



Lung Cancer Screening Update

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May 22, 2016

Welcome to Yale Cancer Answers with your hosts doctors Anees Chagpar, and Steven Gore. Dr. Chagpar is Associate Professor of Surgical Oncology and Dr. Gore is Director of Hematological Malignancies at Smilow and an expert of Myelodysplastic Syndromes. Yale Cancer Answers features weekly conversations about the research, diagnosis and treatment of cancer, and if you would like to join in, you can e-mail your questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. This week, it is a conversation about screening for lung cancer with Dr. Frank Detterbeck. Dr. Detterbeck is Professor of Thoracic Surgery, Chief of Thoracic Surgery and Surgical Director for Thoracic Oncology at Yale School of Medicine. Here is Dr. Anees Chagpar.

Chagpar I remember it was a couple of years ago, you and I sat down on the radio and we were talking about lung cancer screening, remind our listeners about what the state-of-the-art is right now in terms of screening for what I think is one of the deadliest cancers, is that right?

Detterbeck It certainly is. I think one of the things that people do not realize is that lung cancer causes as many deaths as the next four leading causes of cancer deaths combined, so it is a major cause of cancer deaths in both men and women. Screening, because it is such a major cause of cancer deaths, one of the things that has been on the table for a long time is can we diagnose it earlier, can we save lives by doing that, and so there has been interest in that for decades. There has not been anything that really worked as a screening test up until 2010-2011 when a big trial was done in the United States, the National Lung Screening Trial, the results became available and showed that we could in fact save lives by screening people in the right way for lung cancer.

Chagpar Let's talk a little bit about that because I think one of the things that our listeners have really gotten over the last several years that we have been doing this show is that finding cancers late is problematic and that is when people die, if you find cancers early, whether it is a colon cancer, a breast cancer, prostate cancer or lung cancer, actually people can do pretty well, and so screening is important, but do you screen everybody or do you just screen some people because screening has to be cost effective in the current healthcare scenario.

Detterbeck I agree, but even aside from the cost issues and we can talk about those, but even aside from that, I think we have to screen where we can make a difference, where we can actually save lives and not screen where it really is not going to make a difference, and so, we have to recognize that although we have good data that now that screening can save lives, it does not mean unfortunately that we can detect every lung cancer early, that we can save every life from lung cancer. We have to accept that fact that there are limitations to screening. So, we have to screen people that are at relatively high risk of developing lung cancer. To take it to an extreme, would you screen your 10-year-old daughter for lung cancer, the answer is obvious – no, you would say why

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would I give radiation or whatever to somebody who is really not at risk? So, when you take it extremes, I think it becomes obvious for everybody. We have to screen the right people to make a difference.

Chagpar And who are the right people to screen and how do we screen them?

Detterbeck I think that to get back to where we started from, things have evolved somewhat since the last time we talked, so when we talked a few years ago, the data had just come out, NSLT was ages 55 to 74, people that had smoked for at least 30-pack-years, that is a pack a year for 30 years or 2 packs a year for 15 years and had quit less than 15 years ago. So, those were the criteria in NSLT, and those are basically still the criteria for which screening is approved, so CMS has approved, that is the Centers for Medicare and Medicaid Services, screening for that population, with slight modification in the age, upper age limit. But I think we have evolved since then. There are other factors that are risk factors for lung cancer; we have a somewhat better understanding of that, there are risk models that have been developed to try to predict what the risk is for developing lung cancer in people that perhaps do not fit those criteria but still have high risk, and I think that we are gradually evolving to understanding these risk models well enough to start to use those to select the right people to screen.

Chagpar Tell us more about those risk factors and those risk models because there is not a day that goes by that you will hear somebody, say my cousin, my sister, my neighbor, my friend got lung cancer but never smoked a day in their life. And so, those people would certainly not meet those criteria, so what are the modifying factors, the other risk factors that now are available to people who might really need to be screened, what are those risk factors?

Detterbeck Smoking is clearly a risk factor for lung cancer that I think everybody knows. There are nuances of that, so the 30-pack years and having quit less than 15 years ago and so forth, that is sort of a broad sweep, and we can take that down a little bit more. As people get older, they develop more cancers and they have a higher risk of lung cancer, so age plays a role and factoring in the smoking and the age a little bit better is important. Family history is important. If you have a first-degree relative that has had a lung cancer, you are at higher risk of developing lung cancer regardless of any exposure to smoking. People have thought well, that is just because you are exposed to smoking with your parents or whatever, which is correct, you have a higher risk, but even nonsmokers have a higher risk. So, I think those are probably the biggest factors. There are a few others, but those are the biggest ones. Now, to get to another part of your question, what do we do about the nonsmokers? And, it is a misconception that only smokers get lung cancer. Clearly, nonsmokers do get lung cancer and we do not have as complete of an understanding of that as what we need. And I think that in the

past, we were only able to look at lung cancers as one big group, it is like looking at the whole forest and we could not necessarily tell what makes one tree or another tree develop quite as well because we are only looking at the forest. Well now, we can do genetic fingerprinting of tumors and see that there are different mutations that have caused different tumors to develop and to grow, and so it is like being able to figure out what is an oak tree and what is a beech tree in the forest and so now, we can start to develop a better understanding of what makes the oak tree grow, what makes the beech tree grow.

Chagpar How does that play into screening? I mean it is one thing to say this cancer is driven by this mutation and that cancer is driven by that mutation, but screening it seems to me is a step before that, before you have ever got lung cancer. How is genetics or genomics or is it really playing into who gets screened and who does not get screened?

Detterbeck At this point, we do not have an answer for the nonsmokers. We do not have a guidance on which ones of those should we screen or should not screen.

Chagpar Aside from the family history?

Detterbeck Aside from the family history. We really do not have that. Now, we have an ongoing study to look into other factors to get genetic fingerprinting of the tumor, but there is a very careful epidemiologic study, what kind of foods do you eat, where have you worked, various things so that we can identify perhaps what are risk factors, what are predispositions, what types of exposures might lead to certain types of cancers with the idea that that will tell us in the future perhaps how to screen certain people, but may be even better than that how to advise people, we need to not expose people to this or to that so that we can prevent cancers in the first place.

Chagpar That is awesome. Tell us again how screening works, is it a CT scan every year, every 10 years, when do you start, when do you stop, tell us more about the actual screening mechanism.

Detterbeck The screening tool that works, that we have data for, is a CT scan, it is a low-dose scan, so it is very little radiation and that is what we have data for that works. But it is not just a scan, so I think very often people think, I go in and I get a scan and that is it. It is really a process. If you are screening, you are wanting to detect something early, so you cannot get one scan and then say well I am good for the rest of my life. You really have to get a scan every year, that is the current system and there seems to be pretty good data for doing that once a year and not changing that interval. But it is a complicated process of picking the right people, doing a good quality scan, interpreting

that correctly, one of the problems with CT screening is that you find a lot of little things, you pick up a lot of noise, it is just background noise, but you have to sort through the background noise to figure out what is just noise and what is something that I need to may be focus on a little bit more, and so that process of interpretation of that scan is very important piece and the quality of how that is done is a very important piece to making screening either effective or potentially causing more harms than it does good. So, we have to be careful about all of these things.

Chagpar Yeah, I mean that whole conversation brings up the concept of over-diagnoses, which is certainly an issue that we have heard about in the breast cancer world, do you foresee that that will be an issue in the lung cancer world or is this really something that is so lethal really in terms of the prognosis for lung cancer that you can never pick up something that is "not going to have an impact on longevity."

Detterbeck I think this is very true in lung cancer as well, and I do not personally like the term over-diagnosis because I think it is something that is useful for epidemiologists, but I do not think it is really useful for patients or doctors that are trying to take care of patients. What it refers to though is that there is a spectrum of aggressiveness of cancers. There are aggressive nasty cancers, there are sort of middle of the road cancers, there are relatively well-behaved cancers and there are cancers that are probably inconsequential as best as we can tell that are never ever going to cause a problem. And I think that screening is one of those things that certainly brings out the fact that there is a spectrum of disease much more than we ever appreciated in the past. So, as we recognize that better, I think we also have to evolve in how we approach patients, how we figure out what is a tumor that we better jump all over what is a tumor that perhaps the intervention we need to do, can be a lesser intervention, the little less invasive, we do not need to treat it that much in order to be able to cure it and perhaps in some people what are cancers that are likely to be inconsequential cancers that maybe we should leave them alone and watch them and just sort of see do they actually do anything if they are not really doing anything, then maybe we do not need to intervene at all.

Chagpar Such an interesting concept and we are going to pick that topic up right after we take a short break for a medical minute. Please stay tuned to learn more information about lung cancer and screening with my guest, Dr. Frank Detterbeck.

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The American Cancer Society estimates that there will be 75,000 new cases of melanoma in the US this year with over a 1000 of these patients living in Connecticut. While melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths. Early detection is the key, and when detected early, melanoma is easily treated and highly curable. Clinical trials are currently under way at federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital. To test innovative new treatments for melanoma, the goal of the Specialized Programs of Research Excellence (SPORE) in skin cancer grant is to better understand the biology of skin cancer with a focus on discovering targets that will lead to improved diagnosis and treatment. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital. More information is available at YaleCancerCenter.org. You are listening to WNPR, Connecticut's public media source for news and ideas.

- Chagpar Welcome back to Yale Cancer Answers. This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Frank Detterbeck. We were talking about lung cancer and screening, and right before the break, Frank, you were talking about this concept of a spectrum of disease, and we have heard this concept in other cancers for sure, but the idea of over-diagnosis, I think the concept that there may be some cancers that we can simply watch is something that people are still kind of wrapping their heads around. Is that something that occurs in lung cancer, should that occur in lung cancer, where are we at with that?
- Detterbeck It definitely occurs. There is no question about it. I think that that is something that 20 years ago, the vast majority of people would say they cannot see that occurring in lung cancer, but clearly as we are doing more scans and picking up cancers early, we are realizing that there is a spectrum of disease and some of those early, early, early cancers always stay early, early cancers without really doing anything. So, they seem to be well behaved, it might be one term or inconsequential, they do not seem to do anything.
- Chagpar And that is where getting these scans on a yearly basis to make sure that they do not do anything comes in?
- Detterbeck But that is different from screening. Once you have something that you are paying attention to, you are following that. Screening is people that you have no idea have anything, you have some idea they have some risk for lung cancer, but you have not identified something that you need to follow.
- Chagpar I am with you. But in terms of follow-up, is that follow-up with CT scan to make sure that those cancers are not doing anything or is it such that you do a biopsy of that lung

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cancer and based on its genomics or its characteristics or how it looks under a microscope that it is one of these "inconsequential" lesions and then you just say okay, I know that it is inconsequential and you do not need anything further?

Detterbeck No, it is really follow-up by imaging by CT scan once a year.

Chagpar The other question that I wanted to ask you was this whole idea of the nonsmoker and the family history and the screening guidelines that are now being expanded, so let us suppose you are 35 years old, your father who smoked like a chimney his entire life got lung cancer at 75 and passed away, you now have a first-degree family history of a relative who got lung cancer, you do not smoke but you just told us before the break that that does not matter, you are still a candidate for screening, when should that screening start, when you are 35 or do you wait until you are older because more lung cancers happen when you are older, what is the guidance with regard to that?

Detterbeck Let me just correct you a little bit to make sure that we are on the same page. Just because you have a family history does not mean that you are a candidate for screening. It does mean that you are at slightly higher risk than the average person of getting a lung cancer, how high is that risk, is that risk high enough to warrant screening, well you have to bring in other factors like age and so forth. At this point, the guidelines for screening are still age 55 or greater and a smoking history and so forth. I think we are evolving to having good risk prediction models where we can alter that and we can include other patients. The guidelines at this point do not really say that, CMS does not really approve screening in other groups, I do not think we are quite there yet, but I think we are pretty close. I think in another year to two years, we are going to have better criteria. Now, to answer your question specifically, your father had lung cancer, you are 35, I do not think we are going to ever get to a point where we say you should be screened. If you are 50-55, I think maybe then because of the age factor and how that increases your risk of developing a lung cancer, that might end up being somebody that you should screen even if you did not smoke, for example, if you have a high enough family history.

Chagpar It sounds like there is a lot going on in terms of lung cancer screening and how it is evolving, tell us a little bit about how you think lung cancer screening is similar or different from other cancers, I mean it sounds like certainly in breast cancer, we have some squabbles about who should be getting a mammogram and how frequently and it sounds like lung cancer is a bit the same way, tell us about the similarities and differences across cancers that you see in terms of screening.

Detterbeck I think there are a number of differences for lung cancer. First of all, it is newer and so we have not been working at these details as long as in breast cancer for example or

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prostate or colon cancer, so a lot of the details we are still kind of figuring out and working on. I think that the level of understanding that physicians have about it is also not quite the same and it is going to take some time. I think that I have to say that even for myself, I put a lot of time in the lung cancer screening, I had been an author of a guideline for it, I have been a co-author of most of the major societies in this field that have possession papers on how we should do this, I have put a lot of time into this and yet taken me a long time to really develop the inside I think in order to be able to advise people appropriately about it and interpret things appropriately. So, I think that primary care physicians probably do not really have the tools at this point to really be able to do this as easily as they can in other cancers. I think another complexity is that the risk, how do you pick the right patients for it, that is getting to be more complex, but that is an issue, I think that interpreting the CT scan, I told you about that, we pick up a lot of noise, how do you sift through that appropriately, how do you not overreact to noise that is a bit more of an issue. Another issue perhaps is that you do a PSA level for prostate cancer, you get an answer about your PSA level and that is it. You do a CT scan, you scan everything from your chin down to the bottom of your liver and so you pick up stuff about the lungs but you also pick up other stuff. How do you sort through, how to react to the other stuff? So, I think there are differences that make it a little bit more complex, and at this point, I think you really need to have an organized program that has a system for dealing with all of these things in order to be able to do it well.

Chagpar Speaking of an organized system and going back to your comment about primary care physicians and how complex everything is, one of the issues though that I think about is, in terms of screening these are people who do not have cancer, who may be at risk of cancer, but usually they are not frequenting a thoracic oncology program because they do not have lung cancer, they go to their family doctor we hope, maybe once a year for a checkup and so do you think that it is evolving to the point or could evolve to the point with appropriate education where primary care physicians can look at the guidelines and say are you 55 or older? Have you smoked for 30-pack years? You need a CT scan and oh! by the way, here is the program that you should go and see because without that how do they get to these organized programs?

Detterbeck Currently certainly there are some primary care physicians that do refer patients. I think that there are people that refer themselves, say I have been a smoker, I have a family history or whatever and I am concerned. I think eventually yes, we need to evolve in this field and certainly I think it is something that needs to evolve to be a system that it can be implemented in primary care practices. I think another aspect that I did not really touch on before, but I think that the psychological guilt factor of lung cancer and smoking is another issue that makes it a bit different than other cancers where you say well, why did I get breast cancer, there is nothing I did wrong.

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Whereas I think people that smoke, they tend to feel that they are to blame and we have to get over that. Smoking is an easy thing to start, it is a very difficult addiction to get away from, it is not just people's fault that they chose to smoke and not stop, it is not that simple and there is a lot of good we can do for people and in fact the guilt that they have thinking well I am smoking so therefore I do not even deserve this, we got to get over that.

Chagpar Do you think that another potential referral source, I am thinking about how people get to these "organized programs" for lung cancer screening, your point about getting over this concept the guilt associated with smoking, how do smoking cessation programs kind of fit in with those organized platforms because I can see a great deal of synergy there, the people who are going to smoking cessation programs clearly smoke and also could benefit from screening?

Detterbeck I certainly agree, we have integrated one way but not the other way. A lung cancer screening program really needs to have a good smoking cessation program that is part of it. So, people that come in for lung cancer screening that are smokers, we need to do everything we can to help them to quit because the fact is screening can find lung cancers early, but if you can quit smoking, you can actually prevent lung cancers from even developing, and that is clearly better. And the science of helping people to quit smoking has advanced tremendously. The old-fashioned approach of let me pat you on the back and here is some nicotine gum, give it a try, really has advanced a lot more. So, a sophisticated smoking cessation program needs to be part of a screening program. The other way around, we have not really connected with smoking cessation programs that to just say, well would you tell people about lung cancer screening if they do not know about it and have them thinking about it, we have not done that.

Chagpar It seems to me like it would be a good idea, Frank?

Detterbeck I think so.

Chagpar One question, when you mentioned that lung cancer screening programs often refer people for smoking cessation, let us suppose you smoke, let us suppose you meet all of the criteria, so you are a 30-pack-year smoker, you are 55 and above, if you quit smoking today, could you reduce your risk of developing lung cancer even if you smoked for 30 years in the past? Can you erase your previous mistake?

Detterbeck Yes and no. If you continue to smoke, your risk of lung cancer continues to go up pretty steeply. So, if you can quit smoking at any age, you actually will reduce your risk of lung cancer but you will also reduce your risk of stroke and heart disease and all

sorts of other things that take people's lives. And that really is true even at an older age. However, generally the risk that you have built up, you keep that, you do not ever completely lose it, you never go back to as if you have never smoked in the first place, but since your relative risk goes down relative to continuing the smoke, it makes a big difference.

Dr. Frank Detterbeck is Professor of Thoracic Surgery, Chief of Thoracic Surgery and Surgical Director for Thoracic Oncology at Yale School of Medicine. We invite you to share your questions and comments. You can send them to canceranswers@yale.edu or you can leave a voicemail message at 88-234-4YCC, and as an additional resource, archived programs are available in both audio and written form at YaleCancerCenter.org. I am Bruce Barber, hoping you will join us again next Sunday evening at 6 for another edition of Yale Cancer Answers here on WNPR, Connecticut's public media source for news and ideas.