The Present and Future of Imaging in Pulmonary Hypertension

This fall, Guest Editors Jeffrey D. Edelman, MD, Associate Professor of Medicine at the University of Washington in Seattle, and Harrison W. Farber, MD, Professor of Medicine at Tufts University School of Medicine in Boston, Massachusetts, convened a panel of experts to discuss the role of imaging in pulmonary hypertension. Guests included Benjamin H. Freed, MD, Assistant Professor of Medicine at Northwestern University Feinberg School of Medicine in Chicago, Illinois; Paul Hassoun, MD, Director of the Pulmonary Hypertension Program and Professor of Medicine at Johns Hopkins University Department of Medicine in Baltimore, Maryland; Peter Leary, MD, PhD, Associate Professor of Medicine and Director of the Pulmonary Vascular Disease Program at the University of Washington in Seattle; Sudhakar N.J. Pipavath, MD, Professor of Cardiothoracic Imaging and Adjunct Professor of Pulmonary, Critical Care, Sleep Medicine and Medicine at the University of Washington in Seattle; and Anjali Vaidya, MD, FACC, FASE, FACP, Associate Professor of Medicine and Co-Director, Pulmonary Hypertension, Right Heart Failure and CTEPH Program at Temple University in Philadelphia, Pennsylvania.

Dr Edelman: Good afternoon, everyone. Thanks for joining us. This is the roundtable for *Advances in Pulmonary Hypertension* Volume 18 issue 4, focusing on imaging in pulmonary hypertension (PH). I am Jeff Edelman, a pulmonologist at the University of Washington, and my co-moderator is Harrison Farber, a pulmonologist at Tufts University. Before we start, I was hoping we could go around and identify ourselves and our disciplines and where we are.

Dr Pipavath: Yes, I'm Sudhakar Pipavath, chest radiologist at the University of Washington, Seattle.

Dr Hassoun: Hi, this is Paul Hassoun, a pulmonologist at Johns Hopkins in Baltimore.

Dr Vaidya: This is Anjali Vaidya. I'm a cardiologist at Temple University.

Dr Leary: This is Peter Leary. I'm a pulmonologist at the University of Washington.

Dr Freed: I'm Ben Freed. I'm a cardiologist at Northwestern in Chicago.

Dr Edelman: Okay, excellent. Thank you. I'd like to start with the general comment that our imaging studies can play dual roles of identifying and finding patients with evidence of PH as well as in the evaluation of PH, such as assessing the severity and identifying associated conditions. There is fundamental information that's assessed and identified on most studies in routine clinical settings, while more detailed data and evaluation can be obtained in more specialized settings. I think that experts from different fields, as we have in this group, bring different skillsets and perspectives to the table, and our overall evaluation is really enhanced by this multidisciplinary approach.

I hope our discussion today is going to reflect this diversity. I'm not sure where we're going to go in the next hour. I do have some basic starting points, but I think we'll let the discussion move from there. As a basic starting point, I think it's worthwhile to mention and discuss what imaging modalities we think are routine in evaluating patients with known or suspected PH.

Dr Pipavath: I look at imaging (radiology) of PH being useful in three areas. Number one is diagnosis of PH, be it early, or when there are clinical symptoms and signs. In this situation, one tends to employ an additional investigation and then try to make a diagnosis. The second area is to determine the cause of PH that we can figure out at imaging. There are various causes of PH that imaging can help identify. The third area is imaging as guidance for treatment in some conditions. We have not fully explored the ability of standard imaging in quantification, specifically assessment of severity of PH. I don't think the standard imaging modalities are that great in terms of quantification.

Standard radiology imaging signs have certain predictive values for the diagnosis of PH. However, none of these are predictive enough to cross the treatment threshold for you to start treating PH on the basis of imaging signs alone.

You might employ an invasive study such as the right heart catheterization, which is considered the "gold standard." In practice, you may not be able to perform this test in everyone—this is my understanding, you all need to correct me if that's not the case—and that leads to the next best confirmatory test, the echocardiogram, where you are looking for a tricuspid regurgitation jet, I suppose. I'm sure the cardiologists will be able to say the most about its diagnostic value.

Dr Edelman: For the patient with symptoms that lead you to suspect PH, I think the basic imaging studies that we're going to start with are going to be chest x-ray, computed tomography (CT), echocardiogram, and ventilation-perfusion (V/Q) scan. There are some fundamental findings there that are going to further lead us down the PH pathway or perhaps identify some other cause of dyspnea. I think those are our basic workhorse studies. . . yes?

Dr Vaidya: I agree. I would just add, I think the question was along the lines of the routine imaging that's available

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and used, and I think of it as echocardiogram, V/Q scan, and CT angiogram. Chest x-ray is important and can be helpful, but unfortunately, it's not utilized adequately to raise the suspicion diagnosis often enough. While we want to talk about it and teach about it, it's routinely not interpreted as abnormal in PH. The echocardiogram, of course, for basic awareness for PH, and then it has two additional utilities. One is to recognize the likelihood of the underlying hemodynamic profile that can then be confirmed by catheterization. The other utility is to use it as a guide once we're down the road of PH medical management to see if we've achieved treatment goals. Then the V/Q scan to make chronic thromboembolic PH (CTEPH) diagnosis, and then the CT is equally important to assess for underlying parenchymal lung disease, or if we're going to go down the road of CTEPH evaluations at Temple, to include the CT angiography. Those are my three.

Dr Hassoun: Are we talking about all imaging or just heart imaging? I'm a little bit confused there. Are we talking about all imaging in PH?

Dr Edelman: All imaging.

Dr Hassoun: I see. Okay.

Dr Freed: I would add to the discussion. I think that we also have to think about the judicious use of all these imaging modalities because we have a lot of them. We have CT and V/Q and chest x-rays and echocardiograms. We have to figure out a better way than sort of the shotgun approach to providing the information that's needed.

I think one of the big strengths of echocardiogram is that you can use it to not only identify PH, but to also help further refine where the PH might be coming from. There are many signs on echocardiogram that can help you differentiate between pulmonary arterial hypertension (PAH) or pulmonary venous hypertension. I think that can really help you figure out what potential other imaging modalities you might need, if anything else, before you go ahead and order all these other tests for the workup.

Dr Farber: Let me take that thought one step further. There's a paper from 3 or 4 years ago in which the authors, who were not clinicians, but just medical economists, looked at the workup for PH strictly from a monetary standpoint. They concluded that, on a cost-benefit ratio, the most cost-effective way to proceed if you think somebody has PH is, first, get an echocardiogram. If it's abnormal, proceed directly to right heart catheterization, and then do the rest of the workup if they have PAH because, with the prevalence of diastolic heart disease, you're going to do a lot of imaging or a lot of workup before you actually catheterize somebody who doesn't have the disease you're looking for.

Dr Vaidya: I completely agree. Either the echocardiogram has to strongly suggest a pulmonary vascular resistance (PVR) problem, or the right heart catheterization has to confirm a PVR problem before going down the full road of V/Q and CT of the chest.

Dr Edelman: There are nuances in both of those comments because I think Hap said, "if the echocardiogram suggests PAH," and then Anjali said, "specifically a PVR issue." If you were to take that further, the echocardiogram might be a stopping point, either if it was completely normal or if it suggested a left-sided cardiac problem. Am I interpreting those two comments correctly?

Dr Vaidya: Yes.

Dr Pipavath: The question that I have is, how often can you clinically suspect PH? Are there symptoms or clinical signs? Do they help you in any way, or are you mostly doing a study to assess the cause of shortness of breath, dyspnea, or dyspnea on exertion? Then you go through a series of investigations like just radiographs, CT, or echocardiogram. Then you arrive at the diagnosis of PH and then go downstream in terms of becoming more granular in workup?

Dr Vaidya: I think it can happen in a variety of ways. Both of those scenarios you described are quite common. There are going to be multiple providers out there that are just simply working up dyspnea and ordering a host of imaging tests to work it up and then ultimately land on PH. Probably those of us in this conversation are accustomed to recognizing specific symptoms, things like exertion on presyncope, syncope, exertional angina, physical exam findings that are very obvious to us for right heart congestion, the right heart abnormalities. We may go down that route in a more focused way earlier, but I think it can happen either way.

Dr Farber: Also, nowadays, realistically, people who are short of breath usually get an echocardiogram fairly early and/or a chest x-ray. If the chest x-ray is at all suggestive, you get an echocardiogram. If that is abnormal, go directly to catheterization.

Dr Pipavath: This might be a stupid question, but whenever you do an echocardiogram, do you always look for the pulmonary artery pressures?

Dr Farber: Sure. However, I am more interested in what the right ventricle looks like. The only question with the echocardiogram is, do you do tricuspid annular plane systolic excursions (TAPSE) on everybody, right ventricular outflow tract (RVOT), pulmonary artery acceleration time, etc.? The cardiologists can play with that.

Dr Pipavath: What is the sensitivity of echocardiogram? Does it pick up all cases of PAH?

Dr Farber: The false-positive rate was said to be 30% to 40%. That may be a little better now. The false-negative rate is unknown; it's thought to be very low, but nobody actually knows the number because you don't catheterize a whole bunch of people with normal echocardiograms.

Dr Leary: I would like to double back on the false-negative rate of echocardiography. There is a tendency to focus just on the estimates of right ventricular (RV) systolic pressure on the echocardiogram, but when you narrow in on the pressure, you lose a lot of the richness in

the echocardiogram in order to inform the diagnosis. Once you take into account RV dilation, RV dysfunction, and notching of the RV outflow tract Doppler envelope, then even if the RV systolic pressure does not suggest that you have PH, the sensitivity of echocardiogram to pick up meaningful pulmonary vascular disease goes up. When you rely on just pressures alone, you are certainly going to miss some people.

Dr Freed: I couldn't agree more. It's not just about the pulmonary arterial pressure, which we do get on all patients, but you're also looking for septal flattening, RV function, and then some of the things I mentioned in terms of trying to differentiate between left-sided causes of PH versus more a precapillary process. Echocardiogram is very rich, if you use it properly, in providing a lot of information that can really help your diagnosis and determining whether or not this patient truly has PH.

Dr Vaidya: You could go so far as to say that the RV systolic pressure estimation or the pulmonary artery systolic pressure estimation is the least helpful part of an echocardiogram outside of the initial screening and recognition that there's an underlying problem. Everything else is so much more useful in terms of the left atrial size, the E/e′ ratio, the systolic septal flattening, or the pulse wave Doppler in the RVOT, as well as the RV size and function. When you put all that together, I completely agree with what was said, that it is very rich and full of information. The pressure estimation alone has the least utility.

Dr Pipavath: Would you say then that there is no requirement for right heart catheterization because false negativity is pretty close to zero? I'm obviously asking a leading question.

Dr Vaidya: No. I don't think you can say that there is no role for the right heart catheterization; there will also be too many users without adequate expertise making mistakes on this basis. The utility is to recognize early on what the likely underlying hemodynamic profile is and then move quickly to confirm that and move quickly to do the subsequent testing, like Hap said earlier. Get the V/Q. Get the additional chest imaging if it's suggestive of that. Move more quickly to the right heart catheterization when you have features that suggest an underlying PVR problem versus maybe looking more closely for risk factors for left heart congestion when you have the other appearance on the echocardiogram, but the catheterization should still be done. It should be done with a little more insight.

Dr Edelman: In the sixth World Symposium consensus proceedings section addressing PH due to left heart disease, there's actually a nice table that combines echocardiogram and other clinical findings to characterize the pretest probability of left heart disease phenotype. So using echocardiogram findings and other clinical data, one can define scenarios where maybe all you need is the echocardiogram to say there's probably not PH here, or there is PH, but it is very likely due to a left-sided etiology. I think that combination of study findings with clinical suspicion is certainly important in guiding decisions as well.

Dr Leary: I think that it was important how you framed this as a negative, Jeff, and I agree. Echocardiogram is relatively good at excluding a diagnosis of PAH either by arguing against PH altogether or by arguing for left heart disease as the explanation for PH. On the other hand, even if an echocardiogram looks like PAH, it is not adequate to confirm a diagnosis of PAH. Even if you don't see clear evidence of left ventricular systolic dysfunction or valvular cardiomyopathy, if you're playing the numbers, it is still probably more likely to represent heart failure with preserved ejection fraction than PAH. For me, this is still the key reason why right heart catheterization really can't leave our algorithm. If we neglected the heart catheterization, we would likely be mistreating a phenomenal number of people who really have diastolic dysfunction that was difficult to appreciate or misinterpreted on the echocardiogram.

Dr Edelman: I agree with that, Peter. I guess I was framing it in the setting where you may have enough information to determine that there is a likely PH etiology, such as left-sided heart disease, for which you might proceed to treatment without right heart catheterization. I wasn't saying that, if you suspect that there's PAH, the echocardiogram is good enough, but that there are settings where you can, with good reliability, identify an etiology and direct therapy for the etiology without the heart catheterization.

Dr Vaidya: I agree with that. There's another angle of this, too, where we are so commonly discussing how right heart catheterization is the "gold standard" in the diagnosis of PH. That's only the case if it's done accurately. The flip side is how commonly patients with true PAH or CTEPH or a predominantly PVR lesion have an underoccluded technical error when trying to get an accurate wedge pressure. It's because their distal pulmonary arteries are larger in caliber, and this is a very common technical error that leads to an overestimated wedge pressure and missing the accurate diagnosis of PAH. It's part of why it still takes 2 ½ years to make an accurate diagnosis.

That error can be vastly avoided if we are properly interpreting the echocardiogram in advance. Our fellows, for example, know that they are not to scrub in on a right heart catheterization with us until they've looked at the echocardiogram images themselves, so that if they underocclude a pulmonary capillary wedge tracing and the tracing blunts and it looks like it could be a venous wedge waveform but it's 28 mm Hg when the patient echocardiogram has severe septal flattening, an E/e′ of 7, a small left artery, and an RVOT notch, then they know that they've probably underoccluded, and they have to pay more careful attention technically in the catheterization lab.

The echocardiogram can be very helpful both ways to ensure that the right heart catheterization is also providing hemodynamic data that's most consistent with the patient's true overall clinical presentation.

Dr Edelman: All echocardiograms are not alike. All right heart catheterizations

are not alike. When you get information that doesn't fit, sometimes you need to step back and look at where the potential for error is. Some of these studies are being done at centers with different focuses or experience. PH centers can play a role in integrating and further reviewing the quality as well as obtaining more nuanced information from these studies.

Dr Farber: Just one last point about all that: the other part of this is that the echocardiogram is not near 100% accurate in diagnosing or suggesting diastolic heart disease. That's one issue; the second aspect is that there are people who have every risk factor for diastolic heart disease and have true precapillary PAH. So I don't know how, at least currently, you're going to get away from right heart catheterizations, nor should you.

Dr Hassoun: I'll say something about our experience, which is quite skewed at Hopkins, because we're a PH center, and patients come in with a suspicion of PH. They've had sometimes several echocardiograms or other tests. We always start with the chest x-ray, V/Q scan, and CT scan with pulmonary angiogram (CTPA) to exclude either lung disease or thromboembolic disease. V/Q scan is a must for all our patients.

I agree with all that's been said about echocardiograms in terms of the usefulness in ruling out valvular disease, diastolic dysfunction, left heart disease, etc. It's extremely helpful. I agree with the comments made by Anjali about the RV systolic pressure, and this is the thing that I pay least attention to. I look at RV morphology, volume, septal displacement. We do TAPSE on all our patients, not only to assess RV proper function, but also for risk stratification.

We also use TAPSE for follow up. We decide based on the echocardiogram whether it's left heart disease or more likely right heart disease, and that will lead us to eventually do a cardiac catheterization. To give you an example, if I have a middle-aged obese patient who has some systemic hypertension, an RV systolic pressure of 50, but a normal RV volume, I would be tempted to get a sleep study first and treat for 6 months in case a sleep disorder is confirmed before repeating the echocardiogram and deciding on further action.

We eventually perform right heart catheterization on all patients with a PH suspicion. This comes after a set of baseline tests that will lead us to place the patient in 1 of the 5 groups of World Symposium on Pulmonary Hypertension (WSPH) classification of PH. I am saying our experience is skewed because these patients come in with a suspected diagnosis of PH, and the challenge then becomes to decide whether this patient fits mainly in Group 1, Group 2, Group 3, Group 4, or Group 5. This will be very important before doing a right heart catheterization and considering treatment.

In addition, we use the echocardiogram for risk stratification, and if you look at the REVEAL score or the European Society of Cardiology/European Respiratory Society (ESC/ERS) recommendations, unfortunately, there is only pericardial effusion considered in the REVEAL score, and pericardial effusion and right arterial area for the so-called ESC/ERS traffic light table. I think more echocardiogram findings like TAPSE, fractional area change, or degree of tricuspid regurgitation should be used for stratification.

Finally, we use the echocardiogram for follow up after initiation of treatment, mainly focusing on TAPSE, fractional area change, to see if there are changes of function of the RV chamber. We haven't talked about cardiac magnetic resonance imaging (MRI). We do cardiac MRI mainly for research purposes, but this is a modality that can be extremely important, at least for PAH in terms of assessing, again, RV function, such as RV ejection fraction, which has been shown to correlate with survival. There are so many other useful parameters that you can get with cardiac MRI.

Dr Vaidya: I would agree with that comment regarding the guidelines table. I've always thought it's unfortunate that they only include right atrial area and pericardial effusion because that is a little limiting in broad utility, and there are data to support TAPSE and fractional area change and other features. I think of it as overall echo markers of right heart performance. I completely agree that pericardial effusion and right atrial area should not be the only things included in that category.

Dr Leary: I don't disagree with either of those comments, but from a logistical standpoint, what I think that the existing risk scores show us is that where we are right now in PH, we certainly don't have a single magical imaging variable that prognosticates for our patients. So we're left with old-school scales of justice, where we stack data on one side or the other to try and get a sense of whether our patient really is in a low-, intermediate-, or high-risk category. I think that we can broadly agree that imaging markers of the RV, whatever your favorite may be, are an important part of that risk assessment. The degree of derangement in a single marker may outweigh votes in a bunch of other categories, but any given marker rarely stands alone. What I heard from Paul and Anjali is that we have a lot of good markers out there. People have done good work correlating these to disease progression. What can be challenging with the plethora of high-dimensional data is deciding how to weight these things in clinical practice and coming up with a framework to put that into.

I don't envy the people who created the risk scores for that reason. . . to try and make something that's manageable, incorporating all these various inputs, all of which are somewhat colinear and hopefully are telling you similar things. Ultimately, though, I still think that you do want to look holistically at this and not get too married to any individual marker.

Dr Hassoun: I agree with you, Peter. I was complaining about the fact that, whether the REVEAL or the ESC/ERS risk scores, they have a couple of elements of echocardiograms. There are many biomarkers that have been associated with survival. I agree with you that we need to have a more holistic approach. If you look at the work that was done in the Swedish, in the German, and in the French registries using

the ESC/ERS risk stratification, they've looked at between 4 and 8 variables: hemodynamics, a little bit of echocardiogram, function, hemodynamics, etc. I think we need to have a number of imaging parameters to incorporate into our stratification scores.

MRI is not even mentioned in any of these. I think obtaining MRI may be more complicated from an availability standpoint, but I think it gives you so much more accurate information on both the left and the right heart and coupling between the right ventricle and the pulmonary artery and so many other things such as myocardial perfusion reserve by cardiac MRI, which we find correlates with survival. That means that there are so many things that have not been explored from an imaging standpoint.

Dr Edelman: I think we should talk about the role and potential role of MRI. I want to save that for just a little bit later. I'm still sticking to routine tests. I want to come back and talk a little bit about CT and V/Q scanning and their current roles and limitations because I think that, a lot of times, we are seeing patients who come in with dyspnea and often one of the first tests that's ordered is a CT, particularly CT angiogram, to look for acute pulmonary embolism. On many of these studies, there's no pulmonary embolism, but there are findings of PH such as pulmonary artery enlargement.

There is a lot of information that often isn't looked at. You can get fairly good assessments of some of the cardiac structures as well and get some further ideas as to what may be contributing if there is PH present, including information regarding underlying lung disease.

Dr Leary: As with any imaging test, I think it's hugely important where it's being used. There is a ton of information on a CT scan, and I'm going to focus in on CTEPH for a second. If you put a CTPA in the hands of a chest radiologist, particularly one who's focused on CTEPH or at a CTEPH center—even without a V/Q scan, they reliably identify the features of CTEPH that make the diagnosis likely based on the CT alone. In this scenario, I think CTPA really does tell you a ton.

On the other hand, we also know that CT reads from someone who is not focused on CTEPH can frequently miss the features of the disease on CT. In this context, something like a V/Q scan is necessary to really draw attention to the perfusion fall out. I don't think that we have moved beyond the era of V/Q scanning PH patients, mostly because of these differences in expertise or focus in terms of who's reading the scan. While the technology is sound, I think greater expertise and focus than is widely available is necessary to really pull out a lot of the features that are important on a CTPA as they relate to PH in routine practice.

Dr Edelman: Peter, just like you said before about echocardiogram, I think the point is that there's a richness, to use your words, in CT imaging as well that isn't always readily tapped into at every location.

Dr Leary: Yes, that sounds right.

Dr Vaidya: I agree completely with the comments about CTPA and its use in CTEPH. That is certainly our experience at Temple, where the outside scans are sometimes not recognizing the findings that are truly, clinically obvious in our interpretations, but what a difference it makes, based on a center's volume and experience in recognizing the disease state. I agree that the V/Q needs to remain part of the algorithm for the general clinician workup out there.

Dr Freed: I agree, too, that the V/Q needs to remain part of the algorithm. I think there are technological changes coming down the pipeline with CT, like dual-energy CT, that might be able to help in giving both anatomical and perfusion information. It's not there yet, and it's certainly not ubiquitous by any stretch, but I think that, as technology improves, we might be able to get our information out of one imaging modality rather than multiple ones, but certainly in total agreement that V/Q scan is still a major part of this workup.

Dr Pipavath: I don't do nuclear medicine, so do you typically use V/Q scan as a rule-in modality or a rule-out modality? You are probably not, just on the basis of perfusion defects alone, suggesting CTEPH and starting to treat it. You would require a morphologic correlate, wouldn't you say that?

Dr Vaidya: Correct.

Dr Pipavath: You will move onto CT angiogram in someone who has a slightly higher pretest probability at that point and then look more carefully to make sure that there is or there is no physical occlusion or a linear filling defect or a peripheral filling defect indicating CTEPH.

Dr Vaidya: That's correct. The V/Q scan is very sensitive, but not specific, and so the CT angiogram is critical to then rule out other mimickers of CTEPH and to further characterize the location and nature of thromboembolic disease.

Dr Pipavath: What do you do when the V/Q scan is positive but there is no physical correlate? Do you just assume that it is because of Group 1 disease by excluding everything else?

Dr Vaidya: It can be that the description of a V/Q scan being positive in that context needs to again be interpreted by a CTEPH center because sometimes even the interpretation of the V/Q scans can be more complex than realized, and they can be read as false positive sometimes as well.

Dr Freed: Yes, and then there are diseases like sarcoma or vasculitis or pulmonary veno-occlusive disease or fibrosing mediastinitis. All of those can be false positives on a V/Q scan.

Dr Edelman: I think the value of the V/Q scan in this assessment, as Anjali said before, is really more of its negative predictive value. That really takes CTEPH off your list, and that's why it stays in the algorithm. It's readily available. It's got very defined interpretation guidelines as opposed to what we heard about CT, where CT at the right place,

in the right hands, read by the right person, may approach that kind of operating characteristic of V/Q, but I had to add a lot of caveats to get there.

Dr Leary: I said that CT was rich, and I don't back away from that statement. That's not to say that I think we've climbed the mountain and are at the top. I think that, particularly as we've delved further and further into balloon pulmonary angioplasty and are working on chronic total occlusions and distal disease, what we're finding is that we're bumping into the limitations of a CTPA to really define anatomical disease in a way that's as good as we want it to be, as we start targeting smaller vessels and taking different approaches to treat the disease.

Maybe dual-energy or some of these other approaches will get us there. Maybe they won't, but I think there is still room for improvement in imaging around this space.

Dr Farber: To summarize, part of the problem is there are none of these imaging techniques that are specific enough to avoid any of the others. If you're going to evaluate somebody for CTEPH, there are multiple different imaging techniques that are used so the surgeons or those doing balloon pulmonary angioplasty have an idea of what they will encounter.

Dr Edelman: I think we should probably spend some time discussing studies that are perhaps not as routinely used, such as cardiac MRI in evaluating PH.

Dr Freed: I think this was mentioned earlier, but one of the bread-and-butter kinds of things that MRI does is give you accurate RV volumes, RV ejection fraction, and RV mass. You don't need contrast for it, it doesn't take long to get it, and there's no radiation involved. That alone, just giving you that type of information, is huge and really overcomes the limitations of echocardiography because it's a 3-dimensional imaging modality. You can get a more global assessment of RV function, and this is what really helps to prognosticate in these patients.

That's just the basic stuff that MRI can do, not to mention all the other sequences like tissue characterization that could potentially be helpful.

Dr Leary: As a physiologist and somebody who enjoys the idea of thinking about the RV an awful lot, I love MRI. Despite that fact, I use MRI almost not at all in my clinical practice outside of our research studies.

Within the setting of a multipronged risk stratification approach where we're looking at B-type natriuretic peptide and 6-minute walk and some form of RV imaging, I've yet to be convinced that clinically a cardiac MRI has risen to that level where the juice is worth the squeeze, so to speak. Our patients tend to like echocardiography better; it is more accessible and is less costly to the system. I am just not sure that, in a multipronged risk stratification approach, use of cardiac MRI over echocardiogram moves the needle on prognostication. I love it as somebody who likes thinking about the RV, but I will say that clinically I don't actually use it all that much.

Dr Pipavath: What do you think are its limitations? I don't do cardiac MRI. My colleagues do it here. Those who do cardiac MRI, they seem to claim that it is, as you said, much more reproducible, but what—is it just the expense and the patient going into the magnet? Some of my colleagues have said that the expense tends to be very similar sometimes, but obviously the mean might be different at different locations. Is it just the expense, or is it that enough data have not been produced to comment on it?

Dr Leary: I'd say, for us, partially it's the expense and partially just my bias. At least our long-term patients have grown up on echocardiograms, and so MRI feels intimidating. We've had a lot more pushback from patients after they get their MRI than after they get their echocardiogram. That's just anecdotal experience, but it is fairly consistent anecdotal experience.

Dr Freed: I completely appreciate what you're saying. I think that problems come when you're at a center where potentially the echocardiograms are not read correctly, as we talked about before, or you simply have a lot of difficulty seeing the right ventricle for a variety of reasons. I think that's when MRI might be particularly useful. I certainly don't use it for every patient either, but there are still a number of cases where it could be helpful. I think this is also why, in the world of MRI, there's a push to try to find other indications for MRI in this patient population that will make it worthwhile to go ahead and get that test, things that MRI can provide that echocardiography can't and are useful in the management of these patients. I don't know if we're quite there yet, but there are a number of techniques being studied for this reason.

Dr Edelman: Can you elaborate on that a little more? I think your article in this issue talks quite a bit about RV strain.

Dr Freed: Yes. We talk about RV strain both for echocardiography and MRI. There's a lot of literature out there on using RV strain with MRI, in a relatively easy way with no special sequence that you need to use ahead of time. In addition, there is 4-dimensional flow and T1 mapping, which provide data on flow dynamics and diffuse fibrosis, respectively. I think it's still in its infancy in terms of what we can use it for in PH. There are studies out there showing that identifying diffuse fibrosis either in the septum or potentially in the RV free wall can be helpful in figuring out prognosis, for instance.

Dr Edelman: Another information source that may lead to PH identification are MRIs that might be obtained for evaluation of left ventricular issues and then come back with findings that then trigger a PH evaluation.

Dr Freed: Yes. MRIs can provide information similar to echocardiograms in terms of helping you with where exactly the PH is coming from, but it probably goes beyond echocardiography, too. For instance, MRI can help identify both intra- and extracardiac shunts, which 2-dimensional echocardiography might not be able to visualize. I agree MRI can also help in differentiating the

mechanisms or where the PH is actually coming from.

Dr Edelman: We're getting close to the end of our hour here. I think we've covered most of what we had hoped to cover, but also want to give the opportunity for general comments or other things that people feel we may have missed and would like to add in here.

Dr Leary: We haven't even talked about positron emission tomography! I must say, it's a cool idea. As we move forward in imaging, thinking about trying to understand stress at the cellular level is an idea that's out there and has some data behind it. It is certainly not ready for primetime clinically, but I think that, at the end of the day, we are trying to understand the myocyte under stress in the setting of increased afterload**.** I think we use morphology and strain and function as surrogates of that cellular stress, and I wonder if, in the future, we'll be looking at biomarkers that are more focused in on the myocyte under strain. It's kind of pie-in-the-sky stuff, but interesting to think about.

Dr Edelman: There is great potential for these studies to enhance our understanding of disease pathophysiology as well. I think that's really where we would be going with MRI and positron emission tomography and studies that aren't currently routinely used in clinical PH evaluation.

I think we have reached the end of our hour, and I want to thank everyone for your input and participation. It's been a great discussion.