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Panel Discussion: Simulated CTEPH Case Conference

## Announcer:

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#### Dr. Moles:

So, we have about 17 minutes for discussion. And I'll start with a question for Dan, and for John. I think that you talked a lot about how you select these patients. But I'd like to ask a question and see if you have some recommendations of who would be the patients who may not benefit? Who are the patients that you would not select for surgery or for BPA, given comorbidities or because you think that they may not benefit from these procedures?

#### Dr. Haft:

So I think we sort of balance the risk and rewards. So if the patient has a substantial amount of obstructive disease, like the case that you presented, the 80-year-old woman, I look at those angiograms and think, well, wow, I can really change this person's life with an effective operation. But you also have to think is this person can actually recover from cardiac surgery. So, you know, if she had severe pulmonary hypertension, which she did, PA pressures of over 100, if I really felt that a lot of her disability, if she's in a wheelchair, if she's on oxygen, she has a lot of functional limitations, if I felt that most of that was attributable to this particular disease, I might say, I think surgery is a reasonable thing. But if she also had substantial osteoarthritis, if she had, you know, a myriad of other comorbidities that were not going to get better with an operation, then I would agree with the strategy that you guys undertook, which was to do a catheter-based approach in a sort of staged fashion to figure out how do you make somebody, you know, better enough to enjoy their quality of life. But a lot of these patients can really have significant functional limitations, you know, because of their pulmonary hypertension. And if you think that they have an opportunity to have an improvement in their life, then I'm willing to push those comorbidities aside. That being said, I think you sent me a patient who had a BMI of 80.

## Dr. Moles:

I did.

#### Dr. Haft:

And I think I did send her back to you to see if you can make her a little better surgical candidate before she comes back. But anyways, I'd love to get Dan's perspective.

#### Dr. Schimmel:

Yeah, I think there are a couple of things that, one, when you have comorbid reasons for pulmonary hypertension, that's a risky situation, I think for the operating room. Trying to figure out what the attributable amount of symptoms are to one particular comorbidity can be difficult. And so, if there's a question over how much of the symptoms are related to CTEPH, I think sometimes – and we have weekly – as I'm sure you do, we have weekly meetings regarding these patients, trying to hear about their history, look at their images together with our radiologists, our pulmonary hypertension team, and cardiologists, trying to figure out what the best pathway is forward. If the pathway is ambiguous, sometimes we'll take those patients for balloon pulmonary angioplasty with some shared medical decision-

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making with the patient to say, you know, we're going to look and see if you respond to this, if you will feel better or not. I will say in this patient population, my nurses in the cath lab absolutely love to take care of them. Because after surgery, or after a couple of sessions with the responders, the patients, like say, 'I feel so much better,' the nurses feel a lot of value for taking care of these patients, which can sometimes be different post CABG or some of our other cardiac patients where they don't get that much symptomatic benefit. So I think, one, if there's comorbid disease, we have a lot of discussion over, will you be a responder or not. And typically, if I'm concerned, we'll usually give it 3 or 4 sessions to see if they are a responder, and I'm not going to keep doing sessions if someone really is not.

## Dr. Moles:

Okay. Alright. And John, maybe you can talk to us a little bit about how the comorbid parenchymal lung disease kind of interferes with your decision-making, because I think that's an area where we struggle quite a bit in in making the right decision.

## Dr. Haft:

Yeah. So you like to think that all your patients have one diagnosis, right? Occam's law, that there's one explanation for everything. But of course, when you're operating on a population that's in the age of 60-70, you know, they have other comorbidities. And when they have significant COPD or worse, pulmonary fibrosis, you know, is their CTEPH the main driver of their symptoms? Or is it their other comorbidities? And, and so, you know, I was tasked with giving the talk, thou shalt not reperfuse disease lungs, talking about exactly this phenomena that somebody has, you know, bad emphysema or pulmonary fibrosis, and they also happen to have, you know, vascular obstruction, what does Val say, is the juice worth the squeeze? You know, is doing an operation going to make them better, perfusing part of the lung that's bad. In fact, you might even make them worse by getting perfused with areas of the lung that have poor gas exchange. So I guess what I'd have to say is I benefit from working in an environment where there's a lot of people around me that are much smarter than me. And so having our multidisciplinary discussion with you and Val and the rest of our colleagues, radiology as well, that it can be very helpful in deciding what the right approach is.

## Dr. Schimmel:

There's a lot of questions too, I think, after acute PE, this case seemed like there's plenty of hypertension probably early on. I struggle with how long to wait before you pull the trigger. And I think that that timeframe, from acute PE to CTEPH has shortened, in part, just because of awareness. I think our follow-up for particularly patient is submassive, massive PE, those patients should be seen very soon after the discharge; one, to make sure they're on good medical therapy, that their symptoms are getting better. And then what the timeline is and what that testing is in follow-up, I think we're getting to a point where we probably have some consensus because of the Balloon Pulmonary Angioplasty Committees and PERC Consortium and then all these other committees. But they are consensus statements, not really data driven. So you know, 3 months, 6 months, how long after a PE would you take someone to surgery?

## Dr. Haft:

Yeah. I mean, a lot of the patients that I see have already been filtered out by now, and Victor, so I do get the benefit of that. But typically, when a patient has a new diagnosis, I mean, if somebody has a PE, they don't have pulmonary hypertension, right? They have RV failure, but they don't have pulmonary hypertension. If somebody is given a new diagnosis of PE and they have PA pressures of 70 or 80, it's not an acute PE, it's chronic for sure. But if they don't have pulmonary hypertension like that, then we always wait at least 6 months with anticoagulation therapy and then sort of start the whole process again. You know, the best of all worlds is to cure these people with blood thinners. If you can do that, that'd be the greatest thing. And but they, you know, are amazing how effective they are with PE, even massive PEs, how effective it can be. But most of the time we see these patients and they're labeled as having an acute PE. And they have all the radiographic stigmata that suggests there's chronicity here, that they have, you know, mosaic perfusion of their lung, they've got big dilated mean PAs, you may even see big bronchial collaterals that suggests this process has been going on.

That patient that you presented, the 80-year-old woman with PA pressures of 110, there's no question her PAs, her pulmonary embolism happened probably decades ago, right? For her to develop pulmonary hypertension to that degree and have her walking around just suggests that this has been going on a very, very long time. And even if you were able to do surgery and extirpate all the accessible obstruction, she would still have pulmonary hypertension, because she has pulmonary vascular

Changes; this process been going on so long that that's a person that you likely won't cure, but you can make them substantially better, either with BPA or with surgery because a lot of it is still mechanical disease.

#### Dr. Cuttica:

You know, in light of the discussions we had in the first session of PVR and EPI populations being predictive of mortality, mild elevations of the PVR, do you consider this a high PE, not CTEPH, not acute-on-chronic, but an acute PE presenting? Do you consider this a high-risk patient population that should be screened for PH regularly? And if so, how do you do it? I mean, to Dan's point of the timeframe of when you call it CTEPH versus, you know, something else? Or do you do you think every patient with a PE should have some sort of

follow-up to look for chronic disease?

#### Dr. Moles:

Yeah, no, I think Mike, that's a great question and a very important topic. I'll tell you what we do in Michigan, and I think we have a great collaboration with the PERC team that sees these patients consistently in the hospital. And we have rapid access clinic for post-acute PE syndrome that we tend to see the patients about one month after their hospitalization, and Jeff Barnes is the person who leads that acute PE clinic. And we're very – we have a very low threshold to test these patients, even if they have any residual symptom after their pulmonary embolism. So patients who have dyspnea, who – a lot of patients describe just I don't feel back to baseline, and they can't maybe elaborate the fact that they cannot exercise as much as they did before or they cannot climb the stairs as they did before. But those patients are consistently getting a V/Q scan about 3 months after the anticoagulation. They've been therapeutically anticoagulated and they're getting an echocardiogram. And that's when, if there's any abnormality in any of those tests, I mean, they will be seen by us and we'll start that pulmonary hypertension CTEPH diagnosis.

I also want to point out, I think that the testing utilization in post-acute PE patients is very, very low. Our group recently published a paper on using the Optum database. It's a national claims database, and we found that in patients who have any symptoms that may categorize them as having a post-pulmonary embolism syndrome, between 3 and 5% of the patients got a V/Q scan nationally. And I think that that's a test that really has the sensitivity that you need to catch this patient population, especially the distal CTEPH patients, the patients who would benefit from a balloon pulmonary angioplasty the most.

And very interestingly too, CT pulmonary angiograms are in on the order somewhere between 40 and 50%. So, I think that there's a misconception about what is the test of choice to look for residual pulmonary vascular obstructions. But that's what we do. I don't know Ruben, if you want to add to that.

#### Dr. Mylvaganam:

I read a second that. I think, and Mike obviously you know the practice here, but we have a post PE clinic, it's a multidisciplinary clinic that involves both pulmonary interventional radiology and, for the most part, hematology as well to sort of help us with that. And we tend to try and use some of those hazard ratios as odds ratios that we saw there. So submassive, massive PEs, patients who presented with symptoms that sort of presented for longer than 2 weeks or those who may have imaging findings that are suggestive of an acute-on-chronic process to screen.

I think there is a role for screening the acute PE population, I don't think there's a role for screening all comers with acute PE; that just not feasible. And, you know, the good prospective registry suggests that it's only a small fraction of them that go on to develop CTEPH, let alone excluding the disease of CTED.

#### Dr. Schimmel:

I that's a follow-up period issue. Like how long – you know, I feel like the 20-year-old who comes in with a PE, presents as a 40-year-old with their CTEPH, right? So like a 4-year follow-up, 2-year follow-up? Is that really enough to say what the incidence of CTED or CTEPH is after say a submassive or massive PE?

#### Dr. Mylvaganam:

So I'll walk that back. So those trials were acute PE mandated to be tolerating their anticoagulation, and they were following it. So you're right. It's different than actual clinical practice where there's oftentimes medical – or insurance reasons why they haven't tolerated their anticoagulation, haven't been on it for a while, have been lost to follow-up. So yeah, it's hard to answer but I think in those who have tolerated anticoagulation, they're on it for their prescribed, whether it's provoked or unprovoked. I think that the data would suggest that after 2 years, the incidence of CTEPH is pretty minimal. So I think you're, you know, at least the way I practice, and it could be wrong, the way I practice is, if I'm following an acute PE who's at high risk for CTEPH, if I screen them for 2 years, and there's no evidence of CTEPH on RV or in V/Q or CTA, that's the end of our sort of follow-up for CTEPH.

#### Dr. Haft:

You know, Ruben, you presented I think, in your slide deck, that the incidence of prior PE, you know, in the CTEPH population is 75%, that it's only 25% of people had no history of PE. I feel like in our practice, and again, you know, I've already been screening with my medical colleagues, but it seems like more than half of those patients have no known history of PE. And if they do have a history of PE, their – at the time of their PE diagnosis, it was clearly chronic. So their PE likely happened a long time before. And I think that's the large, or a very high percentage of that CTEPH population or people who had PEs, and they chalked it up to indigestion and never got treated,

#### Dr. Mylvaganam:

Yeah, or pneumonia or some other some other disease. Yeah.

Dr. Haft: Something. Yeah.

**Dr. Moles:** Tom had a question.

### Dr. Cascino:

So, we've talked a fair amount about patient selection and comorbidities, and now we're talking about follow-up of patients. I think one of the other challenging situations that comes up is that patient who comes to you, they're still symptomatic at 3 months, you get the V/Q scan, it's positive, you do the right heart cath, and they don't meet hemodynamic definitions of pulmonary hypertension. So their mean PA pressure is less than 20. But you talk with them, and their life's clearly been changed since the PE. Can you talk a little bit about how you approach this situation? And specifically, the management of chronic thromboembolic disease that doesn't have pulmonary hypertension?

## Dr. Mylvaganam:

Yeah, I think it's - I'll take it and definitely fill in there. I think what we would typically do at that point is make sure that they've sort of been adherent to their anticoagulation, there isn't any reason for breaks or failure there. And then I think we would CPET them and I think we'd try to document their symptom limitation is vascular in origin. And if that's the case, then I think as long as it's not proximal obstructions, we would think about moving them towards, Dan, if it is proximal obstructions, I think we moved them towards our surgical colleague, Dr. Malaisrie, because we have operated on patients with CTED, and we have offered them a pretty impressive symptomatic benefit from an exertion perspective too. So think to CPET is what helps you there. As long as you get that pre and then you get that post intervention, it really makes us feel better about offering them something as invasive as an endarterectomy surgery.

#### Dr. Moles:

And I would agree with you, Ruben, on everything you said. I think, you know, once you have a patient who may not have CTEPH because they don't meet pulmonary hypertension hemodynamic criteria, I think I would look at the whole picture and try to make sure that I don't have a patient who was, you know, 80 years old with other comorbidities like heart failure, severe coronary artery disease. But if I can be sure that the obstructive pulmonary disease is the reason why they feel short of breath, we do exercise or heart cath, CPET, invasive CPET. If there's nothing else that can explain their symptoms, I think that revascularization is very, very reasonable.

And then I would go back, if I find myself in that situation, I would go back to the usual pathway for CTEPH patients. Do they have surgical accessible disease? And we may have a little bit of a different threshold because they had CTED and not CTEPH. But we've have operated on a good number of CTED patients who have reported dramatic changes in the quality of life. There was one patient in particular who had most of the right lung completely obstructed and then felt a trillion percent better in balloon pulmonary angioplasty, for sure.

I think that it's a little bit of a misconception that in CTEPH, the reason why patients feel short of breath is their pulmonary hypertension. I think that the pulmonary hypertension is part of the problem, but the vascular obstructions are also a huge part of the problem. And I don't think we have a good way to measure that. And I think in the future, we'll change our diagnostic approach to understand a little bit better how we can measure their degree of vascular obstructions for being responsible for symptoms. Alright, we –

#### Dr. Haft:

You know, the thing I do worry about though, is that there's great variability in CT imaging quality. And not only the quality of the scan, but the quality of the interpretation. And so, I think if you rely on CT imaging as the sole method of determining if somebody has residual clot after PE, you're going to miss a lot of people, I think.

#### Dr. Schimmel:

Yeah, and it's probably not just quality, right? I mean, it's the protocol that they have. Well, what we think quality, someone else might say, 'Well, my scan looks great,' but it's, you know, a cut that's thicker than should be done to find webs.

#### Dr. Mylvaganam:

I think also pushback that we – and I know Mike and I have talked about this, we struggle because a totally normal V/Q scan wave may not be totally normal based on who's reading the V/Q scan. And these webs and these – in non-congenital patients, these webs in these mural thrombi in patients who are symptomatic, I wonder that if there is an element of proximal – or of obstruction that's causing their symptoms. I, you know, the V/Q scan with the bronchial artery collaterals, you can have perfusion. And there is a good paper out there that looked at this, that you can have a V/Q that's normal because of the bronchial artery collateral anastomosis in the supply there and because of the way the V/Q is done. So, yeah, I think, like we said, it's a multidisciplinary conversation with multiple imaging modalities. And I think as the future progresses, the imaging and the qualities of that imaging is going to be pretty good for us.

## Dr. Moles:

Alright, we're done with our time, were up. So we'll go to our next session.

#### Announcer:

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