The Challenging Spectrum of PH in Liver and Kidney Transplantation Patients

On August 16, 2013, a group of physicians with clinical expertise related to management of pulmonary hypertension (PH) patients who are undergoing evaluation for or having liver or kidney transplantation was convened by telephone to discuss this challenging topic. These complex patients represent a spectrum of clinical types of PH and require complete evaluations utilizing a team-oriented and multidisciplinary approach to ensure appropriate treatment and safe transplantation. Facilitated by the guest editors of this issue, Charles Burger, MD, and Paul Forfia, MD, discussants included Michael Krowka, MD, Professor of Medicine, Pulmonary Division, Mayo Clinic, Rochester, Minnesota; José Diaz-Gómez, MD, Medical Director-ICU, Departments of Anesthesiology and Critical Care, Mayo Clinic, Jacksonville, Florida; Anna Hemnes, MD, Assistant Professor, Assistant Director, Pulmonary Vascular Disease Program Vanderbilt University Medical Center, Nashville, Tennessee; and Michael Mathier, MD, Assistant Professor of Medicine, Director, Pulmonary Hypertension Program, and Associate Director, Cardiovascular Fellowship Program of the University of Pittsburgh Medical Center.

Dr Burger: One of the issues that has come up fairly regularly in addressing hepatic cirrhosis patients who are being considered for liver transplant has been those patients who progress with their liver disease and have what we would consider marginal hemodynamic profiles for purposes of clearing them for a safe transplant. From a personal perspective, I struggle with that patient. In the interactions with the hepatologists and my transplant colleagues, I often ask, "Is it appropriate to move ahead with the transplant, despite the fact that we don't have the hemodynamic criteria exactly where we might prefer it to be?" I would ask Dr. Krowka to weigh in on this clinical scenario, which I'm sure he faces on a regular basis.

Dr Krowka: Well, it is a problem. And the main problem is that of the individuals that have pulmonary artery hypertension complicating their liver disease. Most liver transplant centers that I'm aware of do screen for pulmonary hypertension with echocardiography. And centers do have their own criteria for who goes on to right heart catheterization. As you know, there are criteria that exist now to allow patients to have a higher priority for liver transplant, as long as their treatment for the portopulmonary hypertension, as we know it, reaches a certain satisfactory level in terms of measuring mean pulmonary artery pressure and pulmonary vascular resistance. We do run into these individuals that, despite our treatment, they are borderline in terms of satisfying these acceptable criteria. A common problem that we've run into is that a patient will be treated for their portopulmonary hypertension with any one of a variety of pulmonary vasodilator options and their mean pulmonary artery pressure remains above this acceptable cutoff of 35 mm Hg, yet their pulmonary vascular resistance has markedly improved and their cardiac output has markedly improved. So what do we advise for these individuals? In my experience, this is where the echocardiography comes into play. If we have seen changes where the right ventricle is now significantly improved, with normal size and normal function, I am much more comfortable letting those patients go onto liver transplant. Whether or not they'll get a higher priority for transplant or not, I'm a little more reassured that they can at least get through the procedure. I do believe that the individuals that have normalized their right ventricle with treatment have the greatest likelihood of coming off pulmonary vasodilator after a successful liver transplant.

Disclosures: Drs Burger, Forfia, Krowka, Diaz-Gómez, and Mathier indicated no conflicts. Dr Hemnes has disclosed current financial relationships with Pfizer, United Therapeutics, and Annamometer.

Dr Burger: So to that end, it seems like the hemodynamic guidelines are just that, "guidelines." They help us, I think, put together a construct for approaching the patients. But with the more modern era of options for treating pulmonary vascular disease and the availability of methodologies to evaluate the right ventricle, as you said, echocardiography, MRI, whatever it might be in a particular institution, how valid do you think the older transplant hemodynamic guidelines really are for 2013?

Dr Krowka: That's an excellent point, because those hemodynamic criteria were based on two retrospective studies and databases several years ago. There's been no prospective study to look at what would be the optimal or favorable hemodynamics overall. And I think that would be a very important contribution. So right now, we're basing our judgments on data that's close to ten years old and clinical experience in everyone's individual centers.

Dr Forfia: What's interesting about the way that the mean pulmonary pressure of 35 cutoff is utilized in real life is that the resistance aspect of the equation is ignored. And actually in the seminal paper (Krowka MJ, Plevak DJ, Findlay JY, et al., Pulmonary hemodynamics and perioperative cardiopulmonary-related mortality in patients with portopulmonary hypertension undergoing liver

transplantation. LiverTransplantation, 2000; 6 (4):443-450), in the patients with a mean pulmonary pressure between 35 and 50, only those with a PVR greater than 240 were at higher risk. And we've had this conversation with our own liver transplant team many times. And so to Mike's point, when the patient has a mean pulmonary pressure that's still elevated, but yet their PVR has normalized, it seems that the liver transplant community has not embraced that group of patients; those whose mean pulmonary pressure is still high but their PVR is low. In that paper, those with a mean PA pressure between 35 and 50 and a PVR less than 240 did well. Also, to underscore Mike's point, if you have a PVR that's less than 240 and normal RV size and function in the context of persistently elevated mean PA pressure, we do feel this is an optimized group where referral for liver transplant is reasonable.

Dr Krowka: You raise a very good point regarding educating the liver community regarding these observations. And I think that was noted in that paper. Perhaps we've not done as good a job as we could. We are in communication with the OPTN/UNOS liver and intestinal transplant committee to relook and possibly revise the Model for Endstage Liver Disease (MELD) exception criteria. I suspect the committee will want to see some supportive and/or prospective data. Unfortunately, we don't have a good handle on that right now and we don't have those data to show. But I would totally agree, our clinical experience has been favorable. Hopefully over time, we'll be able to see this adjusted.

Dr Hemnes: I would echo that what I think we're all getting around is that mean pulmonary artery pressure really doesn't give you any particular information as to what the underlying pathology or pathobiology is. And if you understand what's driving that increase in mean pulmonary artery pressure, then you can make a more informed decision about whether or not somebody is or is not suitable for liver transplantation or has unacceptable outcomes afterward. So I think use of mean pulmonary artery pressure as a sole decision maker for whether somebody can or cannot undergo liver transplantation may miss patients who could tolerate transplantation. That's sort of how we approach it here, using hemodynamics and right ventricular function together to determine etiology of pulmonary hypertension and suitability for transplantation.

Dr Mathier: I'll just expand on that in maybe the other direction. It's not only what is driving the elevation in mean pulmonary pressure but, as has been pointed out, what effect has that pressure overload had on RV performance? And if the RV performance by our current technologies looks favorable, then I think that that has to be factored into a decision making process more than it often is.

Dr Burger: It just seems that there's a general consensus among the participants that we haven't perhaps pushed the envelope as much as we could in those whose PVRs have normalized with therapy. So I would just ask for the participants to comment on the additional component of assessing RV size and function. Is echocardiography adequate? Or are there other imaging modalities, in this particular setting, pre-liver transplant with portopulmonary hypertension, which you would favor?

Dr Diaz-Gómez: I would like to point out as a practicing anesthesiologist and intensivist that the current advances in transthoracic echocardiography for evaluation of patients with POPH facilitate a better assessment of the right ventricular function. For instance, I would like to highlight the article by Arkles et al. published in the blue journal in 2011 (Arkles JS, Alexander R, Opotowsky JO, et al. Shape of the right ventricular Doppler envelope predicts hemodynamics and right heart function in pulmonary hypertension. Am J Resp Crit Care 2011; 183:268-276) The authors described a method that actually provides a different insight of the interaction between the pulmonary circulation and the right heart function. Indeed,

they aimed to assess the coupling effect between the two components: the right ventricular function and pulmonary vascular resistance. Thus, if the right ventricular outflow tract Doppler flow velocity envelope presents a notch, it means the patient has more severe vascular disease and right ventricular dysfunction. I think right now we have a better capability in the OR to assess this valuable hemodynamics evaluation with echocardiography, even in the postoperative period. Some patients will come to the OR and even they have borderline PAP readings. After the intubation, we can find with the TEE evaluation that the PAP are higher than expected. In this case we have the ability to provide adequate depth of anesthesia, acid base, and intravascular volume status. These are common causes of increased PAP readings. Subsequently, we can reassess the patient, and determine the best strategy to intervene further the increased PAP. In conclusion, I would probably put a lot of weight on perioperative echocardiography in the assessment of this patient population.

Dr Forfia: Mike, I just want to say that I did not call him ahead of time and ask him to say that. (laughter)

Dr Hemnes: I don't believe you, Paul.

Dr Burger: Does anyone else have a comment on the best way to image? I would agree completely with Dr. Diaz-Gómez's comment about the whole business of the coupling and certainly, you know, Dr. Forfia has made a point of this in many presentations. We can't separate out each of these individual measurements in the hemodynamic profile from that of the right ventricle's ability to handle the challenge of the re-perfused blood volume once the new liver is transplanted. That's really the challenge!

Dr Mathier: I don't know that I would say that I favor any kind of different approach, except that I think it's worth emphasizing that we have to have as full an understanding of RV performance as possible. So that in many patients, echocardiography combined with

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hemodynamics is adequate for that. But in some, when the echo windows aren't acceptable, you may need to move onto MRI or you may need to rely more heavily on serial hemodynamic data. But I think the main take home point has to be that a really full understanding of right heart performance is what's important. And how you get it is going to vary from patient to patient.

Dr Krowka: I agree and I think there is a lot to be learned by the evolving methods to look at that right ventricle. The sequential studies are very important. One group of patients that I've found that are very worrisome are those that have, just with a simple electrocardiogram, T-wave inversions in V1 through let's say V4, V5. That tells me, everything else being all right, that there's still a lot of stress and strain going on affecting that right ventricle. And we pay a lot of attention to the improvement in just the basic electrocardiogram to give us another piece of information that perhaps we're taking some stress and strain off the right heart.

Dr Diaz-Gómez: I absolutely agree with you, Dr Krowka. I think we can maximize the understanding of the right ventricular function if we use wisely all the technology we have in place, starting with the EKG. I will add, for example, the utilization of continuous cardiac output monitoring and mixed venous saturation. The trend of the mixed venous saturation, or the limitation at the time of its interpretation in the setting of severe underlying hypoxemia is valid, as well. Other clinically used surrogates, such as lactate, are helpful guiding the management of patients with perioperative right ventricular failure. So if you have a patient who is improving his or her hyperlactatemia, the mixed venous is persistently better, and the hemodynamics looks good, that would suffice to have a good information about the patient's current status, even if you have limited echo windows and you cannot have a very desirable echocardiographic assessment.

Dr Hemnes: The only thing that I would add is that although the echo and

MRI may be useful, a lot of times at the bedside you can even tell when you've made an improvement. As you all know, of course, you can look at right atrial pressure, feel for RV heave, and those can be early and relatively reasonable predictors of hemodynamic response and RV function after changes in or addition of therapy for portopulmonary disease.

Dr Burger: So in that vein, what do the participants think is the best strategy for continued pharmacologic treatment after a successful orthotopic liver transplant? Both in that more immediate perioperative period and then beyond the hospitalization?

Dr Mathier: I'll tell you what our practice is. It's again variable from patient to patient. If I had a patient with portopulmonary hypertension who required intravenous epoprostenol to achieve the hemodynamic benchmarks we look for, I typically will continue that drug postoperatively, at least for a block of time that ranges from several weeks to several months, before I begin to reassess the patient's need for the drug. That typically is a clinical assessment, followed by an echocardiogram. And if the signs are favorable that the drug can be at least weaned, I always start with a right heart catheterization to ensure that I know exactly what the hemodynamics are before I begin. If instead it's a patient who had more modest portopulmonary hypertension and I was able to reach my hemodynamic benchmarks with a PDE-5 inhibitor alone, I'll typically do something relatively similar. But depending on how the echocardiogram looks, I may or may not proceed with a hemodynamic assessment, if it really looks favorable for weaning or discontinuing that drug. So I try to individualize it according to the patient. I tend to not like the idea of removing PAH therapy in the immediate postoperative setting, unless there is a lot of difficulty with systemic hypotension or another indication to do so.

Dr Diaz-Gómez: I absolutely agree with that practice. Spending some time in the operating room, I would say that sometimes it's easier for us to use nitric oxide in that setting. Although we have the capability of actually continuing with the face mask and nebulize it away in the postop period, I absolutely agree with the weaning has to be extremely cautious, especially during the first week. So sometimes we have used intravenous epoprostenol in the acute setting, if we don't have favorable numbers. It may be after the TEE and the same. We will do the weaning the way you describe it. So I don't think there is any unique way to do it. But probably, the most two popular alternatives that we have at this point is even IV epoprostenol or nitric oxide.

Dr Krowka: I would agree with Mike's approach, also. It's variable by individual. We proceed slowly. What I do like to do, regardless of the method that we've used to get them through, whether it's IV preparations or oral medications, just before they're dismissed from the hospital, I do get a baseline echo. We generally would bring them back at about 12 weeks for a reevaluation of their whole posttransplant status. I go very slowly with weaning them off of an IV preparation and an oral preparation. It may take weeks and months. Depending again on factors like what did that echo look like pretransplant with our successful management, if I did get to a normal RV size and function and everything looked good, I'm a little bit more comfortable that, well, maybe I can move a little more quickly, weeks after the transplant. But the other thing I'd like to stress is that when you think about this, this is one of the few times we potentially can cure, at least hemodynamically, pulmonary artery hypertension; what we know as portopulmonary hypertension. So there are folks that have severe hemodynamic impairment before their liver transplant; we treat them, get them through their transplant, and we can get them off of these medications at a certain point later on. And we see this sustained success. The echo looks almost normal, if not normal. We have essentially created a hemodynamic cure, at least in my opinion.

Dr Forfia: We set out to tackle pul-

monary hypertension in advanced liver disease, which it seems is the area with the most data, relatively speaking, compared to renal disease-associated PH. And, of course, it's also the condition, endstage liver disease, where true group 1 disease is a significant complication of portal hypertension. Endstage renal disease, of course, is a different matter, where there's a tremendous burden of left heart disease in the background, as well as heterogeneity of the hemodynamic presentation. There is also a paucity of data in the background to support treatment and management decisions. Nevertheless, there does exist a fear of the presence of pulmonary hypertension in patients with endstage renal disease in the context of transplant that I think we've all encountered. So, that sets up our first question for the panel. Which is, how do you approach a patient prior to renal transplant, whose been referred to you with evidence of pulmonary hypertension, on an echocardiogram? So we'll start with that because this is, of course, by far the most common scenario that we all encounter.

Dr Mathier: I'll tell you what we do. So as you pointed out, Paul, pulmonary hypertension in a patient with endstage renal disease is both common and complex. It can be on the basis of any number of factors, either individually or in combination. These folks often have a diastolic abnormality of the left heart, with elevated left heart filling pressures. They often have volume overload. They often have high cardiac output related to AV fistulas, or even in the absence of a large fistula. And they, at least some of the time, have pulmonary vascular disease. They also often have a comorbidity profile that can contribute to pulmonary vascular disease in an indirect way, whether that's intrinsic lung disease or sleep apnea or something else. So it's imperative in my mind that no assumptions be made when you have a patient with advanced kidney disease, who has evidence of pulmonary hypertension on echo. Even if that echo is very convincing for its being a group 2 type of physiology, with a very large left atrium, hypertrophied ventricle, and Doppler profiles consistent with significant diastolic dysfunction, I still think we're obligated to perform a very careful hemodynamic study. I often insist that this be both a right and left heart catheterization, because I think it's really imperative that we understand left heart filling pressure without any uncertainty related to whether the wedge pressure is accurate or not. And so it's really become my routine to do very careful hemodynamic assessment as the next step.

Dr Krowka: I totally agree with that. I think we've probably been lax in our kidney transplant program, in terms of evaluating these patients beyond echocardiography. We are trying to change our algorithm at this point, because there are so many other subtleties that do occur; and I would also agree, I think it's unusual to see pure pulmonary artery hypertension in these folks. It does occur. More often than not, we are taking people off of pulmonary vasodilator medications when they're referred to us, because I think they're being mistreated in that sense. The other comment I would make, and the issue that's come up from our kidney specialists on several occasions, has been what is the real impact of these large AV fistulas that have been placed? How much of their contribution is really causing a lot of difficulties? And again, I think that's where it's very important to proceed to a good hemodynamic assessment by right and left heart catheterization, so we fully understand what's going on in terms of the possible back pressure that's going to affect kidney outflow and these other cardiac issues.

Dr Mathier: Do any of you guys ask that your catheterizers do temporary occlusion of the fistula to try to assess its impact on either flow or pressure?

Dr Hemnes: Yes, I was just going to bring that up. We routinely do that, regardless of really the size of the fistula. Although lately, it seems like many of the patients who have been referred to us have really large, longstanding fistulae. But yes, specifically when we talk about a careful hemodynamic assessment in this population, I agree a left heart catheterization is almost always useful and informative, in addition to the right heart catheterization. But we usually do it with and without occlusion of the fistula.

Dr Mathier: Is there a protocol for how long you occlude?

Dr Hemnes: I don't think you need to occlude for very long. We usually do it for a few minutes, at most.

Dr Forfia: We do the same thing. I do the caths myself. And we'll do baseline hemodynamics and then we'll do a manual occlusion of the fistula, typically for two minutes, and repeat the hemodynamics. If I could also just share I think a clinical pearl, that after having now fairly extensive experience with dealing with fistula-associated dyspnea and pulmonary hypertension or heart failure, is the location of the fistula is very important in predicting its hemodynamic significance. If you really dig through the data from published literature, it's fairly clear that proximal fistulas are much more common to do this. For example, in the upper extremity, it's the brachial fistula, so it's above the elbow where you're much more likely to have a high flow. We've also seen this with the rare occasion of a fistula in the femoral artery-vein. But either way, it's a proximal vessel. We have not seen very much in the way of high output with grafts, although that's possible, or with fistulas that are at the level of the wrist. And, Anna also alluded to the fact of the duration of fistula, which is relevant. Because the longer that the fistula has been in, typically the larger it gets. And so when we see a brachial fistula that's been in place for many years, that patient is the setup for a high output situation, where our pretest probability for a very high flow is quite high.

Dr Hemnes: But, of course, the other thing to notice though is that pulmonary hypertension is common in people who are getting dialysis through a catheter and also a peritoneal dialysis. So, you know, the Israeli group has done a nice job of characterizing these patients and has suggested that endothelin or poor clearance of endothelin may underlie pulmonary hypertension in this group. So while the fistulas may play a role in some patients, patients that don't have fistulas are at risk, as well.

Dr Burger: While I don't disagree with the catheterization for the hemodynamic profile, almost all of these patients will have elevated left heart pressures. So the question is, what do you do with that information vis-à-vis transpulmonary gradient, diastolic pulmonary gradient, attempts to lower the left heart pressure and then see what happens to the hemodynamics?

Dr Mathier: Charlie, as you pointed out, these patients will nearly always have elevated left-sided filling pressure, but also, elevated right-sided filling pressures are common. I'll try to give some feedback to the dialysis team and, you know, try to have them incorporate the hemodynamic data into how they set a dry weight and how the patient on their own works to manage their volume status. And then the other thing is that a lot of times these folks have verydifficult-to-control systemic hypertension and that will be directly influencing filling pressures. And so you can use the hemodynamic data to also advocate for a more aggressive approach to systemic blood pressure control. And those things can have a very substantial impact on pulmonary pressures. And I think they're important, because without optimizing volume and systemic pressure, you're not going to really stand much of a chance of improving the pulmonary pressures.

Dr Forfia: If I may jump in just for a second and go back to our first question, which was how to approach the patient prior to renal transplant, with evidence of PH on an echo. Mike, you made a great point about how you're going to have a low threshold to refer that patient for a right heart catheterization. But if I could get you guys to comment briefly on how you use the echo to start to make distinctions between the types of pulmonary hypertension prior to invasive assessment. So what does one echo in a patient with PH and endstage renal disease look like versus another? For example, a pure diastolic heart failure patient versus a patient who seems to have evidence of pulmonary vascular disease, How do you make those distinctions?

Dr Krowka: At our institution, I think the echoes have been very helpful in the sense that if we look at, for example, the left atrial volume index, if that's huge, that certainly gives us more of a clue, along with these other indirect measures of diastolic dysfunction that our echo folks give us, you know, would certainly lean more toward the fact that, alright, we're going to probably be dealing with the volume and the diastolic dysfunction issue here, rather than, you know, a pulmonary artery hypertension scenario, which again is probably uncommon. I think the timing of when some of these studies are done is very important. So the nephrologist will call and say, "Well, I have an echo. Take a look at this." Well, it's done the day before or the morning of dialysis. Getting data after the dialysis is probably where we've gone now, rather than trying to select a random set of measurements from echocardiography to decide what our next step is going to be.

Dr Forfia: If I could underscore that a similar approach in the use of echo in endstage liver disease can be advocated in patients with endstage renal disease. So specifically, Mike Mathier and Mike Krowka had emphasized the importance of looking at right ventricular size and function in the context of pulmonary hypertension in endstage liver disease, I'd like to hear what everyone has to say about how they incorporate right ventricular size and function information into the echocardiogram read in the patient prior to renal transplant.

Dr Burger: I think it makes a big difference. I mean, just yesterday, we saw two end-stage renal patients with elevated right heart pressures on echocardiogram. One had the classic grade 3 restrictive left ventricular filling on echocardiogram, with all of the signs and symptoms of restrictive cardiomyopathy in the setting in volume overload. The other patient, had elevated right heart pressures but the diastolic relaxation didn't look bad. The E/e' ratio also looked okay. The pressures were only mildly elevated. The RV looked pristine. And so that creates a situation where one has to use judgment about next steps. In the second case, we made every effort to go over all the things that have been mentioned about maximizing the impact of the systemic blood pressure, normalizing the intra-vascular volume, making sure that they're compliant with sodium and fluid restriction, wearing their oxygen, etc., before moving ahead with a catheterization. Because even if they moved quickly to renal transplant, I think that patient's ability to survive and do very well with the transplant is quite good. I think all of those things come into play for your judgment in this regard. And I think you're exactly right, Paul, the integrity of the right ventricle is very important.

Dr Diaz-Gómez: A quick comment about a relatively common condition as patients with advanced chronic kidney disease may have dual pathology, due to high prevalence of systolic as well as diastolic cardiac dysfunction. In addition, the presence of the cardiac dysfunction does not automatically exclude coexistence with pulmonary arterial hypertension. So I think we probably need to be more rigorous and precise with the echocardiography assessment in comparison with the liver transplant patient population. So, just keep in mind, that both diastolic and systolic dysfunction can be present in patients with end stage kidney disease.

Dr Mathier: I'd like to agree with that. We often see patients who have, in this setting on hemodynamic study, elevated left heart filling pressures, but very high transpulmonary gradients and very high pulmonary vascular resistance, or at least moderately high, in excess of 5 or 6 units. And so you're left with one of these mixed profiles and they're very challenging in terms of really knowing how to attack it. And also, I'd go back to something that I think Paul said right at the beginning of the discussion of the advanced kidney disease patient. We're not really 100 percent sure what the

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impact of the pulmonary hemodynamic derangement is on clinical course and on outcomes with kidney transplant. The transplant group at our facility has gotten concerned that these patients are higher risk. And they cite some less than ideal outcomes in terms of graft function and graft survival in patients who had pulmonary hypertension before transplant. So I think it's a population that we really need to try to get a better handle on through careful study in the near term. Because it's a very common clinical scenario, at least in what we've been seeing.

Dr Hemnes: I completely agree with you. And the most common scenario of the patients referred to us is one of we found pulmonary hypertension on an echo and this person who has endstage renal disease who is being evaluated for a transplant, can they survive transplant? And I feel like the data isn't out there to really know definitively what the answer is to that question. We have our own personal practice patterns and I tend to rely on the RV function, what I think the underlying etiology of the pulmonary hypertension is, etc. But in the absence of any data, that's a very hard question to answer right now.

Dr Forfia: I would say that we can use some epidemiologic data to get at some of these answers. It's estimated that 30 to 50 percent of patients at the time of renal transplant have pulmonary hypertension. And I would say it's closer to 50. In that context, patient survival and renal allograft survival at most renal transplant centers is outstanding. And so that's interesting. What that suggests to me is that in many of our patients with endstage renal disease who have pulmonary hypertension, the pulmonary hypertension itself is not what is conferring the risk. And that whatever is making up the pulmonary hypertension, which many of us feel is the combined effects of fluid overload, high cardiac output, and systemic hypertension, are actually significantly alleviated with renal transplant. So now, that is not to say

that there is not a subset of patients with pulmonary hypertension and endstage renal disease where the PH is actually a real risk factor for perioperative outcome. With that in mind, I just have this last question, which I don't think will take very long to answer. And it is, who is the renal transplant patient who you would consider PH being a relative contraindication, or at least where PH therapy should be attempted prior to reevaluation for renal transplant? Which of these PH patients with endstage renal disease really gives you pause, where you're going to stop and really carefully delve into this and/or treat their PH, but not agree that they are ready to be listed for kidney transplant?

Dr Mathier: I would say high PVR and evidence of significant right heart dys-function.

Dr Krowka: I would agree. That's where the hemodynamic right heart study really is crucial in these folks. And I would agree with that picture of who I'd be strongly concerned about.

Dr Burger: I would also add any strong risk factor for pulmonary arterial vasculopathy such as HIV or collagen vascular disease; that is something else that would make you think that the risk of actual pulmonary arterial hypertension is higher, in conjunction with any evidence that the RV is dilated or hypokinetic.

Dr Hemnes: I would agree with all of those things. And the only other sort of patient category that I'd add is that it's well-described that patients who have had multiple angioplasties of their fistulas are at risk for chronic thromboembolic pulmonary hypertension. So, a patient who's had multiple angioplasties and evidence for chronic thromboembolic disease also gives me pause.

Dr Krowka: I would like to also see some prospective data that characterizes who does have graft failure. What are those criteria for renal graft failure and what are the characteristics of those individuals hemodynamically that perhaps would shed some light on the dilemma.

Dr Forfia: Right. And I think that's the type of study that needs to be done. Because retrospective studies that cite evidence of pulmonary hypertension on an echo, and then without any further information, associate pretransplant pulmonary hypertension on an echo with transplant outcome, are quite problematic. Given hat there is such a huge amount of colinearity between many of the comorbidities that the patients suffer from prerenal transplant and their PH. For example, their body mass index, their systemic hypertension, the size of their fistula, the duration of time on dialysis, the degree of left ventricular hypertrophy, the degree of left ventricular systolic and diastolic dysfunction. These factors cannot really be properly parsed out when someone is doing an association between PH and outcome post kidney transplant. So, it seems likely that PH has to a certain extent been blamed for less optimal outcomes when, in fact, more careful analysis may reveal that the PH itself was not the direct cause of adverse events in many of those patients.

Dr Burger: I'd like to thank the panelists for a very educational and informative discussion and for the time away from their busy days for participating.

Dr Forfia: Yes, I'd like to thank everyone, as well. And I feel it is worth emphasizing that our ability to assess pulmonary hypertension in any individual patient, pointed out from every member of the panel during this discussion, involved the assessment of varying hemodynamics in combination with an evaluation of right heart size and function. We agree that pairing pulmonary vascular load with right heart size and function is seemingly the best way to gain insight into the significance of pulmonary hypertension in any individual person.