Tailoring CTEPH Imaging for Evaluation and Postintervention Assessment—What Works and What's New?

This summer, Dr Richard Krasuski of Duke University; Dr Gustavo Heresi of Cleveland Clinic; Dr Victor Tapson of Cedars-Sinai; Dr Irene Lang of the Medical University of Vienna, Austria; and Dr William R. Auger, Emeritus Professor at University of California, San Diego, gathered to discuss imaging in the assessment of chronic thromboembolic pulmonary hypertension (CTEPH).

Richard Krasuski: As you know, CTEPH is a common problem that we all see in our pulmonary hypertension (PH) clinics. Somewhere between 3% and 4% of all pulmonary embolism patients develop CTEPH afterwards. We're challenged to identify these patients early so we can get them the appropriate treatments they need including surgery, balloon pulmonary angioplasty, and advanced medical therapies. Despite many efforts, it still takes up to 2 years from the time of symptom onset to confirmed diagnosis.

We have collected an amazing group of panelists and friends for today's session. Pretty much a "Who's Who in CTEPH." This includes Dr Bill Auger, guru of CTEPH and Professor Emeritus at UCSD and Temple and now my fabulous colleague at Duke; Dr Vic Tapson, a sage in pulmonary thromboembolism and pulmonary hypertension who I learned so much about pulmonary hypertension from when I was a fellow at Duke; as well as Dr Irene Lang, Professor of Medicine at the University of Vienna and an expert hemodynamicist and pulmonary vascular interventionalist. It's a real pleasure to be able to comoderate this panel today with my esteemed colleague Dr Gustavo Heresi, who is the head of the Pulmonary Vascular Clinic at the Cleveland Clinic and was my colleague for about 10 years when I was at the Cleveland Clinic. He is going to ask most of the questions, and I'll try to interject when necessary. He was a fellow when I joined Cleveland Clinic and collaborated with the PH program, and he is now the head of the whole thing. It's very impressive, Gustavo, please continue.

Gustavo Heresi: Thank you, Rich. Yes, that brings me back to good times. It was really nice to have you here, and it was a loss for us, but I know you're doing great in North Carolina. Anyway, really excited to have you guys here, and I think, without further ado, we'll just start talking. Rich and I went over a template of some of the questions that we wanted to bounce off of you. The first one, as Rich was saying, the challenge of diagnosing this disease even in this day and age: One of the things that we wanted to start hearing from you guys is what kind of studies you think are needed for every patient with suspected CTEPH.

I guess we can start by talking a little bit about the ventilation/perfusion scan, which, of course, we still consider the best screening method, but we wanted to hear some thoughts from you as to how do you view the ventilation perfusion scan (V/Q) scan in 2022? Do you still consider it the best screening method? Should it be different based on a patient history of prior pulmonary embolism (PE) or not? During the COVID-19 pandemic, has SPECT/CT V/Q scanning changed the way you think about this test?

Vic Tapson: I'll just mention the fact that I still believe the V/Q scan is useful. I think it's underestimated and underutilized by many of our colleagues out there. One of the key values of the V/Q scan, as you well know, is when it's normal, we're done. If it's not normal, you need to move on and be certain there is expertise reading the compute tomography angiography. Reading a CT for CTEPH takes tremendous expertise. Acute PE is easy. The ability to accurately read a CT for CTEPH like Bill Auger does, for example, is a rarity. A true rarity. Most pulmonologists, cardiologists, and surgeons can't read CTEPH CT scans like the people on this call.

Irene Lang: I think V/Q scan is a great tool just for the screen. However, COVID has brought in diagnostic uncertainties to the old technique because COVID infection of the lung changes the V and the Q, probably independent of concurrent acute PE. I think we have to sort out the COVID changes before we use the V/Q as a screening tool for PE during or after COVID-19 infection. I think it's not so trivial. A relationship between COVID infection and CTEPH is still unconfirmed. I do think there's a lot of research ongoing currently, at least in Europe. I know of some studies where people are screened with V/Q after COVID and that isn't trivial.

William Auger: I completely agree. If you speak with experts around the world about screening patients for suspected CTEPH, the V/Q scan still plays an essential role, and the test of time clearly shows that, if the perfusion scan is deemed to be normal, CTEPH has been ruled out.

It's also important to appreciate what you're looking at with the V/Q scan. You're simply evaluating for perfusion abnormalities. It's a nondiagnostic study,

so when folks tell me that CTEPH has been diagnosed with a V/Q scan. . . this is overstated. If there is a known history of pulmonary embolism, the VQ scan might be suggestive of CTEPH, but given the wide range of diagnoses that can result in unmatched perfusion abnormalities, a more diagnostic study such as CT, MR, or catheter-based pulmonary angiography [needs] to be performed to accurately diagnose CTEPH.

Vic Tapson: The great thing is, Bill, a normal perfusion scan, like you said, rules out CTEPH. A normal CT scan does not rule out CTEPH unless a true expert reads it. We've seen major medical centers completely miss CTEPH by CT.

William Auger: I think we still rely on a number of studies that look at the sensitivity of CT and CT angiography for CTEPH which were performed at expert CTEPH centers. . . people who knew what they were looking for and knew how to interpret these studies. However, when you look at "real-world data," another story is told and seems more in line with our day-to-day experience. By way of example, there was a recent small study out of Sweden that examined the original preoperative CT reports of patients with known CTEPH. . . patients who ultimately underwent pulmonary thromboendarterectomy surgery. The diagnostic sensitivity for CTEPH in these reports was found to be only 26% (Rogberg et al. *Acta Radiol*. 2019;60(11):1576–1583). This underscores what you just said Vic that the CT scan can be very difficult to read, particularly at the segmental and subsegmental level.

Gustavo Heresi: Vic, you've done some work in the post-PE population, and I think you showed us that the post-PE population is certainly not well studied. Do you want to comment on what's your approach in somebody with persistent dyspnea and also a little bit about whether or not you see a role for exercise testing, cardiopulmonary exercise testing, even invasive cardiopulmonary exercise testing? How do you view the post-PE population in terms of picking up CTEPH or chronic thromboembolic disease (CTED)?

Vic Tapson: We published 1 study not long ago, Gustavo, the INFORM study, and it was a big claims database. You have to be a little cautious with claims database data, but what it told us is, in a cohort of incident PE patients, that clinicians very often do not look for CTEPH. When patients are dyspneic and have pulmonary hypertension, they're not getting V/Q scans ordered. They may work the patient up for pulmonary hypertension, but VQ scans are often not done or are done very late, again, not a randomized trial, not a registry, but a claims database study. Still, I think the evidence and our experience tell us that people are not looking for it.

I wish we did a better job upfront following patients with acute PE long term. I think patients with acute venous thromboembolism (VTE) should be followed by an expert forever. New studies are published. Patients' risk factors change. Our European colleagues have done a great job with long-term follow-up data. Look at the studies that have been done by Meneveau, Bonnefoy, Nijkeuter, and others. All these studies looked for residual pulmonary vascular obstruction (RPVO) and studied its implications. We don't generally do this. We know RPVO with or without PH is common. The percentage of patients that have more than 10% RPVO with or without PH is 20% to 50%. If you have RPVO, your risk of recurrent VTE is higher, and your mortality is higher.

In many situations, post-PE patients go to their PCP, or they go to an internist. They may go to a pulmonologist, cardiologist, or hematologist. Whoever it is, they ideally need to be followed by an expert. If you have cystic fibrosis, you go back to the CF doctor when you're discharged, and you're followed up. If you have PE, you don't. You end up in a PH clinic years down the line seeing one of you guys, seeing an expert when someone could have been following all along. I think the whole PE world needs to be less fragmented and more organized. Re-imaging and considering CPET in symptomatic patients is not done in a systematic manner.

Richard Krasuski: Let's discuss timing when seeing these patients back after PE. I've seen 3 months or 6 months used in the literature. At what point do you think it's important to assess whether these patients still have dyspnea? Should we be doing studies like cardiopulmonary exercise testing (CPET) routinely to try to establish whether they are functionally limited and need further evaluation?

Irene Lang: I just wanted to remind you, there was a very recent study now published in the *European Heart Journal*, the FOCUS study, where 1000 PE patients were followed up prospectively. Actually, if you go through the list of centers in Germany, a majority of those were PH centers. They had both knowledge on PE and on CTEPH, and they found in 2 years 2.3%, with all the care that was part of the FOCUS study, which is a lot. They had several follow ups, very structured follow ups, since the acute event assessing numerous parameters, including exercise testing.

I think it's still rare, and I wonder if you don't find more CTEPH cases if you look in the ED acute PE presentations and rather than in the post-PE because I think, in the post-PE, you get a mixture of everything. When you look in the emergency room for CTEPH, you may find more. Maybe that is not so clear to you, but I do think, if you do CPET later on, you will find more coronary disease and aortic stenosis than CTEPH.

William Auger: Irene, you are making some important points, emphasizing some of the ongoing difficulties that we're having trying to establish a true prevalence of the disease, either being CTED or CTEPH. In the majority of the studies, patients are followed (on average) for about 2 to 3 years after an acute event in an effort to establish the incident rate of CTEPH.

Two comments that can be made about that: One is that the time period following acute PE patients in these studies may be too short to get an accurate sense of CTEPH incidence. Many of the CTEPH patients that I have seen in clinic relate the story of

having experienced their PE 6 or 10 or 15 years ago. I don't have the exact percentage of patients with established CTEPH who share this history, but the timeline between acute PE transitioning to CTEPH remains an unknown. So, the available studies may be limited, as the follow-up may not be long enough to get a true incident rate, and in support of Irene's comment, many of these incident studies may have been combined patients with established disease. If you look at the condition of PE patients at presentation, the presence of significant pulmonary hypertension, right ventricle (RV) strain, and/or RVH may reflect that their initial presentation may actually be decompensated CTEPH and not acute PE.

Vic Tapson: There's a movement now by the PE Response Team Consortium for VTE Centers of Excellence, which I really think we need. Patients need to be followed from the onset of their acute PE; they need to be seen by a PE expert. This is not just to look for CTEPH or to look for RPVO but to look for postthrombotic syndrome, determine how long to anticoagulate, decide when to look for cancer, whether to look for thrombophilia, etc. I follow my PE patients forever because, who knows, in 5 years, we may know their point mutation. We may be able to give them gene therapy, and they may get CTED or CTEPH.

Irene Lang: It's part of the guidelines in Europe to look at persistent dyspnea at 3 or 6 months; it's open. I don't know, to be honest, how many patients will be seen, what the percentage is, but I think quite a few because people have embraced not only CTEPH but also the post-PE impairment syndrome, which is probably even worse than CTEPH and more common, definitely. It was found in 16% in FOCUS.

Richard Krasuski: It's estimated that up to half of patients post-PE will have persistent dyspnea after 3 to 6 months. As you correctly identified, Irene, it's only a small number of those that'll eventually be diagnosed with CTEPH, but there are other etiologies that may need to be assessed, as Vic mentioned.

Irene Lang: Many.

Richard Krasuski: These can be worked up and potentially treated. A lot of these people have numerous comorbidities, including morbid obesity, deconditioning, and other disease processes that can contribute to their functional limitation.

William Auger: Agreed.

Richard Krasuski: Lifestyle modification can be very important for them.

Vic Tapson: Erik Klok, Irene, and others wrote a very nice paper a couple of months ago in the *European Heart Journal*, and it was on optimal follow up after acute PE, a beautiful paper with a nice table that goes through things: bleeding risk, thrombophilia testing, oral contraceptives, when can a patient fly after PE, when can they exercise, and when and how to look for CTEPH. I think that needs to get distributed more. Again, I think our European colleagues are way ahead of us in this disease state in terms of [at] least following the acute patient up.

Gustavo Heresi: Before we move on, I wanted to circle back to a quick point about how, during the pandemic, many centers dropped the V part of the ventilation/perfusion scan and started using more widespread SPECT CT-Q. Is that, in your experience, something that your centers did? Do you think it added any value? Do you think that's the way to move forward, or just the planar V/Q scan is enough as the screening test of choice? Irene, what are you guys doing in Europe?

Irene Lang: We dropped V scans for a while, but also Q, and then started both again. I think we had a period of low referrals as well. I do believe that those went in parallel, so we didn't miss anything. As we speak, patients are coming back, and they get the whole array of diagnostics. As I mentioned in the beginning, the perfusion part of the test is, of course, also altered by COVID infection, so that, I think, has still to be learned. As was pointed out correctly, any V/Q is an unspecific perfusion test.

I think we tend to look more at CT scans and refine those and use the dual source and the iodine map [to] replace the V/Q. I still like to look at the Q, to be honest, if it's about CTEPH diagnosis.

Vic Tapson: I feel the same. We're still getting our feet wet with dual-energy CT and reading it and looking at perfusion. I still think us old-fashioned people are going to probably stick with a V/Q scan for a while, but CT technology is getting better.

William Auger: To address your question, Gustavo, at the onset of the COVID pandemic, ventilation studies were not performed. . . reasonably so, and yes, a SPECT study is helpful in providing more anatomical information that might cause an abnormal ventilation scan. . . as you might expect if a pleural effusion was present. Whether SPECT imaging adds value relative to planar perfusion imaging when evaluating patients for CTEPH is a separate issue. There's no argument that perfusion imaging with SPECT is more sensitive than planar VQ in the detection of perfusion abnormalities, but whether you see 11 perfusion abnormalities versus 8, it doesn't really matter. In many instances, the perfusion abnormalities on SPECT seem exaggerated without adequate definition on CT to account for those findings. Bottom line, as is the case with planar V/Q, further investigation with diagnostic studies is still required to define the cause of the perfusion defects.

Gustavo Heresi: That's a beautiful segue actually into the next point, which is: If the V/Q is done, and it's abnormal, what comes next? Is it a CT for everybody, and if yes, how do you see it? How does it help you make the diagnosis? Perhaps exclude some mimickers? Then also, are you guys using dual energy? What do you see the role for dual-energy CT scan is in this condition at the moment and perhaps in the future?

Irene Lang: I think CT is the next step there. Nobody doubts that, right? I think dual energy—I'm not so sure about

dual energy as yet. It's more radiation. I personally rely on CT scan, 3D reconstructions, as good as they are possible. I think they are very useful. In case of CTEPH diagnostics, I move quickly to a nice digital subtraction because I can do this very well in 2 planes. I know exactly what's going on. This is my little toolbox. I go from V/Q to CT scan, conventional 3D reconstruction to pulmonary angiograms (PAGs).

Gustavo Heresi: In everybody, Irene?

Irene Lang: Everybody with the suspicion of CTEPH or CTED.

Gustavo Heresi: Even if the CT shows you, for example, nice main or lobar disease, even in those cases, you'd still proceed to a PA gram?

Irene Lang: Yes, because you need hemodynamics anyways, even if you do surgery. The PAG is very fast, and it gives you all the details on all mechanical intervention. Balloon pulmonary angioplasty (BPA) may become necessary unexpectedly. We have had a bailout BPA during COVID because there was no surgical theater available.

Gustavo Heresi: Vic, what's your practice after an abnormal V/Q scan?

Vic Tapson: I think what Irene says makes great sense. After an abnormal V/Q, our next move is a CT. If CT is very obvious, this patient is going to get referred for endarterectomy if they're a candidate. We're not doing endarterectomies at Cedars right now. A right-heart cath would be the next move, but since we still refer to San Diego and they will do the cath/PA gram anyway, so we don't, and they will get the usual very thorough work up and therapy.

To have San Diego in your backyard or have Bill Auger on a phone call is worth its weight in gold. Even though we don't have an actual CTEPH center, we see plenty of it and refer it.

William Auger: The CT is just a marvelous tool, and I just think it provides a tremendous amount of information, not only about the pathology involving the pulmonary vascular bed but also the status of the lung parenchyma, mediastinal issues, and large pulmonary vein abnormalities, all of which can result in an abnormal V/Q scan. When done properly and when read properly, it can provide all the information necessary to diagnosis pulmonary vascular obstruction due to chronic thromboembolic disease and to establish whether or not the patient has technically operable disease. At many CTEPH centers of excellence, an abnormal V/Q and a diagnostic CT angiogram precludes the need for catheter-based pulmonary angiography.

However, as we discussed, interpretation of CT angiography becomes more difficult at the level of segmental and subsegmental vessels, and this becomes increasingly relevant from a patient care perspective with the availability of balloon pulmonary angioplasty, an intervention that can be effective in treatment of distal vessel CTEPH. It's in this setting where there may be questions as to the diagnosis, and particularly in the assessment of operability, that proceeding to catheter-based pulmonary angiography is necessary.

The other point to make is just how valuable perfusion imaging can be in the interpretation of CT angiography and even conventional pulmonary angiography. . . essentially asserting that the perfusion scan can be used as a guiding tool in your diagnostic evaluation. I've recently just had this experience with a case where a patient exhibited a large apical right upper lobe perfusion defect, and the initial CT scan reading failed to account for this abnormality. The perfusion scan provoked another look at the CT, with a more care review showing an obstructed pulmonary artery that originated from the main PA at an unusual spot.

Perfusion imaging can also be useful as a guide for conventional angiography. . . focusing the evaluation of vessel anatomy in regions where there are perfusion defects, even if the CT findings have been assessed as "unremarkable," and it's worth re-emphasizing that this effort in defining the segmental and subsegmental anatomy is worth it. Though the patient with chronic thromboembolic disease may ultimately be assessed as inoperable, their lesions may be amenable to BPA. . . an increasingly available intervention that can really help treat patients like this.

Irene Lang: I think it's a great quality control for the surgeon as well because, if the patient comes out of surgery with mean PA pressure of 32 and wants to go and exercise vigorously, you may want to go back and see the segments that have been missed.

Vic Tapson: How do most experienced surgeons feel about hemodynamics before endarterectomy?

William Auger: With my advocacy of CT, I hope I haven't left folks with the impression that a catheter-based PA gram has lost value in the evaluation process. In fact, I prefer having all 3 studies—perfusion imaging, CT, and pulmonary angiography—available, as they each provide different and potentially important information about your CTEPH patients.

I agree with the points made by Irene and Richard. As well, the pulmonary angiogram is often used for "mapping" in planning the surgical approach, especially to more distal disease. Especially with distal segmental level disease and subsegmental disease, surgeons are not necessarily seeing the chronic thrombotic lesions intraoperatively. However, using the available diagnostic studies as guides, such as a perfusion scan or pulmonary arteriogram, they'll start an endarterectomy plane in a normal appearing vessel to access the distal vessel lesions exhibited on these studies.

Vic Tapson: They have to be able to say, "Perhaps I can find a dissection plane here or something because this vessel was abnormal."

Richard Krasuski: Yes, that's a great point, Vic. Getting to that distal plug operatively can potentially improve the clinical outcomes and reduce the need for further intervention afterwards.

Gustavo Heresi: But for that, isn't the perfusion scan just as good or even

perhaps better than the digital subtraction angiogram?

William Auger: Yes, it may well be, Gustavo, but as you know, the remarkable surgeons that we all work with appreciate that perfusion imaging may not correlate well with the pulmonary vascular anatomy, and as such, the findings on pulmonary angiography can be preferred for surgical planning, particularly with distal vessel endarterectomies.

Irene Lang: Just one more comment: If there is uncertainty about the diagnosis of chronic thromboembolic pulmonary disease, we put an OCT (optical coherence tomography) down there, and that really shows you whether there are webs in veins, and I completely agree that PAGs have to be read in conjunction with the CT scan. It's very clear. Chronic lung disease can mimic CTEPH on PAG.

William Auger: You remember the old days in San Diego, right? Now you're using OCT. What did we use? We use angioscopy. Remember? It's the same thing.

Vic Tapson: A bronchoscope with a balloon on it.

William Auger: Pulmonary angioscopy, Irene. It was essentially a very long (120 cm) pediatric bronchoscopy with an inflatable balloon tied onto the tip. That's what we used.

Vic Tapson: Yes, you guys, I remember from 20 years ago going to San Diego, Peter Fedullo was doing a procedure on—did the PA gram on an 18-year-old kid with one lung disease, single-lung disease. I think this could be sarcoma. He went down with the angioscope. As soon as he saw that lesion, he said, "This is thromboembolic disease."

I'm so glad to see that. It was a fascinating study. I don't know now what CT would have shown on that, but that was an exciting moment for me, was a revelation about how good angioscopy was with someone that really knew what they were doing.

William Auger: Yes. It's a passé instrument simply because of the superiority of CT, and with other imaging modalities like OCT, we have the diagnostic capabilities comparable to what was provided with angioscopy. What originally motivated the San Diego group to pursue this approach was to address the problem of the occasional discrepancy between a markedly abnormal perfusion scan and a not-so-remarkable PA gram.

Irene Lang: I'd like to engage Rich in this conversation because, as soon as you become interventionally active, you want to see an angiogram. It's the same in coronary. We have very nice coronary CTs, maybe even further along in development and imaging power than the pulmonary artery CT scan. Best is angiogram for the precision of ballooning or stenting or any other intervention.

Richard Krasuski: The old expression is "dye don't lie," and it still holds today.

Gustavo Heresi: What do you guys think about this? One way we think about it in our group is, if we have a pretty abnormal VQ and a pretty striking CT and we know that patient is going to go to the operating room, we frequently don't do a digital subtraction angiogram, but I can totally see the value of doing that. However, we would never say that a patient is inoperable based on CT alone because I think the case that you were describing illustrates some of the challenges even for experienced people.

Sometimes even on CT scan, the absence of findings is what's important, if you don't see a vessel coming out where it is supposed to, but some of those findings are difficult to identify. In our hands, we will never stop at a CT for operability assessment. Then we definitely move on to a digital subtraction angiogram. Frequently, especially if the VQ scan is abnormal, the angiogram actually shows you particularly segmental disease in a way that the CT sometimes is less striking. Is that fair, or do you guys have a problem with that approach in general?

William Auger: As more experience is gained in CTEPH centers around the United States, your approach is the more common approach than just doing all 3 studies regardless of the situation.

Irene Lang: You all agree that there needs to be a right heart cath, right?

Gustavo Heresi: Of course.

William Auger: I think that the pulmonary hemodynamic information that you obtain with right heart catheterization is so important, not only for prognostic purposes, but if the hemodynamic profile is really bad, there is the opportunity to get patients to a "better clinical space" prior to surgery, and if you're going to do BPA, the hemodynamic results ensure that appropriate patients are on PH-targeted medical therapy before you do angioplasty.

Vic Tapson: You think there's a role for any other novel imaging? We diagnosed acute PE with intravascular ultrasound in the mid-'90s, but we usually don't need it. It hasn't caught on. We have great CT scans. In terms of chronic disease, we use intravascular ultrasound for chronic deep vein thrombosis cases to better assess them. Do you think there's a role for intravascular ultrasound or OCT or other imaging, or do you think we can do a good enough job without those in most cases?

Irene Lang: You mean in acute PE or in CTEPH?

Vic Tapson: In the CTEPH pre-op evaluation, with a VQ scan and CT angiogram, we do a pretty good job, but as you mentioned, Irene, some clinicians may use OCT. Are there particular cases where you're thinking OCT is beneficial?

Irene Lang: That's exceptional. It's really for those where you cannot make a decision like you described this 18-year-old. I think it remains a very rare thing.

William Auger: There may be a role at some point. There's nothing more uncomfortable when a surgeon comes out of the operating room and says they saw more disease than we did with

on our diagnostic studies. Thankfully, I don't think this happens a lot, but I think more aggressive imaging may be necessary for those questionable cases, such as patients with really abnormal perfusion scans, and a CT that's really not all that impressive. I also hear from our interventional colleagues that perform balloon angioplasties that some of the minor vessel irregularities on catheter-based pulmonary angiogram are sites where there's considerable and hemodynamically significant disease. These are sites where it was difficult to pass a wire, or there was a pressure gradient across the lesion. Is that not true, Rich?

Richard Krasuski: Even with angiography, we can still be fooled. Biplane angiography can help at times, but there still may be an area that doesn't necessarily look that diseased. You realize after poking at it for about 10 minutes with a wire that there is a pretty severe web lesion present. As you get more selective into the distal branches, your pictures get better and better. We find that the more proximal in the vessels you are when you do an angiogram, the more the contrast goes everywhere, and the harder it is to see something distal.

The more selective you get, the easier it is to define the anatomy. Before any transcatheter intervention, you really have to perform selective angiography.

William Auger: Is that the equivalent of the surgeon saying they're seeing more organized clot than we're seeing as diagnosticians?

Richard Krasuski: I totally agree with you, Bill. I think we always end up seeing more when we go in and take selective pictures. As you said, the V/Q starts the process, mainly for the purpose of exclusion of CTEPH. You do the V/Q, and if it's abnormal, you move on to the CT. Certainly, for any patient in whom I'm planning a transcatheter intervention, I'm always going to get selective angiograms. With selective angiography, I generally see more disease than I saw on the PA gram. It's not because I'm necessarily better at taking pictures; it's just that the contrast injection is focused into that one spot. There's a lot of overlap in blood vessels on PA grams, and lesions can be missed.

Vic Tapson: I think that gets back to the point Gustavo was making earlier about being careful about ruling out operability with the CT.

Richard Krasuski: True. As always, I'm learning so much from all of you during this session. One of my take-home pearls is how important each of these studies are and that probably we're cutting corners when we don't do a PA gram for a patient going to the operating room. Circling back and thinking about what Bill mentioned earlier, you hate to have that feeling that you've missed more distal disease. The surgeon needs to know this for their gameplan. Like you said, they're planning their attack based on how distally they're going to go for their resections based on the imaging. If there's a better way to provide that for them before the procedure, we should probably be doing this routinely.

William Auger: It's such a different world now. With effective BPA and other treatment approaches for patients with distal vessel CTEPH, a careful and complete evaluation is necessary. This has been an exciting decade for both diagnostic and therapeutic advances for our CTEPH patients. We can help more people now than we've ever been able to help in the past.

Irene Lang: I think we also help the surgeons. My surgeons benefited most from BPA, I think, because they saw pictures they'd never seen. Although they had seen the lesions, their intravascular look is not really capturing the lesions. They only see the vascular explant and not all lesions.

William Auger: Exactly, Irene. That's the thing that Stuart Jameson taught me early on: When they look in the pulmonary vascular bed, the appearance of organized thrombus is quite variable. It could be a straightforward web. It could be some dimpling along the wall. It could be what some people interpreted as a "plaque" or vascular roughening. It could be complete obstruction of a vessel. There's a number of findings consistent with organized clot from a surgical perspective.

Vic Tapson: I know I said it already, but we have to get these patients to experts. We have to get the fragmented acute PE care coordinated and organized. It's a huge problem. Then these patients can, when they have dyspnea at 3 months, 6 months, 1 year, get seen instead of waiting years to get to someone, get seen, and get help instead of being told they are overweight or deconditioned, or it's their asthma. I think it's critical to make sure we move ahead with better coordinated acute PE care.

William Auger: I couldn't agree with you more, Vic.

Vic Tapson: You have a heart attack; you go to a cardiologist. You have a stroke; you go to a neurologist. You have a PE; you go to a hematologist, maybe a pulmonologist, maybe a cardiologist, maybe a vascular medicine person, maybe a hospitalist, maybe a PCP or an internist. It is okay to be any of these, but it has to be an expert.

Gustavo Heresi: Yes, 100%.

Richard Krasuski: One thing I wanted to add and we've not discussed at all today is the role of echocardiography. It's readily available and so easy to get. It's noninvasive, and no radiation or contrast is necessary, which makes it so different from some of the other studies that we've been discussing today.

I think, for any patient that has had dyspnea for a while and has an abnormal echocardiogram, particularly a big right ventricle that's dysfunctional or an abnormal TAPSE or whatever estimate of RV function you routinely look at, in the context of a normal left heart, it certainly makes me focus on the pulmonary vasculature.

I also feel that follow-up echocardiography is incredibly important, particularly after any intervention.

I find that it's probably the most helpful in terms of knowing how patients

have responded because a lot of patients that are persistently dyspneic and have residual disease will continue to have abnormal echocardiograms. I'd love to hear how you utilize echo in these patients.

Vic Tapson: Quick point, Rich, would just be that you guys probably read Akhi Sista and Jeff Klein's meta-analysis on post PE syndrome, and they found that close to 20% of post-PE patients had abnormal RVs on echo. Echo is such a simple test to do. If it's abnormal, figure out why the RV is abnormal.

William Auger: That's correct, and as others have pointed out, the other important trigger point for clinicians to push forward with an evaluation is ongoing cardiovascular symptoms experienced by PE patients having undergone a reasonable course of antithrombotic treatment. Even if an echocardiogram in this setting is normal, that's where I think more advanced exercise assessments are warranted. An invasive or noninvasive CPET can provide an assessment of ventilatory efficiency and other abnormalities that might direct you toward pulmonary vascular disease or other conditions that might be causing ongoing cardiopulmonary symptoms.

Vic Tapson: I think that goes back to the RPVO issue. The fact that you can have RPVO without pulmonary hypertension and still have increased mortality, increased VTE recurrence rates, and increased dyspnea, that's something we need to explore more, I think.

Gustavo Heresi: In the last few minutes, I wanted to ask something that I think a lot of people struggle with. I think you mentioned earlier that the arrival of BPA has changed the field. There's a lot of patients now that we can help, but I also think that presents us diagnosticians with a more difficult task in terms of calling CTEPH. For example, now we can detect tiny little clots. We're getting really good at imaging, sometimes OCT. We use cone-beam CT, and then you have a clot here and there, and the patient has severe PH.

Is that CTEPH, or is that pulmonary arterial hypertension (PAH)? When do you use BPA? I think, before, those patients, you knew they were not surgical candidates. It didn't really matter that much. You will give medical therapy, but now with BPA, do you struggle with that? Is that something that you guys see in your practices? If you do, how do you make decisions as to when to go after lesions that you think you can balloon? The question is: Is this CTEPH really? Are we going to make patients better? I wonder if you guys have any thoughts on that and would love to hear what our interventionalists think, Irene and Richard as well.

Irene Lang: It's a good question. I stick to the rule that I do not diagnose CTEPH BPA able condition unless there have been 3 months of anticoagulation. That's the first rule that I've always tried to stick to. Sometimes, it's hard, but because there's people who find that there's no doubt this is CTEPH for other reasons, but there are some patients where I insist. Then there's, of course, patients with a disconnect between hemodynamic severity and the amount of vascular obstruction.

For those patients, I think it's very good to have an excellent hemodynamic evaluation to assess wedge correctly do an left ventricular end-diastolic pressure because some of those patients have severe left heart disease as well. Then go ahead and do a good PAG with maybe selective injection, and then take the time and put them on dual upfront medical treatment, or we use a lot of prostacyclin still for the very severe, for 1200 dynes, and a few defects.

Then the next step is take the angiograms, send it to Japan, and get Professor Matsubara's opinion. Usually what comes back is, "Please try." Then I have the patient after hemodynamics, angiogram, pretreated, and then I go in, and I do as many lesions as I can reach. Sometimes, it's an eye opener, and you find many lesions that you have missed before because, when you do a distal injection, you see so many things.

Other cases, not so many lesions, I stop. I say there is nothing more to do, but those are very few patients where really there is few lesions, and then you may think there's another reason for pulmonary hypertension. It's possible. Whenever there's a comorbidity of PAH like M Recklinghausen or some of these scary things, then I'm very cautious.

Richard Krasuski: That's so well said, Gustavo. I don't think I have much to add to what Irene already mentioned. That's just a cornucopia of everything you need to know about performing catheterization in patients with pulmonary hypertension. Diagnostically, it's so important to get that wedge pressure measured accurately. You have to start at step one because so many of these patients have left heart disease. Especially on my end, I see a lot of congenital heart patients. There's a big differential diagnosis that comes with PH in these patients.

You probably remember a patient with congenital heart disease and Eisenmenger physiology with calcified vessels that was initially sent to us at the Cleveland Clinic as a CTEPH case. Sometimes stepping back and making sure that you've made the diagnosis properly before you decide on interventional management is so important. I think Irene's point about an adequate period of anticoagulation before you approach any lesion you think could be CTEPH is so important, as well as initiating medical therapy for those patients that are pretty ill before bringing them to the lab for intervention.

From diagnosis all the way to intervention, there are so many steps there. Catheterization can be helpful at any of those. I think we all agree that CTEPH is still a catheterization hemodynamic diagnosis. Every CTEPH patient, just like every PH patient, needs a right heart catheterization, case closed. My takeaways: V/Q scanning for screening, CT for assessment of anatomy, PA gram to know how distal the disease extends out to, then right heart cath. Every single patient undergoing this evaluation should get one. Probably all 4 of these studies are necessary, even though the patient may end up with surgery, transcatheter intervention, or get treated medically (or some combination of each). I think, as interventionalists, sometimes we have to step back and realize that we're all diagnosticians

first, and we shouldn't be ballooning what [we] haven't first fully assessed and understood.

Richard Krasuski: There are a lot of important mimickers of CTEPH, as you mentioned. I think that CT is obviously an important way to exclude those. I want to go around one time last. Any closing statements from each of the panelists?

Vic Tapson: Let me say mine, Rich. I've said it twice already. I want to say this is a closing statement. We need to organize acute PE. We have great CTEPH experts out there, but we need to get the patients to them. Patients need to be seen for acute PE by experts in the hospital, get referred to experts when they go home. This is not a slam dunk internal medicine thing to take care of. You need to know the new studies. You need to know EINSTEIN CHOICE and AMPLIFY-Extension.

How do we extend anticoagulation? When can we drop the dose? When can we stop it? We've got data that shows chronic care with a half-dose rivaroxaban is better than aspirin alone. It's as safe and better. There's a lot of information. Acute PE needs to become unfragmented and focused so we can do a better job getting these CTEPH patients to experts.

William Auger: My final comment would be very similar. The fields of acute and chronic thromboembolic disease and the transition between these clinical spaces continue to evolve. If questions arise, reach out to your local experts in this field. As Irene and my colleagues on this call have pointed out, there's a lot of expertise out there that can help us interpret a diagnostic study or to make the right decision for our patients. It's just a phone call or a Zoom meeting away.