Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/deep-breaths-updates-chest/new-frontiers-in-copd-and-emphysema-personalized-therapies-and-minimally-invasive-options/36585/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

New Frontiers in COPD and Emphysema: Personalized Therapies and Minimally Invasive Options

Announcer:
You're listening to *Deep Breaths: Updates from CHEST* on ReachMD. This program is produced in partnership with the American College of Chest Physicians and is sponsored by Pulmonx, the maker of the Zephyr Valve. And now, here's your host, Dr. Bobby Mahajan.

Dr. Mahajan:
Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I am Dr. Bobby Mahajan, Medical Director of Interventional Pulmonology and Complex Airway Disease Programs at the Inova Health System in Fairfax, Virginia. Here with me to explore the evolving treatment landscape for COPD and emphysema are Dr. Surya Bhatt and Dr. Jonathan Kurman.

Dr. Bhatt is the Director of the Center for Lung Analytics and Imaging Research as well as the Medical Director of the Pulmonary Function and Exercise Physiology Lab and the Pulmonary Rehabilitation Program at the University of Alabama at Birmingham.

Dr. Bhatt, it's great to have you here with us.

Dr. Bhatt:
Thank you for having me.

Dr. Mahajan:
Also joining us is Dr. Jonathan Kurman, who is an Associate Professor of Medicine at the Medical College of Wisconsin and the Director of Interventional Pulmonology at Froedtert and Medical College of Wisconsin Health Network.

Jonathan, great to have you here today.

Dr. Kurman:
Thanks, Bobby. It's great to be here.

Dr. Mahajan:
Alright. Well, let's dive right in, starting with you, Dr. Bhatt. How has your approach to COPD and emphysema management shifted in recent years, especially with the rise of both device-based and pharmacologic therapies?

Dr. Bhatt:
So there have been several exciting advances in COPD management over the past several years. There are now treatment options to make a more personalized approach possible.

Overall, for COPD, there are now several new therapies to target exacerbations and shortness of breath. For exacerbations, we have two new biologics approved in the form of mepolizumab and dupilumab, both of which target type two inflammation, especially for those who continue to exacerbate even when on optimized inhaled therapy. And then for shortness of breath, we have ensifentrine, which is a PDE3/4 inhibitor that was approved last year. It's a bronchodilator with some anti-inflammatory as well as mucoactive properties.

As you know, emphysema is a little harder to treat in contrast to the airway disease that we also see in COPD. For those with significant hyperinflation and air trapping, mechanical deflation with either lung volume reduction surgery or bronchoscopic lung volume reduction with endobronchial valves are good options. And they can significantly improve lung function and lower symptom burden, especially dyspnea.

Bronchoscopic lung volume reduction is associated with far lower morbidity than lung volume reduction procedure, although there have been some advances with LVRS as well with endoscopic interventions and lesser morbidity. But overall, I think the bronchoscopic method is associated with substantially lower morbidity and fewer post-procedure complications.

So I think after a long time, we as pulmonologists have a lot to offer our patients who are complex and hard to manage. I think it's important now more than ever to continuously keep an eye out for patients who may benefit from such treatments and phenotype these patients along the exacerbation pathway or along the dyspnea pathway. It's important to remember that these are not mutually exclusive pathways; some people have both, so we need to manage them both with the specific treatments we can offer.

So when I see a patient now in clinic, I don't just stop at inhalers. Thankfully, I have more options now. I work them up for frequent exacerbations and treat them along that pathway, but simultaneously, I'm working them up for dyspnea and seeing if they're candidates for advanced interventional or device-based therapies.

Dr. Mahajan:
And so do you think there's a true paradigm shift now? I mean, traditionally, we've thought about not having patients feel worse with their breathing, but now we're actually looking at the option of improving their breathing and then making them feel less short of breath.

Dr. Bhatt:
Absolutely. I think previously, the hopes were very low for most people with COPD, especially those with advanced emphysema. I think we'd be happy if the patient didn't progress further or we decreased the rate of progression. But now, I think there's a lot of hope for actually improving their symptom burden and making them feel much better. We've had instances where the lung function improves quite drastically to the point where they almost are to the level they were about five to ten years prior. So I think there's more optimism now for better management of these patients.

Dr. Mahajan:
Turning to you now, Dr. Kurman, if we zero in on endobronchial valves themselves, who's an ideal candidate for this therapy, and what factors help guide patient selection?

Dr. Kurman:
There's a lot of misconceptions about who the ideal candidate for bronchoscopic lung volume reduction might be. A lot of people think that the ideal candidate is somebody who's on triple therapy with a LAMA/LABA and ICS, on chronic steroids with prednisone, on chronic suppressive antibiotics with azithromycin, maybe on roflumilast already, and trying to decide if they need a lung transplant or palliative care.

In reality, the ideal candidate is probably somebody who is not quite that advanced in terms of their COPD management. Yes, you can still evaluate a person who's at that point for bronchoscopic lung volume reduction, or BLVR—it's not wrong. But if you can identify a patient earlier who may benefit from this, that patient is probably going to do better.

The way that I like to think about it is that candidates who receive this treatment as soon as they qualify are probably going to do better than those who barely qualify anymore because they're so sick. So you don't need to wait until the patient is essentially incapacitated by their dyspnea in order to evaluate them for this.

When I like to think about who to evaluate, it's a patient who is on dual therapy with a LAMA/LABA, has hyperinflation, and is still dyspneic, even if it's just dyspnea with exertion. If you want to screen them further in terms of their pulmonary function testing numbers, you want to look for somebody with an FEV_1 less than 50 percent and an RV over 150 percent of predicted. Chances are, if they meet those two criteria, they have a good chance of being a viable candidate for this procedure.

We'll still do additional screening once we see them with things like a transthoracic echo, an ABG, six-minute walk distance test, et cetera. But those key parameters are good screening tools in the beginning.

So when you think about this procedure in that light, you're going to realize that there are probably tens of thousands of patients who qualify for this, who simply haven't been referred for evaluation yet and deserve the opportunity to see if they're a candidate or not.

Dr. Mahajan:
A lot of referring physicians know about the LIBERATE trial, one of the pivotal trials showing the benefits of heterogeneous disease with hyperinflation treated with valves. And they say, "Well, those are the inclusion criteria for this trial. Those are the patients who should be kind of referred." But do you really see that it needs to be within those conclusion criteria? Or can it be outside, meaning a little bit of a higher FEV_1 and a little bit of a lower RV, and these patients still do pretty well?

Dr. Kurman:

We have evolved a lot since the LIBERATE trial and the other early randomized controlled trials. Our threshold for candidate acceptability has increased dramatically. For example, FEV_1s up to 50 percent may be a good candidate. RVs down to 150 percent may be a good candidate. And if a patient looks like a good candidate, but there's one or two criteria that are outliers, even from those values, it's still reasonable to have that patient be assessed at a treatment center to decide on final candidacy.

This is not just black and white; every patient is different and needs to be assessed individually, and that is probably best done at a treating center, particularly if they have some experience with this and can consider patients that are not your classically ideal candidates.

And now that we've developed significant experience with this, we've seen how this can benefit patients who would have been excluded from the clinical trials with their very strict criteria. And this has opened up the door for thousands and thousands of patients across the country. But even though we've done an okay job treating patients, there's still probably tens of thousands of patients right here in the US that can still benefit from this.

Dr. Mahajan:
And Surya, after a valve is placed, what should referring clinicians expect in terms of post-procedural recovery and improvement, and then symptom improvement after the procedure is done?

Dr. Bhatt:
So when bronchoscopic lung volume reduction is performed, one thing we don't have control over is how quickly lobar deflation happens. So if the lobe deflates very quickly, the ipsilateral non-target lobe can get stretched very quickly, and you can develop a tear and a pneumothorax. And that's known to happen in about 25 percent of patients.

The risk is the highest in the first two to three days, and then it gets substantially lower. So we admit the patients for three days for observation to make sure they don't get a pneumothorax. If not, then the risk goes down considerably, and then they can go home.

That said, we now have some strategies to lower this risk. So if we give an FiO2 as low as possible—sometimes even room air, or even 20 to 30 percent of FiO2—the risk of pneumothorax seems to be substantially lower.

And then we also advise some the things to the patients—for example, bed rest. We try to suppress cough with cough suppressants the first couple of days. Anything that reduces the chance of increased intrathoracic pressure, decreases the risk of pneumothorax.

As is usually the case, when the procedure is successful, most patients start feeling better within a few days. But there's the tension between the improvement in lung deflation, and also a slight VQ mismatch that can sometimes happen, and sometimes atelectasis post procedure. So there's always a little bit of tension between improvement in one regard and slight worsening with the other. So it might take a few days for patients to improve. But generally, within about two to three weeks, most patients start feeling better and report symptomatic improvement.

And then this benefit can continue to occur till about four months out. So it doesn't plateau immediately after a few days; you can continue seeing benefit up to four months out, is what we've noted.

And then if patients have heterogeneous emphysema, meaning at least a 15 percent difference in their emphysema score between the target lobe and the non-target lobe, then they can expect about a 25 percent relative improvement in FEV_1. And if they have homogeneous emphysema, meaning more uniform emphysema, and less than a 15 percent interlobar difference, then one can expect about a 15 to 20 percent improvement in lung function FEV_1.

And also important is the improvement in air trapping or residual volume, where about a 350 to 400 milliliter improvement is considered a minimum clinically important difference. And I think if you achieve that, most patients are able to tell the difference.

Dr. Mahajan:
For those just joining us, this is *Deep Breaths: Updates from CHEST on ReachMD*, and I'm Dr. Bobby Mahajan. I'm speaking with Dr. Surya Bhatt and Dr. Jonathan Kurman about current approaches to COPD and emphysema care.

So I'm going to jump back to you, Jonathan. Do you ever combine the novel pharmacologic therapies with endobronchial valves? And how do you navigate choosing between those options versus, say, transplant?

Dr. Kurman:
Historically, we have targeted stability as our goal. But now, the goal is not just stability, but to essentially be symptom free—i.e. dyspnea free. We can't always achieve that, but that's what we should work towards.

And in my mind, a combined approach of minimally invasive procedural interventions using valves in the appropriate patients, combined

with the appropriate advanced pharmacologic therapies like dupilumab and ensifentrine, can give patients the best chance of achieving that.

What valves do is they reduce hyperinflation mechanically. You are intentionally trying to cause lobar atelectasis to reduce hyperinflation and improve respiratory mechanics efficiency, taking pressure off the intercostal muscles and the diaphragm. And valves are really good at that. It accomplishes the same thing that we used to do with lung volume reduction surgery with a fraction of the morbidity and mortality.

Biologics and other advanced pharmacologic therapies can help optimize patients from an airway standpoint. And together, these are going to give patients the best chance of having a minimal symptom burden.

Dr. Mahajan:
Well, we are coming to the end of our discussion, but Surya, I want to ask you one last question. What's really exciting you about the future of emphysema care?

Dr. Bhatt:
Quite a lot, actually. There's a lot of excitement in the emphysema world related to alpha-1 antitrypsin deficiency, with several new pharmacologic treatments being tested. Whether they'll work in alpha-1 antitrypsin or not remains to be seen. And more broadly, for all emphysema. But more immediately, I'm excited by how we are now able to offer a treatment option that's specifically tailored with alterations in lung physiology that is quite patient-specific.

The accurate estimation of collateral ventilation, now using both CT and balloon occlusion procedures, makes the patient selection more precise and more likely that a given patient that is selected in such a fashion is going to achieve a lot of benefit. That is really important rather than guessing which patient might improve. So I think the precision in identifying patients is a significant advance.

And then the newer advances in management of frequent exacerbators, like Jonathan was mentioning with biologics, make it likely that we can get some patients who were previously considered unstable because they were getting frequent exacerbations to a more stable point—we can now do this procedure safely and then target the dyspnea pathway and then get them better that way.

And also, I'm excited about the degree of improvement in symptoms with lung volume reduction, both in heterogeneous and homogeneous emphysema. I think we should remember that emphysema is a CT diagnosis, and therefore it's often underrecognized until it becomes very severe. So I think we need to have a low threshold of suspicion in people who are quite symptomatic—they may have emphysema that may be separately treated.

We need to raise awareness in the community, especially among private primary care providers, as almost 90 percent of COPD is managed in primary care.

And finally, with advances being made in AI and high-throughput image analysis, my hope is that we can use existing CT scans, for example, with cancer screening, and so on, that we can more easily detect these patients and offer the right treatment and help them.

Dr. Mahajan:
Jonathan, I'm going to give you the same question to finish up.

Dr. Kurman:
There's a lot that I'm really excited about. I think that bronchoscopic lung volume reduction with endobronchial valves has laid the foundation for a future of COPD management that combines minimally invasive procedural intervention with pharmacologic advancements. Don't get me wrong, launching a bronchoscopic lung volume reduction program takes work. It is a program. It requires resources. It requires devotion of time and energy. But by laying that foundation now, you're going to set the stage for everything that is coming next.

There are a number of minimally invasive procedural interventions that are currently in clinical trial that may become commercially available in the coming years that could substantially alter how we address other aspects of COPD such as chronic bronchitis and frequent exacerbations.

One of the trials that's currently ongoing that pertains to valves themselves is bronchoscopic fissure completion, in which we can offer valves to patients who were previously ineligible because of collateral ventilation.

Dr. Mahajan:
I think that is a great way to round out our discussion. I want to thank both of my guests, Dr. Surya Bhatt and Dr. Jonathan Kurman, for joining me to discuss the treatment and patient selection strategies for those with emphysema. Dr. Bhatt, Dr. Kurman, it was great having you on the program today.

Dr. Bhatt:
Thank you for having us.

Dr. Kurman:
Thank you, Bobby. Appreciate it.

Announcer:
You've been listening to *Deep Breaths: Updates from CHEST* on ReachMD. This program is produced in partnership with the American College of Chest Physicians and is sponsored by Pulmonx, the maker of the Zephyr Valve. To access this and other episodes in our series, visit *Deep Breaths: Updates from CHEST* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!