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## Management Tools for Early-Stage Lung Cancer

### Announcer:

Welcome to CME on ReachMD. This CME activity, titled, "Surgical approaches to early-stage lung cancer" is presented by Dr. Tim Murgu. This activity is brought to you by CHEST and supported by an independent educational grant from AstraZeneca.

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Here is your host, Dr. Murgu

### Dr. Murgu:

Surgical resection is the guideline recommended first choice for curative intent therapy for patients with limited stage lung cancer. This is an increasing problem because of the high prevalence of pulmonary nodules seen due to screening practices per guidelines, and due to a higher rate of lung nodules that are detected incidentally on CT scans done for advanced lung disease. There have been tremendous advances in robotic surgery and bronchoscopy, which may create a paradigm shift on how we diagnose, treat and stage early lung cancer. I'm the host today. My name is Septimiu Murgu. I'm faculty at the University of Chicago, and I would like to welcome my guest, Dr. Janani Reisenauer. Dr. Reisenauer is a thoracic surgeon at Mayo Clinic, Rochester, where she also the Vice-Chair of Innovation for the Department of Surgery. Dr. Reisenauer is joining me today to speak about the role of thoracic surgery for early lung cancer in the area of robotic-assisted surgery and bronchoscopy. Dr. Reisenauer, welcome to the program.

### Dr. Reisenauer:

Thank you, Dr. Murgu. It's a pleasure to be here and join you today.

### Dr. Murgu:

Thank you for making time for us. So let's get into it. There have been lots of discussions in tumor boards for patients who are not surgical candidates for lobectomy, on what treatment to offer. So how do you decide on whether a patient should undergo sub-lobal resection or SBRT?

### Dr. Reisenauer:

Yeah, that's a great question. When most surgeons are evaluating a patient, and making this decision, and as we discuss this in Tumor Board, it really comes down to patient factors and tumor factors. Tumor factors – we think about the size, the nodal status, and the location of the nodule, meaning is this something that's a peripheral nodule that might be amenable to a wedge resection, or is it more central where you're thinking about a segmentectomy, the implications of which we will get into, I'm sure, a little bit later. There's been multiple reports that have been published about the utility and efficacy of SBRT as it relates to surgery. There were three prospective, phase 3 trials that were started and actually closed, due to selection bias, but the seeming belief is that SBRT in medically inoperable patients is equivalent to surgery. I would say there's still, in real time, a bias towards surgery in a patient that we think can tolerate an operation, even if it means a wedge resection, and I believe the reason for that bias is because of the ability to truly adequately sample lymph nodes at the time of the resection, and confirm that that patient is, in fact, a stage 1. These are the tumor factors that we think about.

In terms of patient factors, there's obviously the tolerability of a general anesthetic, as well as single lung ventilation, and some of that is contingent upon not only the patient's pulmonary status in pulmonary function testing, but also that patient's cardiac status as well. In some situations, it has to do with the patients, whether they're still smoking or not. Personally, I think if it's just a wedge resection, I'm willing to offer a resection to a patient that is still smoking, but there are many that believe that if the patient is still smoking, that they are not a candidate for surgery, and particularly in the era of SBRT could be referred to stereotactic body radiation therapy. A quick note, that there is the STABLEMATES trial that is currently going on, that will compare the two-year disease-free trial and overall survival, in patients who are high-risk surgical candidates that are undergoing sublobar resection versus SBRT.

**Dr. Murgu:**

And Dr. Reisenauer, how do you decide whether to proceed with segmentectomy or a wedge resection, when you're a decision to go for sublobar resection? Can you please describe your practice bias and maybe a quick reference to the literature?

**Dr. Reisenauer:**

Sure. So, there's no great data that parses out segmentectomy versus wedge resection. Most of the terminology is a sublobar versus lobectomy, like the recently published JCOG 0802 trial, that suggests perhaps superiority of segmentectomy for patients with early stage 1A non-small cell cancer. We are hoping that the CALGB trial, whose results have yet to be reported will show some difference, as they did parse out patients for segmentectomy versus wedge resection, and so maybe there will be some data there that we can extrapolate and consider practice guidelines. In the current era, for me, the decision to perform a segmentectomy versus wedge resection is primarily driven by the location of the nodule, and if I believe I can obtain a good margin. If the nodule is very, very peripheral, or subpleural, and it's possible to get a two one to two centimeter margin that might be more favorable, as a wedge resection is a much shorter operation, is generally an overnight length of stay, and generally the complication profile is fairly low. That is in comparison to a segmentectomy, which removes the anatomic vasculature and airway associated with the nodule, but is technically more challenging than even a lobectomy. Takes a little bit longer, and confers a higher risk of air leak and potentially a longer length of stay. That being said, from an oncologic perspective, many believe that a segmentectomy is a superior oncologic operation, because it is an anatomic dissection. I think we need the data to tell us exactly which direction to go and that's where the results of the CALGB trial are much anticipated. But for now, I think it's primarily driven by size, location and ability to achieve a satisfactory margin without compromising the remaining lung parenchyma that you are not resecting.

**Dr. Murgu:**

Thank you. Now in regards to approach, you know, we talk a lot about robots – in bronchoscopy, in surgery. When it comes to resection – lobectomy or sublobar resection what is the difference in regards to outcomes between video-assisted thoracic surgery and the robotic-assisted thoracic surgery? Can you comment on the available data, and then maybe you can comment on your practice at Mayo, and reflect on the popularity of robotic thoracic surgery.

**Dr. Reisenauer:**

Sure. So, I think that most importantly, when we talk to patients, I group robotic and thoracoscopic into minimally invasive surgery, versus open surgery. And the reason for that is that recently, the Society of Thoracic Surgeons came out with a benchmark initiative which they used to grade hospital system star ratings. And one of those metric is how many of early stage 1, noncomplicated lung cancers are performed in a minimally invasive setting? So it is important to make that distinction between minimally invasive and open surgery. Minimally invasive surgery does have the benefit of a shortened length of stay, less pain equivalent and less risk of intercostal nerve pain following the surgery, with equivalent oncologic outcomes. When you dissect it out farther into robotic-assisted and video-assisted, the data is really muddy, and the reason for that is most of the data is not randomized, prospective, controlled trials. It's either meta-analysis data, or retrospective data. And when you look at some of the data that's out there, they're heavily biased towards one technique or another.

For example, they're comparing an expert thoracoscopic surgeon with a beginner robotic surgeon, or they're comparing a robotic surgeon that's primarily robotic compared to somebody who doesn't do that much VAS, but is only doing VAS for the purpose of the study. So it's really difficult to separate these two and look at the data, other than looking at a large cohort in a meta-analysis. There was a meta-analysis published in BMC Cancer in 2021, which included approximately 11,000 patients – 5,000 in the robotic group and 6,000 in the VAS group. Compares with VAS, robotic was seemingly associated with less blood loss, lower conversion rate, more harvested lymph nodes, and a shorter duration of chest tube drainage. However, I would reiterate that most of the surgeons that were robotic surgeons were expert robotic surgeons, compared to the thoracoscopic surgeons. From a cancers perspective, however, there's been no study that has shown a difference between robotic and thoracoscopic surgery. There is currently a prospective trial that's looking at this, that's been enrolling since 2017, and hopefully that'll provide us with some more answers.

**Dr. Murgu:**

Very, very informative. Thank you. Now switching gears a little bit in tumor boards, every month or so – at least at our institution – we

have – we have patients that may not be candidates for surgery or for SBRT. So how do you manage these patients with early stage lung cancer, that you cannot operate, and the radiation doctors are reluctant to provide SBRT?

**Dr. Reisenauer:**

Yeah, that comes up, I would say, pretty sparsely, because most patients, we are able to get to one treatment algorithm or the other. But I think it's not – it – it's important to not count out percutaneous ablation as a treatment modality for early stage lung cancer. If you look back at the trends of the utility of percutaneous ablation, it really hasn't changed all that much over the last ten years. And one has to ask themselves why that is, because it seemingly is a minimally invasive approach that has a relatively low complication profile, and patients are either discharged the next day, or perhaps it's done as an outpatient basis. The reason for that is the paucity of literature. If you go back and look at the data that's out there on ablation – percutaneous ablation – there's a mixture of modality. Cryo, RFA and microwave are sometimes all reported in the same series.

There's a mix of primary and secondary tumors. and there's not great long-term follow-up. In fact, one of the better studies that's out there, is actually a five-year study. Most of the studies that are out there for ablation are unfortunately only two or three-year follow-up, and not the standard five-year follow-up that we look to. One of the few five-year survival cryoablation trials for stage 1 that's out there showed a five-year survival rate of about 68%. And the five-year progression-free survival was only about 88%, and when you compare that to the 85-90% associated with SBRT, or the 85-90% associated with surgery, it is somewhat inferior. I think for the individualized patients and the individualized treatment approach percutaneous ablation is certainly an option when those other two are not particularly available for a patient, but this is an area where we clearly need more data to understand what the implications are, before we recommend it as first-line alongside surgery and SBRT.

**Dr. Murgu:**

And if I may add to that, Dr. Reisenauer, percutaneous ablation does pose the risk of complications like pneumothorax, BB fistula, plus one has no staging information, and people may be committed to several procedures – which brings me to my next question, Janani. I know you're an early adopter of robotic bronchoscopy and incorporate it at – in your thoracic surgery practice. So can you comment on how you use robotic bronchoscopy in your practice?

**Dr. Reisenauer:**

Absolutely. So, as you mentioned, I am an interventional pulmonologist by training, as well as a thoracic surgeon, so I do use the robotic bronchoscope to perform lung biopsies as part of the diagnostic, part of the workup for the patients, but we have recently started incorporating the diagnostic element into a single stage anesthetic approach for the patient. So, if a patient presents with a high suspicion of malignancy on a CT scan, we enroll those patients into a program where they receive a consultation by virtual telemedicine, and after a brief visit in the preoperative area, they then undergo a single-stage diagnosis with the robotic bronchoscope, and then if we can confirm or prove malignancy, the patient goes on to an EBIS for staging and either a thoracoscopic or a robotic resection under the same setting. We're doing this to essentially reduce the wait time and the delay times that are associated with lung cancer care, which has led to upstaging in various reports, and also, to reduce some of the anxiety that's associated with a lung cancer diagnosis for our patient. Further, as other technological tools for therapeutics evolve, meaning bronchoscopic either ablation or chemotherapeutic injection, developing these platforms and understanding the risk profile of these technologies is critically important, and I think being able to do this in a single stage fashion sets up that platform for some of those other experimental therapeutics that are coming down the pipeline.

**Dr. Murgu:**

Thank you, Dr. Reisenauer, for speaking with me, and to our ReachMD audience. I do have a final question, though, if I may. Looking to the next five years, what's your wish list in regards to diagnosis, staging and treatment of early lung cancer?

**Dr. Reisenauer:**

I think if I had to answer my wish list, it would be that any patient, anywhere in the United States could receive the same degree of care as a patient that's living in an area that's close to an academic health center that expeditiously treats patients with lung cancer. Being able to use some of the technologies and the tools that we have, to eliminate the health care disparities that exist, that are centered around lung cancer, would be a dream come true. I think alongside that, opportunities to investigate other therapeutics, such that not every patient has to have a conventional lobectomy, or even a segmentectomy, and prove that that's oncologically equivalent. So-called natural orifice surgery, so to speak, with some of these bronchoscopic techniques, I think is very exciting. And I think it's all about developing the appropriate tool kits and evolving the data, and having a true multidisciplinary collaborative approach to cater individualized treatment to each patient.

**Dr. Murgu:**

Well, I surely hope and I trust that that vision will become a reality. Thank you.

**Dr. Reisenauer:**

Thank you.

**Announcer:**

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