

Current Status of Lung Cancer Screening in the Wake of the National Lung Screening Trial (NLST)

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Introduction

Andrew Schorr:

Lung cancer detection can be tricky. Who should be screened and when? Well, there are now new study results that are being released from the National Lung Cancer Screening Trial—which has been going on across the country for several years—and the results are significant. Coming up, Dr. Eric Hart, a chest radiologist from Northwestern Memorial Hospital, will discuss the latest news from the study and how this may affect you and your loved ones. It's all next on Patient Power.

Andrew Schorr:

Hello and welcome to Patient Power sponsored by Northwestern Memorial Hospital. I'm Andrew Schorr.

When you think about different types of cancer, the deadliest one unfortunately is lung cancer. As a matter of fact, in 2010 it was estimated that lung cancer killed 157,000 people in the United States. As a matter of fact, lung cancer kills more people than the cancers that affect the breast, prostate and colon combined.

Now, there are more than 94 million current and former smokers in the United States, and many of those folks are at high risk for lung cancer, and as we've always been told with cancer typically early detection can save lives. So you wonder, 'well, if we could detect lung cancer at its earliest stage couldn't we save lives?' And then the question follows, if that is true, what's the best way to screen for lung cancer so we can spot it early, do something about it and allow people to live longer and live better?

So that was really the focus of a trial that went on for a number of years, called the Lung Cancer Screening Trial. We're going to learn more about it on this program from a radiologist who specializes in chest imaging at Northwestern Memorial Hospital in Chicago. We will also come to understand what the results were of this trial—which were significant and are still being digested, what it means for people who smoke a lot, should they be screened and how should they be screened, and should more people be screened. And depending on what's found, what should be done and what does it mean for the future as far as saving lives from lung cancer.

Understanding the National Lung Screening Trial

Andrew Schorr:

To help us understand this is Dr. Eric Hart. Dr. Hart is an associate professor of

radiology at Northwestern's Feinberg School of Medicine. He's at Northwestern Memorial Hospital in Chicago. Dr. Hart, this trial's results came out in November of 2010, and it, I believe, is a big deal, but why don't you help us understand this better. First, is it big deal? And what were the results?

Dr. Hart:

Well, first of all, I would like to thank you for having me on the program. And to answer your question briefly it is a very big deal. The National Lung Screening Trial, as you mentioned, has been ongoing since 2002, and it is the first research trial of its type, which is a large, randomized controlled trial, to show that screening for lung cancer reduces lung cancer mortality and specifically with the trial screening with low-dose helical CT scans reduced lung cancer mortality. So, yes, it is a very big deal because the mortality statistics, as you said earlier, are just horrible from lung cancer.

Andrew Schorr:

So how much did it show people if they were screened early with helical CT scans—which we'll understand what those are—how much did the death rate go down?

Dr. Hart:

So the patients—excuse me, the participants really who were screened with the helical low-dose chest CT showed a 20 percent reduction in mortality versus people who were screened with a chest x-ray.

Andrew Schorr:

So what's the difference between chest x-rays (and so many of us have had them) and a helical CT scan? What's the difference, and for you as a radiologist, what does it enable you to see that you might not see otherwise?

Dr. Hart:

Well, a chest x-ray is a two-dimensional picture basically of the organs of the chest, and so, you know, as we exist in our lives we're all three-dimensional beings, and so we compress information into two dimensions and we display it and try to interpret what's going on inside the chest. The helical CT scanner gives us effectively a three-dimensional view of whatever organs of interest we're studying. In our case we were looking for lung cancer so we were screening the chest, and it's that additional information in three dimensions that really allows us to look for smaller objects and again in this case, smaller lung cancers. It just gives us a better overall picture of what's going on inside the body instead of compressing all of that information and making us take more of an 'educated guess' at it.

Andrew Schorr:

So more defined imaging allows trained radiologists to spot things, see things more clearly, and then you can determine if there is evidence of cancer. And does it allow you to see things, tumors, if you will, that are smaller?

Dr. Hart:

It does. Typically we see nodules in the lungs which may be lung cancers that are

less than a centimeter in size and in many cases down to just a few millimeters in size—two, three, four millimeters. Whereas with a chest x-ray typically we detect nodules in the lungs that are between one and two centimeters or maybe even slightly larger, so there's a significant difference in the size of the lesion that we can ultimately see.

Andrew Schorr:

So my understanding with the study is you had folks who were pretty heavy smokers over many years and some of them had chest x-rays and some of them had these more sophisticated CTs, and more cancers were spotted, earlier detection, and that enabled intervention as appropriate, and there was a 20 percent reduction in mortality for the people who had the CTs. Did I get it right?

Dr. Hart:

That's correct.

Andrew Schorr:

So that's a big deal. With lung cancer we're talking about thousands and thousands of people.

Dr. Hart:

Correct. If the 20 percent mortality reduction holds up, going back to your earlier statistic of about 157,000 anticipated deaths in the US in 2010, and we're looking at tens of thousands of people whose deaths we could potentially prevent. And "potentially" is a key word there. Obviously no testing is perfect, and so we wouldn't necessarily pick up every lung cancer at an early stage if we were screening a large amount of people, but we certainly feel that there is the potential that we can save a significant number of lives in this country.

Andrew Schorr:

Now, I mentioned that the folks who were in the trial were heavy smokers. What does that mean? How were people selected?

Requirements for Trial Participants

Dr. Hart:

Heavy smoking for the trial was defined as being a number called the 'pack-years,' and in our case we used a cut-off of 30 pack-years. And pack-years really are just an easy way to represent things. So if you're a smoker who smokes two packs a day and you've done it for 15 years, it's simply that number two times the number 15. That gives us 30 pack-years. So another example would be if you smoked one pack a day you would have to smoke for 30 years to hit that number. So it gives us a way to quantify how much people smoked both over time and on a per-day basis to get to a number that we feel is a high-risk cut-off.

Andrew Schorr:

So some of the folks had x-rays, some of the folks had CTs. And I understand in many cases there were urine samples and blood tests taken as well?

Dr. Hart:

Yes. For the major design of the trial, it was called a randomized, controlled trial, and approximately half of the people who agreed to enter the trial were randomized to get a chest x-ray and about half were randomized to get the CT scan. And in one arm of the trial, the arm run by the American College of Radiology Imaging Network, about 40 or 45 percent of those participants agreed to supply what are called biospecimens. And in this case they provided blood samples, sometimes sputum samples if they could cough anything out, and urine samples that can be used for future analysis.

Andrew Schorr:

And of course we also have...I'm sure history was taken, like 'did anyone in your family have lung cancer,' and other things. So as you crunch the data, and I understand that will go on for quite a while, we may well learn more than just the difference between chest x-ray and CT, correct?

Dr. Hart:

Absolutely. Historical data was very important in terms of who in your family was a smoker and who had lung cancer, was it a first-degree relative or second-degree relative, those kinds of things.

And remember too, another thing we haven't touched on yet is that the people who agreed to enter this study skew relatively older in that they had to be at least 55 years old to enter, and they could not be older than 74 years at the time they entered to be included in the study. They could be one day before their 75th birthday, but they could not have reached that point. And those choices were made to hopefully increase the number of people who had truly heavy smoking histories, but also when you're screening for any kind of disease you want to make sure that the people you're screening are actually able to undergo the potential therapy or else the screening test will not be of any utility.

Andrew Schorr:

Right. And the therapy, if something is found--and we're going to talk about what do you do based on what you see--but it could be lung surgery, certainly biopsies, lung surgery or in some cases some people might even have systemic therapy, like chemotherapy, right?

Dr. Hart:

Correct. And the hope would be that we find the lung cancer early, and generally the accepted therapy for early-stage lung cancer is to have it surgically removed. So the goal would be to find people who can undergo surgery that would be done with what's called curative intent because by the time patients, or people, depending on how you look at things--they're people when they enter the study. They may be patients when they come out of the study. But by the time you're into systemic therapy it's in most cases not felt to have the same curative potential for early lung cancer as does surgical removal.

Andrew Schorr:

Right. We should mention that the five-year survival rates of lung cancer when it is found when it's stage I-A, where it can be easily removed surgically, I understand is about 70 percent, but more than 75 percent of individuals have incurable locally advanced or metastatic disease, and that just has a five-year survival rate of less than 5 percent.

Dr. Hart:

Yes.

Andrew Schorr:

Hence the high mortality from lung cancer. So let's go back to finding it early. So this study had people who were pretty heavy smokers. One would say, well, gee, nobody wants to develop lung cancer. What if you're a less heavy smoker, you know, or you smoke occasionally. And we're talking about 94 million people who smoke, well, shouldn't we now be broadening this out? I know that in the study the National Cancer Institute, they were paying for the imaging, but now we say, 'well, gee, okay, we have this groundbreaking result. Let's just roll it out to a lot more people.'

What does this Mean for the General Smoking Population**Dr. Hart:**

Well, and I think a lot of people would think on the surface that that's the right thing to do, but we do have a groundbreaking result but we have a groundbreaking result in a select population, and so I think we need to maybe go slowly here and say for this select group lung cancer screening reduces mortality, so we need to figure out the way to roll out screening for the larger heavy-smoking population in the country other than just the people who were in the study. But to say that we can--or to try to generalize the results, to less heavily smoking populations or to other people with occasional smoke inhalation, I don't think we're ready to do that yet. I think it would be unwise to say that these results generalize to a larger population.

We may find more information about that as the number crunching of the data from the study goes on, but it may in fact take additional studies to try to prove whether someone with a slightly lesser risk factor profile from their smoking history would truly benefit from screening. So we don't want to get into the situation where we screen everyone who thinks that they have some exposure history only to later find that, you know, when you do that screening doesn't make a difference. We want to screen in those that we know it's going to be effective first, and then try to figure out who else might be effectively screened as well.

Andrew Schorr:

We should make the point that really screening is so important but what--the big, key message here, knowing that lung cancer does not only develop in smoke but it develops mostly in people who smoke, that the key message is don't smoke or stop

smoking.

Dr. Hart:
Absolutely.

Andrew Schorr:
And is it ever too late to stop smoking, doctor?

Dr. Hart:
It is never too late to stop smoking because smoking doesn't just cause lung cancer. Smoking causes a whole host of other systemic problems, other cancers, including the GI tract like the esophagus, the head and neck, the bladder, and emphysema. Smoking exacerbates heart disease. All of those things can be improved or further declines can be prevented if people stop smoking. So we should always encourage current smokers to stop first, we should encourage people who have never smoked to never take up the habit, and then kind of for the people who unfortunately became addicted to the nicotine in cigarettes if they have a heavy smoking history we should consider screening them going forward.

Andrew Schorr:
Well, we've talked about this on a number of programs, and one former Chicagoan, President Obama, we hear finally quit smoking, so that's good. So when someone quits do their lungs begin to recover?

Dr. Hart:
The first benefits are that their lungs stop getting worse, and actual--for patients who have developed emphysema, for instance, recovery of lung tissue we don't currently see as happening although there are lots of people who are working on making that happen in the future. I think it's probably most important to think of it as preventing additional damage specifically to the lungs.

Things that do improve are certainly heart disease risk, blood pressure issues, and the risk of developing lung cancer and others cancers does go down over time, although if you were a heavy smoker it probably never goes back to the same risk as a nonsmoker.

Andrew Schorr:
All right. It certainly has benefits though, folks, and we just want to underscore that. So if you smoke, there are so many programs. I know it can take for some people 14 tries to quit, but there are a lot of resources to help you now and it's so important.

So let's go back to radiology for a minute. So there you are, you're screening, and now you have CTs and you can see in different dimensions and you can spot smaller tumors. So one would say, well, I know you don't have the guidelines yet of saying, you know, how this is going to roll out, but one would say, well, if you can spot this, you know, why not just intervene? You can do biopsies and maybe somebody needs surgery. Let's just rush ahead to do that as you spot something

that's suspicious. But I understand there are risks for that.

The Risks of Treating Too Early

Dr. Hart:

There are definitely risks, and one of the things that I think it's important to understand is that lung cancers to a radiologist start off as a nodule in the lung. They're an abnormal area of density in the lung which is otherwise not very dense.

But there are a lot of other things that start off as nodules as well, including lots of infections. And depending on where you live in the country you have a very high chance of having been exposed to some of those infections. They're typically fungal infections. One of them being histoplasmosis, another being blastomycosis, and a third being coccidiomycosis, and these can all appear as small nodules, or they can heal leaving small nodules behind.

And the problem for me as a radiologist is when a nodule is very, very small is doesn't have any specific characteristics that I can see to try to distinguish is this an infection or the result of an infection or is this going to be a lung cancer. And so we can't really just rush in because we might be performing a procedure or might be performing a surgery that turns out to have been medically unindicated. We need to have a better idea that something is going to be lung cancer before we take those steps.

Andrew Schorr:

And when we say intervention like that, there are risks that go with any interventional procedure, right? So you don't go into it lightly.

Dr. Hart:

No. I mean, the risk that I was talking about just now of the scans themselves is called the false positive. There are lots of little nodules that generally don't turn out to be lung cancer, so just from the screening test itself, the images that we get will have these false positives. There is also then if we find something that looks suspicious there's the risk of any additional imaging or intervention, such as a lung biopsy either done through a bronchoscope or using a needle and going through the skin into the lung, or a surgical biopsy or even ultimately surgery or chemotherapy or radiation for treatment, so all of these things add additional potential risk making us stop and consider what we're doing so that we don't injure patients.

Andrew Schorr:

I have another question. So when you look at a nodule, and let's say that you're pretty confident that it's a malignancy, I understand not all malignancies in the lung are alike, that some may be not benign but not aggressive, and others would be more aggressive. Is that always clear? Like this is one that's not going to really go anywhere, we can watch it, or should this is something where, boom, we've got to

rush this person to surgery.

Dr. Hart:

It's not always clear, but we're definitely gaining a better understanding of it, both as a result of this trial and actually as a result of the fact that the number of CT scans of the chest being routinely used for other indications has gone up, so we just have much more experience now than we did five or 10 years ago. Certain nodules do have an appearance that suggests to us that they may be relatively nonaggressive. Those have been called minimally invasive adenocarcinoma most recently, and they've had other names in the past. We tend to--they tend to have a characteristic appearance, and we generally then suggest that they be followed up unless there are other reasons for more intervention.

The ones that are going to be aggressive don't have any specific features that say 'I'm going to be an aggressive tumor,' but they tend to be more solid in appearance to us. And some of the solid ones will be slightly less aggressive, some will be more aggressive, but anything that looks like it is relatively solid and has other characteristics that suggest to me that it's a lung cancer, those are the patients who then get referred on quickly for additional diagnosis and intervention and hopefully quick therapy.

Andrew Schorr:

So, Dr. Hart, let's talk about this. During the trial the CT scans, I believe three, were paid for by the government, but until we have all the results and new guidelines out, which we don't as we're producing this program, it's still a question as to if a heavy smoker went to the local doctor, wanted to get a CT or a series of CT as were done in the study, whether it would be paid for by even Medicare or other insurance. Right?

Dr. Hart:

Correct. The Centers for Medicare and Medicaid are definitely interested in the results of the trial, and they will be starting their considerations of what they think is appropriate once the formal results are published in the upcoming few weeks, so we're looking forward to that. But at this point there are no insurance carrier decisions to pay for this that I'm aware of. And so if someone wants to be screened it's a decision that they certainly should discuss with their physician, and, you know, then having had that discussion and I think probably just more full information of what the potential upside and downside of screening is they can decide if they're willing to pay for it on their own at this point.

Should You Be Screened?

Andrew Schorr:

So, Dr. Hart, say there is someone listening now, thinking, we're in this limbo about what's paid for, what isn't, and they have been or are a heavy smoker. So is there a recommendation, or is that really just a discussion between them and their doctor?

Dr. Hart:

I think at this point it's a discussion between them and their physician. Certainly it is something that insurance carriers all across the country will be interested in formulating policies for in the very near future once the formal results are published. Medicare has said that they are interested in looking at the formal results so that they can come up with a decision, and I think we'll see a lot of interest in this over the next several months to, you know, a year or a year and a half.

Until that time I think someone who is a heavy smoker or who would otherwise have met the entry criteria to get into the National Lung Screening Trial if they are interested in being screened should talk it over with their physician. There certainly are programs whereby people can pay to be screened if that's the decision that is ultimately--that they come to between, you know, their discussion with the doctor and their looking up information and listening to programs like this.

I don't think that we can make a blanket recommendation that people go out and be screened right now until the formal results come out and until we have a better idea of exactly who we think might fit into guidelines that will be developed in the future.

Andrew Schorr:

All right. Let's talk about the future. So we mentioned earlier that blood samples were taken from some folks and sputum and even urine and family histories. So looking in your crystal ball, and I know it's really just thinking about the future, while we may get better imaging techniques to let folks in radiology really make better recommendations based on what you see and see things even smaller and their characteristics, will we maybe have a blood test with biomarkers some day or you know, if you have this family history and this blood test result and you've been smoking this long that we can make certain conclusions and treatment recommendations based on that?

Dr. Hart:

That would be one of the big hopes that come out of this study. I mean, the--the initial big hope is that we can obviously prevent lung cancer deaths if we screen, and we've proven that with the 20 percent mortality reduction in the people screened with CT.

Another big hope for the study is that these biospecimens that were obtained will prove useful in coming up with biomarkers that might show us who is at highest risk for development of lung cancer or who in the best-case scenario may be protected from risk of development of lung cancer or some combination. And we might see that someone who's got, let's say, a 30 pack-year smoking history and has had a negative screening exam now but has a marker that shows up in their urine in two years' time, those folks need to be more intensively screened in the future so that when something does appear we can remove it and, you know, not have them die from lung cancer.

So there are all kinds of laboratory groups right now that are hoping to use these biospecimens to validate either early work that they've done or ongoing work that they've done to give us additional tools in our armamentarium of trying to detect lung cancer early. And I think that that is just a fantastic future potential for some of the specimens that were obtained in this study. And really we probably won't know anything from those kinds of ideas for another five or 10 years, so this is going to be a really ongoing, long-term discussion of what turns up to be best.

Andrew Schorr:

Well, lung cancer is, we said at the beginning, our biggest cancer killer by far, and so the results already and the people who benefitted being in the trial with the CT scans, talked about 20 percent reduction in mortality, and I understand not just from lung cancer but we've been saving lives in picking up other things, I guess, too, and with their health screening, so it's had lots of benefit already.

Dr. Hart:

Right. There was in addition to the 20 percent reduction in lung cancer specific mortality the people who were screened with CT had a 7 percent overall reduction in mortality compared to those who were screened with chest x-ray. So there was something about being in the study and being followed by the researchers that helped save additional lives there.

And I think, kind of on a tangent to that but I think an important tangent, is, you know, we definitely showed that there's a mortality reduction, but I don't want people to think that all the people in whom we found lung cancer had their lives saved. That's not the case. It's just that we did decrease the number of people who actually died from the disease. There were still a significant number of people who entered the study who we found lung cancer in who unfortunately died from the disease, but we did decrease that number. So it's like any other testing. It's not perfect, but we did make a difference.

Andrew Schorr:

And what's so beautiful about this is these were centers across the country working together in really what has probably been the most significant trial of its kind related to lung cancer screening. So I know you're excited about it and continuing to work towards really understanding lung cancer with the underlying message, please, please, please don't smoke, and if you smoke stop, right?

Dr. Hart:

Absolutely. And that's actually an interesting--there's an interesting side story that will go along with that because one of the things that we took information on at the beginning of the trial was people's smoking behaviors. Are they current smokers, have they quit? If they had quit they had to have quit within the previous 15 years.

And one of the things that comes up in studies like this, not necessarily lung cancer but has been seen in other studies, is that if you tell people that their result is negative sometimes they will then kind of backslide and say, well, I'm okay. I can

go back to my old bad habit. And one of the things that's going to be assessed as part of the study in the future is what happened to patients'--or participants' smoking behaviors once they were screened? Did they stop smoking, did they smoke more heavily, did they not change?

And I think that will be an interesting sideline result from the study because my concern would be that people would say, well, I didn't have lung cancer so it's okay to continue to smoke, and that's absolutely not the case. And I can't be strong enough about it. It's not okay to smoke. If you're still continuing to smoke, you really do have to quit.

Closing Comments

Andrew Schorr:

Amen to that. I think it is so important to underscore. Well, I think just to sum it up for folks, so the National Lung Screening Trial and the results that have come out are very significant, but they're still really processing immense amounts of data. And what does that mean for guidelines? What does it mean for you if you're a heavy smoker, quit, and lots of programs, turn to so many resources to really try to do that. If you don't smoke, stay that way. And then as far as a discussion with your doctor about how this applies to you if you're concerned about lung cancer.

Dr. Eric Hart from Northwestern Memorial Hospital in Chicago and your specialty in radiology, chest radiology, thank you for what you do and thanks for really participating in the trial and helping us understand the significance of it.

Dr. Hart:

Well, I don't think you should be thanking me for participating in the trial. Actually I think you should be thanking the over 53,000 heavy smokers who agreed voluntarily to participate in the trial--

Andrew Schorr:

True.

Dr. Hart:

--who really have provided us with the result that we have now. Those people who participated have spent years, going back to 2002 with us, and without them staying active and staying involved in the trial and allowing us to collect their health information, we wouldn't have this information. So really our hats should collectively be off to them.

Andrew Schorr:

Well said. And I think that really underscores the point, as I always say, participating in a clinical trial may well help yourself and it certainly can help others, and here's a great example of that. Dr. Hart, thank you for being with us on Patient Power.

Dr. Hart:

Thank you for having me. I appreciated the time to talk.

Andrew Schorr:

Yes. Well, this is what we do on Patient Power, and lung cancer is certainly a hot topic for us always. Thank you for joining us. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.

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