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Lung Cancer Screening and Treatment of Early Stage

Announcer Intro:
Welcome to CME on ReachMD.

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Dr. Edell:
Good afternoon or evening, depending upon which time zone you are in. My name is Eric Edell. I'm a pulmonary and critical care physician at the Mayo Clinic in Rochester, Minnesota and I'm honored to be here with my co-chair Septimiu Murgu from the University of Chicago. It's a real honor for us to have you join us in this first of five webinars on non-small cell lung cancer.

We're fortunate enough to have our corporate sponsors that have provided independent educational grants for this program and the sponsors are listed on this slide. The content was completely created by the faculty and I think you'll be- appreciate the expertise that we have today.

The description of the course is before you. I would i- give you an opportunity to read this and also the learning objectives that we hope to convey to you through the materials that we'll share today.

As I mentioned, my colleague, Dr. Septimiu Murgu and myself have the privilege of co-chairing this and fa- four subsequent webinars on non-small cell lung cancer. Joining us today are Drs. Nicole Tanner from the University, from the me- Medical University of South Carolina, Kimberly Sivertsen from the University of Chicago, Dr. Janani Reisenauer from the Mayo Clinic, and Dr. Andreas Rimner from Memorial Sloan Kettering in New York.

The dic- disclosures are displayed for you.

And as I mentioned, we want to invite you to join us for the f- next four webinars on the topic of non-small cell lung cancer as well. I think you'll enjoy not just this but the subsequent webinars i- in addition to this one.

Finally, I'd like to encourage you to send your comments and any questions that you have through the chat box. We'd like to engage as best we can with the format that we've been, become accustomed to in this pandemic world. Please don't hesitate and enjoy the rest of the hour.

Dr. Tanner, I'll turn the first presentation over to you.

Dr. Tanner:
So, I'm Nicole Tanner, I am a Professor of Medicine at the Medical University of South Caroline in Charleston. I also have a joint employment at the Ralph H. Johnson VA. I'm fortunate enough to direct lung cancer screening at both institutions and so we will start

this off with the following questions.

What is the current U.S. Preventive Services Task Force eligibility criteria for lung cancer screening? Is it a, ages 55 to 74, actually the, the poll has started so I'll let you all read that and give it a second instead of reading it to you just in the interest of time.

Hopefully everybody's seen the poll. OK. And I think we were going to potentially share those results. OK. So that's interesting and hopefully we'll see that answer as we go through the presentation.

So, I'd like to go through the history of lung cancer screening very quickly. I think the wins that we've had is that there is definitive evidence that screening those at high risk based on age and smoking history does confer a mortality benefit, and that screening with low-dose CT scan. And I've put up there for you the two trials, the seminal trials including the National Lung Screening Trial which was conducted in the United States and the NELSON Trial conducted in Europe. And both of these it showed a mortality reduction through using low-dose CT scan in those that are eligible.

And so as, by way of timeline you can see what the eligibility criteria are and were for lung cancer screening. You'll see the ages have varied but the initial trial, the National Lung Screening Trial i- showed, enrolled patients ages 55 to 74 who are current or former smokers with 30 pack-year history, quit within the past 15 years. And you can see how that's evolved. So, the U.S. Preventive Services Task Force in their first iteration of their guidance for lung screening for the first time gave a grade B recommendation to lung screening in 2013. CMS or the Center for Medicare and Medicaid Services did some modeling exercises and decided to approve lung cancer screening for their beneficiaries up to the age of 77. And what you'll see, the most common thing that spans all of this is that patients is- that should be screened should be asymptomatic and must not have comorbidities that would preclude definitive surgery and that's a debate in and of itself. But those are the criteria. And most recently, in 2020 and most recently approved the U.S. Preventive Services Task Force lowered the age criteria to 50 with a 20 pack-year history in order to include those individuals who were still at high risk but were not being captured by the initial eligibility criteria and those individuals include blacks who have lighter smoking histories and might've started smoking at an earlier age.

So, we do have wins in that there has been guidance over the past 10 years for implementation and best practices, and that's the goal of this discussion is to kind of highlight some of the best practices for lung cancer screening. So, you have to look no further than our only, than our very own CHEST Journal to look at the components necessary for a high quality lung cancer screening. This was published in collaboration with the American Thoracic Society in 2015 and really this is what provides the guidance and in fact if you look at the first CMS or Medicare guidelines, it actually followed the qua- qualities for a high lung cancer screening very closely. Then in fo- further along in 2015 there was an official ATS CHEST statement on how to best implement low-dose CT scanning. And I would encourage anyone on this webinar who is interesting in starting lung cancer screening to pull these two papers. And then we've actually seen an evolution of the guidelines for lung cancer screening from CHEST. There was an initial iteration and most recently one that was published in 2021.

So, let's backtrack a little bit and highlight the components necessary for a high quality lung cancer screening. This involves eligibility with who is being screened, how often, and for how long. Technical aspects of how the low-dose CT scan is performed from a radiology standpoint, guidance for structured reporting by the radiologist interpreting the scan, lung nodule management algorithms, tobacco treatment, education of patients, and data collection really to verify that lung cancer screening is being done in a good way.

So, I would highlight the 2021 CHEST Living guidelines and this was a first really I think adventure into living guidelines where they changed pretty rapidly with the U.S. Preventive Services Task Force recommendation. And so, if you look at the eligibility criteria based on the CHEST guidelines I've highlighted here in red, who the high recommendation is for lung cancer screening and these mirror the original CMS guidelines, so 55 to 77, 30 pack-years, quit within the past 15. Th- these actually mirror the new U.S. Preventive Services Task Force 2021, so this is an addition. So, patients who are asymptomatic and that keeps coming up who don't meet that first recommendation at our younger age and have a lighter pack-year history and they're saying the quality of the evidence here is moderate and with a weak recommendation.

And this is actually the newest criteria here which is a big change from the initial CHEST guidelines. And so these actually say that in folks who do not meet criteria based on number one and number two but are projected to have a high net benefit from lung cancer screening as assessed by a validated clinical risk prediction calculator could be offered lung cancer screening with a low-dose CT scan with moderate quality evidence and really this is augmenting the criteria with risk prediction on life years gained and the whole purpose of this is really to lead to greater equity across race and eligibility for lung cancer screening. So, I think this is a really important addition that is not necessarily supported by the new U.S. Preventive Services Task Force guidelines; they are in support of it but say there's not enough evidence for it but I applaud the folks on the guidelines for this because I think this is important for certain populations.

And so, one of the things I was tasked with doing as we talk about lung cancer screening was really highlight the best practices for

smoking cessation, so I'm going to spend a little bit of time and take you through what the recommendations are and what we know about tobacco treatment within lung cancer screening. So, over 34 million adults that live in the United States continue to smoke cigarettes and it remains high among certain groups and these are typically those in, at the lower socioeconomic status below poverty level. And so, the question then becomes is lung cancer screening a teachable moment? And so, what is a teachable moment? It's supposed to be this naturally occurring life transition or event that happens that motivates someone to spontaneously adapt a new, good health behavior. Now, does the process of having a low-dose CT scan really indicate this type of spontaneous life transition? I'm not so sure but when polled, a- approximately two thirds of screened patients said that they were, you know, ready to quit, 25% said within the next month, 40% within the next six months, and 60% wanted nicotine replacement therapy sand counseling and I think that's really important in the take-home message is that we need to be providing patients undergoing lung screening that are still currently smoking options.

So, these are the two questions that have come up, are there, is tere an added value of increasing quit rates to a screening program and what are the best methods for integrating smoking cessation? And so, to address that first question, our group published back in 2016, and what we really wanted to see was that within National Lung Screening Trial participants and those who had quit smoking, at what point and how many years did we actually get that same mortality benefit in absence of doing LDCT? And so, when you look at the chest x-ray arm and the spiral CT arm, you can see that former smokers, or people who quit smoking that were abstinent for 7 years had achieved that same 20% mortality reduction without getting and LDCT. Now, if you combine this with doing an LDCT, you get this maximum benefit of a 38% mortality reduction. So, with each additional year of smoking abstinence, there was a reduction in lung cancer related death by 6%, and this increased to 9% when combined with LDCT. So, I think this is the data that shows us that doing both is really important.

What about the cost effectiveness? If you look at approved screening procedure or acru- proved medical procedures in the United States, usually you have to hit that threshold of less than $100,000 for quality-adjusted life year and the data from the NLC showed that it was 81,000 for quality-adjusted life years, so, check, we meet that. But look at the cost of smoking cessation. So, around $1,000 for quality-adjusted life years. So, you could argue that you get your most bang for your buck with smoking cessation and if you increase the rate of people who are eligible for lung cancer screening of quitting, you actually cut the cost of LDCT screening in half. So, there's a- an economic advantage there, not to mention the additional health benefits of stopping smoking cigarettes.

And so, what is the best method, like how do we integrate this into our lung cancer screening programs? Well, we don't know yet but we do know a few things and I will give a, highlight that there's a huge trial that's ongoing right now that was funded by the National Cancer Institute at eight different sites, it's called the SCALE trial, looking at different ways to incorporate this. So, more on that to come. But if we look at what we do know is that there's a lot of misconceptions about lung screening. So, this is a great qualitative project that was done in a group of veterans, and 49% of these participants said that there were mechanisms where screening actually lowered their motivation to quit. So, they thought having a cl- clean scan was a license to continue to smoking, and everyone who participates in screening will benefit and you know I think this is the fallacy there and where patient education really comes into play.

We, in our group, wanted to see what the amount of tobacco-dependence would be that predicts a higher lung cancer and mortor-mortality rates in the National Lung Screening trial. And so, we did a secondary data analysis of the ACRIN arm of the NLST. This was a sub- subset of centers that were participating in the National Lung Screening Trial where they did details smoking questionnaires and what we, what was found was that more of the people participating in lung cancer screening were of a higher nicotine dependence than the average U.S. smoker and not surprisingly, the more dependent, the less likely the individuals were to quit smoking and more likely to die of lung cancer. So, if you have someone who was a high nicotine dependence, this is really someone that deserves intervention and how do we a- address nicotine dependence? That's a very simple question and it's been validated a- along with other scales. But the time to first cigarette. If someone's having their first cigarettes within the first five minutes of waking up, they are highly nicotine dependent and you can see there by the lung cancer diagnoses and comparatively across the board, they have a higher rate of dying from lung cancer and all causes. So, if you ask that simple question, you will learn a lot.

The other question we wanted to know is does type of cigarette matter? And so, this was a trial that we had published in JAMA Internal Medicine where we again looked at the NLST ACRIN dataset and compared the different types of cigarettes and again looked at lung cancer incidents, mortality, and all causes. And so, what we found is that all cigarettes are bad and I need to highlight that, all cigarettes are bad. But unfiltered cigarettes are the worst. So, if you're going to ask two questions, how early do you smoke when you wake up and what, kind of, cigarette are you smoking? I think that's really informative and so, what you can see here is that unfiltered smoker-unfiltered cigarette smokers were 40% more likely to develop lung cancer, twice as likely to die, and 30% more likely to die of any cause. And you can see the differences between the rest here with light and regular verus ultra-light, etc. And there was no difference between menthol and regular cigarette smoking as it relates to lung cancer incidents, mortality, and all cause mortality. A and I think that was a question that has been out there is, you know, are menthol or flavored cigarettes worse than regular cigarettes?

The next question we wanted to know was if smokers of unfiltered cigarettes, you know, if the type really d- lead to the type of dependence? And so, I think this sh- continues to tell the story that those who smoke unfiltered cigarettes actually have a higher nicotine dependence. And I think this next point is really important because you'll have people that come in and say, oh I smoke o-, you know, lights, it's OK, you know, they're not as bad for me. So, the interesting thing is that while light or ultra-light cigarette smokers happen to be less dependent, they're actually less likely to quit probably because they think that it's OK. So, this again is an opportunity for intervention.

And so, then the last question that we have asked and this has been submitted pub- for publication is what are the predictors of smokers ces- smoking cessation? And so, again, we looked back and we wanted to see what was going to tell us if someone was more or less likely to quit smoking. And I think this really just speaks to an area for improvement, right? So, of the people who were actively smoking at the time of enrollment in lung cancer screening, over 73% received no pharmacologic treatment. And what we do know is that getting medicines like nicotine replacement therapy really increases the chances of trying to quit and being successful. And so, you can see here tho- more who attempted to quit were offered prescriptions versus those who did not but it was still a low level. Those who continued to smoke, females unmarried, and those with less than a college education, and those were the higher dependence, again time to first cigarette who received dual therapy have the highest likelihood of a quit attempt and that's really important as we talk about how we are going to talk to patients.

So, I will end here and just summarize. There are a number of guidelines and best practices available for lung cancer screening. Implementation should be thoughtful and quality should be continuously reevaluated. There's a lot of information about tobacco treatment with lung cancer screening is actually very paramount from a cost standpoint. Cessation and lung cancer screening also results in greater mortality benefit. All cigarettes are bad but unfiltered cigarettes confer the worse incidence in mortality and people who smoke unfiltered cigarettes are more dependent. Time to first cigarette indicates dependence and so, you should ask about it. And treatment with pharmacotherapy is really important so, you have a captive audience, ask them what they are smoking and offer them some treatment.

And so, we will end with the last question. Which additional group outside of the U.S. Preventive Services Task Force and Centers for Medicare and Medicaid Services recommendation should be offered lung cancer sc- lung cancer screening according to the CHEST 2021 guidelines?

And here is the poll.

Dr. Edell:
Dr. Tanner while we're waiting for the results, that was outstanding. Excellent job. Thank you very much.

Dr. Tanner:
Thank you.

Dr. Edell:
We, we're waiting for it and what we'll have if you can stop your screen sharing and we'll get Mrs. Sivertsen to get hers up and going.

There was a question from the audience that wanted to know if there is a well-validated lung cancer risk calculator that you recommend for using for people who don't meet criteria for screening?

Dr. Tanner:
Yes. I would recommend the PLCO modified 2012. This has been the most validated in a number of populations and is currently the calculator that's being used in Canada as they do risk-based screening. And that is available for download. It's the paper by Martin, Tammemägi, and colleagues. There is a tool that you can use online called ShouldIShare- or ShouldIScreen.com and that will allow you to interface and plug in those inputs. It's a little bit cumbersome but I think it is probably the most robust and most well-validated.

Dr. Edell:
Excellent. Thank you.

Dr. Murgu:
Dr. Tanner, Dr. Tanner, if they, if you, if you can include the reference in the chat room for the person who asked in regards to the validated calculator, I think that would be very, very useful. And I will also take some of the questions that were pre-submitted and put them in the chat room for you to answer via chat as we proceed with our presentation because we're real short on time to discuss that live.

So, Mrs. Sivertsen.

Mrs. Sivertsen:
Hi, I'm Kimberly Sivertsen. I'm a Nurse Practitioner at the University of Chicago. I work in our Interventional Pulmonary Program and also a coordinator for our lung cancer screening program. I thank Dr. Tanner for that excellent presentation on the most up-to-date lung cancer screening guidelines. And that's a nice segue into our discussion, which is strategies for shared decision-making and lung cancer screening.

I'll start with the question. The process of shared decision-making in lung cancer screening includes: choose your best answer. You waiting for the results?

OK. So, let's get started. So, if we take a step back and think about what shared decision-making in healthcare means on a daily basis we're having discussions with our patients as we prescribe medications and recommend treatments and procedures. Oftentimes that's us talking at our patients often it's in the form of a consent form where we run though a list of risk and have them sign the form. In shared decision-making, it's allowing the patient to know that there's always a choice in their opti- in their decisions. It's the process of involving the patient, making it a two-way discussion by incorporating their values and beliefs. And as we know for lung cancer screening, this is a CMS recommendati- or requirement for reimbursement.

As we talk about shared decision-making and lung cancer screening the components, we spend a lot of time talking about the t- the eligibility and the discussion of the risks and benefits. It's important to know that there are other things that you should be covering in that shared decision-making visit and one of those is counseling on the importance of adherence. So, this is definitely not a one-and-done scan. We see that a lot in patients who have had one negative screen and do not want to come back for another one or fall off the radar to come back for another one. And it's important to know that the majority of lung cancers are at- found in screening are actually found on follow-up scans. And then also discussing with your patient that the ability and willingness to undergo diagnosis and treatment, so, while It's difficult to predict surgical resectability in an initial visit, then evaluating their comorbidities, functional status, and then understanding from the patient perspective what they want to know and what they want to go- undergo any recommended diagnosis and treatment. And of course, smoking cessation counseling. CMS specifies that one or more decision aids need to be used in the shared decision-making visit.

So, how are we doing? When we look at some studies looking at this, we're not doing great. We're lacking in providing decision aids to patients, patients perceive that providers often over-state the benefits but they don't recall hearing about the risks. We do pretty good on smoking cessation counseling and then we know that adherence rates for lung cancer screening vary quite rat- w- widely. And al- and the NLST in order to achieve that mortality reduction, there was a 95% adherence. And this recent metaanalysis pooling together multiple centers, the average was 57%. And in some places, following up after two years the adherence rate has fallen to as low as 2%.

There are many barriers to shared decision-making from both the provider perspectives and the patient and we're going to get into that now in our talk how we can overcome some of these barriers, particularly understanding from a provider perspective, training, and decision aids.

So, for those of us who have been in lung cancer screening since its inception, we know that in the beginning, there was a lot of confusion around shared decision-making. And things have changed rapidly over the last couple years. There is a really nice website from the American Thoracic Society and the American Lung Association for a lung cancer screening implementation guide. And what it does is it takes those papers that have provided guidance for developing a program and gives concrete information and so, you're not needing to reinvent the wheel. And this particular website, there's a five-minute shared discussion making visit between a patient and provider. There's a link to that. In our program, we've actually imbedded that into the order. So, as you're ordering the scan, if you have questions or you want to review, you can actually hyperlink into that and review those before you have a discussion with a patient.

For your patients that might be more visual learners, there is this excellent resource that c- reviews both the benefits outlining for patients that not everybody does benefit from screening. And so, this can be a really powerful aid to use. We use this as an i- in an iPad in our screening program. And then online tools for risk assessment. So, I know on the Chicagoland area, you see the Saved by the Scan on billboards and buses, that's not a personalized risk score, it's just going to use the USPSTF task force guideline to plug in that data. But that's one way that you can get patients into your program and then be able to discuss with them the other things to proceed in your shared decision-making visit. And then we were just talking about this website which is excellent. So, this is ShoudIIScreen.com and that uses the PLCO modified 2012 or the Tammemägi risk calculator. And what this does is utilizes the criteria about age, pack year, and smoking status but also incur- incorporates family history, and the presence of underlying lung disease such as emphysema. And there is an app for that.

Now, you can use from the patient perspective-

So, this is a really nice questionnaire to understand where your patients' values are around lung cancer screening. It asks if the patient

would want to know if they have lung cancer, it asks them about their willingness to want to proceed every year with lung cancer screening. And again, being a really useful tool to understand where you're coming from, where your patient is coming from. It doesn't provide a recommendation as to whether or not you should proceed. And I should say that all of these tools that I'm mentioning here, if you go to that initial website from the American Thoracic Society and American Lung Association you can reference all of them.

So, we spent some time talking about smoking cessation, so I will just add a personal story here which is that for our patients and as we talk about adherence and the annual scan, we want them to be coming back. So, keep that in mind as you have your discussions with them about smoking cessation. Oftentimes I'll have patients tell me that they were scared to come back in for their follow-up scan, they almost didn't come because they hadn't quit smoking and they didn't want to tell us that. So, it's important to always, kind of, assess where your patient is at and make sure that you're meeting them at their level.

So, who performs a shared decision-making visit? Right now, the CMS guidance sates that it should be a physician or a non-physician provider. So, this can be a primary care doctor or a centralized lung cancer screening program with a physician or advanced practice provider. The recent decision memo from CMS for updated guidelines may have removed the provision that it has to be done by a provider and were awaiting those final recommendations.

What we are seeing in the literature is that a centralized counseling and shared decision-making visit does improve patients' knowledge of lung cancer screening. And so, as we move forward, regardless of who is doing the shared decision-making visit, it's likely beneficial that it's done in the standardi- standardized and centralized approach.

There's a course through st- CHEST that if you do shared decision-making visit or if you ha- if you are a coordinator or share with your coordinator, it's a free course that talks about shared decision-making in lung cancer screening and I highly encourage you to check that out.

So, documentation and billing for shared decision-making visits is necessary. What we have done in our program is as much as we can, imbed things int he elec- electronic medical record we have. So, best practice alerts show up if your patient may meet criteria for lung cancer screening. And then within the order itself, and you can do this on a paper order or electronic order, you're ensuring that you've met all the criteria for the shared decision-making visit. And then also providing standardized phrasing for documenting that in the note. And then making sure that you're meeting that criteria for the use of a decision aid by automatically providing patient education materials.

And we will end here with our final question.

Dr. Edell:
Execl- excellent. Very nice, Mrs. Se- Sivertsen, I've learned so, much you know I've heard that talk before so, you, you educated me once more.

Really appreciate the questions coming into the chat box. We'll continue with that format

Dr. Murgu:
Ther- there's a question, Dr. Edell, there is a question fr- that was pre-submitted that is pertinent to screening before we move to the surgical and radiation oncology talk-

Dr. Edell:
Stop sharing there, doc- or Mrs. Sivertsen. There you go. OK. What was the question, Tim?

Dr. Murgu:
So, it was related to the strategies to increase lung screening volume and the DRSW annual follow-up exams. So, Mrs. Sivertsen, if you can comment on our strategies at the University of Chicago to increase the lung screening volume and adherence to this follow-up CTs.

Mrs. Sivertsen:
So, we're constantly trying to increase our volumes. We are continually engaging our primary care providers because that's where our patients are going to come from. And then also do a lot of community outreach to patients. In terms of adherence, w- the thing that has made the biggest difference is implementing a da- an electronic database. So, and changing our program from, into a more of a hybrid approach. So, we have a decentralized entry into the program meaning anyone can order the scan. Any scan that's done is then automatically in this database. That was a long time coming and through EPIC but there is multiple databases out there. And then that allows our screening program to track every single patient that has a stand and allows us to do the outreach. And so, then after that initial scan, the program becomes centralized and then we take over and call them and do their shared decision-making visit and evaluation for the subsequent years. And we've seen about a 30% improvement in our adherence rates.

Dr. Edell:
Perfect.

Dr. Murgu:
Thank you.

And as we move to the next talk, Dr. Tanner, there is a question in the Q&A chat room in regards to the websites for the risk calculators that you are referring to. It seems like there I some difficulty finding that link, if you want to, if you want to resend that, that would be appreciated.

Alright, let's move to the next talk.

Dr. Reisenauer:
Good evening everybody I'm Janani Reisenauer. I'm a thoracic surgeon and interventional pulmonologist at the Mayo Clinic in Rochester, Minnesota. Today I'll be focusing on the former side of my hat, which is the surgical workup and evaluation of patients with early lung cancer. And again, once again, thank you to CHEST for being able to put this program out and for inviting my participation.

We'll start with the first question, which is which of the following is not part of the routine workup for early stage resectable lung cancer?

And as we pull up the results here, the answer will be divulged, maybe not directly but through the next few slides.

So, I took the approach of presenting a case but hopefully it highlights the tenants of what factors come to my mind when considering a patient for surgical evaluation. This is a 61-year-old woman who was a former smoker who had quit several months prior who presented with a 2.4, left lower lobe, spiculated nodule which was incidentally discovered on screening CT. So, again, credit to Dr. Tanner and Mrs. Sivertsen's talk about the importance of lung cancer screening. This patient is part of standard workup as directed by the NCCN guidelines, underwent a PET scan for a lesion that's greater than 8 mm in size and a high risk in dividual and was noted to have an esume- SUV max of 16 which would suggest a fairly aggressive nodule with a fairly short doubling time. She did, however, have no evidence of lymph node or extrathoracic metastases and a brain MRI was performed which was negative.

So, just to talk about the different types of lung cancer surgery, which I think is important as you're seeing these patients and counseling these patients and the amount of lung that you're removing is contingent upon what their pulmonary function testing shows, which also is contingent upon their functional status as a patient, as well. And so, in terms of surgical treatments, we can do what's called a wedge resection, which is just a simple, non-anatomic segment of the lung. This is typically done minimally invasively if it's a, and is typically geared towards more peripheral lesions where you're not taking or dissecting out critical structures. And in our practice here, most of these patients go home within 24 to 48 hours.

The next most invasive in terms of amount of lung that's resected is a segmentectomy where the anatomic segment of the lung is removed. This is actually s- probably a slightly higher complication compared to a standard lobectomy because you are creating somewhat of an artificial plane that doesn't exist. So, these patients do tend to lend themselves to a slightly higher risk of air leak and a slightly longer stay in the hospital. But you do preserve a significantly more lung function trying to do a segmentectomy. There's a lot of debate about which patients are good candidates for segmentectomy versus lobectomy which maybe we can get into if some time allows.

Lobectomy is obviously removal of the whole lobe of the lung. Again, can be done open or minimally invasively, generally with a two-night length of stay. A bilobectomy typically only applies, typically to the right side because of the, because you're either removing the right upper and right middle lobe or the middle and the lower lobe, otherwise, a pneumonectomy would involve removal of an entire lung. As part of a good cancer operation, mediastinal lymphadenectomy should be done at the that time, which removes lymph nodes from the mediastinum. I would argue that anything down to wide resection deserves a good hilar lymph node dissection as well, to truly understand that N1 nodal status.

Any and all of these operations can be done open, thorascopically, or robotically. The literature would indicate that there is no difference in outcomes between thoracoscopic and robotic, although the adoption rate from open to robotic is seemingly higher as that transition appears to be less technically challenging than the transition from open to thoracoscopic surgery.

The STS or the Society of Thoracic Surgeons is now considering all stage 1 lung cancer and many stage 2 cancers should be given an MIS approach and centers are now being tacked based on what percentage of early stage lung cancer patients are being offered minimally invasive surgery. I would also add that the administration of neoadjuvant treatment, prior surgery, or the presence of a central tumor or larger tumors are not absolute contraindications for minimally invasive surgery.

So, in terms of assessing a patient for their functional status again, this will guide how much lung can theoretically be resected during an

operation. The most routine, least expensive test to start with is pulmonary function testing and this is kind of the algorithm that most of us follow if the patient has borderline fu- pulmonary function testing, which is defined as either an FEV1 or a DLCO that is less than 60%. As you can see in that case, the patient typically gets su- subjected to a quantitative ventilation profusion scan, which we'll show in just a second and potentially cardiopulmonary exercise testing.

So, when you're calculating the post-operative FEV1 and post-operative DLCO, it's important to take into the account the number of segments that you're actually removing and the number of functional segments that you're actually removing because if somebody has a segment that's completely taken out from post-obstructive pneumonia or post-obstructive atelectasis, you might have one less functional segment that you're removing compared to somebody who does not have that problem. And so, when these numbers are given, this is given as a relative amount relative to the amount of segments that you're taking.

When you're sitting in the office with a patient and you want to do the quick math, I tell a patient that roughly a segmentectomy is about 8 to 10% and a lobectomy is somewhere between 12 and 15%, obviously it varies depending on which lobe. Those are kind of the rough estimates that you can give a patient.

Criteria that strongly suggest inoperability include a post-operative calculated FEV1 of less than 40% or a DLCO of less than 40% post-op or a pO_2 of less than 45, a pCO_2 of greater than 60 or a VO_2 max of less than 10. So, in this patient for example, her FEV1 was 40% and her DLCO was 45%, and this is pre-operative, so, obviously this patient is a very, very borderline candidate and some would say is not a good candidate for surgery. The patient was very adamant to have surgery. She had a previous family member that had had radiation and although it was a different type of radiation for a different type of disease process, there was significant anxiety associated with her mind with going down that route and wanted to do everything that she possibly could to increase her chances for surgical candidacy.

So, we put the patient through an aggressive pulmonary rehabilitation program and then we sent her for VQ scan, particularly because she doesn't endorse any shortness of breath a- at her visit which also makes you wonder is she anemic or was her MVV low suggesting poor compliance with the test? So, we sent her for a ventilation profusion scan. As you can see here, you, the profusion is the amount or the quality that you want to look at and for the left lower lobe, you are taking away about 9% of her overall functional capacity. So, again if you recall back to her PFTs, that would render her with a FEV1 of 31% and a DLCO somewhere in the high 30s.

So, we finally sent her for cardiopulmonary exercise testing, which is a stress test that measures your exercise capability. Information about the heart and lungs is collected to understand if you can respond to the stress associated with surgery. Anything less than 10 is considered prohibitive. Anything greater than 20 is considered acceptable and this patient was 15. So, she was borderline.

So, again, this goes back to having some very detailed discussion with the patient about risks versus benefits. A- and the patient felt absolutely compelled to go on with surgery. The other thing that we did with her in the office is put her on a pulsaple- pulsa- a portable pulse oximeter and walk her up two flights of stairs to see if she desaturated. And she did not. And so, based on that, we decided to go ahead and perform a minimally invasive lobec- s- lobectomy. The advantage of this that's been documented int he literature is that it does avoid breaking the rib or cutting the muscles, is associated with a shorter length of stay, less pain, faster recovery, and less scar tissue formation. The patient underwent a left lower lobectomy. She left the hospital in two days. She was very motivated to participate in pulmonary rehab, which we have on our floor while patients are recovering from lung surgery and has done well since.

A couple of comments that often come up is do you operate on patients that are smoking? The data on this would say that patients that are actively smoking have twice as many complications as those who did not smoke a cigarette within four weeks of surgery. Again, it's all about risk versus benefit. If you're doing a wide resection on the patient, you might be more compelled to go ahead and operate as opposed to if you're doing a complicated lobectomy or i- a lot of this has to do with the eyeball effect in the pulmonary function testing, as well. It seems counterintuitive, but if a patient is actively smoking and they for whatever reason is medically urgent that they have surgery in the next couple of weeks, it's actually better for them to continue to smoke though the surgery than it is to stop within two to three days prior to surgery.

And then in terms of how long can I wait? Perhaps the most relative questions that we can ask around the time of a pandemic, based on the literature that exists, most of the time the delays are routinely related to evaluation, meaning surgical candidacy if the patient has other problems relating to smoking such as heart disease or peripheral vascular disease. Additional procedures sometimes rela- related to staging or additional testing to determine staging and smoking cessation. There are some studies that suggest four weeks is OK to prevent up-staging but I would caution the audience to say that this is very patient-specific and certainly in this case, where this patient had a very aggressive lung cancer with a high SUV is quite different from that patient that presents with a low grade adenocarcinoma that's been present for two years and is slowly growing on CT. So, the individualized patient approach should really be taken into consideration if you are s- considering more than a four-week delay.

This is just a quick screenshot of a VATS approach. You can see the pulmonary artery there is exposed and we've already taken the left lower lobe pulmonary artery as well as the fissure dividing the middle lobe from the lower lobe. This is the same dissection that's done in a robotic view as you can see both i- the tips of both instruments there are dissecting around the pulmonary artery.

That's all I had, I'll close here with a question and we'll give it a few minutes here for people to look at and answer, or a few seconds. Which of the following is a contraindication of surgery?

Dr. Edell:
Excellent job, Dr. Rei-

Dr. Reisenauer:
Alright.

Dr. Edell:
-senauer.

Dr. Reisenauer:
Thank you.

Dr. Edell:
Thank you very much. I think there's going to be, Dr. Murgu mentioned that there's a question. Do we have time for a question Dr. Murgu?

Dr. Murgu:
Yeah, I think we, we're actually on time, so, (throat clearing) Dr. Reisenauer, appreciate the concise review on the literature. And there are a few questions from he audience then I actually have a question and if you can satisfy my curiosity, I would appreciate it.

But let's start with the audience questions. W- I think you alluded to it but what do you think is the impact of the pandemic on the diagnosis of early stage lung cancer? And that's somewhat related to your comments in regards to the risk of up-staging if we delay the, the procedures for diagnosis or therapeutic intent?

Dr. Reisenauer:
Yeah, I can speak a little bit to what our practice evolved into when we were right in the height of things and we were asked to prioritize cases for example. I think a lot of it goes back to the individualized patient approach and in size and doubling time as estimated by PET scan and serial CT scans. I do think that we saw probably more up-staging than we have seen in the past simply because patients were so, afraid of going into surgery for fear of contracting COVID through multiple hospital visits or being in the hospital and then chose to defer surgery, You know, Dr. Rimner is going to follow my talk but we did a fair amount of sending patients to radiation oncology during the period of the pandemic and fortunately our radiation colleagues were not as limited as we were in terms of access. And so, they were the frontlines and treating these people and I think that's really important.

Dr. Murgu:
Thank you. A- another question from the audience which I think is pertinent to your practice is what would be the most appropriate modality for treating a tumor, non-small cell lung cancer 3.0 to 5.0 cm in size that's invading the chest wall without any lymph node or extrathoracic metastases?

Dr. Reisenauer:
Yeah. I think that patient does need pathologic proof of no metastases, so, I would send all those patients to EBUS first and assuming there's no N1 disease if the patient is a good functional sta- c- candidate o- ou- our bias is to still go ahead and perform the resection first. Now, it all depends on what that reconstruction is going to look like. Most of the time, if it's just removal of a couple of ribs and sewing in a gore tex patch, that's probably better to do up front. If you anticipate that the patient is going to be needing i- i- or if for some reason is a frail patient that you don't think would tolerate a chest wall resection, that might be the situation that you le- neoadjuvant treatment first.

Dr. Murgu:
Appreciate it. Thank you Dr. Reisenauer.

Dr. Reisenauer:
Thank you.

Dr. Murgu:
I think we need to move on.

Dr. Rimner?

Dr. Rimner:
Good evening everyone. Thank you fo- to CHEST and to Dr. Murgu and Dr. Edell for having me. I'll be talking about radiation treatment as an alternative to surgery as the definitive treatment for early stage lung cancer.

Here are my disclosures.

And we start with a question. What is the long-term local control achieved with full dose SBRT and you see the presented just there. Please go ahead and vote.

So, I also s- will start with a case. This was a 75-year-old gentleman initially presenting to us in 2015, a current smoker at the time with a significant smoking history who underwent a screening CT scan that showed this nodule here in the left lower lobe, 1.2 x 1.0 cm. There are some small, scattered node- nodules, as well but the SUV was 2.1 and he was evaluated by one of our surgeons who found a DLT of 22% and as you just heard from Dr. Reisenauer that sh- precluded surgery for this patient. A CT-guided biopsy demonstrated a poorly differentiated non-small cell lung cancer and the patient came to us for radiation. Here is the stereotactic body radiation therapy plan. As you can see here, this is the nodule with some safety margins of a few millimeters around it and then that dose cloud, you can see is hugging really cl- tightly the area that we want to target. The patient tolerated radiation well and quit smoking in 2017, had a gradual decline in lung function over the years because of his worsening emphysema and started pulmonary rehab. Eventually he started using some intermittent oxygen but it was, sort of, a gradual decline not thought to be related to radiation.

In 2018 and 19 we followed him for multiple waxing and waning lung nodules until 2020 when he develop another left lower lobe nodule separate from the one that was treated in 2015 and this left lower lobe nodule was biopsied and confirmed to be a metachronous lung adenocarcinoma pointing to the importance of following these patients closely with CT scanning. And then this nodule was treated with 48 Gy in 4 fractions which the patient tolerated again well and had no change in pulma- pulmonary function following the second course of radiation.

We continued to follow him and then a year later he developed a right upper lobe nodule this time measuring 1.3 x 1.0 cm and much more FDG-avid than the two previous ones with an SUV of 14.3. He had a biopsy that was delayed by a COPD exacerbation and then had nuance and atrial flutter, was on Eliquis and loop recorder and eventually had a CT-guided biopsy that re- resulted in a pneumothorax required a chest tube placement but the patient recovered from that. And then we treated that in a third course of radio- of SBRT here seen to again at a dose of 54 Gy in 3 fractions and the patient again tolerated his radiation extremely well.

So, what is stereotactic body radiation therapy? It is also known as saber, CyberKnife, which is a brand name of one of the radiation machines, or stereotactic radiosurgery, those are all a lot of acronyms which really refer to the same thing, delivering a high-dose per fraction or per treatment as we call the f- we call them fractions in somewhere between one to five treatments. And it is the standard of care for curative treatment for patients that cannot undergo surgery and have early stage non-small cell lung cancer. It is a competitive alternative to surgical resection, especially when compared to the sub-lobar resections or especially the wedge resections specifically in patients that are marginally operable. And the reason for that is that there are mo- now multiple prospective clinical trials showing local long-term control of more than 90%. Here's one example from Chang et al. And you can see it goes beyond five years and the curve is completely flat in terms of overall survival, progression-free survival, and cancer-specific survival. The five-year overall survival is somewhere between 80 and 90% depending on the studies that you look at and remarkably the toxicity is really low with grade 2 pneumonitis rates of somewhere between 5 and 10%; something that we ourselves were unsure about because we had never, d- we before SBRT had come along because we had never treated with these radiation doses before. But apparently we can do so, safely with these very precise radiation techniques that- targeting small lung nodules.

There are some advantages to SBRT. It's not invasive, there is no anesthesia involved. There's really no limitation regarding tumor location. We may have to adjust the radiation dose a little bit ta- based on tumor location but it's not that we cannot treat them. We can treat larger tumors, up to 5.0 to 7.0 cm and here is an example on the right side of this tumor and the right lower lobe that disappeared to just this little nodule that in 6 months after radiation treatment had very little inflammation around it. Here's another example from a different patient who had from, who presented with this mass extending from the chest wall almost to the hilum and it completely disappeared after 9 mo- after f- 4 months after the radiation treatment.

We can treat multiple tumors, as I showed in the case. And it's just really an excellent option for the frail and the elderly patients. And the average age of the patients that I treat is actually 80 years old, so, that's the median. We also now frequently use it in the oligoprogressive or oligometastatic patients now that we have data in that setting, as well, that local control with local therapy such as surgery or SBRT can matter and delay and improve progression and overall f- survive- survival.

The toxicity profile is really favorable. Really generally it's a little bit of fatigue, about a month after and some mild dermatitis, if that.

Pulmonary toxicities, as I mentioned is somewhere in the range of 5 to 10% and is actually lower than with conventional radiation treating to larger fields, like for- s- locally advanced lung cancer. And something that is unique to SBRT is chest wall pain can occur in about 20 to 25% depending on how close the nodule is to the chest wall and develop within 9 months but even years later and is usually managed conservatively and usually self-limited. And more than half of our patients don't have any side effects at all, ever, not even fatigue or dermatitis. And my favorite question during follow-up is when patients ask me whether I forgot to switch on the radiation machine because they never felt anything from the radiation.

Now, I'm not one of the people who believe that SBRT has no impact on lung function. I think any intervention that we do has some impact on lung function. But the question is to what degree and it is statistically significant and there are two examples here from RTOG 0236 which was a prospective phase 2 trial where they looked at PFTs before and after, 2 years after radiation and s- found a non-significant absolute difference somewhere in the rage of 5 to 6% in FEV1 and DLCO decline. And the AAPM, the Association for Medical Physicist analyzed 88 SBRT studies and found accrued rate of grade 2 radiation induced lung toxicity of 9.1% and grade 3 or higher of 1.8%. So, it's not 0 but it's remarkably low given the radiation dose that we deliver.

I mentioned that we sometimes have to adjust the radiation dose depending on the tumor location and by that I really mean the central locations in the perihilar areas and near the mediastinum or the esophagus, that's where the full dose radiation that I showed you in our case presentation of 3 or 4 Gy that four fractions of full dose radiation is not indicated and we have to fractionate or spread it out a little bit more over 5 to 15 fractions to make it a safer treatment because they can be damage to the proximal bronchial tree or esophagus and that can be seen here when overdosed as in, as done in the early days of SBRT.

Now just to give a sense of how competitive SBRT haf- ca- has become, there are randomized trials ongoing comparing surgery and SBRT from marginally or even operable patients. And because surgeons and radiation oncs can never agree on who is operable and who is not we, the VALOR trial is one example that's happening in the VA where the pulmonologist makes the decision and refers at the same time to the surgeon and the radiation oncologist. This study is targeting 670 patients and is currently accrued 200 patients and this slide is courtesy of the PI of the study, Drew Moghanaki. And so, patients th- then get randomized to surgery or SBRT and followed for overall survival.

So, in conclusion, SBRT is the standard of care for inoperable early stage lung cancer, the local control exceeds 90%, severe toxicity and pulmonary toxicity grade 2 or higher is in the range of 5 to 10%. Caution needs to be used when we are talking about are ultra-central perihilar masses and these need to be treated in a level with more for protracted regimen of 5 to 15 treatments. And SBRT is often possible when surgery or radiofrequency ablations are contraindicated in extremely frail patients and difficult locations, we can treat them still with adjustment of the fractionation or enlarged tumors.

And I'll end with the second question: what is the gr- risk of grade 2 or higher radiation pneumonitis with full dose SBRT?

Dr. Edell:
Spectacular Dr. Rimner.

Fantastic group presentations. I think we have time, Dr. Murgu if there is a question or two for Dr. Rimner or doctor- or any of the other panel members, we have a couple minutes, we want to be cognizant of peoples' time. You have one that you want to address?

Dr. Murgu:
Y- yeah, there, so, there are a few questions from the audience that we haven't addressed yet and I think they are pertinent to everyone.

So, please reflect on that while I ask you a question Dr. Rimner.

So, the question from the audience is in regards to the multiple small ground glass nodules, so, think about up to five ground glass nodules in the range of 4 to 7 mm incidentally found on CT in asymptomatic patients. W- how do you address that at your institution?

And as you are all thinking about that, I do have a question for you Dr. Rimner in regards to SBRT. So, we at our institution we tend to stage patients prior to SBRT mainly because of knowing the local regional recurrence being in the range of 15%. What's your take on that? Is that, is that guideline-recommended, is there something you perform at your institution or not? Th- can you justify your rationale?

Dr. Rimner:
Yeah, so, well I think th- there's no good or strong data looking at SBRT with or without mediastinal staging. That study I don't, to my knowledge, has not been done. We take a pragmatic approach as I mentioned, our patients are on average 80 years old and, you know, we as a, as a hospital our intake mechanism is through surgery so, a- almost all my patients come from the s- thoracic surgeon, that's where they would get referred from and I'm always happy when they do mediastinal staging before they send them to me because, you know, more information is always helpful. The reality though is that many of these patients come to use because they are

not surgical candidates and they're extremely frail and sometimes the surgeons don't even want to do a mediastinoscopy or an EBUS on them. And then what I do pay attention to is the time interval from the last PET scan and to make sure that that is not, no older than 6 weeks before the start of radiation because there is data that there is up-staging if it, if there's an interval of more than 6 weeks from the last PET scan.

My personal opinion is that PET scan is not that terrible at mediastinal staging. I mean this sensitivity is somewhere in the 85 to 90% range and even an EBUS or mediastinoscopy is not 100%, so I think we may be losing 5 to 10% or so, but given the patient population we're delaying with, I think that's acceptable when there is no other option.

Dr. Murgu:
Yeah, m- my question on that is, you know, is there truly a regional recurrence, nodal recurrence after SBRT, or was that actually progression of disease since you have never sampled those lymph nodes. And now for patients going to surgery will have that pathologic staging, for SBRT patients we never do. Which is the reason we, we implemented that in our practice.

And the other question I have which is something that puzzled me recently from reviewing the literature on all these resection studies and ablative modalities, especially as we entertain the concept of bronchoscopic rese- a- ablation, it looks like the requirements right now for a trial are to treat and resect, you know, to look at the tumor death and margins. What SBRT studies subject to the same kind of protocols. Do we have evidence to justify the truly would kill the tumor through SBRT based on that concept treat and resect?

Dr. Rimner:
That, that an, that a very interesting question and from a, from a biology perspective actually really interesting. There has been one well-publicized study by Dr. Palma et al. From JAMA Oncology last year that looked at SBRT followed by resection ten weeks after. And they found that there was a path CR rate of 60%. Now, surgeons said, oh look, SBRT doesn't work, it only works in 60% of patients. But that flies counter to what the SBRT studies show that if you follow these patients long enough, you know, only 5 to 10% actually recur radiographically and then, you know, get biopsy-proven. I think the challenge with these is that r- radiation death, clonogenic cell death from radiation is a progressive event. It's not at one point all the cells are dead and we see even radiographically that the nodules that we treat can shrink for up to 12 months. So, we don't know when the optimal time point is to do that resection. You know, 10 weeks might've been too early, is- it may be 60% at 10 weeks, it may be 80% at 6 months and then 90% at 12 moths. So, it's hard to determine that based purely on a resection specimen.

Dr. Murgu:
Thank you.

Dr. Edell:
Excellent conversation, I want to be cognizant of time and respectful to people who may have other schedules. This was been a, this hour went through so, went by so, quickly.

Thank you again to the outstanding faculty and their presentations. If there are other questions that have come through the chat, we'll try and address those for you if we can get the information out there.

Again, also thank you to CHEST for allowing us to put this webinar together. I just want to let people know that the next webinar in this series will be April 12th, so, we hope people will sign up and I wish everybody a pleasant evening and again thank you for attending and thank you faculty for an outstanding session.

Announcer Close:
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