seen a 21 percent point prevalence quit rates. So we're helping them to be able to become tobacco free. And what we've seen in our program on multivariate analysis is the patients who are able to stay in the program for longer periods of time who are more likely to quit tobacco use. And so we're really excited about that.

The other thing we see in the screening program is the diagnosis of non-thoracic malignancies. So we're not specifically looking for non-thoracic malignancies, but this patient population, given their history, their age, and tobacco profiles, for every 7.5 lung cancers that we diagnose, we diagnosed 1 non-lung malignancy. So cancers such as renal cancers or breast cancer, hepatocellular carcinoma. So we are finding other cancers; that's not our intent. But when you do a CT of the chest, you just end up seeing other parts of the body. And so that's something that may contribute to that overall mortality benefit that you mentioned.

The other thing that we find when we do a CT lung exam, we find coronary artery calcifications for patients. Understandably, they're older and they have a history of heavy tobacco use. And so some of our primary care physicians are using that information to help their patients and counsel their patients regarding their cardiac history. We find emphysematous changes in the lungs. And some of our pulmonologists are using that information to help patients to optimize their lung health. So there's a lot that can be done within this patient population, given the unique characteristics of this patient population. And so it'll be interesting to see, you know, how those other the pieces of information get folded into care plans in the future.

Dr. Sands:

For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands and I'm speaking with Dr. Andrea McKee about lung screening. Now, the other part of risk-benefit is the risk. And certainly people talk about things like false positive rate and overdiagnosis. And can you outline some of the risks to lung screening?

Dr. McKee:

Absolutely. So we know more about the risks now that we've been doing it for longer. So there is more information that we have now that we didn't have when the NLST was first published. One of the things that we have is the long-term data from the NLST. So the NLST investigators published their 11-year follow-up data not too long ago. And what that was able to confirm, which, you know, those of us in the field sort of suspected this, but the overdiagnosis rate for CT lung screening is actually quite low in the NLST. The 11-year follow-up data published a 3 percent risk for overdiagnosis. And this is really important because what it underscores is the deadly nature of lung cancer. You know, we know it's the number one cancer killer in the United States, claiming more lives than breast, ovarian, and uterine cancers combined for women in the United States. And overdiagnosis really shouldn't be a big concern for these patients, given how deadly the disease is. And that's what the long-term follow-up data for the NLST demonstrated.

The false positive rate is something that has been published actually in the peer-reviewed literature many times as being much higher than it actually is. And this is something that, we're trying to make sure people know the facts about the false positive rate. The false positive rate in the NLST was actually in the first round of screening about 23 percent. It has been misquoted in the medical literature as being 96 percent. And it's really important that physicians understand that there is not a 96 percent false positive rate. If there was a 96 percent false positive rate, I would never recommend a screening test; that is just simply too high of a false positive rate.

What it actually is in clinical practice, because we're using systems to really categorize the findings in a lung screening exam. We use a system called Lung-RADS, which was based off of the BiRADS system that has been used for screening mammography for many, many decades. And we actually developed that system at Lahey because we knew that we needed to categorize these findings and be able to track patients and understand when is it appropriate to refer patients for care escalation and when is it appropriate to just keep patients within the screening program and not do workups on these patients. So what we see through the use of Lung-RADS, which defines a positive nodule at 6 millimeters as opposed to 4 millimeters, which was the nodule threshold side in the NLST, is that the rate of false positive findings is about 10 percent in the baseline round of screening, and it goes down to 5 percent thereafter because now you have comparison exams to be able to compare prior studies to your current CT exam. So 10 percent and 5 percent are actually

false positive rates we see with screening mammography.

So the false positive rate is lower than what many people believe it to be. BAnd it's similar to what we see mammography. And that's a good way of describing it to patients when they are asking about risks and benefits of screening, when you're counseling them for shared decision making.

The other potential harms associated with CT lung screening. There's a small amount of radiation that patients are exposed to with a low-dose CT lung exam. It's really less than a millisievert; it's about 0.2 millisievert or even lower. So this is something that is extremely low, about that of, what we see in the screening mammography programs. And we know that from women who have undergone mammograms for many, many decades, there really were not able to detect a higher risk of secondary malignancies from these low-dose radiation exams.

It is important that you are screened at a center that is focused on making sure that radiation levels are within that low-dose environment that is recommended by the guidelines from ACR to AAPM to a variety of different people who have weighed in on the issue of what's an appropriate low-dose screening test.

Of those 10 percent who have a positive finding on the exam on the baseline round of exams, the vast majority of those patients actually go on to have a three- or six-month follow-up CT scan as opposed to a biopsy or surgery or whatever it might be. In our program, it's a little over 2 percent in the baseline round of screening who actually have lung cancer. So that's the other thing to think about.

The NLST showed that 1 percent of patients in the NLST had lung cancer on the baseline round of screening. In clinical practice, we're actually seeing that to be higher, which is an important feature when we look at the performance of screening exams. It makes the exam much more effective when you have a higher rate of lung cancer amongst your screened population. And that's probably because there was a little bit of a healthy bystander effect for the patients who enrolled in the NLST. And that when you actually bring that out to clinical practice, there are patients who, you know, have smoked more or, you know, just end up being a slightly higher risk. And so it depends on which population you look at.

In the military populations, we're seeing even higher rates. There are some publications with the 4 percent, 5 percent, lung cancer at the baseline round of screening. And that may have to do with some of the additional exposures that people in the military see, such as Agent Orange, diesel fumes of the burn pits, a variety of risk factors that our servicemen and women are exposed to, that the general population don't see.

Dr. Sands:

Another thing I hear people mention is just, you know, is there being a nodule and now somebody is really anxious. But the follow-up scan three months later shows that it's nothing and that everything's fine and now is considered a negative. And that never really seemed like a reason to not do scans that save other people's lives, just because you're causing some anxiety for some others who end up where fortunately the scan is good. But what are some of the things that you can say to them? I mean, this seems very much like just discussing things and helping patients understand the perspective and that a nodule isn't necessarily cancer. So how would you recommend having that discussion with patients?

Dr. McKee:

I find it helps to use analogies when speaking to my patients. I try to talk about things that they're familiar with, like breast screening. If it's a female patient, they understand that sometimes they'll be called back for things that end up not being breast cancer. And so we talk about that analogy.

The other thing is we talk about the fact that, you know, your lungs are filters. And as we live throughout our life, things get caught in our lungs just like they do in your -the filter in your car and the filter in your house. And so you can have little things in your lungs that turn out to be nothing. And that's what we're seeing when we're looking for small lung cancers, then we can run into, you know, this is a very, very sensitive test. We can run into little things that end up being nothing. I use the analogy of freckles on the skin. Like we all have freckles all over our skin and the freckle's not a problem unless it turns into a darker area or develops irregular borders, and there are features that are concerning. And the way we discern if something is concerning in the lung is by looking to see if it grows over an interval period of time. And if it does grow, then we're going to need to care escalate, then we're going to need to do something. And if it does grow, you want us to intervene. But also We're still going to intervene when something is really early stage. And that the five-year overall survival for a screen-detected stage I lung cancer is 90 percent. And that's not something that the general public or even many physicians are aware of, that when we find early-stage lung cancer, it's actually highly curable because we're just not used to finding early-stage lung cancer so often in the absence of screening.

Dr. Sands:

Well, you've covered a lot in this very important topic of lung screening and the potential for substantially impacting cancer mortality

numbers, I want to thank you, Dr. McKee. Absolutely a pleasure having you on the program.

Dr. McKee:

Well, thank you, Jacob. It's been a pleasure talking with you.

Dr. Sands:

I'm Dr. Jacob Sands. To access this and other episodes in our series, visit reachmd.com/projectoncology, where you can Be Part of the Knowledge. Thanks for listening.