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Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about surgical care for lung cancer with Dr. Andrew Dhanasopon. Dr. Dhanasopon is an Assistant Professor of Thoracic Surgery at the Yale School of Medicine, and Dr. Chagpar is a Professor of Surgery at Yale and the Assistant Director for Global Oncology at Yale Comprehensive Cancer Center.

Chagpar Andrew, maybe we can start off by setting the stage. Tell me about lung cancer, how common is it, who gets it, at what stage does it present?

Dhanasopon Lung cancer is the #1 cause of cancer death in the United States. Most of the time, we associate people who have smoking history with lung cancer, but also people who have not smoked do develop lung cancer as well. Several years ago, there was a National Lung Cancer Screening trial that was published in the New England Journal of Medicine in 2011, in which they demonstrated for folks who are between the ages of 55 to 74 years have had a prior smoking history of 30-pack years, meaning about a pack a day for 30 years, or those who have quit within the past 15 years, and had yearly CT scans, they found lung cancers in those folks and were able to show a reduction in lung cancer death by 20% of relative risk reduction. At Yale, we have a lung cancer screening program that allows us to detect lung cancer earlier.

Chagpar Lung cancer is something that everybody has heard about and everybody knows that it is bad. We often put lung cancer together with smoking, and even the screening program that you described really puts an emphasis on smoking. But you mentioned that people who have never smoked can also get lung cancer. How do you know what to watch for? What are the symptoms that you would present with? I think that if you have been a smoker for a long time, you might be thinking about lung cancer, but certainly if you have never touched a cigarette in your life, it is not something that is going to be top of mind. So, what are the symptoms that people should be looking for?

Dhanasopon One aspect that we look at when evaluating patients for lung cancer is also family history; in addition to a personal family history, we also ask about symptoms such as cough, any coughing up of blood-tinged sputum, sometimes wheezing can also be an indicator. Obviously, these are very generic and very common symptoms when we evaluate the patients. In addition to the symptoms, we do take into account a variety of other factors into the determination of how likely this person is to have a lung cancer. Often, lung cancers are detected on a CT scan that is found incidentally for a variety of other reasons. And that sort of begins the workup of lung cancer.

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Chagpar I want to unpack that just a little bit more because as a lifetime nonsmoker, I am sitting here thinking I have had a cough before and I can wheeze when it is cold outside and I've run up 10 flights of stairs. Hopefully, that does not mean that I have got lung cancer. Help me to understand when should people be going to the doctor? When should we be saying, I might need a CT scan or how do I know it isn't lung cancer but just exercise-induced asthma due to cold or something.

Dhanasopon As I had mentioned, for folks who have had a smoking history, that is the #1 thing that raises the suspicion. For the less common situation where folks who have had a cough for a period of time that has not gotten better with a course of antibiotics or the traditional therapies for cough, an x-ray is done by a primary care physician and that shows a spot that has not gone away for a period of time, those are some situations where that would raise the suspicion to get a CT scan to follow that.

Chagpar And the other question that I have is, everybody knows that smoking causes cancer, I do not think that anybody can say that is fake news. But what is also true is that it is incredibly hard to quit smoking. So, I have two questions for you. The first question is, if you manage to quit smoking, do you actually reduce your lung cancer risk? And then the second question which may be more difficult is, how exactly does one go about quitting smoking?

Dhanasopon Quitting smoking is one of the most difficult things that anyone can do. We often counsel our patients in clinic that if they do quit smoking, it is of course beneficial to the health. They do still have that inherent risk of lung cancer because of the history of smoking, but they would be able to improve their future health by quitting smoking.

Chagpar But they are still at risk?

Dhanasopon They are still at risk.

Chagpar Because even in the screening trial, even if you have quit less than 15 years ago, you are still considered high risk.

Dhanasopon Exactly.

Chagpar But some people are going to be listening to this saying then why should I quit smoking?

Dhanasopon Quitting smoking has numerous health benefits aside from the respiratory aspect. It affects the cardiovascular system, which is the #1 cause of health-related

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hospitalizations in the United States. For the general health benefits of quitting smoking, we do recommend that. But you are correct that just having

had smoking in the past, that is your risk of lung cancer.

Chagpar I guess the key message there is to anyone who is listening who has not started, do not because if you do start, it is kind of with you for life, it is like the scarlet letter that you cannot get rid of.

Dhanasopon Right. At Yale, we have a smoking cessation program that helps folks quit smoking. They are often with us in our clinics and can counsel the patients on a variety of methods. We all know these over-the-counter products that are in the forms of gums or medications that can help with reducing the cravings for smoking.

Chagpar Let's say you have been a smoker, you are trying to quit or maybe you have quit and you develop a cough that does not go away and you are coughing up blood and you go to your family doctor and get a chest x-ray and lo and behold it finds a spot. And because of your history, your doctor is worried and sends you to see a specialist. Take me through how lung cancer is diagnosed.

Dhanasopon If a patient has high-risk characteristics as you mentioned and there is a spot on chest x-ray, the next step is to obtain a CT scan, a diagnostic CT scan that will help better characterize the spot in the lung. On the CT scan, the radiologist would be able to describe the spot; often it is in terms of the size, the morphology – meaning is it a smooth border, does it have what we call speculated or irregular borders, is it solid, is it not so solid or sub-solid. So, there are a lot of characteristics from the CT scan that we can obtain. And based on the level of suspicion for this nodule, then there are several ways to then work this up. The patients often get a PET scan. A PET scan is different from a CAT scan in the sense that the PET scan shows metabolic activity of areas of the body. For example, a cancer that is metabolically very active, the cells are actively dividing show up as being very bright on the PET scan. If the CT scan has high-risk features and if the PET scan shows that this is bright, it would be concerning for lung cancer. Depending on the location of the nodule, this could be biopsied in a variety of ways. The most common way is a CT-guided biopsy. This is an outpatient procedure, it is done under local anesthesia; and under CT guidance, a needle is passed into the nodule to obtain cells to examine under the microscope.

Chagpar Let me get this straight. You do a CT scan, you see a lump or a mass and it is speculated and you are worried about it and the patient has been a smoker and you are thinking, this might be a cancer. You then do a PET scan that lights up, but then you still do a

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biopsy to prove that it is a cancer. My question is, do you really need the biopsy or did you really need the PET scan because it sounds like either way, you are going to need some sort of test to confirm that it is a cancer, but do

you need both?

Dhanasopon In the workup of lung cancer, a PET scan is often helpful to not only look at the lung nodule, but to examine the rest of the body to see if there is any spread, any activity elsewhere that looks suspicious. So, that would be another reason to obtain a PET scan. You are right in that the CT-guided biopsy is not always necessary if the CT scan and the PET scan look suspicious enough. Patients then can be referred to the appropriate specialist to go ahead with particular treatment depending on what preliminary stage or clinical stage that this seems to be.

Chagpar Tell me about the staging of lung cancer. What are the factors that go into that, how do you figure out what stage you are and how does the treatment vary by stage?

Dhanasopon As with other cancers, the staging for lung cancer follows a stage I, II, III and IV, and within each stage that is determined by a classification for the TNM stage that is tumor, node and metastasis. So, for lung cancer, the T aspect refers to the size of the nodule, the N or the nodes refers to the involvement of any of the surrounding lymph nodes and the M refers to the determination if there is any metastases throughout the rest of the body. For stages I and II, surgery is the first step in treatment for lung cancer.

Chagpar And so, presumably for the others, there are other modalities. I would like to pick up on that conversation and talk more about the treatment of different stages of lung cancer where surgery does play a role, where does medicine play a role, right after we take a short break for a medical minute. Please stay tuned to learn more about the surgical care of lung cancer with my guest, Dr. Andrew Dhanasopon.

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Chagpar This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Andrew Dhanasopon. We were discussing surgical care of patients with lung cancer and right before the break, Andrew was talking to us about how lung cancer is staged and very much like other cancers that we have talked about on this show, we use the TNM staging system – how big is the cancer, the tumor – T; does it look like the lymph nodes are involved N; and are there distant metastases or spread throughout the body M. How do we really divide people up, so stage IV in many cancers is spread to distant organs, is that the case in lung cancer too?

Dhanasopon Correct.

Chagpar How is that treated? Does surgery play a role there or no?

Dhanasopon Surgery at this stage does not play a direct role; with stage IV, at Yale, we are considering a certain very select groups of people with stage IV disease for surgical treatment, for which we are developing clinical pathways and potential trials in the future. But as a gold standard throughout the United States, stage IV is treated with chemotherapy and immunotherapy.

Chagpar So, the reason for that really is because it has got distant spread and surgery cannot really treat distant metastasis?

Dhanasopon Right. We think of distant spread as a systemic issue, we think of surgery as treating a locally contained cancer. And so, for systemic disease, systemic treatments like chemotherapy and immunotherapy would be helpful.

Chagpar Tell me more about surgery in the metastatic setting because certainly in a number of cancers people have started wondering about whether there is a role for surgery of the primary disease – in some cancers even of the metastases in stage IV disease. So, tell me more about this study that is going on at Yale or the pathway that you are developing because I think that that is interesting and certainly something that we think about in breast cancer as well.

Dhanasopon This is a very exciting, very new topic in which we are selecting for patients who for example have a lung nodule, who do not have any other spread except for perhaps a small number or just one spot of metastasis for example in the brain. I actually did have a patient like that a few weeks ago who I operated on, she was a middle-aged woman, prior smoker, had a small 1-cm nodule in the lung but had 2 additional nodules in the brain. The brain metastases were treated with radiation and once she was determined to not have any further progression of the disease there, she was then

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referred to surgery to consider surgical resection of the primary nodule in the lung. She did well after her lung surgery, was able to go home after day #3 and she has so far done very well.

Chagpar Interesting because previously we would say to people if you have got distant metastatic disease, there really is not much we can do for you locally and yet that local primary might be the only site that really is left after people have treated with systemic therapy, small clusters of disease in single organs. Really exciting work there and certainly something that we talk about in colorectal cancer where it has now become standard of care that you can resect not only the primary but up to 4 liver metastases has become pretty standard and something that we are working on to really figure out in breast cancer as well. Let's talk now about the other stages. If we look at the other end of the spectrum – stage I, tell me about what that is. Is that cancer that has no lymph nodes?

Dhanasopon Correct. So, stage I lung cancer involves just the primary site of the lung cancer within a particular region of the lung without any involvement of any lymph nodes.

Chagpar And how are those treated?

Dhanasopon Those are treated with surgery.

Chagpar And surgery alone, so no immunotherapy, no chemotherapy, no radiation, just surgery?

Dhanasopon Correct. Surgery is the gold standard treatment for stage I lung cancer. There are throughout the country starting to be trials looking at if immunotherapy combined with surgery would be even more effective, but as of right now, the gold standard is surgery for stage I.

Chagpar And what is the prognosis of stage I patients who are treated with surgery?

Dhanasopon For stage I lung cancer, it depends on the particular division -- within the stage I there are a few subdivisions, but in general and we talk about 5-year survivals on the order of the high 70s to 90s.

Chagpar Okay. And when you talk about different divisions, tell me what do you mean?

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Dhanasopon For example, in stage I, there is IA and IB – within IA, there is IA1, IA2, IA3, there are a very few different subdivisions depending on basically the size of the tumor.

Chagpar So people are just trying to mince the salami really, really thinly.

Dhanasopon Exactly.

Chagpar I see. And in terms of surgery, I remember back in the good old days, people who underwent lung surgery, this was a really big surgery. I mean a stern to stern kind of cut around the side and opening up, spreading ribs, maybe even taking a rib or two, and doing major resections, people staying in

the hospital with chest tubes and things like that. but these days, especially in some cancers, the urology people doing prostate cancers have now used robotic surgery, tell me about advances in surgical treatment for lung cancer. Where are we with that?

Dhanasopon Over the past 20 years, there has been rapid development of minimally invasive techniques to treat lung cancers. Twenty years ago, this was mirroring the development of laparoscopic surgery which is what I tell a lot of my patients who know more about laparoscopic surgery than what we do, which is thoracoscopic surgery or VATS – video-assisted thoracoscopic surgery. It uses the same basic technology, small cameras on the order of 5 mm in width as well as small instruments to go in between the ribs instead of as you were saying cutting muscle in between the ribs and spreading the ribs and what we call a thoracotomy. So, with VATS that has helped patients to have less pain after surgery to have decreased length of stay in the hospital and to return to work and life earlier than with a big open surgery. In the past 10 years, there has been development of robotic surgery as you mentioned, which essentially is a minimally invasive tool just like VATS; however, the ability to use instruments in a way that is different than VATS allows for better enhancement of manual dexterity and very fine and minute dissection around the critical small structures that are required to do lung surgery.

Chagpar So, just to be clear, because sometimes when we talk about robotic surgery, the image that people get is we have got these little robots inside of you that are doing the surgery. It is still a surgeon sitting at a console using this robot-like technology to do this surgery right?

Dhanasopon Absolutely. The surgeon is at a console next to the OR table, there is an assistant at the OR table with the patient. The robotic aspect of it refers to the arms of the robotic platform that is used to perform maneuvers; however, the surgeon is in complete control of the instruments as he or she uses it in the operation.

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Chagpar So, it sounds like you now have more tools in your armamentarium. So, you can do the big open thoracotomy, you can do the minimally invasive VATS which allows you to do the smaller procedure but might not give you all of the dexterity of the third option, which is the robotic surgery. So, what is the breakdown in terms of lung cancer surgery between the three modalities?

Dhanasopon For example, at Yale, we do over 90% of our lung cancer operations minimally invasively either by VATS or by robotic surgery. Robotic surgery does require additional training and so about 25-30% of our cases that are minimally invasive are done robotically.

Chagpar And so, is there less because of the greater ability for surgeons to

have more dexterity and so on and so forth, is robotic surgery "better," I mean would you have less blood loss, shorter operative time, shorter length of stay or is it really just that the surgeon can manipulate the arms of the device a little bit better?

Dhanasopon I think throughout the country we are still trying to figure out if robotic surgery does in fact translate into those important patient-related outcomes that are better than VATS surgery. As of right now, both are viewed as better than open thoracotomies – big incisions in terms of allowing patients to recover quicker and return to work faster.

Chagpar And so, are there certain patients that you would say – you would advocate more for one option versus the other?

Dhanasopon At this point, not necessarily. I think it is ultimately up to the comfort level of the surgeon. I think that the important thing is that minimally invasive surgery is offered. I think if the surgeon has been well trained in robotic surgery and they are more comfortable with approaching this robotically, then that is a fantastic way to go. I think that if the surgeon does VATS surgery, I think that is also a great modality to use. The key point is to choose a surgeon that is trained in some minimally invasive platform.

Chagpar Good questions to ask your surgeon when you meet and to know what techniques they feel comfortable using and what technology is available at your particular hospital.

Dhanasopon Absolutely.

Chagpar In our last minute Andrew, we talked about the metastatic setting where the patients get systemic therapy and now maybe surgery, clinical trials pending, and we talked about early breast cancer, stage I, where they get surgery alone. What about that gray zone in stage II-III?

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Dhanasopon Stage II patients tend to have some spread of the cancer to local lymph nodes, and often that is discovered after the operation once the tumor and the lymph nodes are sent off to the pathology lab and sometimes what happens is we do determine there is lymph node involvement. In those cases, we have patients see a medical oncologist for consideration of chemotherapy.

Chagpar Before surgery?

Dhanasopon After surgery.

Chagpar Okay. And then, stage III the same?

Dhanasopon For stage III, it is a controversial field in which we are trying to figure out which patients benefit from which treatment first. A common pathway for these patients in which they have involvement of the lymph nodes

not near the tumor but closer to the middle of the chest, those patients tend to undergo chemotherapy and radiation first before undergoing surgery.

Dr. Andrew Dhanasopon is an Assistant Professor of Thoracic Surgery at the Yale School of Medicine. If you have questions, the address is cancer-answers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer here on Connecticut Public Radio.