

The Crossover From Child to Adult With PH and Congenital Heart Disease

Guest editor Dunbar Ivy, MD, Chief of Pediatric Cardiology and Director of the Pediatric Pulmonary Hypertension Program at the University of Colorado School of Medicine and Children's Hospital of Colorado led a discussion among Editor-in-Chief Harrison (Hap) Farber, MD, then Professor of Medicine and Director of the Pulmonary Hypertension Center at Boston University/Boston Medical Center; Mary P. Mullen, MD, PhD, Assistant Professor of Pediatrics at Harvard Medical School, associate cardiologist at Boston Children's Hospital and Associate Director of the Pulmonary Hypertension Service as well as a member of the adult congenital heart program; Jeffrey R. Fineman, MD, Professor and Vice Chair of Pediatrics, Director of Pediatric Critical Care Medicine and Pulmonary Hypertension, University of California, San Francisco, Benioff Children's Hospital; and Gareth Morgan, MD, Associate Professor of Pediatrics-Cardiology at the University of Colorado School of Medicine and Director of the Cardiac Catheterization Lab at Children's Hospital of Colorado.

Dr Ivy: I am pleased to be the guest editor for this issue of *Advances in Pulmonary Hypertension*. This issue is dedicated to the crossover between the adult and child with pulmonary hypertension and congenital heart disease. Several important gaps are recognized between our knowledge and treatment of adults and children. These are readily apparent in the guidelines, which have been published recently by the European Respiratory Society, as well as in the journal *Circulation*. These are the adult guidelines for PH and the pediatric guidelines for pulmonary hypertension. In the adult guidelines, there are very strict criteria for operability. And these criteria do not allow for a so-called treat-and-repair approach, where the patient would be treated with medication and then undergo a repeat catheterization and then a reconsideration of defect closure. In contrast, in the pediatric guidelines there is a potential for a treat-and-repair strategy, whereas patients who would not be reactive—and we can discuss these criteria—could be treated and then reconsidered for surgical operability. So, I'd like to start our roundtable with Dr Mary Mullen, who can talk a little bit about these differences between children and adults.

Dr Mullen: There are clear differences between the adult and pediatric guidelines for operability in pulmonary hypertension. Regardless of patient age, predicting successful short-term and longer-term outcomes in patients with

congenital heart disease is essential and really requires careful consideration of hemodynamics. We assess PVR, PVR to SVR ratio, and pulmonary-to-systemic blood flow in all patients. There are, however, differences in the guideline-based approaches between adult and pediatric populations. With regard to simple shunt lesions such as ASD, VSD, and PDA, European guidelines for adults state that patients with indexed PVR greater than 8 Wood units would not be correctable while those with indexed PVR less than 4 Wood units could undergo operation. Those with PVRI between 4 and 8 may have individual approaches. The pediatric guidelines take into consideration short-term acute vasodilator response to determine ability to proceed with operability and may include a treat-and-repair strategy. Again looking at simple shunt lesions, pediatric guidelines state that an index PVR less than 6, potentially with complementary response to acute vasodilator testing, would allow proceeding to operation. With PVRI greater than 6 you would definitely need a positive acute vasodilator response to proceed to repair. For PVRI >6 without a response to acute vasodilator testing, one should consider a treat-and-repair strategy with target pulmonary hypertension therapy, which would require repeat catheterization. At this junction those with acute vasodilator response could undergo high-risk surgery, considering fenestration while those without positive AVT are probably inoperable.

Dr Farber: So, the question I have is, because all I do is adults: it seems like we're seeing more and more patients, probably because of certain immigration patterns as well as patients diagnosed later in life, who have either an ASD or anomalous pulmonary venous drainage and have fairly significant pulmonary hypertension. Nobody really wants to operate on them because most of them have a PVR >6 or >8. And so, we're forced to treat them medically. Let's say we do have a patient who has a reasonably good response to PAH-specific meds and gets their numbers down. What a lot of people have done, at least in adults, is to look at RV cardiac index and RV end diastolic pressure combined with the PVR and see if we can make it to a manageable number that somebody thinks they could survive surgery. Does that make any sense?

Dr Ivy: I think it makes sense. We have certainly used a similar approach in some patients. We've been referred some adults that have sinus venous atrial septal defect, partial anomalous pulmonary venous return, who have been treated with triple therapy and after several years of therapy, we can get the pulmonary vascular resistance <6 and have elected to do surgical repair with a fenestration. I think that the challenge that I don't think we know as a field is none of these are prospective studies.

Dr Farber: Oh, no, not at all.

Dr Ivy: They are all case series, or a retrospective look, saying, “Oh, we got through the surgery and this is how we did it.” If you look at some of the papers from Professor Galiè and some from the pediatric literature, one of the groups with the highest risk of late mortality is those patients who have had complete repair of congenital defects with existing pulmonary vascular disease. So, I think there is a lack of knowledge, and I think in the adults maybe because of the length of time these patients have had significant pulmonary vascular disease. There’s less appetite for risk. Whereas in a young child, I think we’re more willing to take that on. But again....

Dr Farber: There’s another potential point, just listening to this: the fact that in those people that seem to have a reasonably good response to pulmonary vasodilators, maybe they’d do better if we just left them alone and treated them medically, rather than surgically. But as far as I know, there are no studies looking at that, either.

Dr Fineman: So, I don’t take care of any adults, but certainly in the pediatric population, we’ve been pretty aggressive about this treat-and-repair approach. And perhaps, well after we’re all retired, we’ll know whether we’re doing the right thing or not. In other words, will these patients’ PVRs remain low or re-emerge with PAH? But I could tell you that certainly, particularly with some of the children with complex cyanotic lesions like TGA/VSD that we’ve done, there is no question they feel better and thrive. Their saturations are better. They start developing normally, etc. The big question for us is just what you brought up, Dunbar, is are they going to show up 5 or 10 years from now with advancing pulmonary vascular disease and then, clearly, they would have done better if we would have left them alone? And so, the question that we always entertain is not really should this be a treat-and-repair, but should it be treat, repair, and continue to treat? And should we treat for how long and with what?

Dr Mullen: Right. Well, I think the point you raised is a very good one.

Because clearly, we need to reassess by catheterization any patients with elevated PVR who undergo repair and certainly continue treating if there is residual elevation in PVR or elevation in mean PA pressure. Generally we would repeat catheterization 3 to 6 months post surgery. In both pediatric and adult patients we also need to assess comorbidities, including obstructive sleep apnea, co-existing lung disease, or aspiration, and continue close follow-up, so that there are no other issues that increase propensity to pulmonary vascular disease long term.

Dr Fineman: Well, the other thing is should we, particularly with the atrial septal defects, should we be doing genetic screening on them? Would that change our approach in terms of how aggressive we would be?

Dr Ivy: We saw a child who had a sibling that died from pulmonary hypertension many years ago. She had a moderate to large atrial septal defect; was incredibly reactive; had acute Qp:Qs on room air of greater than 2-1/2:1. We elected to completely repair the defect at that time and then treated her with pulmonary vasodilator medications, including intravenous epoprostenol. Ten years later, she moved back to her native country and was able to continue her therapy, but she died suddenly from a pulmonary hypertensive crisis. So, if you had a patient with familial disease, that may make me want to see a lower PVR and consider fenestration before considering correction. But again, that’s a case of one. I think Dr Morgan had something to add?

Dr Morgan: I’m not a pulmonary hypertension specialist, so I’ve enjoyed listening to the conversation. I have just a couple of comments. I always find the “PH with ASD” conversation particularly interesting because I haven’t yet really been convinced by the data that ASDs cause Eisenmenger syndrome. I’m always, therefore, interested in the interaction between the presence of an ASD and pulmonary vascular disease. But I wanted to take a step back. We talked about data available in adult practice for

degrees of vascular resistance that make complete repair appropriate. Again, you guys may be familiar with it, but there is certainly some work from the group that I used to work with at King’s College in London led by Dr Kuberan Pushparajah and Dr Tarique Hussain (who is now in Dallas, Texas) looking at MRI-calculated pulmonary vascular resistance and operability, both in the single ventricle and biventricular groups. And they got some pretty convincing data that in the pediatric population procedural reversibility is not as important as the baseline vascular resistance number that is calculated. They certainly felt that for the biventricular patient that a PVR of <6 meant that patients could be pretty confidently operated upon with a complete repair.

Dr Farber: Meaning no fenestration?

Dr Morgan: Yeah, with no fenestration. And likewise for single ventricle patients, patients with functioning univentricular hearts, that they could safely complete the Fontan procedure with a PVRI of <4, irrespective of reversibility with those numbers. So, I’m not sure how much more quantitative data that there are in the pediatric world, but it is starting to creep out obviously and guiding numbers are starting to become available. I do think that a lot of our discussion about congenital patients is qualitative and based on gut feeling a little bit. And it would be nice to see a little bit more science developing this conversation to allow us both to determine when complete repair or fenestrated repair is possible. Another question that was raised during this roundtable is which patients need to continue on therapy for at least a period of time after the repair is done?

Dr Ivy: The presence of a PFO is a positive long-term predictor for patients. Julio Sandoval in Mexico City for years has done balloon atrial septostomy for patients with idiopathic pulmonary arterial hypertension, with pretty reasonable results. So, it’s a very complex decision that you would think would be quite easy.

Dr Farber: It’s interesting. Because in his case, he started doing them really out

of necessity, because they really had no alternative, as there weren't PAH-specific medications available in Mexico. But he has done so many that he is really good at it. And their numbers are far better and far exceed anything that any of us in the adult world have ever come close to doing. It's probably once again this issue that they've done so many; they pick the patients much better than we do; and they're just better at it.

Dr Morgan: Do you think he's better at it because he's good at determining how big a hole to make? Or is it patient selection?

Dr Farber: I'll bet it's a combination of that and likely other factors.

Dr Morgan: Yes.

Dr Ivy: It's certainly patient selection. Predictors of procedure-related death include a mean right atrial pressure >20 mm Hg, a pulmonary vascular resistance index of >55 Units, and resting saturation <90%. So, Dr Fineman, I was curious what your insights were in terms of what we really know about ASD and Eisenmenger. I hear people that are strongly on one side or the other.

Dr Fineman: I'm advocating for genetic testing on all of these isolated ASDs. I just wonder how much of a subset of them happen to be, for a better word, idiopathic, and have a coincidental ASD. You know, there's such variability in both the frequency and the age that it presents, it just makes you wonder. In some of the animal data, which I've put a little bit into the paper in this issue of *Advances*—and we have a much larger paper in review right now—we compare the effects of a pressure and flow stimulus on the pulmonary vasculature versus just increased flow alone. There clearly, not just from a physiologic and biochemical perspective, but from a broad transcriptional perspective, are marked different transcriptional patterns, depending on flow alone versus pressure plus flow. In other words, an ASD versus an unrestricted VSD. And the heat map, the transcriptome pattern of the flow alone, is not that dissimilar

to normal. There are some intermediate effects that make it vulnerable to a secondary insult. But there's no question that the two stimuli, pressure and flow combined versus flow alone, are very, very different on the pulmonary vasculature. And so for me, one of the arguments about treating prior to repair is that you're going to take a kid who may have a Qp:Qs of 1.2 to 1 and give him a Qp:Qs of 3 to 1 for a period of time. I'd be happy obviously if we can generate such a large Qp:Qs, because we're obviously decreasing PVR. But for that period of time, I mean, in terms of increasing pulmonary blood flow at a lower pressure for 6 months prior to surgical correction, at least from the animal data, doesn't concern me that I am causing more harm during the pre-op treatment period. Obviously, you need to treat them symptomatically. But I don't think flow alone is nearly the negative stimulus than when you put a pressure head with it. I don't know if that answered your question or not?

Dr Farber: Well, no. But in a way, that makes sense because as an adult pulmonary hypertension person, a lot of these people we see with an ASD, even a large one, don't present until they're in their 50s or 60s

Dr Fineman: Right, right, right.

Dr Farber: And they've just had increased flow their entire life and probably minimal, if any, increase in pressure.

Dr Fineman: Right, right.

Dr Morgan: Jeff, I think your commentary there is really interesting to listen to. And again, as a nonpulmonary hypertension, nonscientist, indeed from the viewpoint of a clinical plumber, I found that to be a very clear explanation that fits with my nonscientific concept of ASDs and PH; the whole idea of upregulation of all the things that are at play in patients who've got increased flow. But I do think a lot of people, in my experiences particularly in the adult pulmonary hypertension setting, a lot of clinicians find that a difficult concept and find it difficult to separate the con-

genital ASD patient from the patient who's had maybe a pressure-driven VSD or PDA-type shunt for a long period of time, who then has a much—in my opinion—easier to understand, vasculature change that's occurred because of a pressure head pummeling the pulmonary circulation.

Dr Fineman: Sure.

Dr Mullen: Clearly there is a different phenotype in the pediatric patient who presents with a large ASD and has elevated resistance from the very start of monitoring—this may be a completely different phenotype. I think the discussion about genetic testing is very provocative and very important, you know, because it would be helpful to understand both subgroups. I was interested in what Dunbar said about taking that into consideration in terms of repair. I think we need more follow-up information about operability of such phenotypes to discern true differences. It may be that certain groups or subsets of genetic mutations causing pulmonary hypertension may be more susceptible to flow and we would really want to make sure that we close them early. I think the data are just not there yet.

Dr Ivy: So, there's a recent paper from a consortium across the US that Wendy Chung wrote, that a gene called *SOX17*, which produces a transcription factor that's involved in embryonic development, may be an early clue as to why some people with congenital heart disease develop early pulmonary vascular disease. It will be interesting to see how things play out in the next few years, in terms of again our ability to predict who is going to do well and who won't.

Dr Farber: There's a large study of PAH patients in Britain. The government actually funded it to sequence all PAH patients. And the British now have collected about 1,000 individuals who have true PAH. And when you look at all the genetic defects they found, *SOX17* does show up every once in a while.

Dr Farber: Maybe that it is another mutation among who knows how many

mutations that we know and most that we don't know that might play a role or increase your risk for PAH or idiopathic disease.

Dr Ivy: So, I think I'd like to take the opportunity to discuss the scientific manuscript in this issue on use of the Occlutech® device. And I'd like for Dr Morgan just to give us a brief overview of the paper. And then maybe we can all comment on how a device like this might change our clinical practice.

Dr Morgan: Yes, thanks, Dunbar. Conceptually, I don't think there's anything new about the concept of this device. In fact, Kurt Amplatz actually developed a fenestrated device similar to this more than a decade ago, but for various market reasons, Amplatz withdrew it from their shelves. Occlutech, who are pushing quite hard at the concept of fenestrated devices, both fenestrated ASD closure devices, but also related to this, the device that is known as the AFR, the atrial flow regulator, which is a controlled septostomy-type device, to give you a defined-sized hole in the septum. This AFT is planned to be used for patients with both pulmonary hypertension and those with left ventricular diastolic dysfunction to allow passage of flow between the atria in a controlled way. And so, as a concept, I think this whole idea is quite familiar to us all. The senior author is Joseph Vettukattil from Spectrum Health Helen DeVos Children's Hospital in Grand Rapids, Michigan. And basically, we gathered all the compassionate cases around the world for the Occlutech fenestrated ASD closure device, including some patients from the USA, but also a lot of patients in Europe and in Britain. So, it's a motley crew of patient characteristics and pathology, as it describes compassionate use cases gathered together. But from a technical point of view, it does show that the device is easily deployable and does create a reliable fenestration that stays open in at least the medium term. Therefore, it can allow potential decompression in the face of rising atrial pressures in events such as a pulmonary hypertensive crisis. Although it's not a prospective controlled study, I think it

does give some early hope for the device to gain some credibility and perhaps move toward FDA approval in the US, maybe allowing us to get good quality data to see if this is the right way to go for these ASD patients that we've been discussing.

Dr Ivy: So, Mary, how would this change your practice?

Dr Mullen: I think that this could be a very useful device for transcatheter closure of atrial septal defects for patients in the borderline PVR category. We frequently consider the need for a fenestration, perhaps through the ASD device sometimes; we have even positioned devices such that we leave a residual hole. Potentially the patients that have an elevated PVR—pediatric patients that maybe is older than 6, approaching 8—and that respond to vasodilator testing, but that we think that we may want to leave a hole that we could go back and close later on. So, I think that it's a very useful tool.

Dr Morgan: Yes, Mary, just to follow up on that, like I said, the concept is long-standing. But I think what we've had previously is a very difficult procedure. I mean, we've done it several times, where we've placed a coronary artery stent through the material of the ASD device and tried to hope that this creates at least a medium-term persistent hole. There are many people around the world that have done that or variations on that. But I think maybe this development gives us safer, quicker, hopefully more reliable, ability to leave a fenestration in place while still reducing the overall effect of the shunt.

Dr Mullen: Oh, absolutely. There are patients that we have had fenestrations or holes that were not reliable and that we have needed to go back to recreate those holes many times in the cath lab. So, the ability to have one there right from the first closure is terrific.

Dr Farber: It would seem to me that this would potentially allow us to at least partially close people that you wouldn't consider before because you were

worried about their right ventricle, even above what you're worried about in kids. Because we worry that closing this hole is going to eliminate their right ventricular pressure release and they are going to develop acute right heart failure. But this—adjustment of the fenestration—might get you past that issue.

Dr Morgan: Yes, I completely agree. And again, this paper and, in fact, most of the experience that I've had with this device has been in adults. The first one of these I did was in a gentleman in his late 40s in London for exactly the reasons you mentioned. I think the interesting thing about this for me, and I think the thing that foxes many of us, is how big a hole do you leave? And although I've been interested, sitting talking to Dunbar and other people, trying to look at equations to work out pressure, decompression, and flow, looking at blood viscosity, etc, I'm still worried that we are in a position of using gut feelings to determine whether there should be a 5, a 6, or an 8 mm fenestration left. I'm going to be interested to see as practice increases whether we can get that to be more scientific or whether we are still left with gut feeling about the correct size of the residual hole. I do worry about leaving a large hole that doesn't effectively benefit the patient, because they still have a significant left to right shunt afterwards, versus a hole that closes because it's too small, doesn't allow adequate decompression, and then clots off after a couple of weeks.

Dr Ivy: Jeff, do you have any comment?

Dr Fineman: Nothing additional, I agree with what's been said. I think the ability to be able to size it reliably is very, very important.

Dr Ivy: So, I'll ask Gareth: we might see a patient with significant pulmonary vascular disease who has an atrial defect. Is there a level of shunting or another measure that you feel like that's the patient that we should consider putting in one of these fenestrated devices? How do we choose the right patient?

Dr Morgan: Well, because I am a simple plumber and not a PH specialist, I'm

not sure whether I'm the right person to answer that. But I always worry about patients who require therapy to get their shunt to a point that they justify an ASD closure. I think if we want to treat a patient with pulmonary hypertension who has a significant ASD and we find that we can increase their shunt to a pathological level with pulmonary vasodilators—and again pathological level—does that mean 1.6:1? Does it mean 2:1? I don't know. But I do worry about patients that require pulmonary vasodilator therapy to get them to a point where we can safely close the ASD. And I wonder, maybe it's a bit of a blanket approach, if these are the patients that we should be putting fenestrated devices into. Patients who require therapy to generate enough of a shunt to need to close should maybe have a fenestration left over, to allow their body's homeostatic mechanisms to get used to having less of a shunt while maintaining the ability to decompress if their right ventricular pressure and right atrial pressure increases.

Dr Fineman: Yes, I think that's an excellent point. I'd like to ask a question to the group, if I may. What do you use, a PVRI of 6 or 8 as operable? I mean, if you had a patient that was above that threshold initially but then got to a 6 or an 8 after a year of triple therapy, do you still think a 6 or an 8 is adequate? Or would you change that if we can't normalize this patient's resistance; maybe we should rethink this approach?

Dr Mullen: Are you talking about a 6 to an 8 at baseline, without additional change with...?

Dr Fineman: Let's say you argue that you're going to operate on anyone <8, okay? So, you have a 5-year-old VSD and their resistance is 7.8 and you're going to go ahead and operate. What if I bring you a patient the same age, who now has a resistance of 7.8 after a year of triple therapy? Would you feel the same way about that patient, or should that number be different? I know there's no data to drive that but...

Dr Mullen: I think that would be concerning. I would have hoped that there

might be some difference and would hesitate to operate.

Dr Fineman: Because there's nothing magical about the 8, right? We were in a room when we made it up. The approach that we've taken, and we've been lucky enough to get dramatic decreases with triple therapy, where they're basically normal, so we haven't really had to ask ourselves that question, but that is always in the back of my mind. I mean, I wouldn't feel comfortable with a relatively late, unrestricted VSD who we get down to 6 after a year of triple therapy. That really worries me, in terms of operability.

Dr Mullen: Yes, I would agree.

Dr Ivy: I would agree, also. I think some of the interesting papers come from countries where there are not as many therapies available. For example, in Brazil one of the main criteria they use for simple shunts is normal resting saturations and normal saturations with exercise. And I believe there's a group in India who said similar things, because of the cost to treat with these very expensive drugs and multiple re-catheterizations. I think that does make me feel more confident about recommending a surgery, if a patient during exercise does not desaturate.

Dr Mullen: Yes. But one of the things I found very interesting about the Occlutech ASD closure paper was that 63% of the patients had either bidirectional or right-to-left shunting across the fenestration at TEE post procedure, is that correct?

Dr Morgan: That's correct, yes.

Dr Mullen: So that's certainly a group of patients that you'd think when they're awake and exercising would also have some degree of desaturation. So that points to the potential use of the fenestration while exercising in that group of patients.

Dr Farber: So, to comment on what Jeff said: in my mind, an adult with an ASD who presents with a PVR of 8 versus somebody who has been on triple ther-

apy for 1 or 2 years and decreases the PVR to 8 from a higher value is a totally different human being. Their pulmonary circulation, their pulmonary vasculature is very different from the one who has a PVR of 8 on nothing.

Dr Fineman: Right, I agree. I agree.

Dr Morgan: Can I ask you another question, guys, that's slightly related? And I'm very much being the plumber in the conversation here. Consider a patient who has an unrestricted VSD, who's got pulmonary vascular disease due to a pressure-driven VSD pathology over time? You feel that you need to close the VSD to take away the driving shunt. If you close that VSD and try and replace it, ameliorate this with an atrial communication to protect from PH crises, does that make any physiological sense at all? Does that provide any genuine reassurance? Or do you think that's treating our own paranoia? Do you think it's something that is beneficial to basically place a device that might open the atrial septum up in a patient who has been driven by a VSD physiology before?

Dr Mullen: We've done that successfully in children who are in that grey area, closing the VSD and creating an atrial communication surgically. And it's been successful in that group of patients, but I don't think there's a large series of those patients. And I would very much hesitate to do it in an older patient. You also wonder whether a patient who doesn't have a lot of tricuspid regurgitation would actually be able to utilize that as an appropriate pop-off.

Dr Morgan: Yes. Then maybe you could discuss the concept of placing a shunt in a different position? The idea of the "reverse" Potts shunt in those patients, because it fits more into the pressure-driven pathophysiology that they have in the first place. Are they better having a direct communication between their pulmonary arteries and their aorta, rather than just a diastolic flow between their atria?

Dr Ivy: So, I think one of the considerations that we're seeing, all of us, is

the Potts—or reverse Potts I guess is maybe the better way to call it—shunt is used more and more. And I think there's a certain advantage to that. One advantage is maintaining normal cerebral saturations; also having a systolic pop-off for the right ventricle. But the patients then continue to have irreversible disease. Once you create a large communication between the pulmonary artery and the aorta, then you're not going to see if it's successful, reversal of shunt to any kind of repairable situation. And that also means that you have to choose those patients wisely. So, I guess what I'm wondering is, in a patient with sub-systemic pulmonary hypertension, would you consider an atrial shunt and supra-systemic, more of a reverse Potts? Obviously, we don't know. But what's the group's thought on that?

Dr Farber: So, I can tell you, mine is fairly simple. I've been involved with just endovascular placement of it in adults with pulmonary hypertension who had failed all available therapies and, for whatever reason, were not deemed transplant candidates, and had failed IV therapy. So, this was sort of like a last-ditch kind of thing.

Dr Ivy: And what were their results?

Dr Farber: The short-term results, except for one horrible case, were pretty good. The longer-term results, the numbers are small, I think I've been involved with about 6 or 7 that the long-term results have been not so great. I mean, I guess you really don't know what you're headed for and what you're comparing it to, because these

are people who, for all intents and purposes, were terminal in one way or another. And some of them have survived for several years after. I assume, compared to what they would have done, that's a good outcome. But in the bigger picture, I'm not sure it is.

Dr Morgan: I think if your experience is 6 or 7 of these, my understanding is that that's actually pretty big for most people who have any interest in this. Certainly, in the congenital groups that I've taken advice from about this, there are only a handful of units I think that have got experience and most of them have done fewer than 5 patients.

Dr Farber: I mean, we actually published a series, I think there were 6 or 7 of them.

Dr Mullen: In the series 7 patients were evaluated and 4 patients underwent transcatheter Potts shunts. There was one procedural mortality and 3 patients with longer-term follow-up. One of those did well for several years post procedure and ultimately underwent transplant with preserved RV function. We've also recently performed a surgical Potts. I think for the right patient, who has clearly maximized targeted therapy, triple therapy, or whatever is tolerated for that patient, and perhaps has preservation in RV function, the reverse really is worthy of consideration.

Dr Morgan: I find it really fascinating. Again, as a plumber, I'm interested to find the correct patient who will benefit from the transcatheter Potts. But I'm cautious because having spoken to Younis Boudjemeline, who has the biggest

congenital interventional experience with these, having done as many as 9 or 10. There are still a lot of parts of the procedure that we need to have a better understanding of the safest possible technique. It's still a procedure that's requiring some tweaking to make sure that we're doing it properly. And given the procedural complexity combined with the fragile patient population, I think it's going to remain a very high-risk procedure.

Dr Mullen: Yes, I agree. And I think this might be one of the groups that we really have to collect data and do very careful phenotyping to understand the time course of progression of pulmonary vascular disease in the patients themselves.

Dr Fineman: I don't have a lot of experience with the reverse Potts. You know, we talk a lot about waiting for the ideal patient. Dunbar, your comment is very interesting. In fact, we have a patient coming in who is just what you had talked about. The patient is quite symptomatic on maximal therapy but she's not quite supra-systemic. And so obviously, we're reluctant to do a reverse Potts, but wondering whether we should just open up the atrial communication. So, we have a lot of discussion about it, but I don't have a lot of personal experience.

Dr Ivy: In closing, I think observational registries may provide at least some initial thoughts as to questions to be answered or potential directions. Professor Rolf Berger is looking for new biomarkers and the Necker group in Paris is evaluating circulating endothelial cells for determining operability.