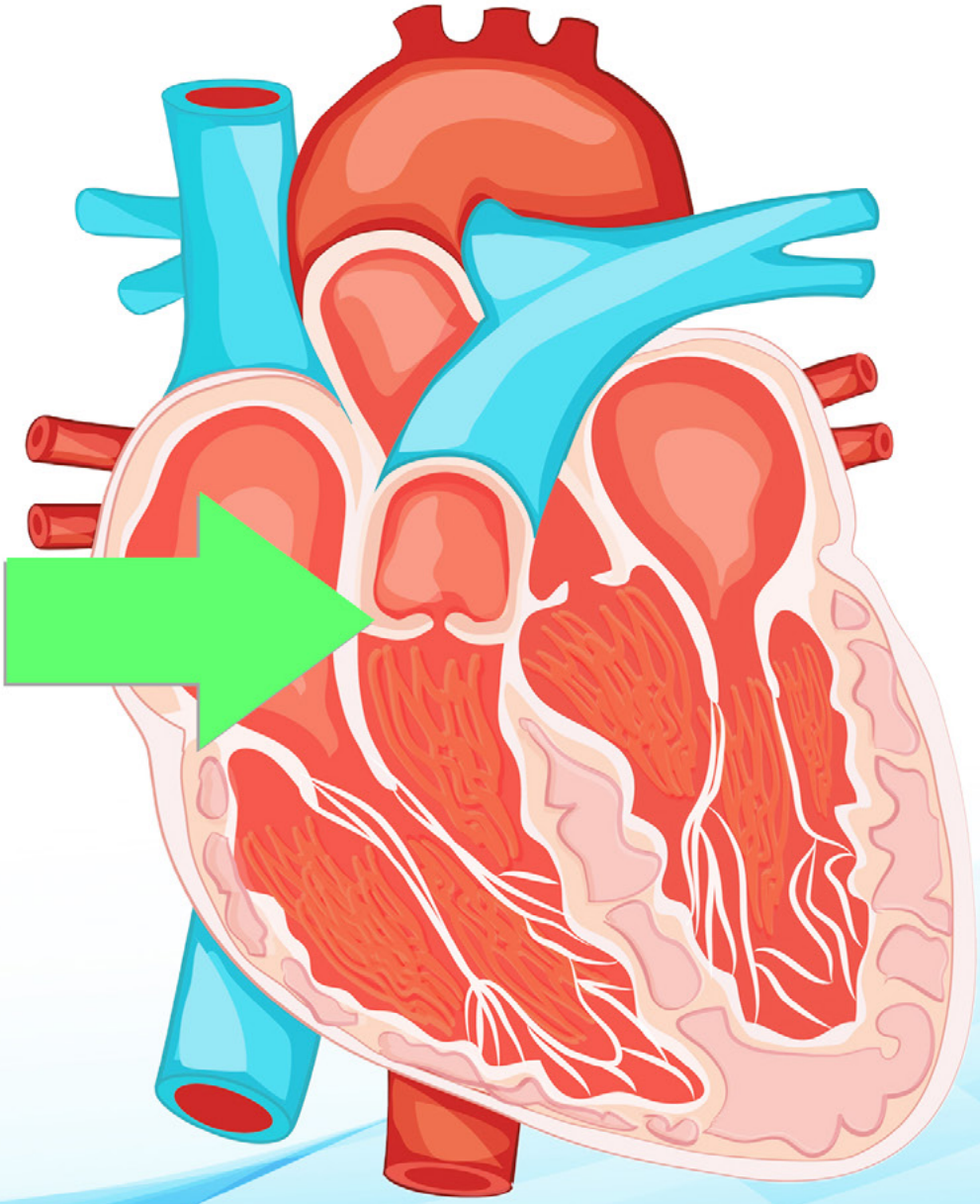
HeartValveSurgery.com

LIFETIME MANAGEMENT OF CONGENITAL PULMONARY VALVE DISEASE



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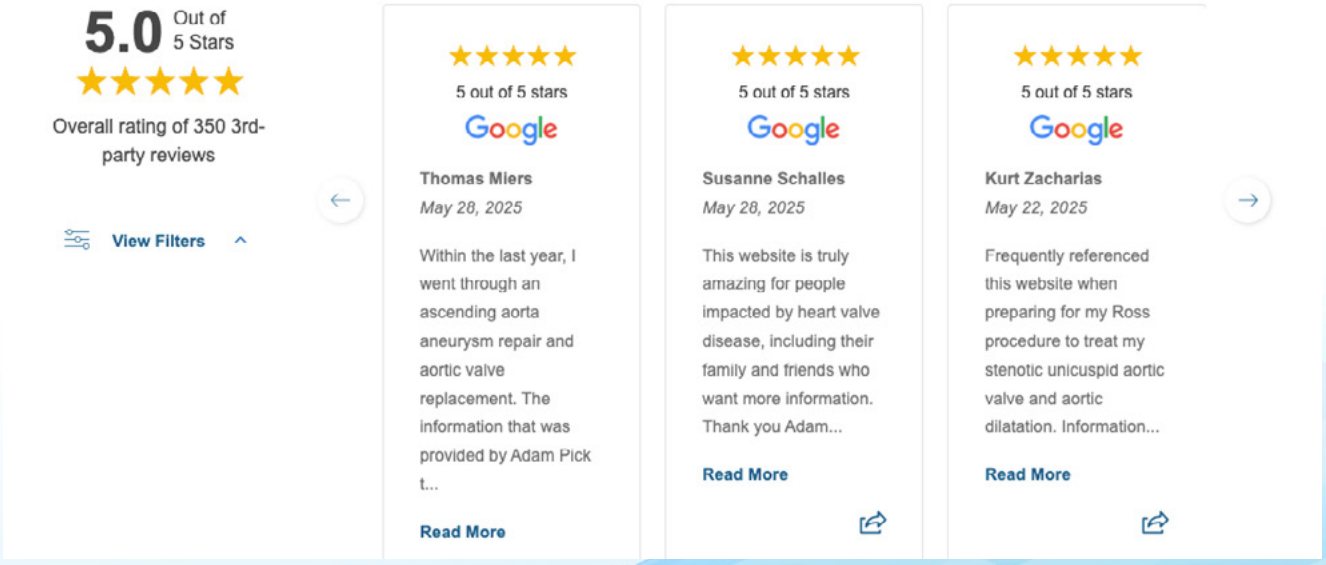
We are happy to announce that HeartValveSurgery.com was just named the #1 Heart Disease Website by Feedspot for the **fourth consecutive year**! Learn more.

To see patient reviews of HeartValveSurgery.com, please visit our new "Patient Reviews" page. See 300+ patient reviews here.



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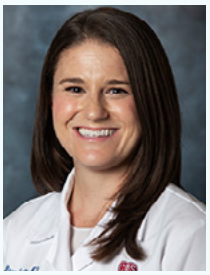
Featured Speakers



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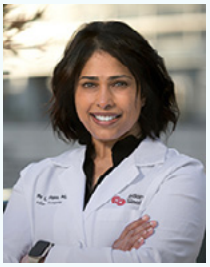

Dr. Melita Viegas
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Please note: A complimentary video playback of this eBook is now available on YouTube at this link.

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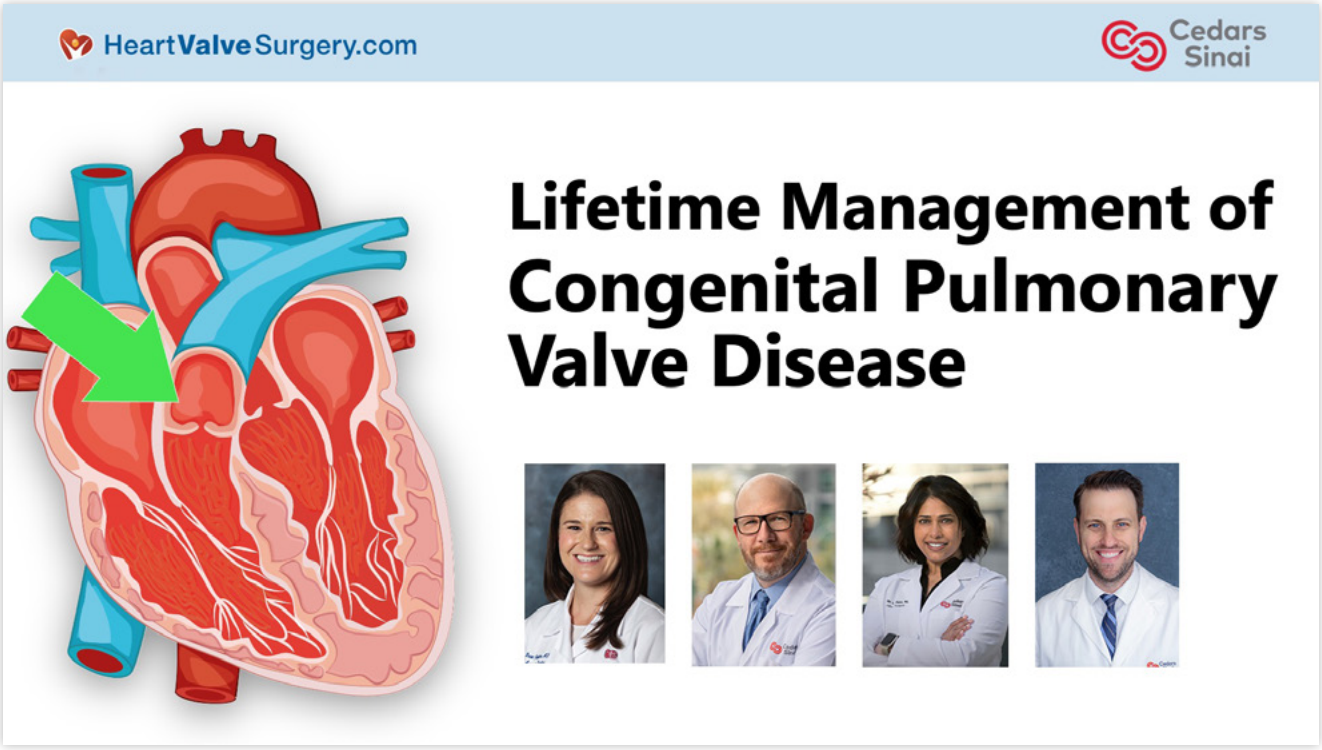
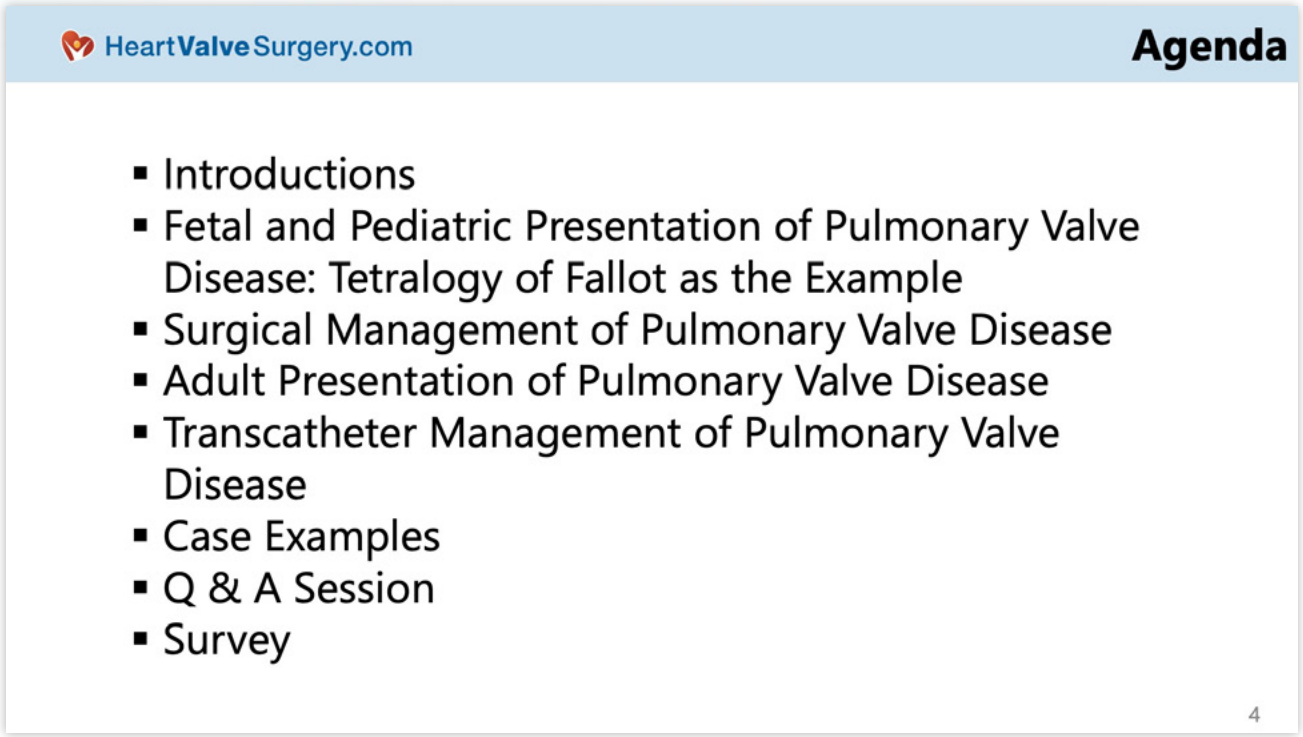
Introduction



Adam Pick: Hi, everybody. My name is Adam Pick, and I'd like to welcome you to the webinar titled, "The Lifetime Management of Congenital Pulmonary Valve Disease". If I have yet to meet you, I'm the patient who started HeartValveSurgery.com all the way back in 2006. The mission of our website is really simple. We want to educate and empower patients just like you. This webinar, which has had over 350 registrations from patients in countries all over the world, was designed to support that mission.

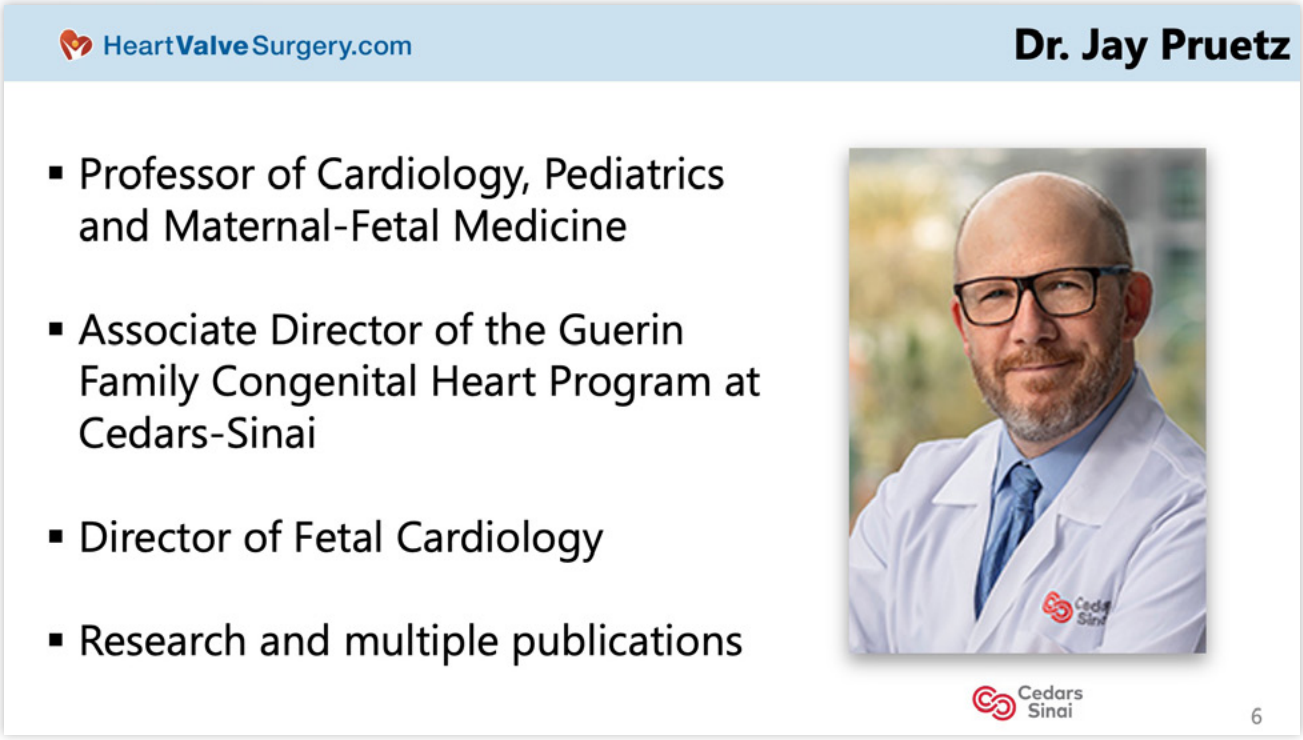
Now, throughout the webinar, you're going to be in what's known as listen-only mode. I'd encourage you to submit your questions in the control panel that's on your screen.



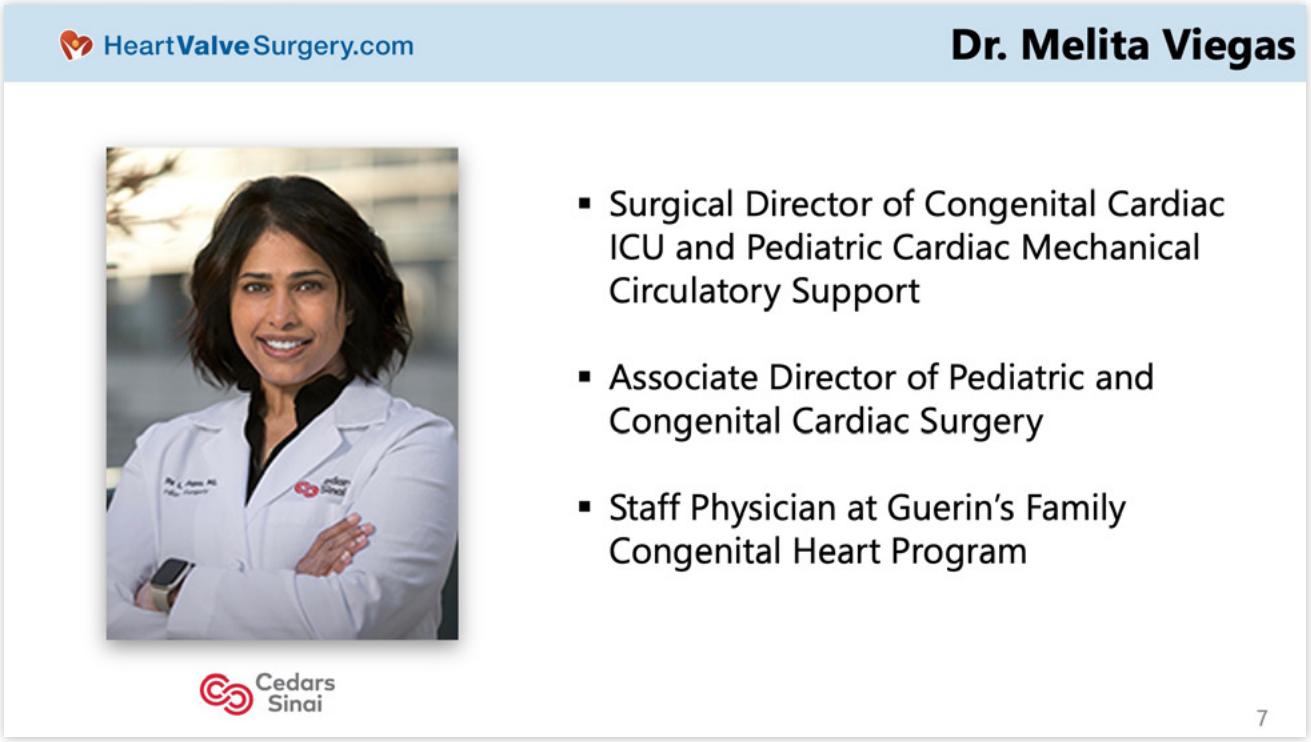
As we look at the agenda, you'll see why. So first, we're going to introduce the featured speakers. We're going to talk about fetal and pediatric presentation of pulmonary valve disease. We're going to look at the surgical management of pulmonary valve disease, the adult presentation. We're going to look at newer transcatheter management strategies and devices of pulmonary valve disorders. One of my favorite parts of the webinar is that we're going to contextualize a lot of what you have heard in actual case examples so you can see how the Cedars team is approaching the congenital treatment of pulmonary valve disease. We're going to get to that Q&A session. Then at the very end of the webinar, I'm going to ask you to complete a very quick five-question survey.

When it comes to the featured speakers of today, I would submit to you that we have a "Fantastic Four" with us today. The reason I say that is because when it comes to congenital pulmonary valve disease, we have physicians who cover all aspects of it. We have a cardiologist; we have interventional cardiologists. We have a cardiac surgeon. Let's take a look at who they are.

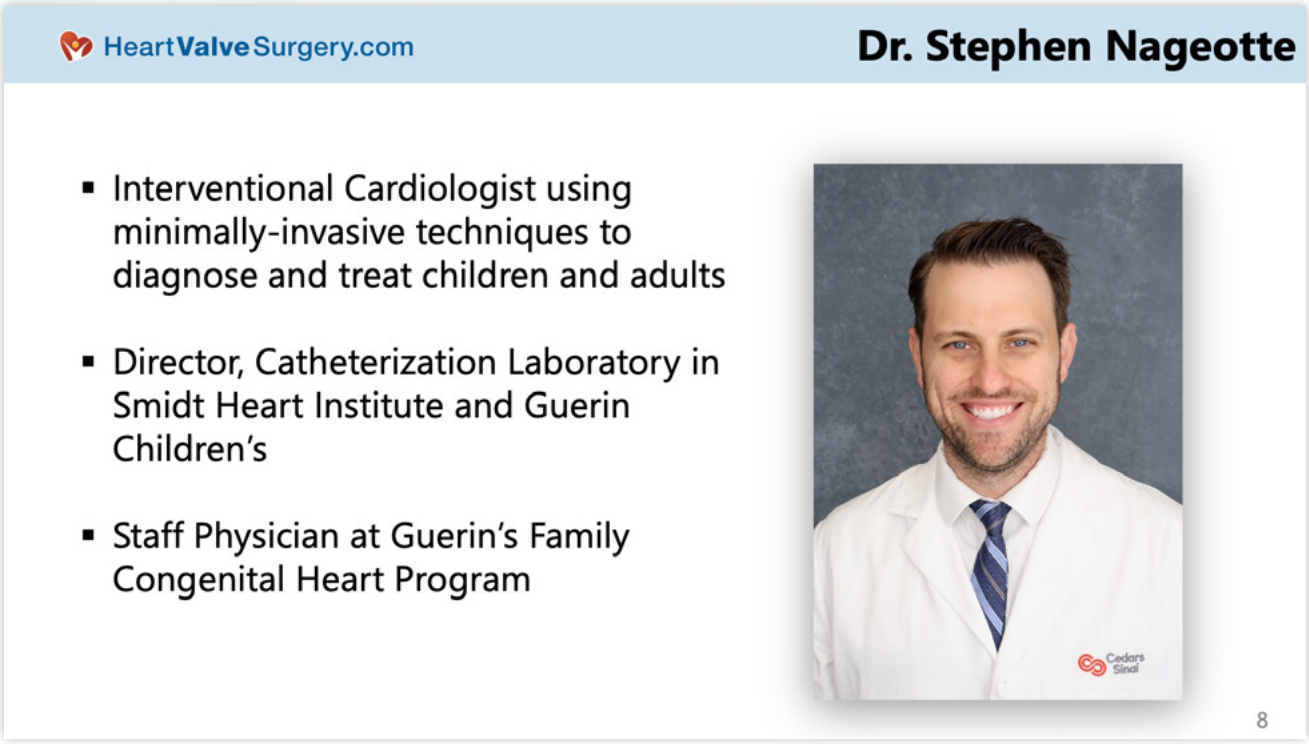
They are Dr. Rose Tompkins, who is the associate professor of cardiology at Cedars-Sinai. She's also the director of adult congenital program. She's board-certified in adult congenital heart disease, and you may have seen a lot of her research in publications -- just recently in how to navigate a higher-risk pregnancy.



Dr. Jay Pruetz is a professor of cardiology, pediatrics, and maternal fetal medicine. He's also the associate director of the Guerin Family Congenital Heart Program at Cedars-Sinai. He's the director of fetal cardiology and has multiple research publications as well.



Dr. Melita Viegas is the surgical director of congenital cardiac ICU and pediatric cardiac mechanical circulatory support. She's also the associate director of pediatric and congenital cardiac surgery, and she's a staff physician at Guerin's Family Congenital Heart Program.



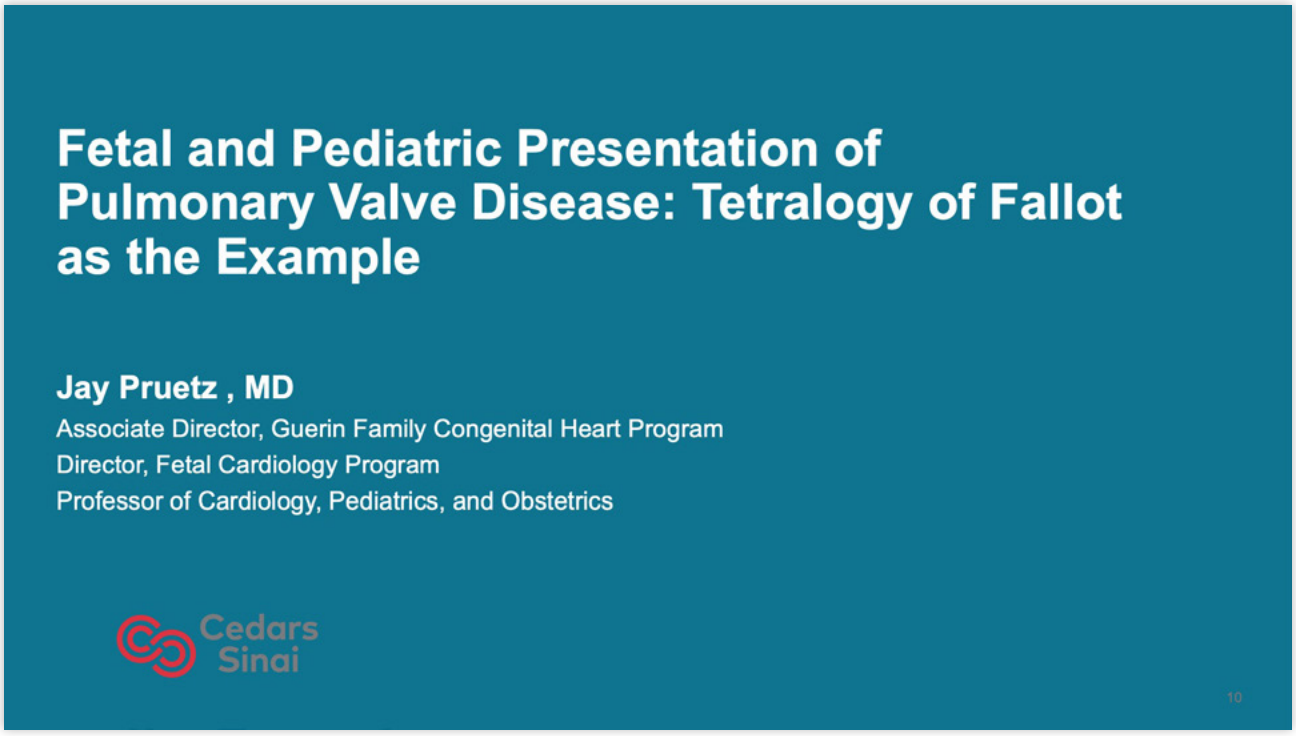
We have with us Dr. Stephen Nagoette, who's an interventional cardiologist. What that means is he's using very minimally invasive techniques to diagnose and treat children and adults. He's also the director of catheterization laboratory at the Smidt Heart Institute and Guerin Children's Family. He's a staff physician with Cedars and Guerin's Family Congenital Heart Program.

Cedars-Sinai Success Stories

I can go on and on about all the achievements and the accolades of this incredible panel. What I'd like to do is show you this. These are actual patient names of folks from the heartvalvesurgery.com community. Whether it's Janice, or John, or George, or Stan who have gone from the heartvalvesurgery.com website to Cedars-Siani for their care. It's one thing to see some names on a screen, but it's another thing to see the actual smiling faces of their patients, whether it's Josh or Wendy from Florida or Jerry or Lailani or Steve or Patricia. Thanks to this team, the entire Cedars team, we're taking folks in very fragile disease states and bringing them to places of great outcomes and excellent care.

With that being said, I'd like to turn it over to Dr. Jay Pruetz to begin the webinar.

Fetal and Pediatric Presentation of Pulmonary Valve Disease: Tetralogy of Fallot



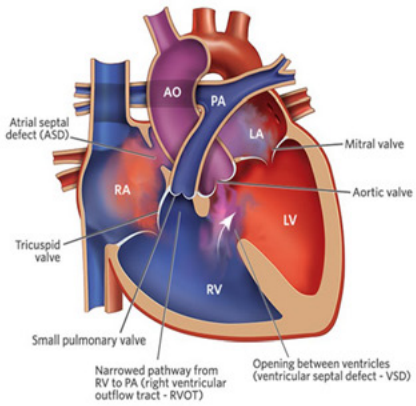
Dr. Jay Pruetz: Thank you, Adam. I really appreciate being here today. I'm going to talk to you about fetal and pediatric presentation of pulmonary valve disease kind of through the lens of a diagnosis called tetralogy of Fallot. This could apply to many different diagnoses that involve the pulmonary valve.

So Tetralogy of Fallot is a congenital heart defect. The key anatomic findings with it are that it has a hole between the two lower chambers of the heart, a ventricular septal defect between the right and left ventricles. Those are the

Tetralogy of Fallot (TOF): Key Anatomic Findings

- Narrowed right ventricular outflow tract (RVOTO), pulmonary valve stenosis (PS)
- Ventricular Septal Defect
- Over-riding Aorta
- Right ventricular hypertrophy
- Enlarged Aorta

- Associated lesions:
  - Pulmonary artery anomalies
  - Left SVCLSVC
  - Right aortic arch
  - Aortopulmonary collaterals



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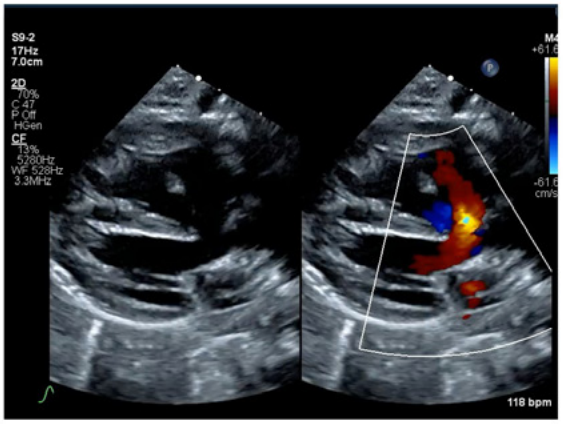
lower chambers. It has – the aorta has shifted over this hole, so it straddles over both the right and the left heart. Then there's usually narrowing in the blood vessel that goes out to the lungs, the pulmonary artery. That's where the pulmonary valve is. The pulmonary valve is the gatekeeper for flow from the right heart out to the lungs. That often can be small, underdeveloped, and when we say that it's small and underdeveloped, we call that stenosis. When it's completely closed so there's no connection, we call that atresia. So those are the basic features of tetralogy of Fallot and then sometimes associated with that, you can also have additional findings such as anomalies of the pulmonary arteries themselves. Sometimes you can have an extra vein connected to the left side of the heart. Your aortic arch can be on the right side instead of the left side, and sometimes you can have extra blood vessels feeding the lungs. I'm not going to get into the details of that, but this sets the stage for with this diagnosis, how do we approach this?

Diagnosis

- Fetal diagnosis with prenatal screening US and Fetal echocardiogram
- Postnatal Diagnosis: Heart murmur vs. Cyanosis
- Diagnostics:
  - CXR
  - ECG
  - Echocardiogram
  - Chest CT
  - Cardiac MRI



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So the diagnosis, we actually can make this diagnosis in utero now many times. This is actually an echo here, a transthoracic echo that we're seeing on the screen. Actually, you're seeing on the top part the right ventricle, on the bottom part, the left ventricle, and then that red flow is across the hole between them. That's the VSD. This is a pediatric echocardiogram but many times, we can detect this even before the baby's born. Sometimes it's not detected before the baby's born and when that happens, we call that a post-natal diagnosis or after birth. That can present in one of two different ways. Sometimes it's detected because the child has a heart murmur or the baby has a heart murmur, so it gets sent to the cardiologist for evaluation. Sometimes it's because there's such obstruction to blood flow the lungs that the baby's color is actually blue.

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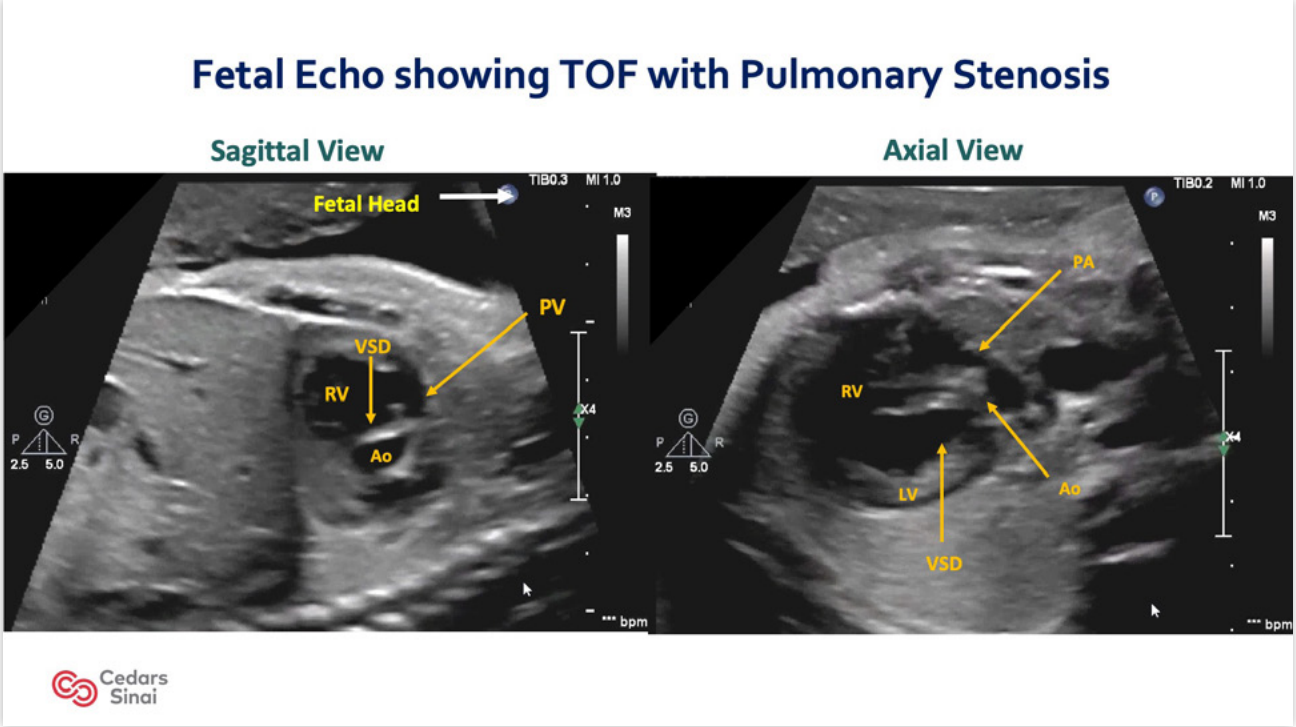
We call that cyanosis, because there's not enough blood flow to the lungs. We use a number of different diagnostic tests to evaluate these children, including chest x-ray, EKG, echocardiogram and then occasionally if we need even more high-resolution imaging structures, sometimes we also do a chest CT or a cardiac MRI as well to delineate the anatomy.

Fetal Echocardiogram



Dr. Jay Pruetz: So this is actually an example of a fetal echocardiogram. This is a baby inside the mom. To the top of the screen is the fetal chest and at the bottom, you can make out the vertebrate. That's the spine. You can see the heart here and if you click another time, there will be some labels that come on that show you the different heart chambers. Here you have the right ventricle. There's the pulmonary valve, which is usually obstructed and narrowed. Then you can see that hole between the right ventricle and left ventricle.

So this is how we diagnose it. You don't really have to obviously understand all the nuances of ultrasound but just to give you an idea, this is really the bread-and-butter of how we figure these diagnoses out.

Spectrum of Disease

- **Pink TOF (normal O2)**
  - Large VSD; minimal PS
- **Blue TOF (low O2) = cyanosis**
  - Large VSD with severe pulmonary stenosis or pulmonary atresia with confluent PAs
- **Complex TOF**
  - Pulmonary atresia with pulmonary artery anomalies (MAPCAs)
  - TOF/APV
  - TOF/CAVC

Feature	Pink TOF	Blue TOF
RVOT Obstruction	Mild	Severe
Cyanosis	Minimal/Absent	Marked
Pulmonary Flow	Increased/Normal	Decreased
Presentation	Murmur, CHF symptoms	Cyanotic spells

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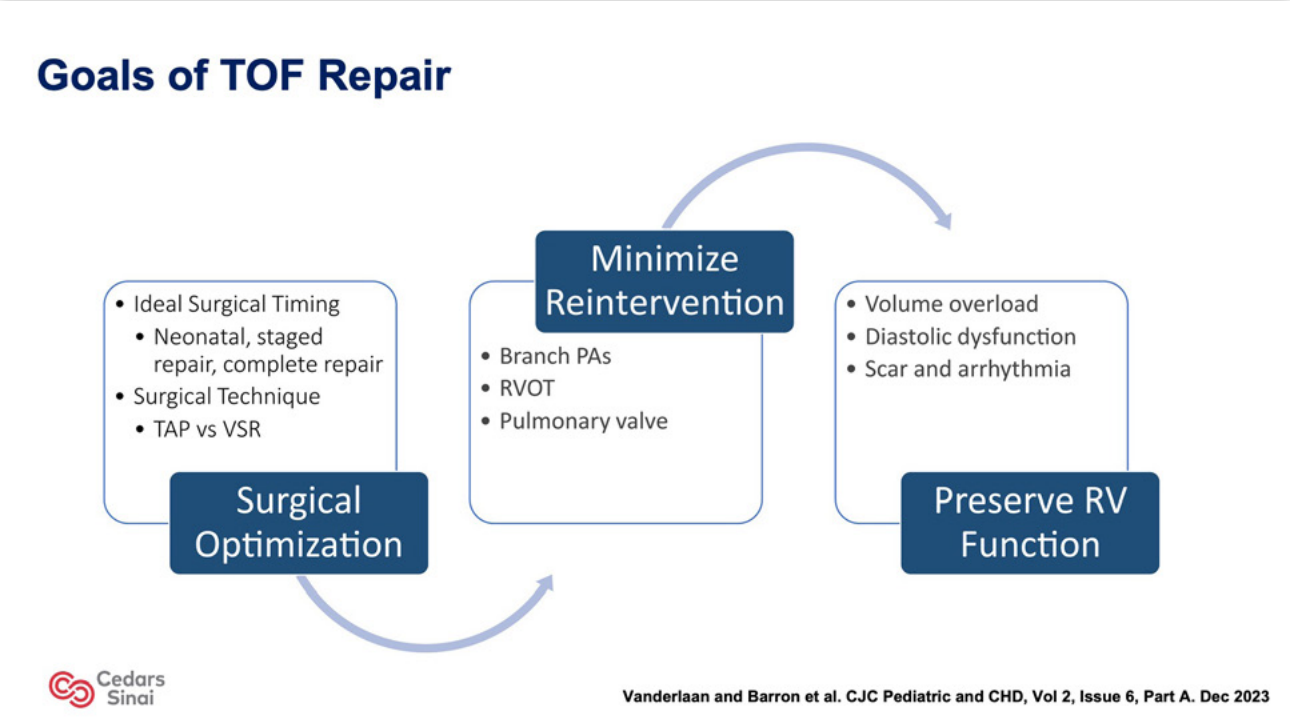
So in talking about tetralogy of Fallot, I'm going to just talk broadly how we categorize this. You may have heard the terms before, a pink tet or a blue tetralogy of Fallot and really, what that has to do with is where are the oxygen levels. If the oxygen levels – we call them O2 saturations – are normal, then the baby or the child appears pink on exam and their oxygen levels measure normally. In that scenario, if you look at this table, and that's the second column of pink tet, they have very little obstruction of outflow from their right heart. They don't have cyanosis, so they're pink. They have a decent amount of pulmonary blood flow, so they have enough blood flow going to their lungs. They are usually the ones that present with less symptoms. They often will just have a murmur or a very minor symptoms of some increased work of breathing

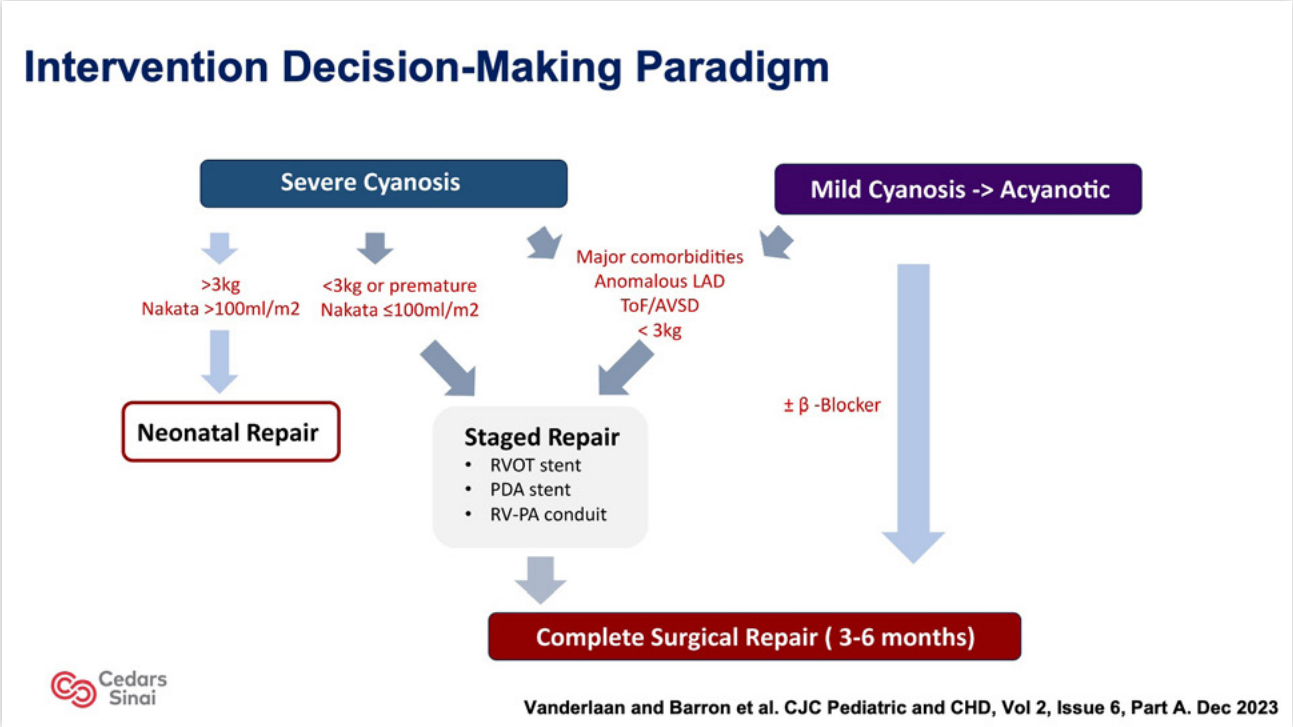
or congestion versus a blue tetralogy of Fallot, when the O2 saturations are very low. There's a very significant amount of obstruction of blood flow to the baby's lungs and the baby is blue and also can have what are called cyanotic spells. These, you can see these two categories are going to be approached very differently. There are also more complex forms of tetralogy of Fallot that we're not going to get into today where you won't have a pulmonary valve at all or you have anomalies of your pulmonary arteries. We're going to focus on this main category right here.

Goals of Tetralogy of Fallot Repair



Dr. Jay Pruetz: So then how do we approach this? What are the goals of repairing this? We know that this can be repaired surgically. The first thing is to try and figure out what's the best timing. Do we need to repair this in a newborn, or can we wait until the baby's a bit older and figure out this surgery at a later date? What technique are we going to use? I'm going to get into that a little bit more. Really, the goal is we want to try to minimize re-interventions. Ideally this would be a one-off surgery and done. Unfortunately, that's not always the case and you're going to learn a lot about that today, particularly because the pulmonary valve often needs to be fixed or replaced down the road. We want to preserve the right heart function. We don't want to overload it; we don't want to cause dysfunction of the heart. That plays into our scheme of what – the timing of surgery and how we're going to repair things.

Intervention Decision-Making

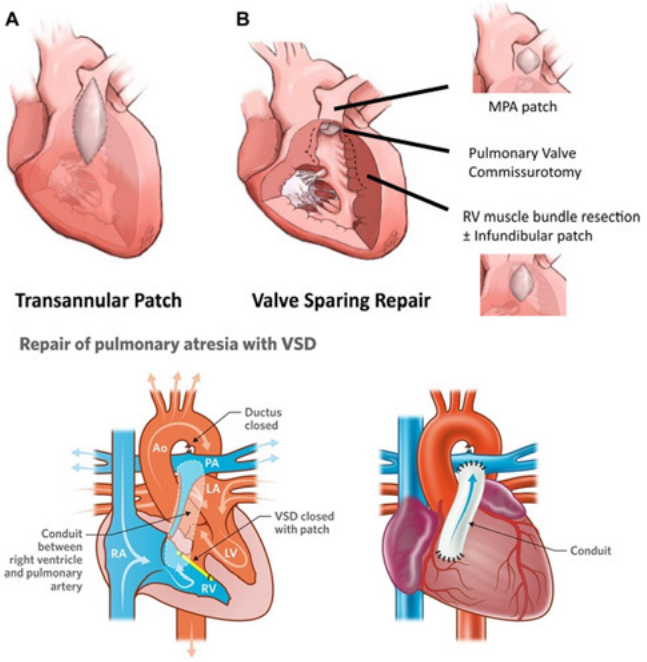


Dr. Jay Pruetz: So this is just a quick chart of if you present as a baby or a young child with severe cyanosis – that means you're blue – and you are at least over 3 kilograms, you may go for a complete repair, a neonatal tetralogy repair right away. We don't have a choice. You're blue; the anatomy's good. You're a good size; we'll fix it.

More often than not, though, the baby may be a little too small or there may be other comorbidities that we want to do more of the staged repair. What that means is we don't go fix everything all at once. We may actually augment the pulmonary blood flow first for a short time by either providing increased blood flow to the lungs, an additional source of pulmonary blood flow, and then coming back at a later date at the bottom of that pathway at three to six months and do the complete repair or if you're a so-called pink tet, you're at the very far side of the screen where you have mild cyanosis. You may not need any initial treatment. You may be able to go out to six months and then go for that complete repair. I'm going to talk to you about the two general approaches to that on the next slide.

General Approach to Complete TOF Repair

- **Surgical Options in TOF with outflow tract:**
  - Valve Sparring
  - Non-Valve Sparring (Transannular patch)
- **Surgical Options in TOF with pulmonary atresia (no outflow tract)**
  - RV to PA Conduit



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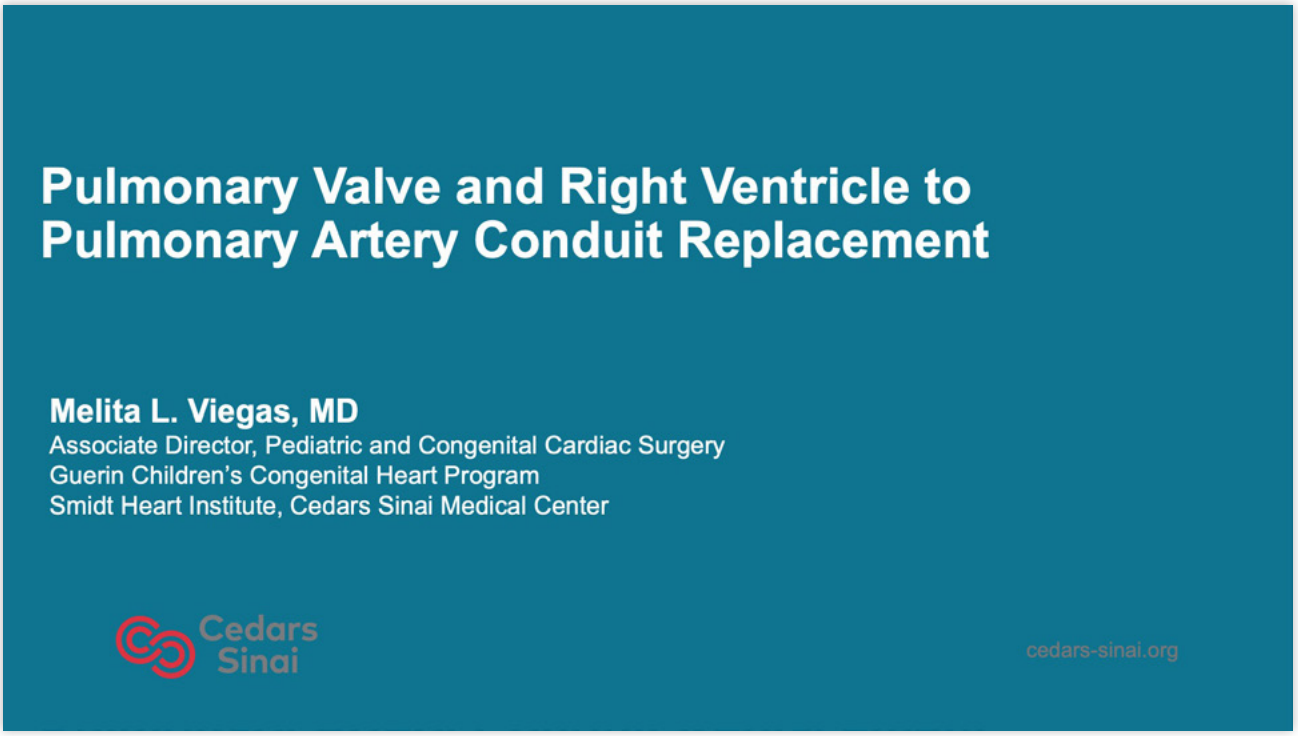
So the approach typically has to do with how much pulmonary valve there is. If you have a decent outflow track from the heart to the lungs, if you have a decent sized pulmonary valve, we would try to do what's called a valve-sparing TOF repair. That's under letter B there where there is an outflow track. What we would do is we would leave your valve alone, and we would patch above the valve in the main pulmonary artery and then we might patch below the valve in the right outflow track but not try to influence the valve too much so that it could grow with the patient. That's the valve-sparing.

However, if the valve is too small or too obstructed, then we can't do that because if we did that, we would leave you with a lot of obstruction. So then it's under letter A. It's called the transannular patch. We would cut all the way across the valve. You'd essentially have to remove the valve and put a big patch there to open up and relive the obstruction. That would leave the patient with no effective pulmonary valve, which is okay for a time, even for years, but eventually would need to be addressed.

Then in the case of there's really no valve or no outflow track, that's at the bottom. When you have something called pulmonary atresia, you actually have to sew in a completely new connection from the right heart to the pulmonary artery, and that's called a conduit, RV, right ventricle, to pulmonary artery conduit. That often will have a valve inside of it. The issue with that is that those are a fixed size; they don't grow with the patient, so depending on the age and the size we put it in, they may have to be upsized with another surgical procedure over time.

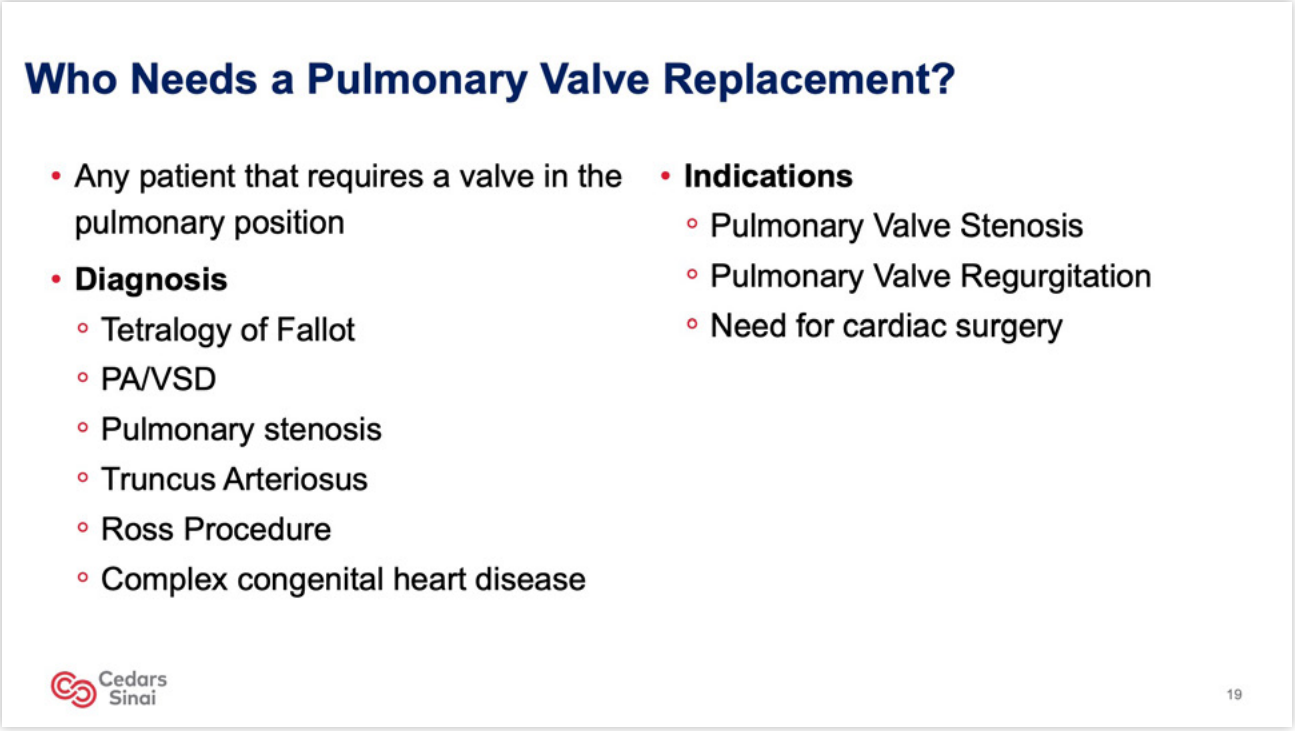
Now I'm going to pass it on to my surgical colleague, Dr. Melita Viegas, to talk about the nuances of these different surgical repairs.

Pulmonary Valve and Right Ventricle to Pulmonary Artery Conduit Replacement

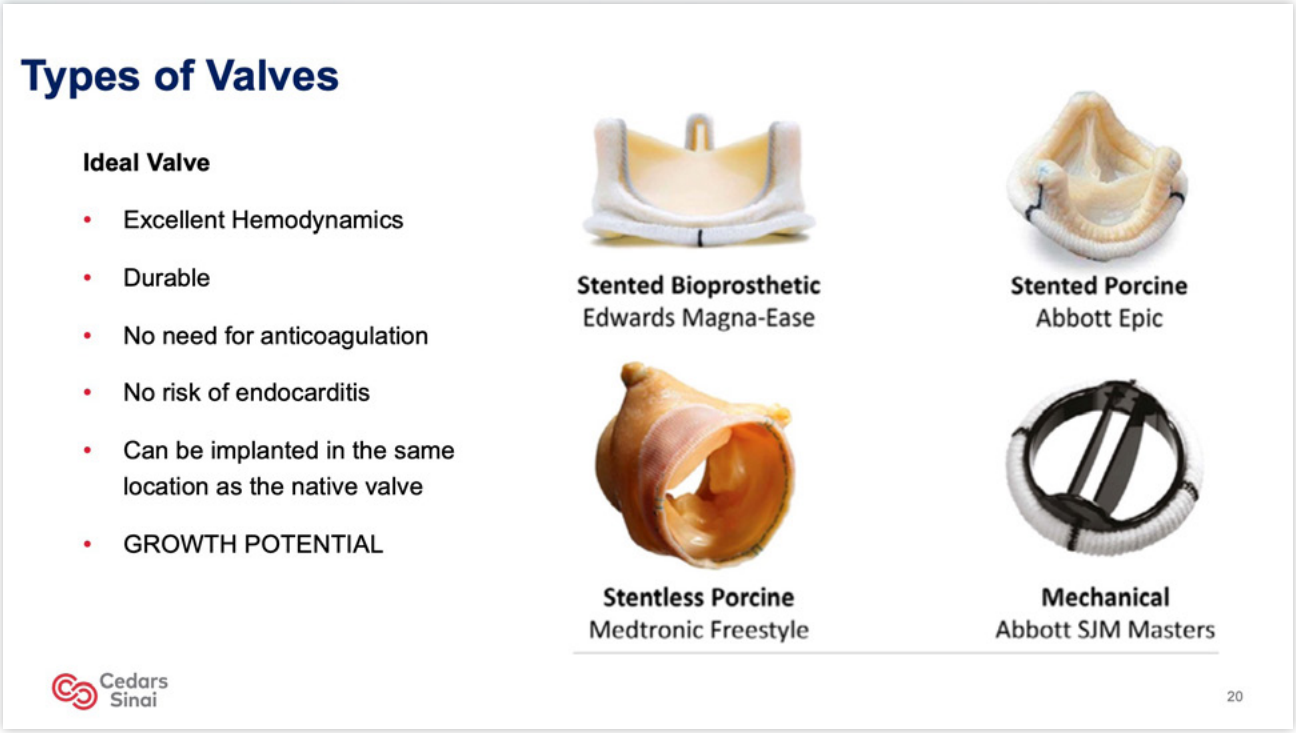


Dr. Melita Viegas: Thanks, Dr. Pruetz. We're going to fast-forward a few years and just focusing on what Dr. Pruetz was just talking about with tetralogy of Fallot. Each one of those repairs within somewhere, it can be as early as four or five years or even ten to 20 years will need an intervention. Sometimes our valve-sparing tet repairs, about 16 to 30% of those actually require a pulmonary valve in the future. The ones that get transannular patches, they also will at some point require a pulmonary valve. I'm actually going to let Dr. Tompkins talk a lot about indications. I'm going to try to focus on what the pulmonary valve replacement surgery is and how we make our choices for the valve.

Who Needs a Pulmonary Valve Replacement?

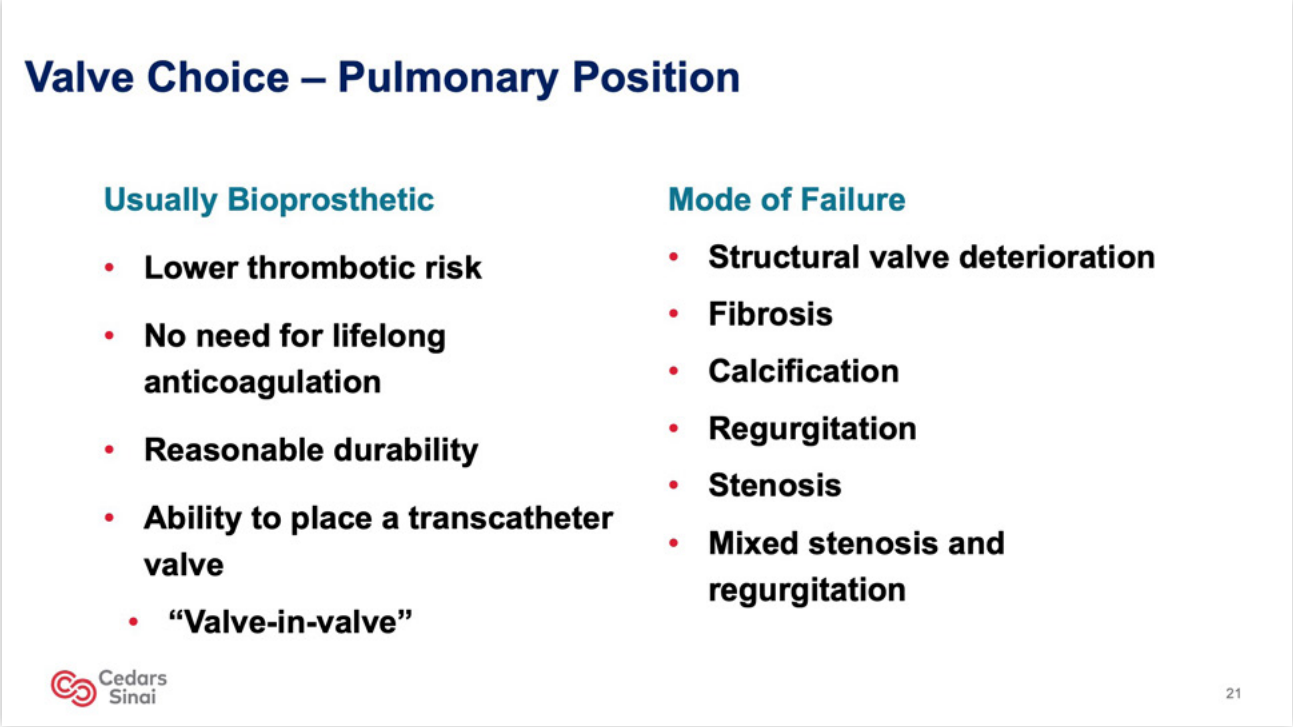


Dr. Melita Viegas: So who needs a pulmonary valve? So any patient that requires a valve in the pulmonary position, so we already talked about tetralogy of Fallot. There's pulmonary atresia VSD, which is on that tetralogy spectrum; pulmonary stenosis; truncus arteriosus, patients that have had a Ross procedure. Sometimes they have conduits and at times, we can actually place a valve in those conduits if there is dysfunction or some other complex congenital disease. The indications themselves are if there's severe pulmonary stenosis or regurgitation, if there's some ventricular dysfunction, or if a patient has a pulmonary valve that's close to needing something done but is getting something else done to the heart at the same time.



So the search for the ideal valve continues, but the things we would like the most are, number one, that they function correctly so that they have excellent hemodynamics, that they're durable and last a long time, that they don't need anticoagulation or blood thinners, and have minimal risk of infection or endocarditis. It's also nice because these valves tend to function better if they're implanted in the same location as the native valve and if they have either growth potential or what we've settled on is if they're amenable to transcatheter intervention.

Valve Choice



Dr. Melita Viegas: The choices – so the valve choices include pericardial valves, so it's the pericardium of a cow, so bovine pericardial valve, porcine valves, and a mechanical valves. Those are the big ones that we choose for or choose. Usually in the pulmonary position, we're going to go with the bioprosthetic valve. That's for a few reasons. Number one, there's no anticoagulation needed. They overall have a lower incidents of having clots thrown from the valve themselves. They have very good durability and there's also the future ability to place a transcatheter valve and even a valve-in-valve in the future.

The downside is they aren't going to last forever. They tend to last somewhere between 10 and 15 years is usually what we tell patients. The reasons for failure include structural valve deterioration, fibrosis of the leaflets, calcification, and over time, they can have either regurgitation or stenosis.

Durability

- **Freedom from Reintervention**
  - 82-98% at 5 years
  - 52-83% at 10 years
- **Factors to Consider**
  - Type of valve used
  - Diagnosis of the patient
  - Age of patient

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Table 1. Summary of Contemporary Retrospective Studies of Bioprosthetic Pulmonary Valve Replacement

Author	Y	N	No. of Centers	Valve Types	Patient Diagnoses	Age Range	Reintervention Rate	Risk Factors for Early Reintervention
Caldarone[5]	2000	945	Single	Ionescu-Shiley (bovine), Mitroflow, CE Porcine, Hancock, Polystan, homograft (aortic and pulmonary)	All diagnoses	Pediatric and adult	82%, 58%, and 41% at 5, 10, and 15 y	Younger age (<13 y)
Shinkawa[9]	2010	73	Single	Stented bovine pericardial valves only	All diagnoses	Pediatric and adult	98% at 5 y	None reported
Zubairi[6]	2011	169	Single	CE bovine valve, Hancock valve, pulmonary homograft, pulmonary heterograft	TOF and isolated PS	Pediatric and adult	72% freedom from reintervention at 10 y	Younger age (<10 y) was a risk factor for reintervention; homografts had higher risk of early PVF
Lee[7]	2011	181	Single	Hancock, CE Perimount, Freestyle, CE Porcine	All diagnoses	Pediatric and adult	94% and 52% at 5 and 10 y	Younger age (<10 y). PA-VSD, use of stentless valve were risk factors.
Jang[8]	2012	131	Single	Hancock, CE Perimount, St. Jude Biocor	TOF only	Pediatric and adult	66% freedom from reoperation at 10 y	Younger age (<15 y); larger valves do not fail faster
Chen[9]	2012	229	Single	Stented valves only (CE Perimount and Magna, Sorin, Porcine)	TOF only	Pediatric and adult	94% and 74% at 5 and 10 y	Younger age (<20 y), larger indexed valve size in patients younger than 20 y (but not in those older than 20 y)
Lee[10]	2012	170	Single	Stented bovine, stented porcine, PTFE biospid, stentless porcine	All diagnoses	Pediatric and adult	75% at 10 y.	None reported

(continued on next page)

Table 1. (continued)

Author	Y	N	No. of Centers	Valve Types	Patient Diagnoses	Age Range	Reintervention Rate	Risk Factors for Early Reintervention
Chen[11]	2013	170	Single	Stented valves only (CE Porcine)	All diagnoses	Pediatric and adult	99%, 94%, and 36% at 1, 5, and 10 y	No difference in reintervention by valve type (stented porcine v. bovine pericardial), controlling for age and valve size; age <15 y was a predictor of reintervention.
Nomoto[12]	2016	611	Single	CE Perimount and Magna, Sorin Mitroflow	All diagnoses	Pediatric and adult	94% and 76% at 5 and 10 y	Younger age (<12 y), Sorin MitroFlow valve (in comparison to CE Magna and CE Perimount)
Egbe[13]	2019	807	Single	Stented pericardial and porcine, RV-PA conduit, homograft, transcatheter valves	All diagnoses	Adults only	83% and 61% at 10 and 15 y	None reported (adult-only study)
Spigel[14]	2020	79	Single	St. Jude Epic only	All diagnoses	Pediatric and adult	96% at 5 y	None reported
Baird[15]	2020	1278	Multi (8)	CE Perimount and Magna, Sorin, St. Jude Epic and Biocor, Sorin Mitroflow, Mosaic, Hancock, Melody, Freestyle, CE Porcine	All diagnoses	Pediatric and adult	99%, 97%, and 92% at 1, 3, and 5 y	Smaller valve size, younger age (<18 y), and Sorin and St. Jude valves

CE, Carpentier-Edwards; PTFE, polytetrafluoroethylene; TOF, Tetralogy of Fallot; PS, pulmonary stenosis; RV-PA, right ventricle to pulmonary artery

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So let's just talk a little bit about durability. Like I said, they function pretty well. At five years, the freedom from reintervention is somewhere between 82 and 91%, and that's been validated by several studies that you can see here. Then at 10 years, it's about 52 to 83%. The variability that occurs depends on many things. It depends on the type of valve used, the diagnosis of the patient, where the valve is placed, and also the age of the patient.

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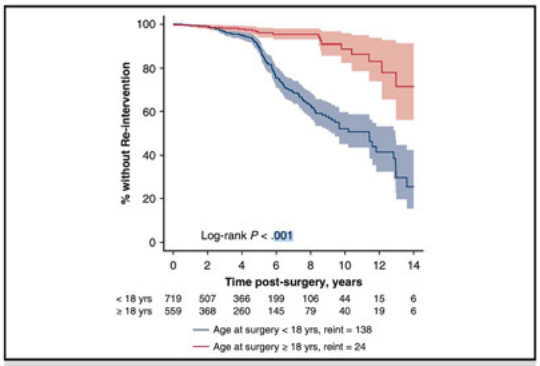
Reintervention rates after bioprosthetic pulmonary valve replacement in patients younger than 30 years of age: A multicenter analysis

- **Largest Multicenter Study for Bioprosthetic PVR**
  - 1278 patients <30yo, 8 US centers
  - Conclusion:
    - Age <18yo was associated with a higher rate of reintervention compared to those in the older age range

Risk Factor for replacement: Younger age



Freedom from reintervention estimated probability by valve type, $P < .001$.

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J Thorac Cardiovasc Surg 161:345–362.e2, 2021

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This is one of the largest multi-center studies or multi-center trials that looked at bioprosthetic pulmonary valves and what their actual durability and reintervention rates are. This is just looking at over 1200 patients. Ultimately, they found that the biggest risk factor for needing replacement is the actual pulmonary valve being placed at a younger age. That's one thing that because there is no growth potential, obviously the younger you are, the higher the likelihood that you're going to need a valve and then like I said, they peak at their full function somewhere between 10 to 15 years.

Valve Choice – Tailored to the Patient

Older patients, pericardial valves tend to perform better

Porcine valves may perform better in younger patients because the leaflets are less stiff and require a lower opening pressure

Mechanical valves *rarely* used unless the patient already has a mechanical valve in another position or has failed a bioprosthetic valve

Stented Bovine Pericardial Valves

Edwards Magna-Ease | Edwards INSPIRIS Resilia | Sorin MitroFlow

Stented Porcine Valves

Abbott Epic | Hancock II | Medtronic Mosaic

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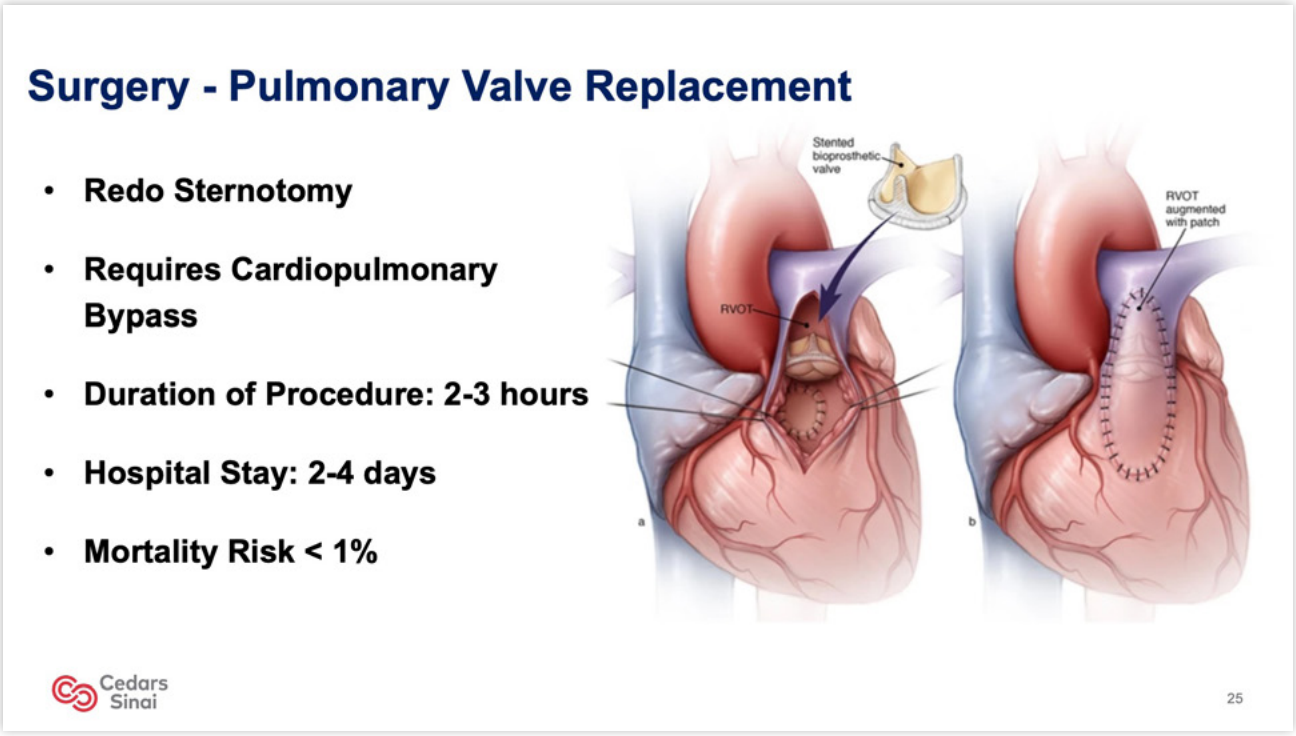
So the valves that we choose for each patient is truly tailored to the patients themselves. Older patients, we tend to use pericardial valves or those bovine pericardial valves. That's the valve that's there in the top in the middle. Those leaflets tend to be stiffer and can tolerate high pressures. The porcine valves or pig valves, which is the bottom left, they tend to perform better in younger patients because their leaflets are a little less still and they require a lower pressure to actually open up those leaflets.

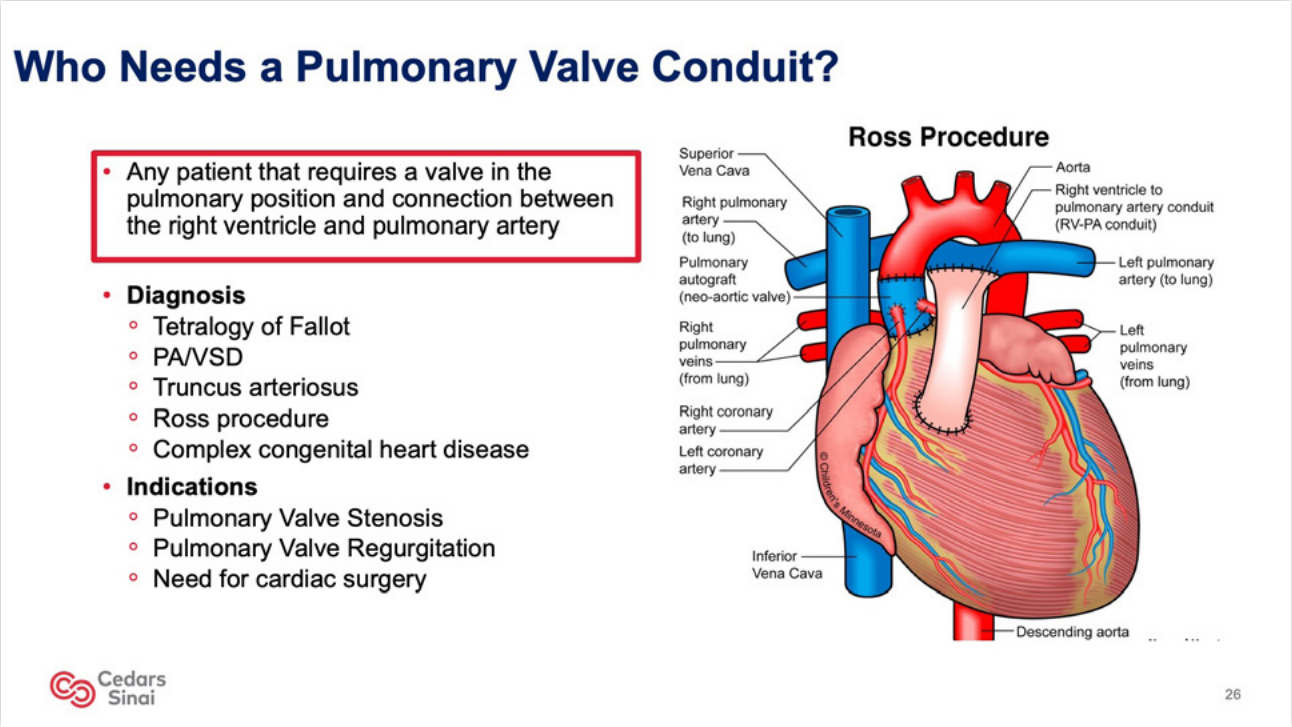
Mechanical valves are an option, but they're really rarely used just because of their issues with potential thrombosis, the need for life-long anticoagulation and honestly, if something goes wrong with that valve, in order to fix it, surgery is the answer as opposed to a trip to the cath lab.

Surgical Pulmonary Valve Replacement



Dr. Melita Viegas: So the pulmonary valve replacement surgery itself is a very common surgery in our field. It does often require a reduced sternotomy because most of these patients have had surgery before. It does require the heart/lungs bypass machine, but the surgery itself takes roughly around two to three hours. The overall hospital stay is about – average at about three days, and the mortality risk is very low at less than 1%.

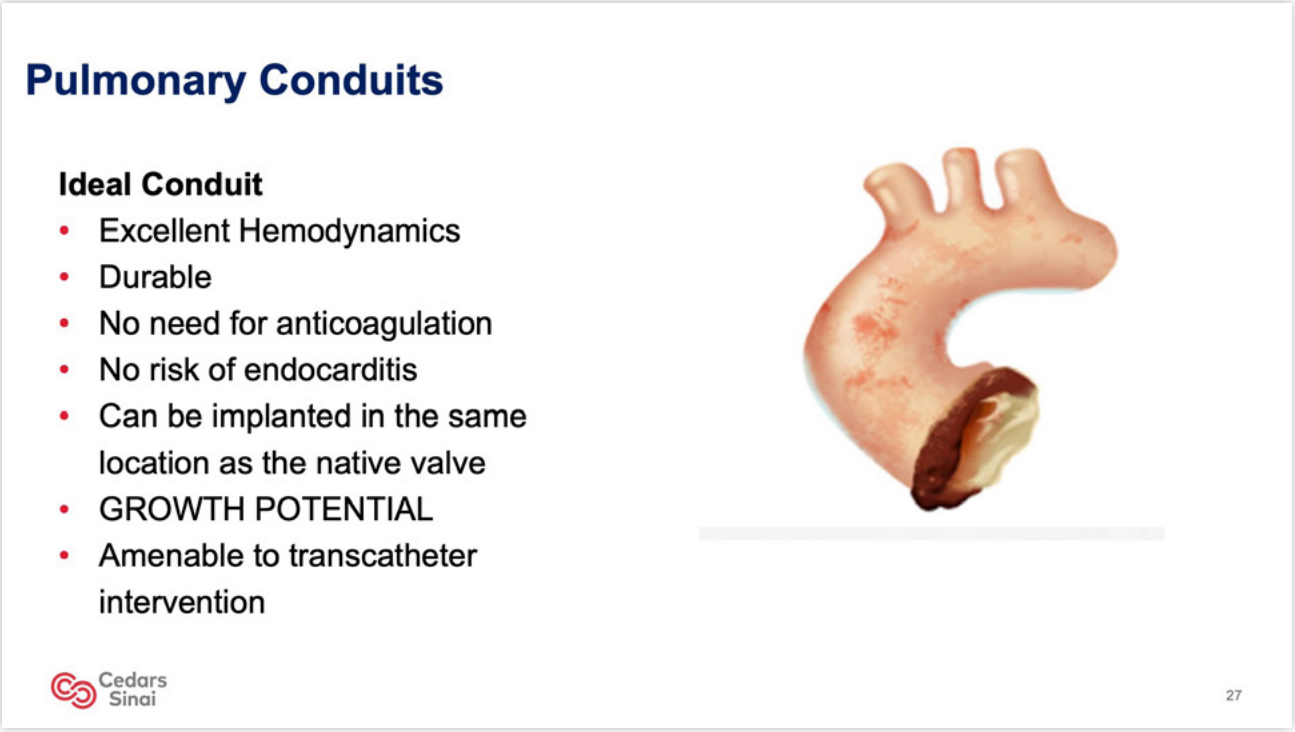
Who Needs a Pulmonary Valve Conduit



Dr. Melita Viegas: So let's quickly move on to who needs a pulmonary valve conduit. So this is any patient that actually requires that connection between the right ventricle and the pulmonary artery with a valve in between. It's pretty much very similar diagnoses that we talked about with pulmonary valves and very similar indications that Dr. Tompkins will go further into.

Again, just as we're looking for ideal valves, we're looking for ideal conduits as well. We want them to function well, so excellent hemodynamics, be durable, last forever, no need for anticoagulation, minimal risk of infection. We want it to be implanted where the native valve is, have growth potential and again, be amendable to transcatheter intervention.

Types of Conduits



Dr. Melita Viegas: So types of conduits we have, the top two are homografts, which means these are vessels that actually come from cadavers. There are valve conduits and some of us make these and some companies make these. But a valve, just like I said, a bioprosthetic pulmonary valve, and it is actually in between two pieces of tube or Dacron tube. There are also PTFE valve conduits, so PTFE is like a Gortex. We actually create some of these in the operating room. Ther eis one company that is starting to make these. That's very early stages and there's also something called Contegra, which is actually bovine jugular veins, so it's the jugular vein from a cow themselves.

Adam Pick: Dr. Viegas, before we move on, a lot of patients in our community, when they hear about getting a homograft and it's from a cadaver, they have this ongoing really important question, which is do I have to go onto a donor list? How is it that you are able to get a cadaver conduit?

Dr. Melita Viegas: So these are actually often harvested at the time of procurement for a donor heart, per se. It's actually the leftover pieces or people that actually donate them themselves. The companies that help with allocating everything, they also help with actually harvesting these. Then they go through several – some of these get decellularized, so that's the idea of trying to make it more inert. It's not 100% but it's helpful. Then they are preserved in several ways, one of which is cryopreservation. These are truly gifts from other people, but it also means they don't have wide availability, which makes it a little difficult. As you can imagine the cost, pretty high.

Adam Pick: Great, thank you so much.

Table 1 Summary of three main classes of valved RVOT conduits [homograft, pulmonary valved conduit (Contegra), porcine valved conduits (PVC)] including specifications, processing, and clinical advantages and disadvantages

	Homograft	Contegra	PVC
			
Description	Biological homograft obtained from cadaver (either aortic or pulmonary)	Bovine jugular vein with natural three-leaflet valve and sinuses in center	Porcine aortic valve suture into center of woven fabric conduit
First described use	1966 (1984 for cryopreserved)	1999	1975
Processing	Placed in antibiotic sterilization solution followed by DMSO cryoprotectant and stored in liquid nitrogen	Preserved in buffered low concentration glutaraldehyde to maintain leaflet flexibility	Preserved in stabilized 0.2% glutaraldehyde with a pressurized aortic root fixation process
Sizes available	6mm–32mm	12mm–20mm	12mm–25mm
Advantages	· Resistance to infection · Excellent hemodynamics	· Increased availability in range of sizes · Versatile handling properties · Reduced cost	· Availability in wide range of sizes · Lack of anticoagulation requirement
Disadvantages	· Limited availability, particularly in smaller sizes · Cost	· Increased incidence of endocarditis · Distal stenosis common	· Structural valve degeneration

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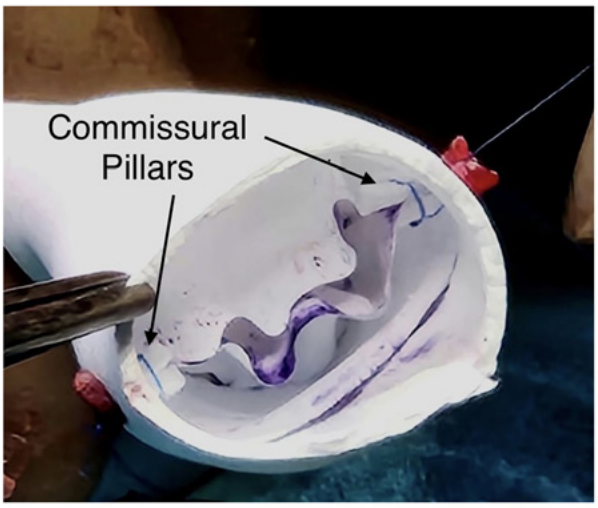
Melita Viegas: Yep. So this is just a quick look at some of the advantages and disadvantages of these three and then I'll talk a little bit about the PTFE. So homografts are great. They are available in a whole spectrum of sizes. We just talked about how we get them. They are pretty resistant to infection. They have great hemodynamics because they are functioning as they were functioning from where they came.

Their disadvantages is that they have limited availability. It's hard, especially as you can imagine, to find smaller sizes of these. While they exist, there's not that many and they're quite costly. The Contegra or the bovine jugular vein, they're also nice because they have increased availability. Their sizes range from 12 to 20 millimeters, which is roughly infant size to adolescent size. They do not cost as much as homografts. However, they do have a higher risk profile for infection as well as calcification.

Then lastly on this slide, at least, you have the valve conduit with the pig valve in between. These are nice because you can tailor them to whatever size. The problem is our smallest bioprosthetic valve is 17, 15 or sometimes you can find 15 but usually it's 17, so you're limited on size. Then you're going to be subjected to the structural valve degeneration that all porcine valves have.

PTFE Valved Conduits

- Handmade
- Inert
- Sizes 10-24mm
- Can be expanded in the cath lab



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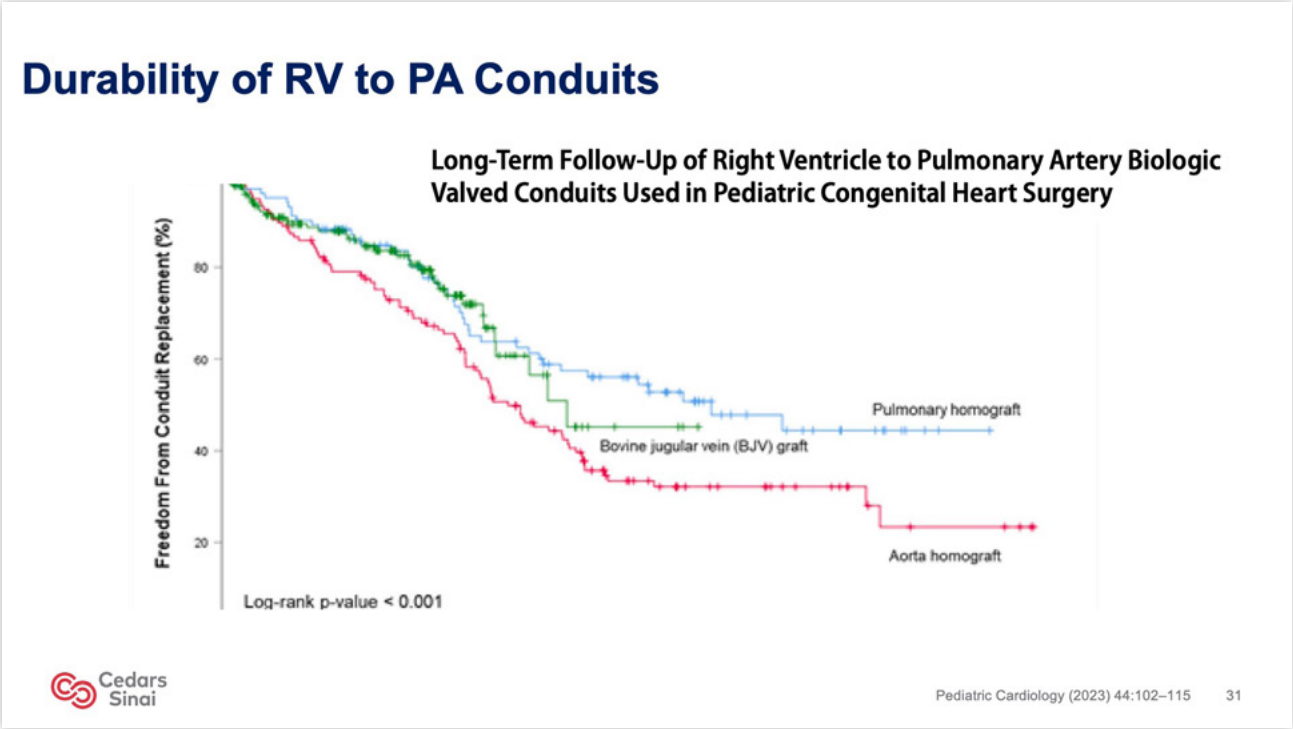
So the PTFE valve conduits, these are about 15 years in their – I guess ever since they were introduced. So these are very specific valves. Not all centers do them, but these are actually valves that the surgeon creates themselves in the operating room. We take thin Gortex leaflets, so that's what's in the center of this tube. We sew them on the inside, and then the outside is a tube that's made out of Gortex. For us, we use a particular graft; it's called – it's just expandable; it's an expandable graft themselves, which is great in the cath lab because we can actually make them bigger over time and place more and more valves inside and limit how many times we need to do open heart surgery.

Durability of Conduits



Dr. Melita Viegas: So just looking at the overall durability, so overall for all conduits, the freedom from replacement at ten years is about 50% and their freedom from intervention is about 40% at ten years. If you look at just pulmonary homograft and the Contegras and the aorta homografts, pulmonary homografts in this position tend to function the best. At ten years, their freedom from intervention is about 80% at 30 years, so it's about 66%, so they do well. As you can see, they're pretty close to one another and depending on the anatomy of the patient will choose which one is best.

Durability – PTFE Valved Conduit

- **Perform well**
  - Single Institution Studies:
    - 92.7% freedom from reintervention at 5 years
    - 88% freedom from reintervention at 15 years
  - Amenable to future transcatheter interventions

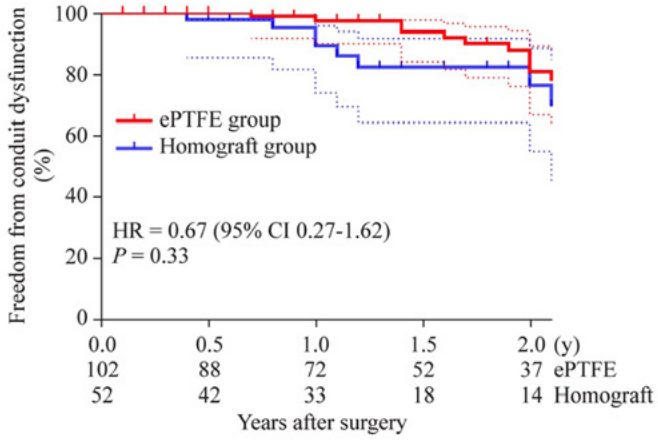


Fig. 3 Kaplan–Meier: freedom from primary end points. Dashed lines indicate the upper and lower limit for 95% CI. *ePTFE* expanded polytetrafluoroethylene, *HR* hazard ratio, *CI* confidence interval

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There hasn't been a big study to compare the PTFE valve conduits, so I just wanted to do these separate. The other thing is because not all institutions have these available, most of the data comes from single institution studies. They perform very well. They have a 92.7 freedom from re-intervention at five years and 88% freedom from re-intervention at 15 years. Like I said, their biggest selling point is not only are they amenable to future transcatheter interventions, they're amenable to multiple transcatheter interventions, which make them very versatile.

RV to PA Conduit: Which one?

- **Tailored to Patient**
  - Age
  - Size
  - Anatomy
  - Medical History
  - Preference
- **Surgeon and Institution Preference**

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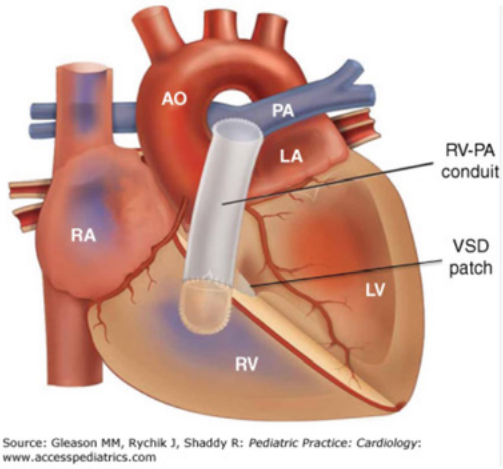
So which one do we choose? Again, just like with the pulmonary valves, we're going to tailor it to each patient, the age, their size, their anatomy, medical history, patient preference, and of course, the surgeon and institution preference all play a role in this.

Surgery - RV to PA Conduit Replacement



Source: Gleason MM, Rychik J, Shaddy R: *Pediatric Practice: Cardiology*: www.accesspediatrics.com

- **Redo Sternotomy**
- **Requires Cardiopulmonary Bypass**
- **Duration of Procedure: 2-3 hours**
- **Hospital Stay: 2-4 days**
- **Mortality Risk: <1%**

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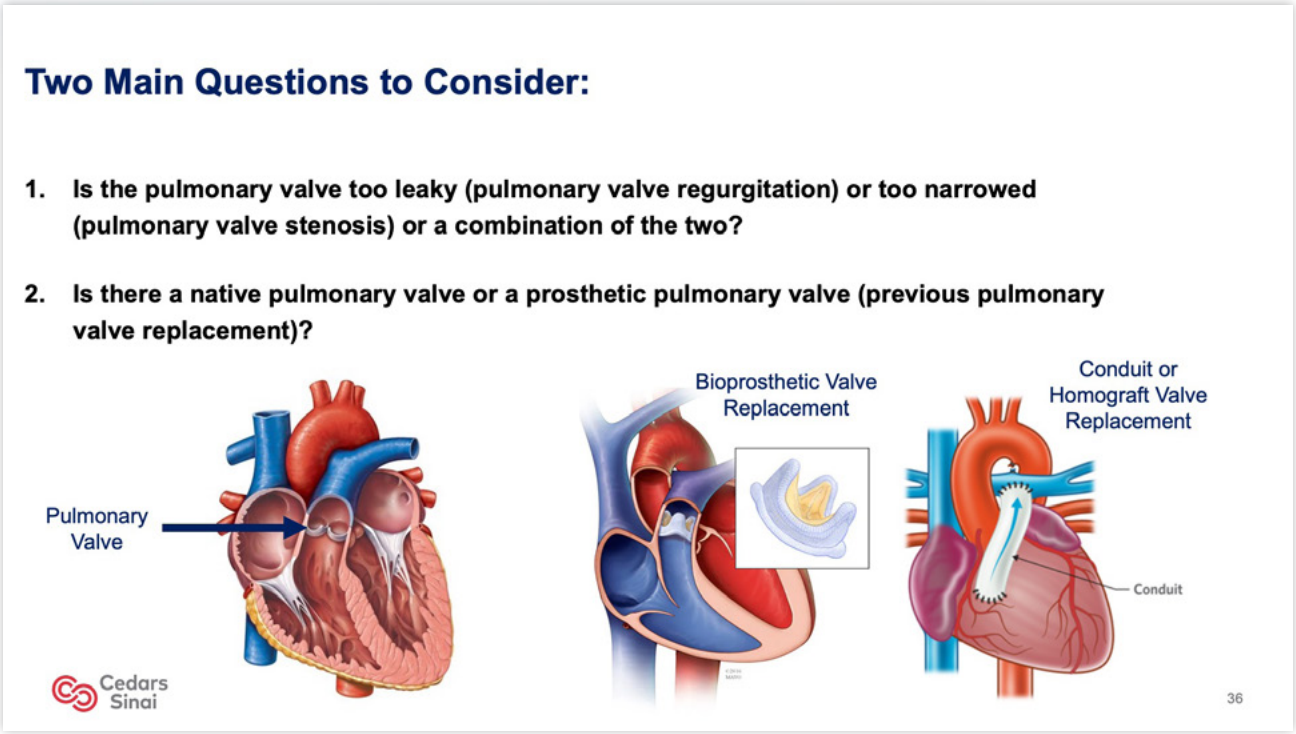
The surgery, this is just really short but it's very similar to pulmonary valve. It is a common surgery that we do. It's a reduced sternotomy, again requires the heart/lung bypass machine. The procedure takes about two to three hours and generally, the hospital stay is about three days with a very, very low mortality risk.

All right. With that, I'm going to pass it on to Dr. Tompkins so she can tell us how these patients do as they continue to grow.

Adult Pulmonary Valve Disease

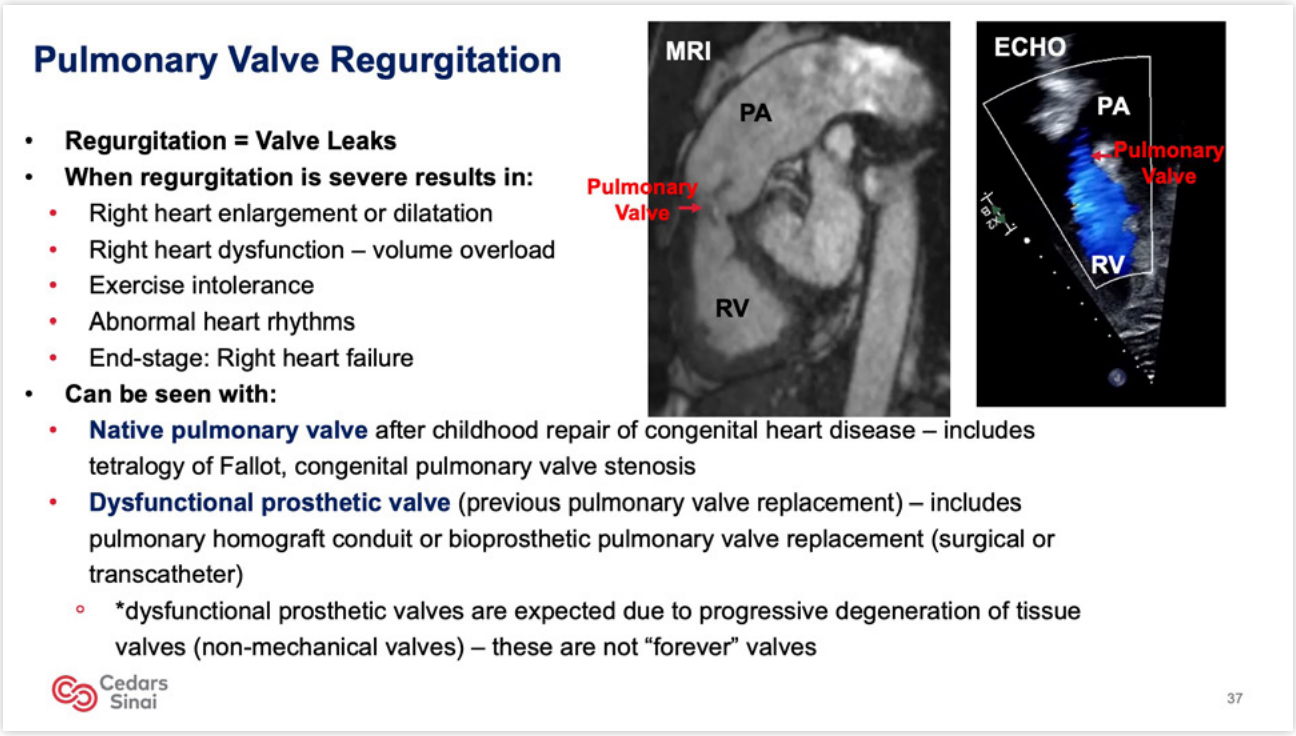
Dr. Rose Tompkins: Thank you so much, Dr. Viegas. So Dr. Pruetz and Dr. Viegas had really planned to show the landscape, if you will, of the patient population that we start seeing as patients age and grow up and come into the adult clinic.

For most of the patients that I see that I'm evaluating for pulmonary valve disease, by and large, are going to be congenital heart patients, meaning that the pulmonary valve became dysfunctional related to a born disease, that they came with a congenital heart, less so for acquired but does exist, so we may have some cases of that. The patient may be getting a valve infection. You can see that even with intervention, many of those valves, as Dr. Viegas pointed out, are not forever valves. We do need to keep a close eye and keep people engaged in care because they may need that re-intervention and trying to figure out the timing.



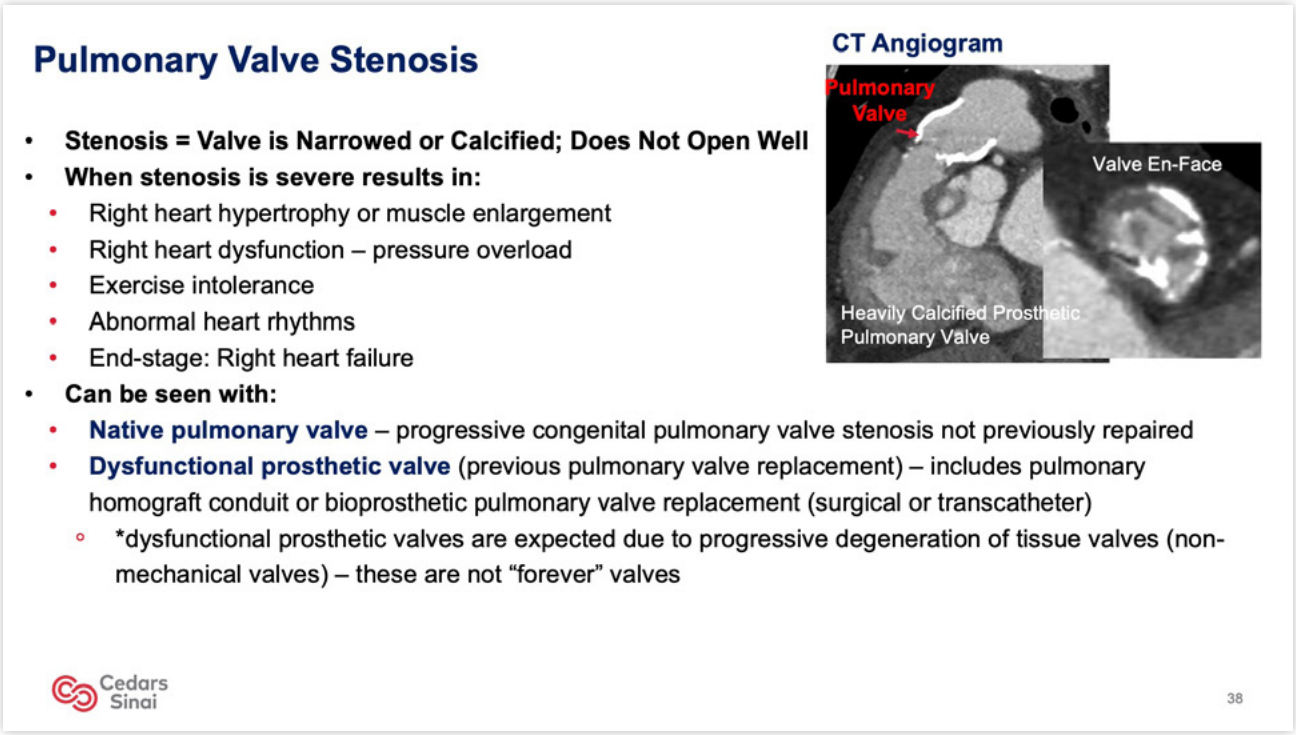
There's two main questions that I really consider when I'm evaluating a patient when I'm looking specifically at the pulmonary valve. Number one is what's the function of that valve? Is it too leaky, meaning that it's starting to develop severe regurgitation, or is it too narrowed, meaning more severe stenosis or a combination of the two? Then I'm looking at is it their native pulmonary valve or is there a prosthetic pulmonary valve in place? Have they already visited my surgical or interventional colleague? If so, I'm going to be thinking a little bit differently about their function and potential interventions down the line based on those questions.

Pulmonary Valve Regurgitation



Dr. Rose Tompkins: Okay, so starting off with pulmonary valve regurgitation, so regurgitation equals leak, really that the valve is not closing well and blood is able to go backwards, if you will, into the right ventricle instead of all the blood going forward out to the lungs. What this is going to result in over time is right heart enlargement or dilatation and can eventually lead to dysfunction. This is because it's a volume overload. That heart is not meant to carry that much volume over time. Patients may start to experience symptoms of exercise intolerance when really their stamina is not able to keep up, abnormal heart rhythms. End-stage is really something we call right heart failure where they may be retaining a lot of fluid on the body, really not feeling well, and even having symptoms at rest. Adam, if you advance, just going to show some examples of how we evaluate the pulmonary valve.

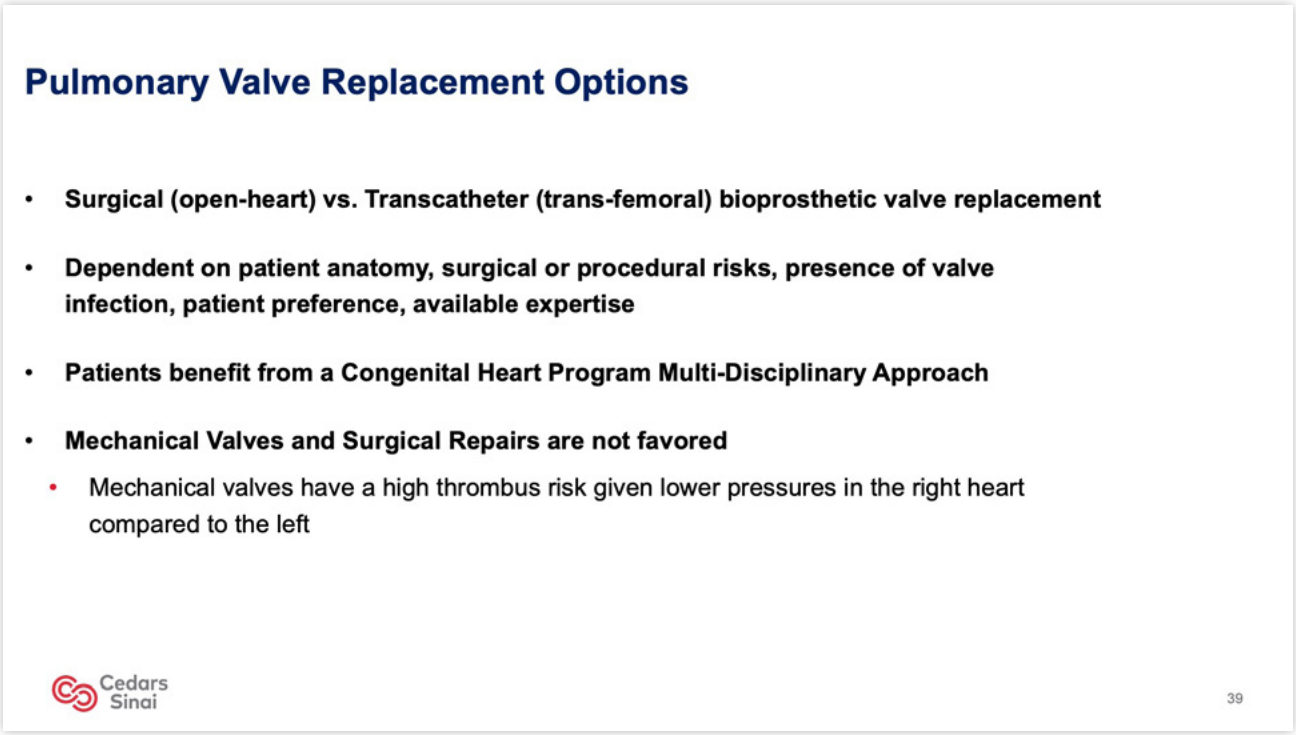
Pulmonary Valve Stenosis



Dr. Rose Tompkins: So our workhorses are really the echocardiogram and the cardiac MRI. I just tried to label here on the MRI image where the pulmonary valve is. You can see above that is the pulmonary artery and below that is the right ventricle. We can see that this is a leaflet that's not sealing well, and so there's a lot of backflow coming into the right ventricle. By MRI, we're able to get more quantification and determine regurgitative fraction. That's how we help determine severity. Then on the echo, kind of a similar image but you can see more color there. There's this whole rainbow. You shouldn't be seeing a rainbow, so what that's implying is there's to and fro flow across that valve and really there is no seal at all. It's almost like an unguarded orifice. There's really not any pulmonary valve leaflet tissue, so that's a pretty extreme example of severe regurgitation.

Now, children live this way for quite a while but eventually, that will catch up with them in adulthood. They'll start to manifest those indications that I mentioned and why it becomes important to consider timing of intervention.

Pulmonary Valve Replacement Options



Dr. Rose Tompkins: So with regurgitation, so can be the native pulmonary valve and this is often after a child had repair congenital heart disease. Most commonly, it's Tetralogy of Fallot. As Dr. Pruetz mentioned, if we're doing things like a transannular patch, we may not leave much pulmonary valve tissue but they do fine with that if they don't have any stenosis. Eventually, that regurgitation, like I mentioned, will catch up with them in adulthood, or congenital pulmonary valve stenosis that might might underly a surgical or balloon valvuloplasty where they enlarge the valve, again, alleviating any of the stenosis or blockage to blood flow but then they're left with regurgitation that does take a few decades where we start thinking about intervention at that time.

Now the next is dysfunctional prosthetic valve, and I'm meaning a previous pulmonary valve replacement. This can include a vast array of pulmonary homograft conduits or all the other different conduits that Dr. Viegas had mentioned, in addition to the surgical bioprosthetic pulmonary valve replacements that can be either surgical or transcatheter, which Dr. Nageotte will be going through shortly. Dysfunctional, again, this is really important with these essential prosthetic valves. The reason is there is going to be progressive wear and tear or tissue degeneration. These are nonmechanical valves and again, these are not forever valves, so this is all anticipated and expected.

So then other conditions, pulmonary valve stenosis, so this is where the valve is too narrowed and often can become calcified. It's not opening well. That stenosis is going to result in similar manifestations as regurgitation but instead of being a volume overload of the ventricle, it's going to be more of a pressure overload. The ventricle has to work that much harder to squeeze blood flow through that little narrowed passageway. That's going to lead to right heart hypertrophy or muscle enlargement and then can also start to cause right heart dysfunction. Patients symptomatically will have similar symptoms as we'll see with severe regurgitation and including that exercise intolerance, abnormal heart rhythms, and then the end-stage is quite similar as heart failure, again manifesting as overload and feeling pretty symptomatic at rest and not doing well.

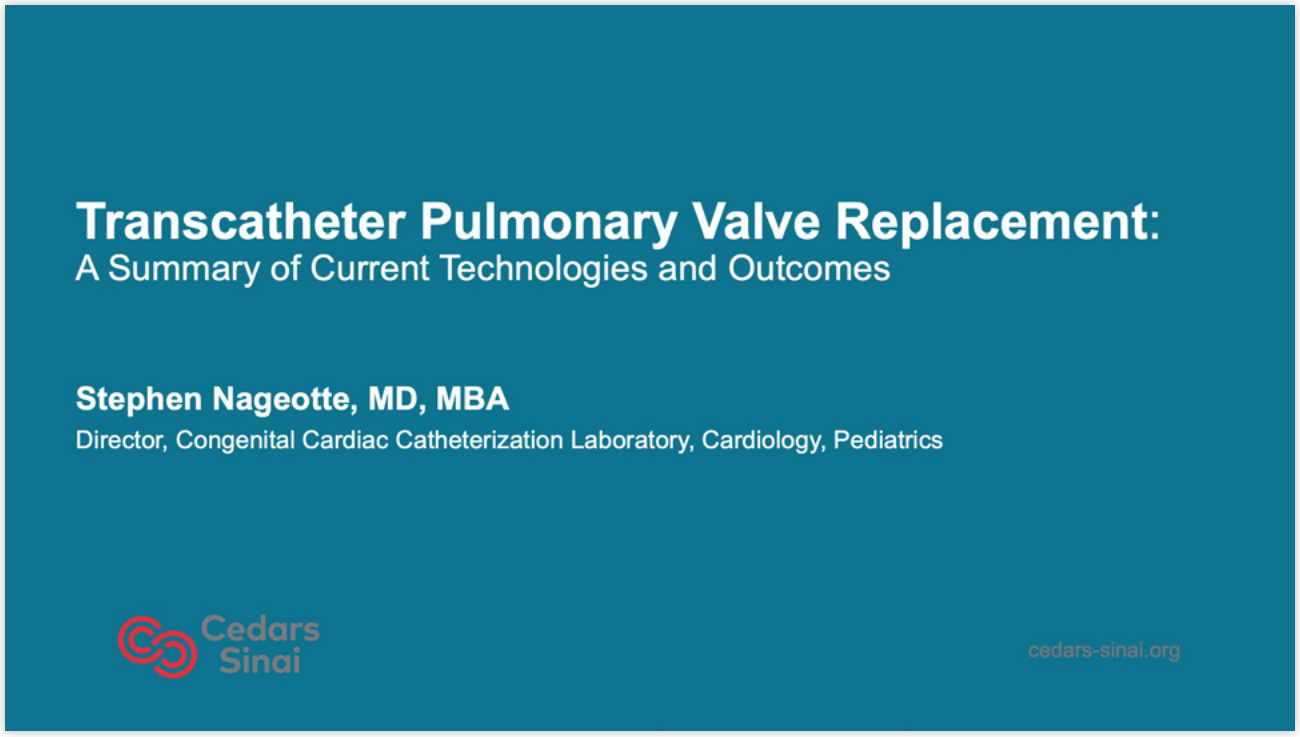
I show a classic picture here on a CT really highlighting the brightness, so that brightness is calcium. What we can see here is a prior prosthetic pulmonary valve that had been put in a patient. This is the wear and tear that can happen to these valves over time. This is a degeneration or the calcification. Then that other view of the valve en face really showing how that opening really gets narrowed down, so not a lot of area then for that blood to push through and go out to the lungs. I always equate to traffic, for some reason, being in Los Angeles. We're on a major interstate at 404, and instead of a five-lane highway, maybe we're going down to a two or a one-lane highway and then that's when we really need to go in and intervene.

So similarly, we can see this with native pulmonary valves. This could be progressive pulmonary valve stenosis that wasn't previously repaired but was advancing as the patient is getting older and may ultimately need something done. More commonly, dysfunctional prosthetic valves are probably by and large where we see more stenosis in the adult clinic. This is going to include pulmonary homograft conduit or bioprosthetic pulmonary valves, again, surgical or transcatheter and again, that little caveat. This is all anticipated and things that we are looking for, especially as patients are nearing that 10 to 15 years or beyond, as Dr. Viegas mentioned, because we're anticipating that's a typical life span of many of these valves.

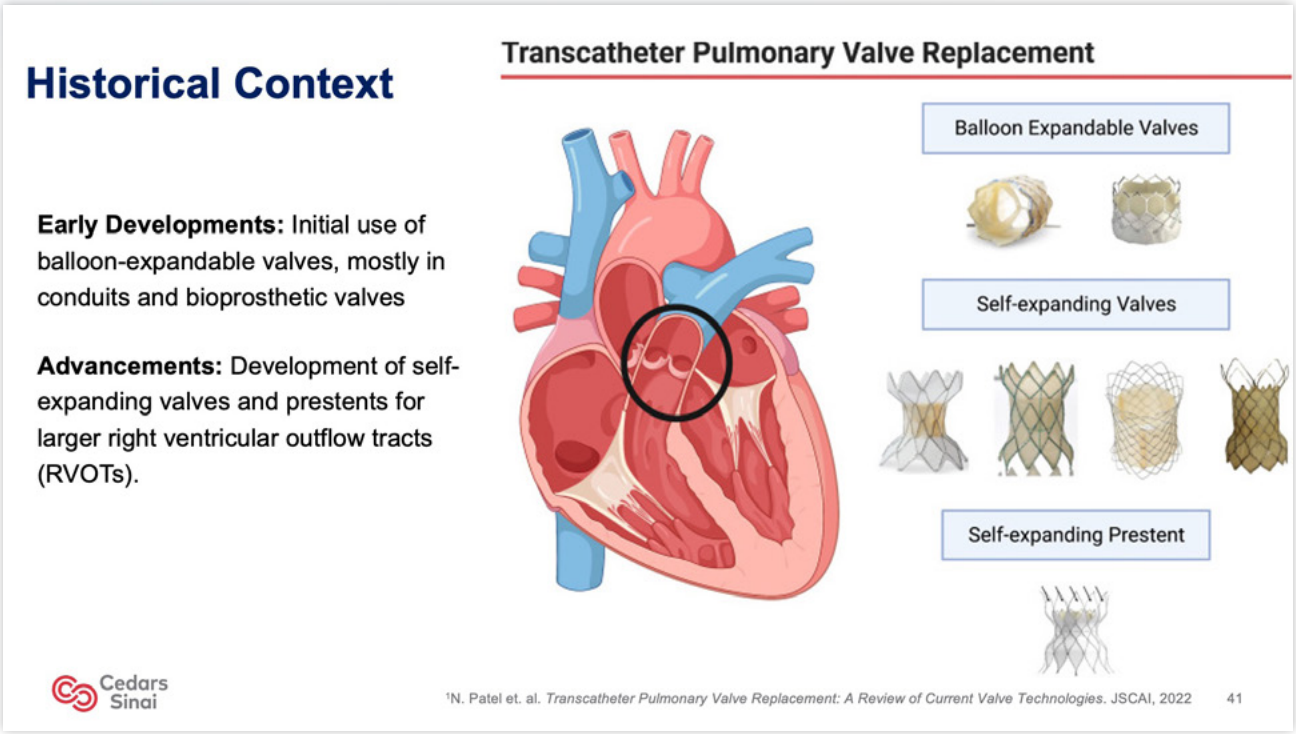
So when we think about options, once we have determined patient has met indication to get a new pulmonary valve, really it's two main avenues. It's either surgical, which is open heart, or transcatheter, which is transfemoral through the groin. So we're very fortunate now in 2025 to have a lot more options form a transcatheter perspective that we get to think about in addition to all the surgical options Dr. Viegas went through. Dr. Nageotte's going to mention this a bit, but this is really important to understand this landscape has changed so dramatically really in the past 15 years and continues to evolve with new devices and approaches as recently as two years ago.

This is truly a remarkable field and why the benefit of coming to a place like Cedars with a multidisciplinary team that includes all the experts that you see now. We really go through all of the different nuances for determining the best valve type for patient. It's going to be based on anatomy, the surgical or procedural risks, whether or not there's a valve infection, a patient preference, and then obviously the expertise that's there. This is why again, it's not a one-size-fits-all by any means for our patients. I do want to highlight again, mechanical valves and surgical repairs really aren't favored. An issue with mechanical valves, is flow of pressure on the right side of the heart relative to the left side, which his mitral and aortic valves which are much more common to have mechanical options. The risk of that valve thrombosing in the pulmonary position, even with anticoagulation, is still quite high. So that's why it is not standard of care to do these other options and why really it's focusing on the valves that you're hearing about today.

Transcatheter Pulmonary Valve Replacement

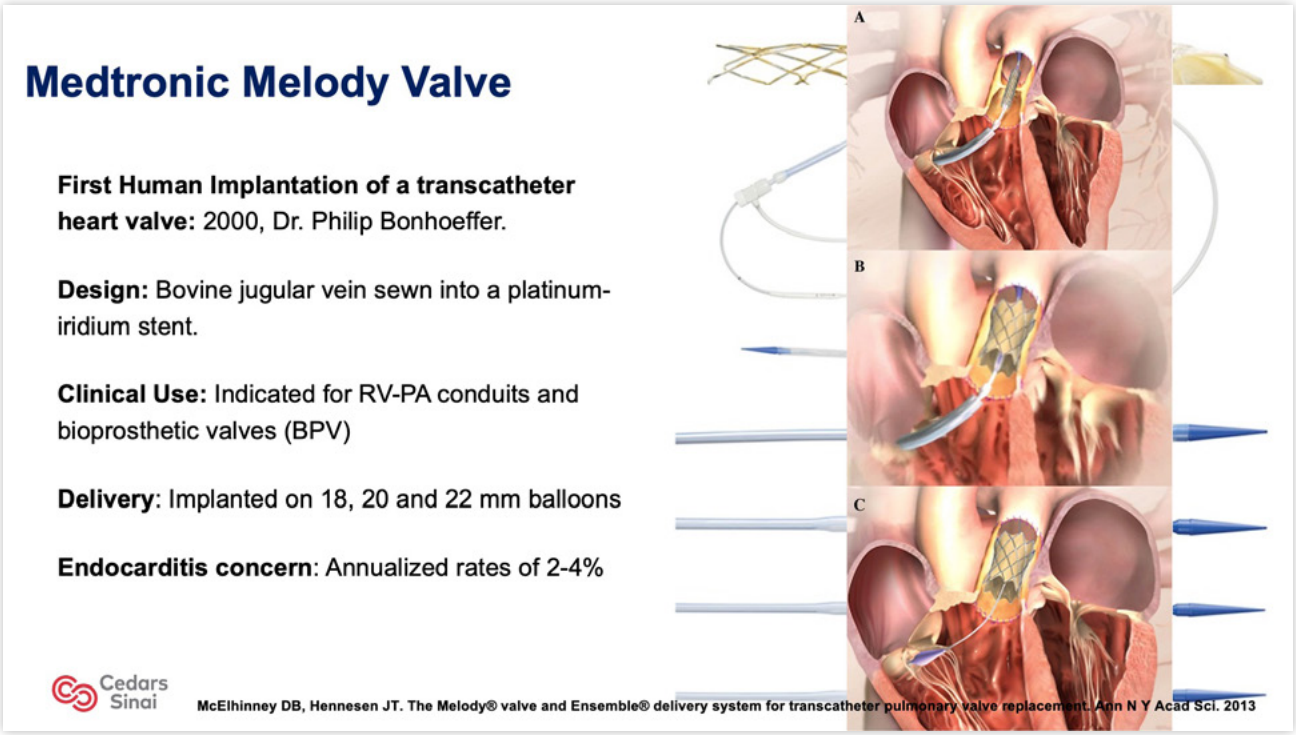


Dr. Stephen Nageotte: Awesome, thank you so much, Dr. Tompkins. So yeah, if you want to hit the next slide, I'll be going over the transcatheter pulmonary valve replacement options. When we're talking about transcatheter, what we mean by that is that what are nonsurgical options? When we say transcatheter, we utilize catheters or soft tubes to enter through the veins, usually through the leg but sometimes through the neck to maneuver through the heart and get into position across the pulmonary valve. We do this on a beating heart, so we're not needing to stop the heart or anything like that. If we're successful in replacing the pulmonary valve, usually the patients will stay overnight and most likely go home the next morning after a period of some observation. Usually it is not a particularly painful procedure, and the morbidity is relatively low for patients who are a good candidate for it.



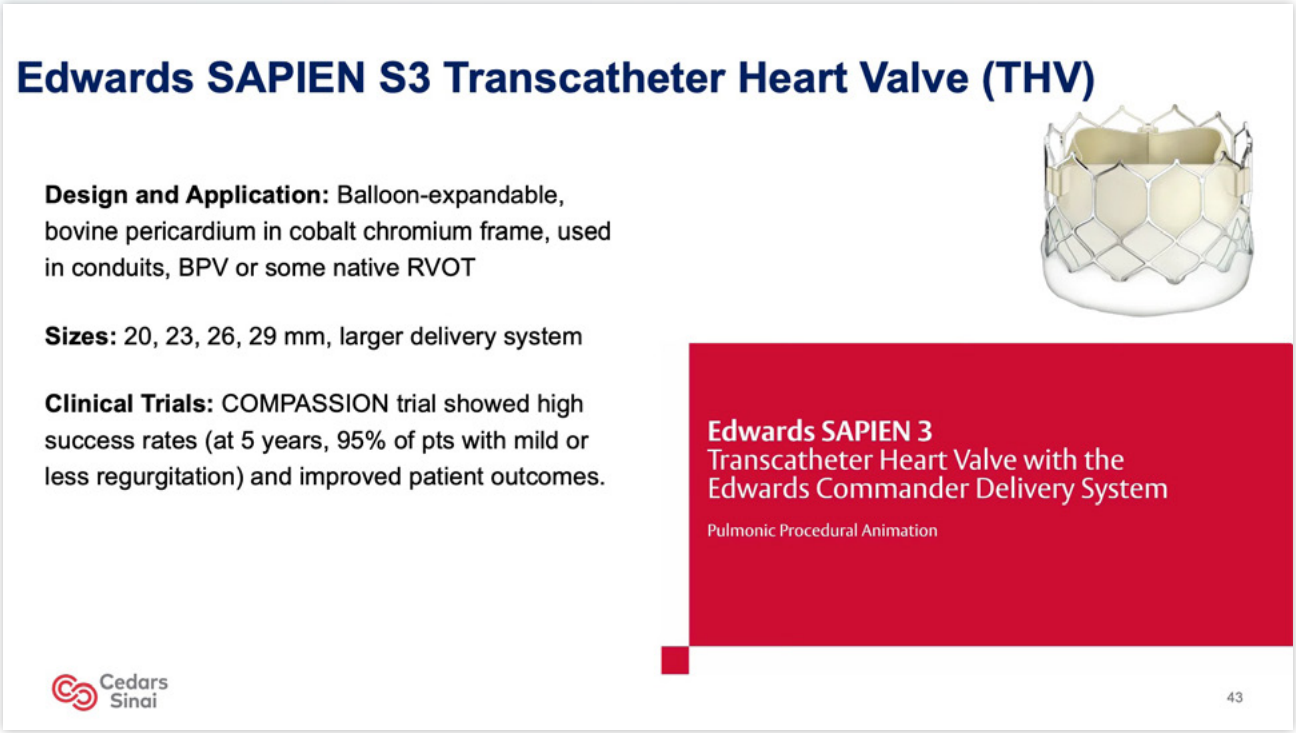
As Dr. Tompkins was mentioning, really the landscape has completely evolved over the past 15 years. Over the past five years, it's continued to evolve. What we can offer now is significantly different. This landscape will continue to evolve into the future.

Types of Pulmonary Replacement Valves



Dr. Stephen Nageotte: So looking at the historical context on the right side of the screen, what you'll see is basically the full spectrum of all the transcatheter pulmonary valves that we have. At the top, we have the two balloon expandable valves, which are the Medtronic Melody valve and the Edward SAPIEN valve. Then we have some self-expanding valves. Historically, we first started with balloon expandable valves. Our targets with those were mostly within these conduits or bioprosthetic valves, but we found that about 75% of patients were not able to be treated with balloon-expandable valves alone because the outflow tracks were so large. That really pushed for the development of self-expanding valves.

Over the past several years, the number of self-expanding valves continues to develop. There, you see the Harmony valve and then at the bottom, you see the Altera self-expanding pre-stent, which are the two valves that are available in America, but I put three other valves. There are three other valves in that picture that are international valves that I'll touch on at the end as well.



So the first transcatheter valve, period, whether it's pulmonic or aortic, implanted was the Melody valve, and that was implanted in the year 2000 by Dr. Bonhoeffer. If you could advance the animation once, this is how they are made. You have a platinum iridium stent, and they take the bovine jugular vein of a cow and they sew that into the stent. This is hand-sewed into place. This is similar to the Contegra graft that Dr. Viegas was talking about earlier. This comes in sizes that are implanted between 18 and 22 millimeters typically in conduits or within bioprosthetic valves, unless frequently in a native valve tract. These are outstanding valves and have wonderful durability.

What we've noticed over time is they seem to have higher rates of endocarditis, which is becoming more and more of a concern. Wherever possible, our field has actually started to move away from utilizing these vales unless, for the right patient, it's still a good option.

So this is what they look like on their ensemble or delivery system. You can see that is how they go in and then on the very bottom of that screen, you can see the balloon expanding and then slowly deploying the valve. Then if you can advance the animation one more, this is the same kind of thing just within a heart. You get the valve in position; you inflate the balloon. Then you deflate the balloon and take everything out and the valve stays in position.

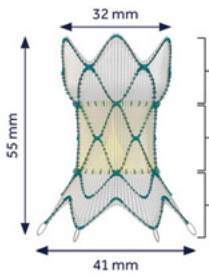
Medtronic Harmony Valve

Harmony Valve: Self-expanding valve for native or patched RVOTs.

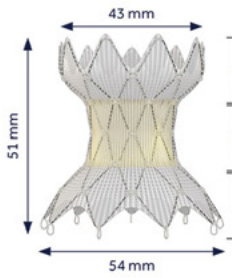
Design: Polyester knitted on nitinol wire frame with porcine pericardial leaflets.

Larger, self-expanding frame accommodates larger "landing zones"

Outcomes: Demonstrated low PR (<4% at 3 years) and high procedural success (>96%)[2].



Harmony TPV 22 PA section	Anatomical Size (perimeter-derived diameter)
Outflow — Distal PA/Bifurcation	22–28 mm
Valve Housing	> 22 mm
Inflow — Proximal PA/RVOT	23–39 mm



Harmony TPV 25 PA section	Anatomical Size (perimeter-derived diameter)
Outflow — Distal PA/Bifurcation	25–38 mm
Valve Housing	> 25 mm
Inflow — Proximal PA/RVOT	32–48 mm

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[1]https://www.acc.org/Latest-in-Cardiology/Articles/2023/01/19/13/08/Advancements-in-Percutaneous-Pulmonary-Valve-Therapeutics

[2] Morray et. Al. *Midterm Outcomes in a Pooled Cohort of Harmony Transcatheter Pulmonary Valve Recipients.* Circulation: Cardiovascular Interventions. 2025

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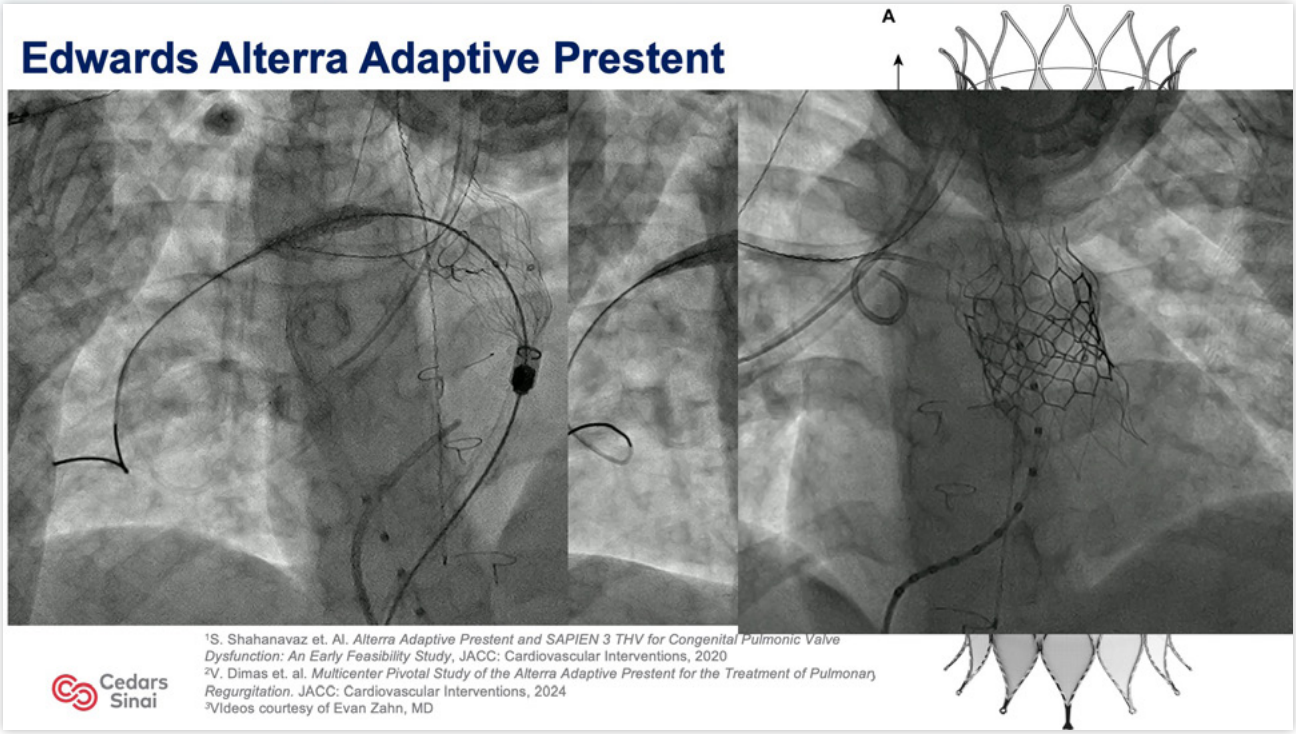
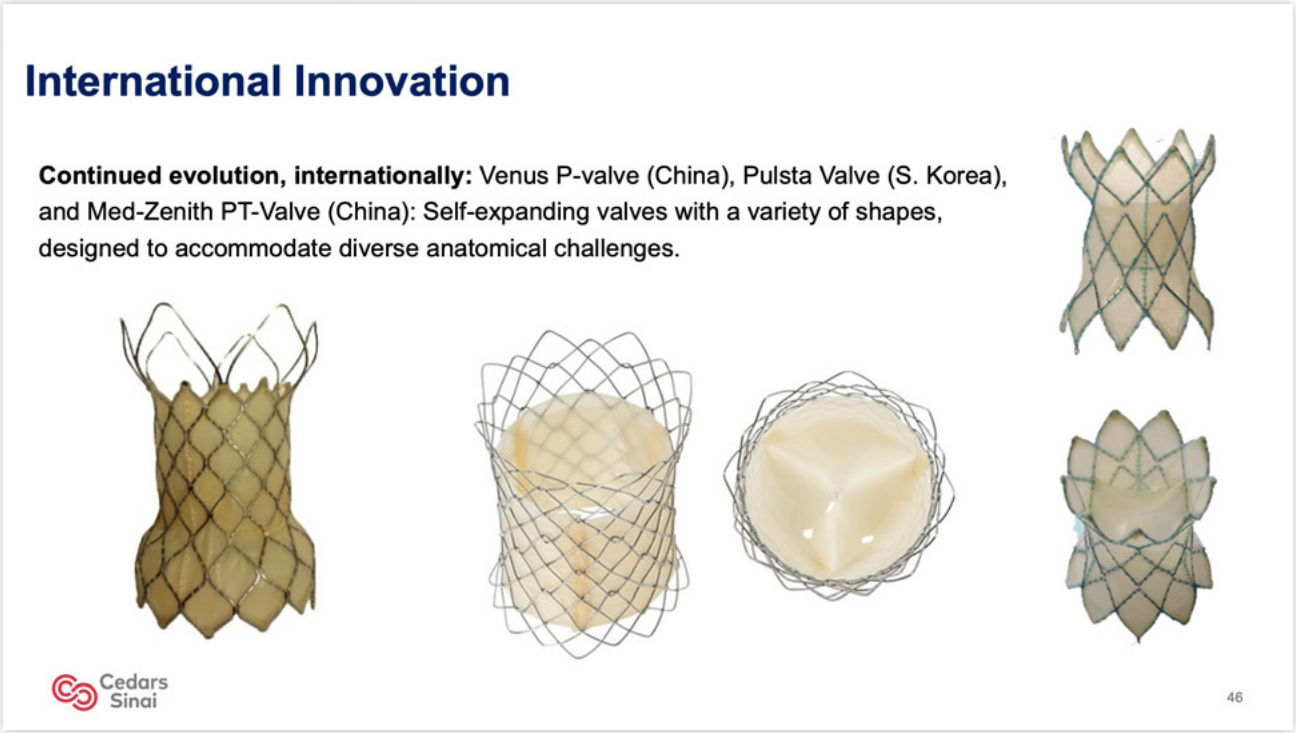
So more frequently now, we've gone more often to the SAPIEN valve, which is a valve that is very, very frequently used in adults for transcatheter aortic valve replacement. This is a balloon-expandable valve with bovine pericardial leaflets in a cobalt chromium frame. This is also used similarly in conduits by prosthetic valves or actually now in some native right ventricular outflow tracks. It's a larger delivery system, but the size of the valve is also much larger, coming between 20, 23, 26, and 29 millimeters. You see in the animation how we are able to manipulate the catheter up through the heart. This is a picture coming from the femoral vein up the inferior vena cava through the heart, and then we deploy the heart actually across the pulmonary valve once in position.

This has not been utilized in the pulmonary position for all that long, so we only have good five-year data. The five-year data is actually excellent with 95% of patients with mild or less regurgitation and significant improvement in patient outcomes in terms of their functional assessment. In those patients in whom SAPIEN valve is an option, it's proven to be an excellent option in these patients. We only need to follow with time to make sure that long-term durability appears to last as long as it's seeming to in the aortic position.

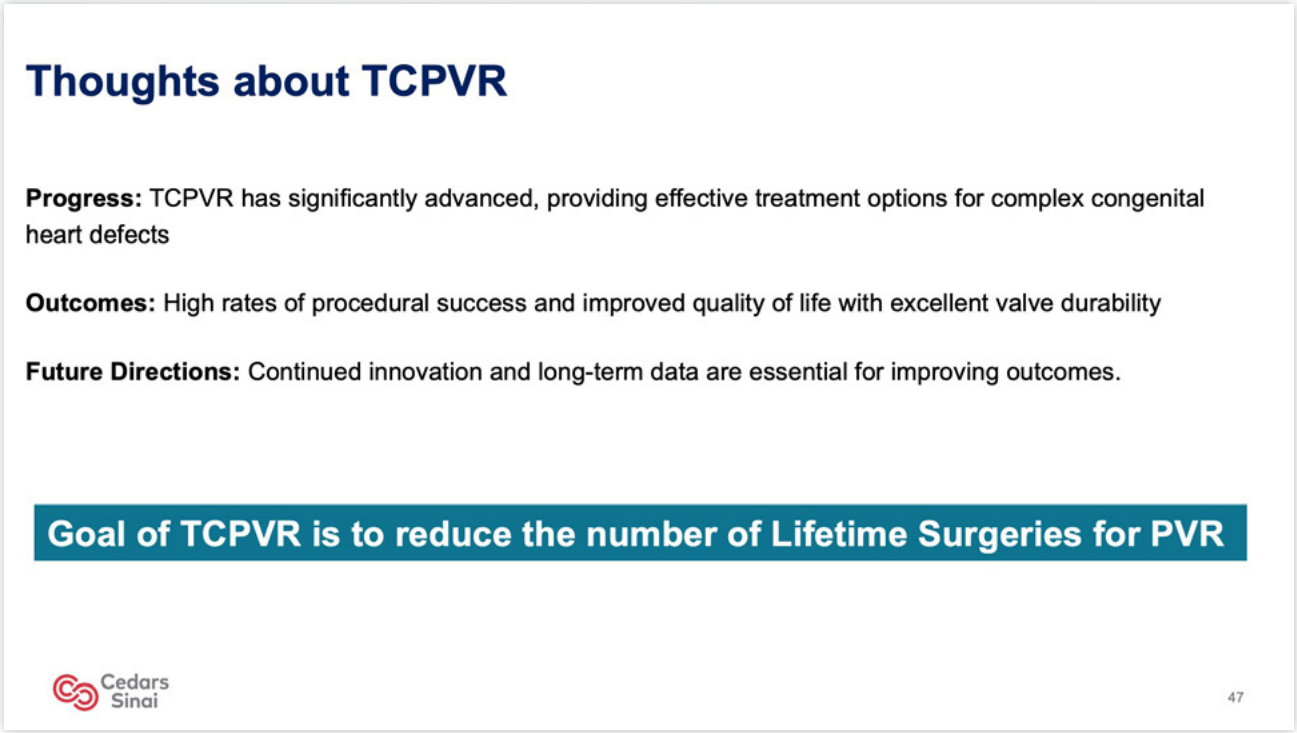


So those first two were what we call balloon-expandable which is what the animation was showing, which means these valves are mounted on the outside of a balloon. They go into position and we inflate the balloon. Those valves only go up to 29 millimeters and what we're finding is that many patients actually need much larger valves. Those valves would not be able to seed safely into the patient. There's been the development of what we now call self-expanding valves, meaning when they're uncovered, the valves pop open and are shaped – most of them are shaped like an hourglass. These are designed to go in the native outflow tracks or patched outflow tracks of patients with pulmonary valve disease.

This is the Medtronic Harmony valve. This is one example of one of these self-expanding valve. It has a polyester – polyester's knitted onto a nitinol wire frame and the valve itself – it's not really shown here. It's on the inside of the valve. It's porcine pericardial leaflets. These are designed to accommodate much larger landing zones. As well, these have not been implanted for very long, either, so we only have about three to four year outcomes. Those outcomes are demonstrating low levels of pulmonary regurgitation, less than 4%, and very high rates of procedural success. With these procedures, the whole name of the game is pre-procedural planning, so utilizing MRI to figure out which patients are the right timing of when they need a pulmonary valve replacement and then CT scans as well in addition to MRI typically in order to plan our procedure and see who would be a good candidate. Again, technically, the technical success rates are so high because we spend so long ahead of the procedure making sure we're determining who is a candidate for this valve and who actually would not be a great candidate for it.



Again, this is just showing the inflow. Advance again, please. Just showing the sizes, it's much larger getting up to about 48 millimeters or 39 millimeters with the smaller Harmony valve versus the 29 millimeters with the SAPEIN. These can treat much, much larger outflow tracks in patients.



This is the Edwards or this is a pre-stent in which we put a SAPIEN valve. This is called the Alterra pre-stent. Very, very similar idea to the Harmony valve. There is certain pros and cons to each of those different valves. The design, though, is similar. This is self-expanding nitinol wire with a PET covering as opposed to polyester, and it's designed to remodel in the right ventricular outflow track in which to land one of those SAPIEN S-3s I was showing two slides ago. Again, this is for larger – this is larger to accommodate the larger landing zones. Additionally, the outcomes have been excellent with very low rates of pulmonic regurgitation and high rates of procedural success. If you could advance, I have some videos showing the implantation process.

So this is inside of the right ventricular outflow track where the Alterra is being released there. You can see at the beginning here at the bottom of it being constrained and we then slowly release the pre-stent. In the middle of the pre-stent, you can see some dots. If you hit the – if you advance it one, please, now we have a SAPIEN valve that's then being implanted within the Alterra which has remodeled the outflow track so that we can put a valve inside it. That SAPIEN valve is being expanded right now or right about now. Then perfect, if you could advance it one more. This is a final picture showing that there's no regurgitation after the valve has been implanted.

In the interest of time, I'm going to skip through this. These are just some international innovations. There's three different valves, the Venus P-valve, the Pulsta, and the Zenith valve from China and Korea, very, very similar idea to the valves we have here in the United States. The more valve options we have, the better for us, so also keeping it – making sure we're keeping an eye on these valves and seeing their durability.

So just to summarize transcatheter pulmonary valve replacement has significantly advanced. The number of treatment options for which patients has come a long way over the past 15 years and even over the past few years has continued to evolve and I anticipate continued evolution in this field. High rates of procedural success, improvement of quality of life with the goal of decreasing the total number of medial sternotomies and surgeries that are needed. What the goal of all of this is to try to pick the right option for each individualized patient to set you up for a lifetime of success, whether that be surgical or transcatheter, really going to a center that works as a team and has all the options available.

All right, perfect, next slide. You can just advance it one more now. We can go to the case examples. I'll kick it to Dr. Pruetz for the first one.

Patient Case Examples

Dr. Jay Pruetz: All right, this is going great so far. So pediatric case of tetralogy of Fallot with pulmonary atresia means that the child was born without a pulmonary valve.

Pediatric Case: Tetralogy of Fallot with Pulmonary Atresia

Newborn born with Tetralogy of Fallot with Pulmonary Atresia

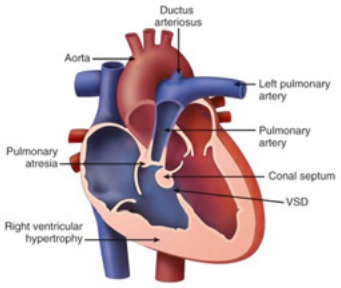
- No outflow for the blood to enter the pulmonary arteries
- Underwent neonatal intervention including stenting of the patent ductus arteriosus (PDA) to provide a source of blood flow into her pulmonary arteries to allow her to grow before more definitive surgical repair

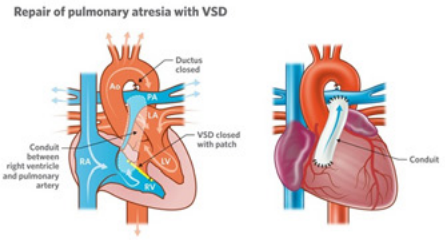
6 months-old underwent complete TOF repair

- VSD patch closure, RV muscle bundle resection, and **13 mm RV to PA conduit (aorta homograft)**, and take-down of PDA and stent

3 years-old developed RV-PA conduit stenosis

- Multi-disciplinary discussion – patient taken to cath lab for conduit balloon angioplasty and stenting to relieve stenosis and delay surgical re-intervention





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It's completely obstructed. In these scenarios, we have no outflow track. From the right heart and lungs, you have to provide some source of pulmonary blood flow. In this case, we used a fetal structure called the patent ductus arteriosus. We kept it open with the medication, and then we put a stent in there like one of the stents that Dr. Nageotte showed you but much smaller to kind of give flow for a temporary time period to the baby's lungs so that they can maintain oxygen levels.

This is the whole idea of stage repair. By stenting the ductus, then we can get this child out to six months of age before actually having to do surgery, at which time, Dr. Viegas can perform a complete TOF repair by patch-closing the VSD shut and placing an RV to PA conduit. In this case, it was an aortic homograft. It was approximately 13 millimeters in diameter. They take down the PDA and the stent at that time because they're no longer needed.

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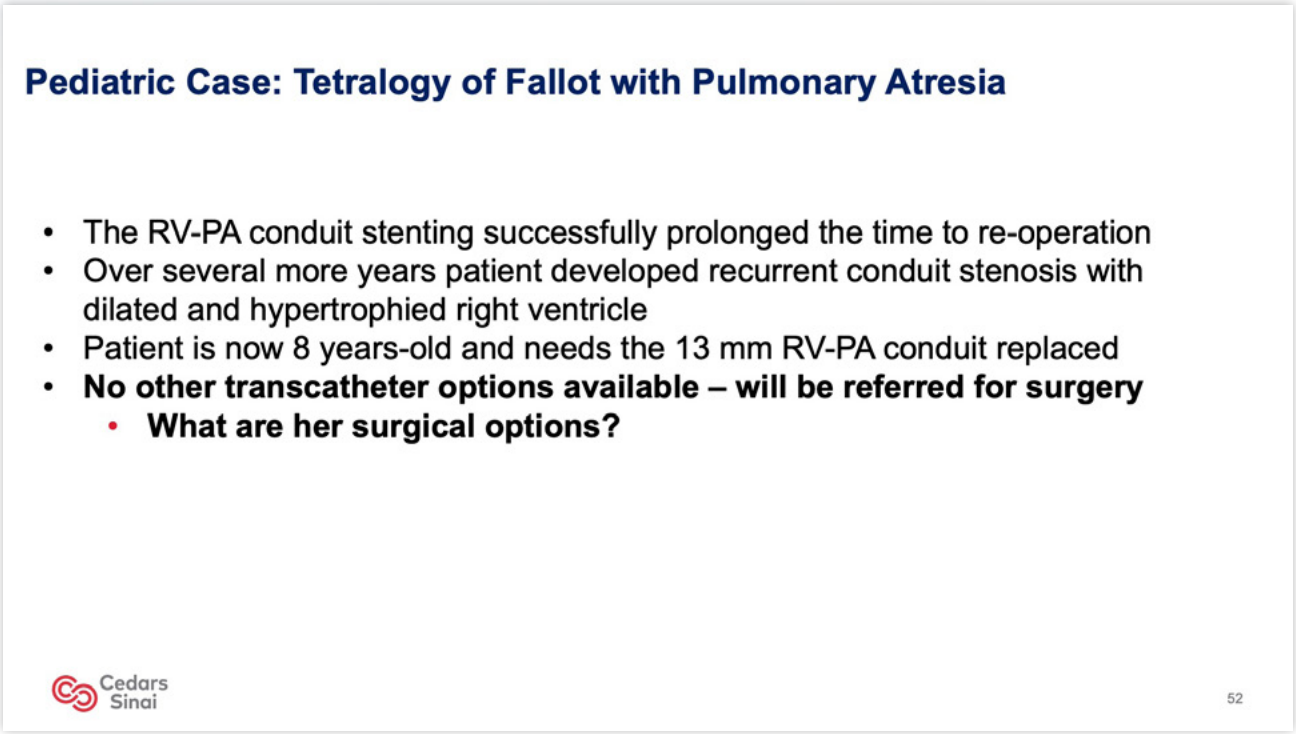
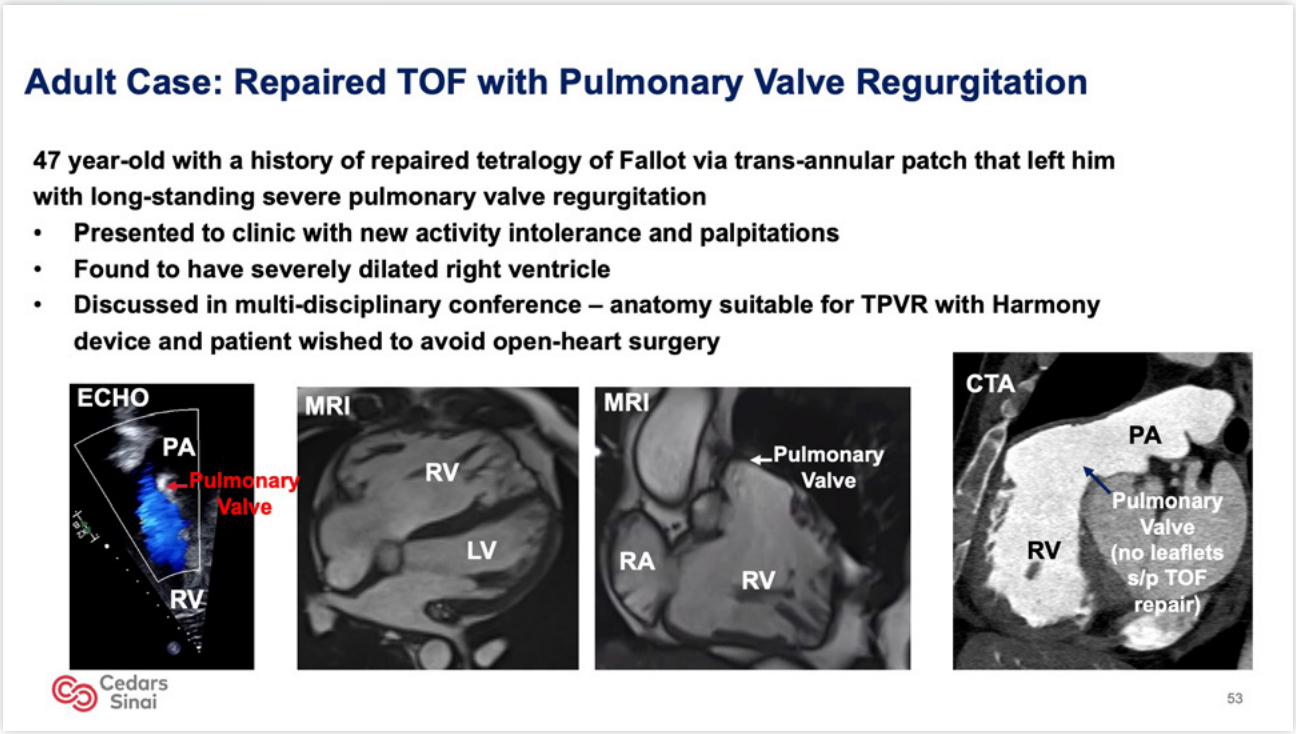
Then this child progresses to about three years old. Unfortunately, the largest size conduit that could be fit in at that time based on the patient's size was 13 millimeters. Now the patient's growing rapidly and starting to develop conduit stenosis. So you don't want to have to take that patient back into surgery, so we're actually going to go to the cath lab now.

Oh, actually before we go to the cath lab, we're going to do – click another time. We'll do some more investigation. We can do the 3D reconstruction of the pulmonary arteries and then stenting within the conduit, which actually gave the child more time. So by not having to replace the valve at that time, we actually stented open the conduit to allow more flow to the lungs temporarily.



Then eventually, this child now at eight years old, even with the stent in place, there's now with continued growth more obstruction. That right heart is starting to become dilated, thickened, so there's not a really great transcatheter option. This is a patient that at that point we would refer for surgical care and I think Dr. Viegas did a really nice job of going over the surgical options for that.



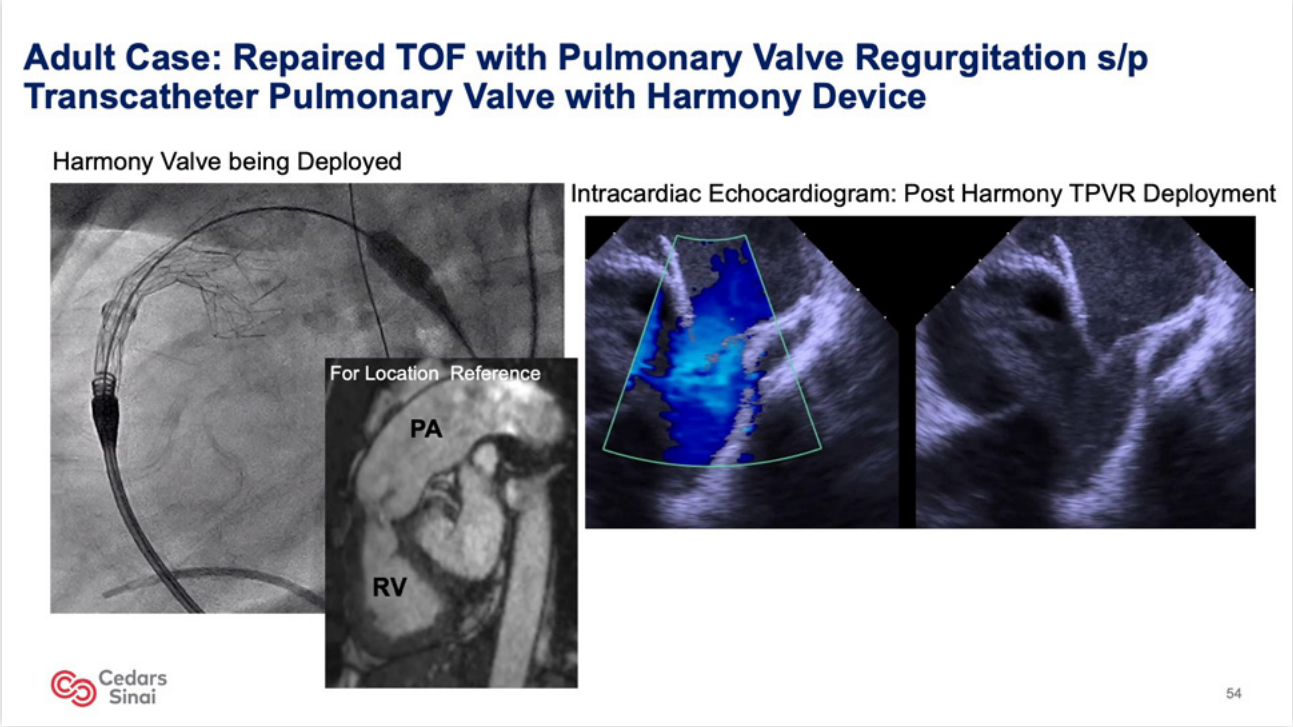
Dr. Rose Tompkins: Okay. I'll round it out with an adult example. So we have a repair tetralogy of Fallot patient coming to clinic with pulmonary valve regurgitation. He was repaired via transannular patch that left him with long-standing severe pulmonary leak or regurgitation. He came to clinic with new activity intolerance and palpitations, really not feeling well. He was found to have a severely dilated right ventricle.

So the echo image that you can see there on the left, again showing that rainbow of flow across the pulmonary valve, so really to and fro flow. If we look

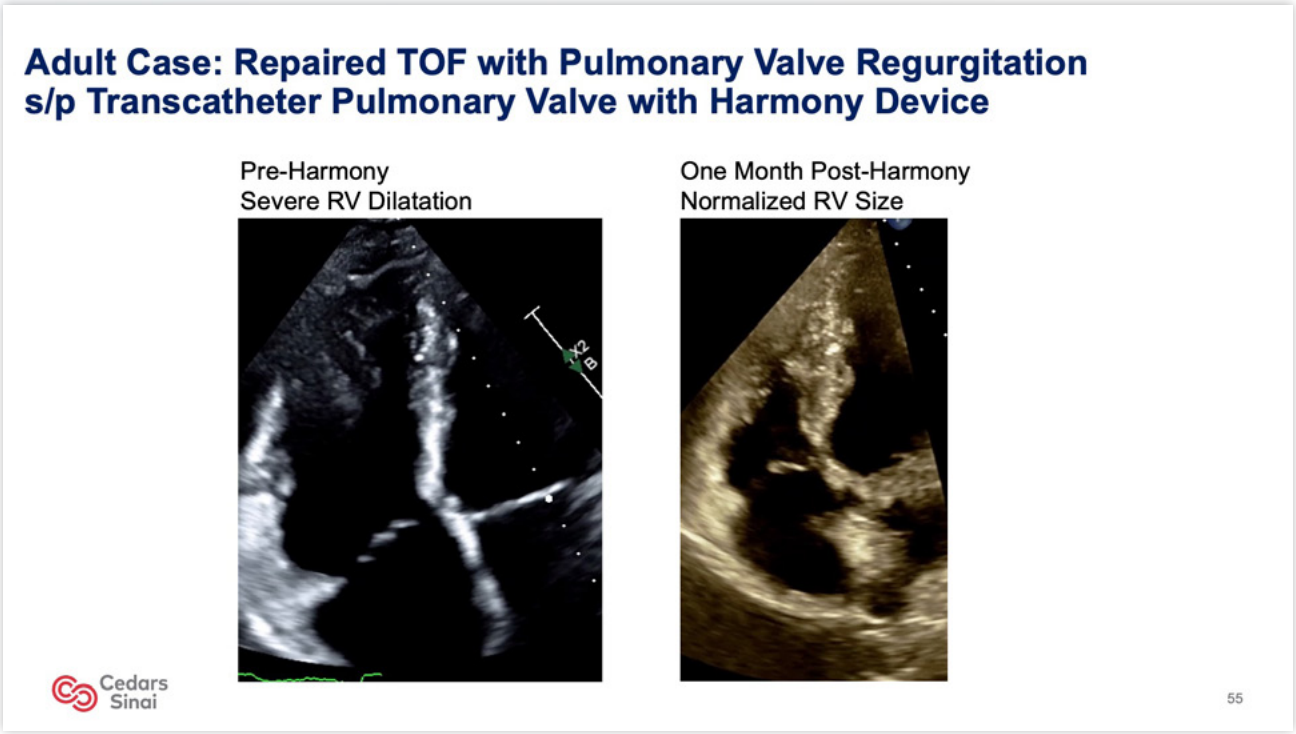
at the MRI next to that, I showed you the RV relative to the left – right ventricle relative to the left ventricle and it is significantly larger. It should actually be a bit smaller than the right ventricle, so letting you know how dilated that appears. Then on the MRI, a moving image, again we can see that to and fro flow across the pulmonary valve, that big right ventricle. Then on a CT angiogram, just because we have to get all the imaging, but I'll go why we did a CT in a moment. What's really striking is you can see there's no pulmonary valve leaflet tissue at all, so there's actually no pulmonary valve that was removed at the time of the transannular patch and complete repair of the tetralogy of Fallot.

At that point, he was a child. You can see the large patch actually at the top right above where the pulmonary valve would be. It's nice and open but it's quite dilated now, and that's going to play a role into some of the transcatheter options, as Dr. Nageotte mentioned, because with the balloon-expandable valves, there's no place for a valve like that to sit; there's no anchor point. So he really wouldn't have had transcatheter options historically and would have been referred for a surgical valve replacement.

However, being 2025, we were able to discuss all of this options and he was determined to be a candidate for the Harmony valve that we mentioned. The patient really wanted to avoid another open heart surgery. After all the careful evaluation, including the CT scan for us to determine anatomical suitability, Dr. Nageotte was able to deliver a Harmony valve there and have that one CT scan just for a location reference. You can see how that stent is sitting within the heart. On the image next to that, that's actually intracardiac echocardiogram, so I'm showing you all the bevy of ways we can evaluate the pulmonary valve. This is at the time the Harmony valve was released and look, he suddenly has beautiful prosthetic valve leaflets that look excellent. There is absolutely no leaks, so we don't see any rainbow of flow at the top of the screen, which would be back into the right ventricle. So it was an excellent procedural success, and the patient was able to go home the next day from the hospital with just a Band-Aid on the leg. So obviously a big change from an open heart and why these new valve technologies are so significant for this patient population and being able to have more options.



So he was seen in clinic about a month later, and so I have the echocardiogram on the left that shows that right ventricle really dilated before the Harmony valve implantation and then just a month later, you can visually really see how nicely there has been some reverse remodeling of the right ventricle, and that size has actually normalized. Patient is feeling excellent, cannot wait to go back to snowboarding this January and looking forward to that. Really exciting for him and exciting time to be in this field as we just have a lot of ways to be able to treat patients and really get them back on their way and having an amazing quality of life really for the long-term.



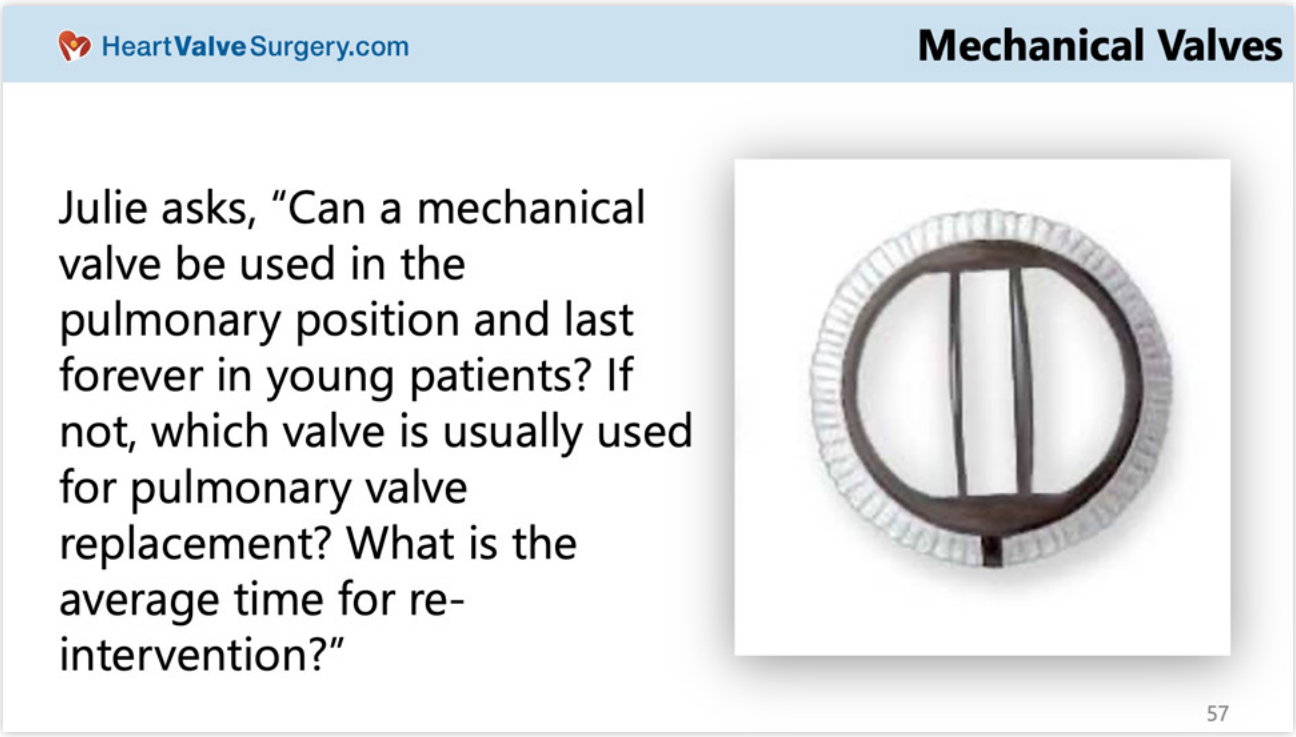
Now this patient will need to continue to see me, so he's not cured, repaired. That's something I always emphasize with my patients is you do need to stay engaged in care; we need to continue to keep an eye. As Dr. Nageotte mentioned, the Harmony valves, those were FDA-approved in 2023. So we don't have a lot of long-term data. We have some clinical trial data that's a few years out now. these values are performing quite well. However, we don't have the length of follow-up like we do for surgical valves. I do tell patients that's important that we keep an eye and they're going to teach us as first generation with these new devices of how they really do in the long-term. That's a little bit of the flipside of taking on new devices. There's just a little bit more uncertainty and unknown that we do discuss as part of our consenting process as we go through all these options with patients.

Okay, so I think with that, we're ready for Q&A.

Q&A

Adam Pick: Great. Well, thanks so much to the Cedars team. That was really fascinating. I love how you ended on the note with the snowboarder getting back onto the mountain. That is just a great way to end the formal prepared remarks and get right into the Q&A. We got some great questions.

Mechanical Valves



Julie sent me three questions, three emails about this question. She's from China. I think we just have to answer it explicitly, even though you talked about it earlier. "Can a mechanical valve be used in the pulmonary position and last forever in young patients? If not, which valve is usually used for pulmonary valve replacement? What is the average time for a re-intervention?"

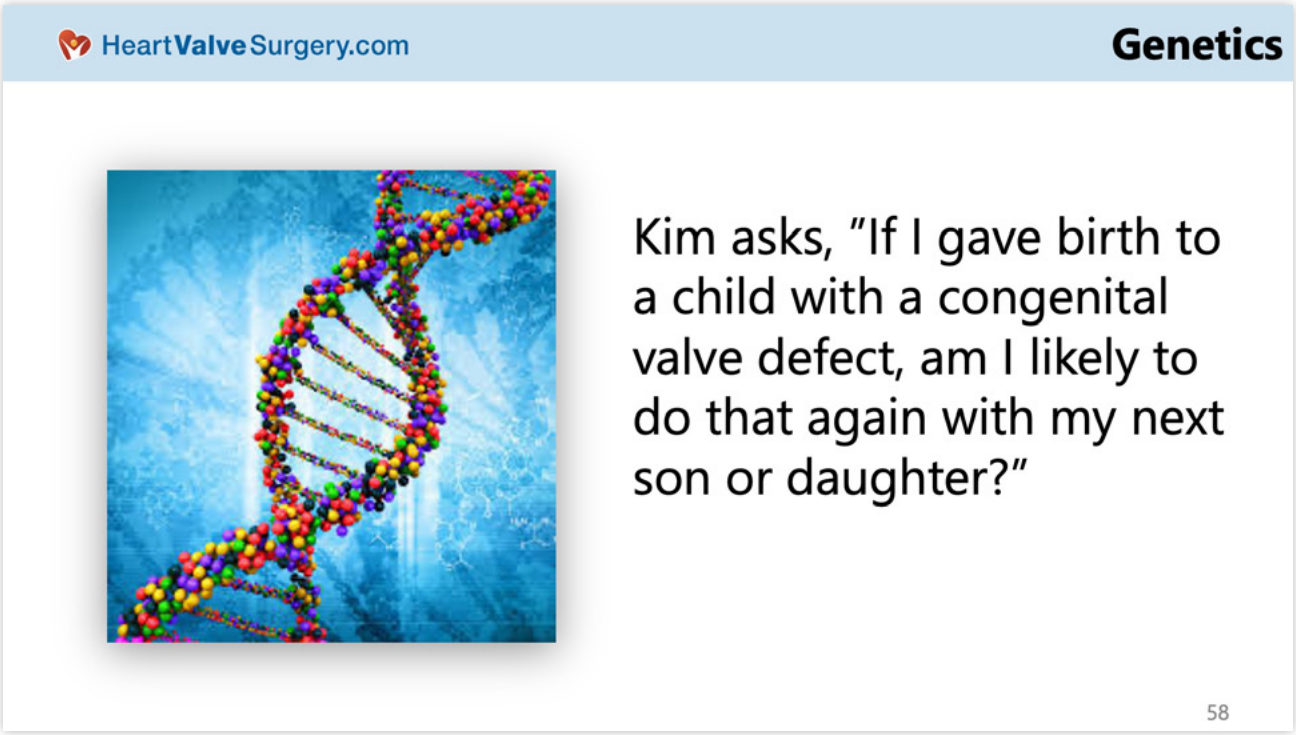
Melita Viegas: So I'll go ahead and take that question. As we said before, we're still all in the search for that ideal valve. Mechanical valve would be great; sadly, it doesn't have any growth potential at all. That being said, it won't last for a very young patient because eventually, that patient will outgrow the valve. Also, very importantly, and Dr. Tompkins touched on this as well. The pulmonary or right side of the heart has very low pressure, so this mechanical valve itself is just a very high risk for clotting or having thrombosis, so it also doesn't make it

ideal and comes with the added cost of anticoagulation, which can really limit activities, especially in young kids, and that'll have a life-long effects as well.

Usually the valve that we use is a bioprosthetic valve and again, they are quite durable. It's usually -- depending on the age, right? If you're older, I would say it lasts about 10 to 15 years. Patients that are younger, it's going to depend on how much they grow and potentially, they need another valve in that interim. They can stretch and really last somewhere between 10 to 15 years. It's only about a 50% chance needing to be replaced.

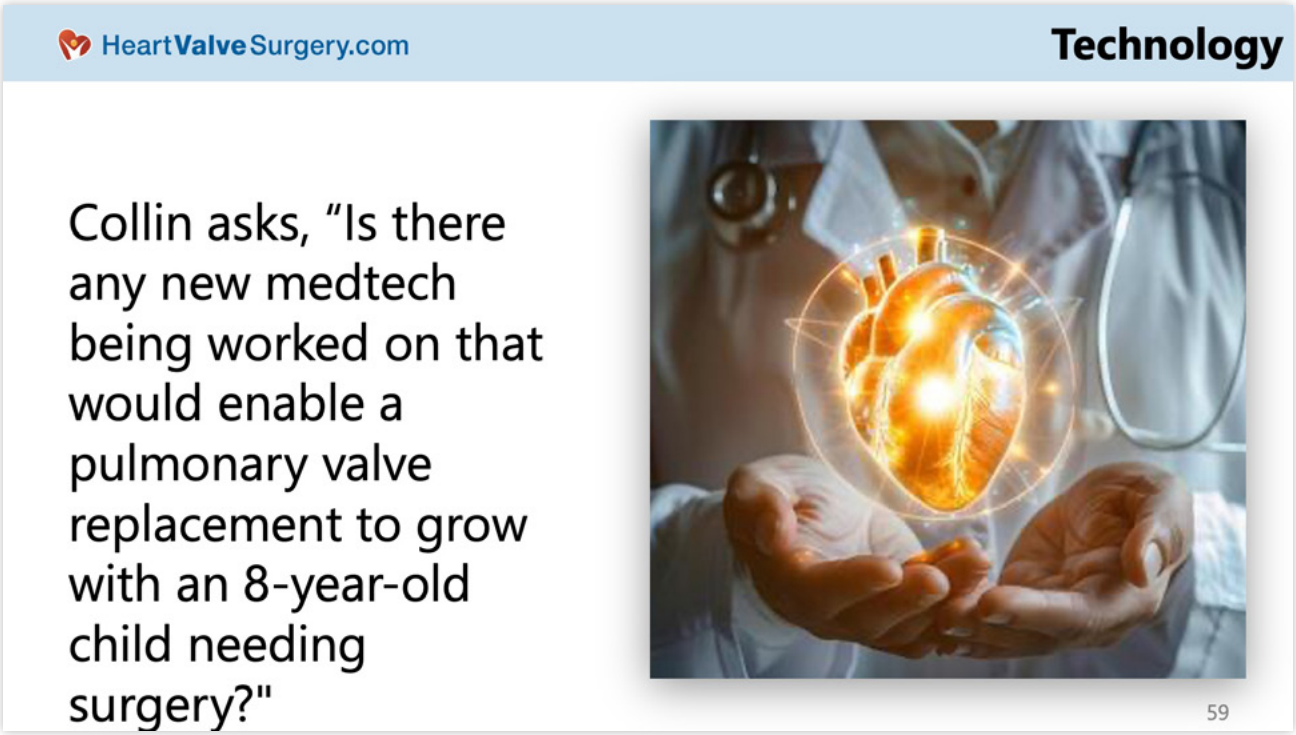
Adam Pick: Great, thanks, Dr. Viegas. This one is a really interesting question from Kim. She asks, "If I gave birth to a child with a congenital valve defect, am I likely to do that again with my next son or daughter?"

Genetics



Dr. Jay Pruetz: I can take that one. So yes, there is increased risk, but it really depends on exactly what the diagnosis is. We do know that congenital disease, when you have one child with it, you do have with subsequent pregnancies increased risk of recurring. What I like to say is that's not given. I think you should get good genetic counseling. There is some tests that can be performed prenatally or even preconception to look at those risks. Then I definitely recommend getting screening during the pregnancy, including a fetal echocardiogram to figure these things out before the baby's born.

Technology



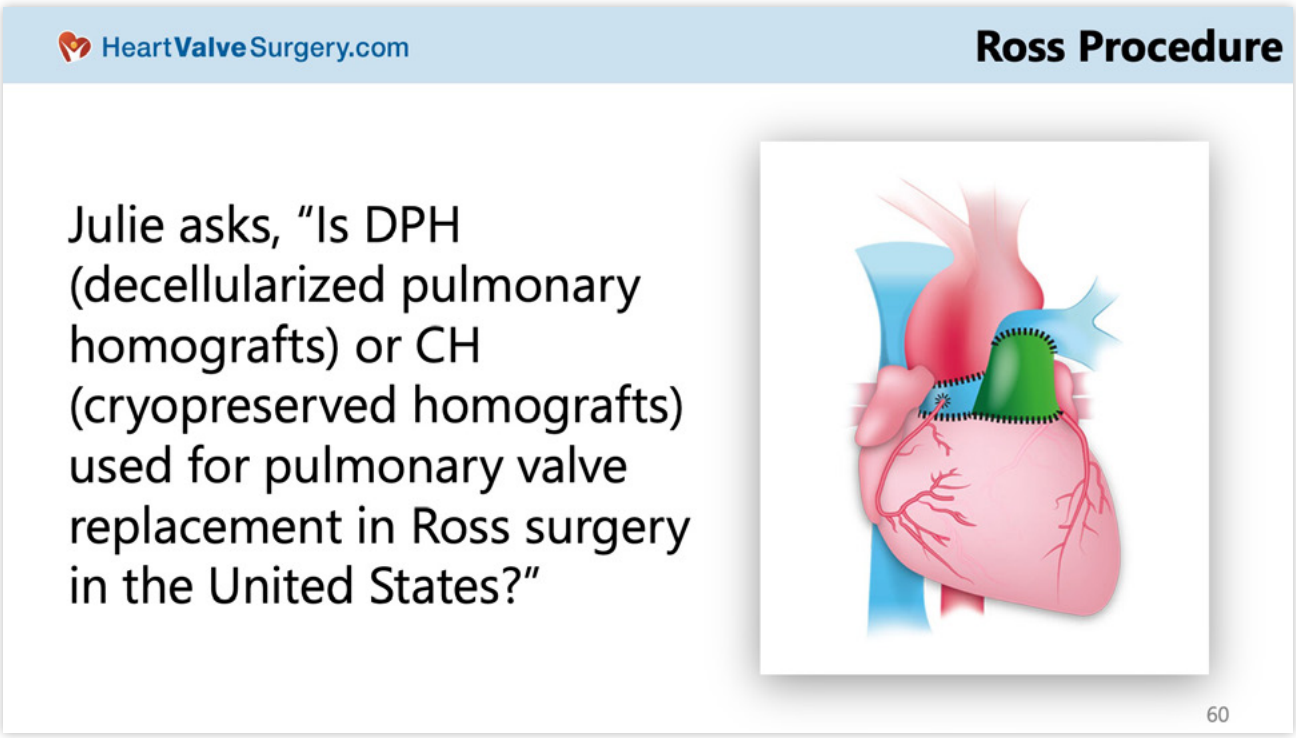
Adam Pick: Great, thanks, Dr. Pruetz. This comes in all about technology, and Collin asks, "Is there any new medtech being worked on that would enable a pulmonary valve replacement to grow with an eight-year-old child needing surgery?

Dr. Stephen Nageotte: Yeah, I can start on at least looking at the transcatheter options. Unfortunately, none of the transcatheter options grow on their own, but they can be grown further. It is not uncommon that we could put in a pulmonary valve even in someone as young as eight that can be dilated further. Eight is a little on the young side, but there is technology being developed out there. It's not available yet, but there are valves that can be put in even at younger ages, two, three, four years of age that can be further dilated. Those things won't grow on their own, but I can kick it to Dr. Viegas if she has any comment on any surgical valves that might be able to do that.

Dr. Melita Viegas: Yep, and then from a surgical prospective, any valve that's going to grow, either there is an RV to PA conduit that lets – had been reintroduced to the market. The idea was that it was a conduit with a valve inside. Eventually, the graft material actually absorbs and is repopulated by native tissue. It is called the Zelta valve. It is still very early. Their first group of patients only had one-year follow-up. There's more to come because they have taken it back and they're adding more to that.

Different from that completely, the world of partial heart transplants does exist. That would be, say, someone is getting a heart transplant but their currently heart actually had a good pulmonary valve. We would actually take that valve and part of the pulmonary artery and part of the right ventricle and we could implant it in. There's a lot more steps to it. There's lots of stuff involve. It will require some element of immunosuppression. We're not really sure about that, but that's one of the forefronts from the surgical perspective in this field.

Ross Procedure



Adam Pick: For the patients and the parents on the line, this is really what I consider to be such a strong point about having a very good heart team to help manage your valvular defect. You're getting feedback from a group here, whether it's from the interventional side or general cardiology side or the surgeons. I had never heard about partial heart transplants, Dr. Viegas, so that is fascinating to me.

This was a question that came in about the Ross procedure. Julie asks, "Is DPH (decellularized pulmonary homografts) or CH (cryopreserved homografts) used for pulmonary valve replacement in the Ross surgery in the United States?"

Dr. Melita Viegas: Yes, actually they're both available. They're just – what decellularized pulmonary homograft means is basically the DNA or as much as possible in the cells of the cadaver have been removed so that it will be inert so that it's not supposed to stimulate the recipient's immune system and cause any low-level rejection but more importantly antibodies in that patient. Almost all of our homografts that we use especially are cryopreserved, so yes, they're being used.

Adam Pick: Great. On that note, I want to respect everybody's time. we're going to conclude the webinar, but I'd ask you to not just jump off the line just yet because I'm going to ask you to complete the survey for all the patients and the parents joining us today. I also want to stop and just thank Dr. Tompkins. Pruetz, and Viegas and Nageotte for taking the time to really help our community understand this idea of congenital pulmonary heart valve disease and how to manage it for your entire lifetime of yourself and/or your child.

So on that note, thank you, Dr. Nageotte, Dr. Viegas, Dr. Tompkins, Dr. Pruetz. Thanks for being with us today, and we'll go ahead and if you'll just stay on the webinar for another ten seconds, you're going to see a survey pop on your screen. As we always say here at heartvalvesurgery.com, keep on ticking. Happy holidays, everybody.

Patient Resources

Since 2006, HeartValveSurgery.com has developed several resources to help you better understand your diagnosis, your treatment options and your recovery.

Listed below, please find resources created exclusively for patients and caregivers. We hope they educate and empower you.

- Adam's Free Patient eBooks - Download 10+ free eBooks about heart valve disease and treatment options for aortic, mitral, pulmonary and tricuspid valves.
- Heart Valve Learning Center - Visit the Heart Valve Learning Center to access over 1,000 pages of educational information about valvular disorders.
- Patient Community - Meet people just like you in our patient community. There's nothing better than connecting and learning from patients who are sharing their stories in our community.
- Surgeon Finder - Find and research patient-recommended heart surgeons that specialize in heart valve repair and heart valve replacement procedures.
- Heart Hospitals - Learn about medical centers that have dedicated teams and resources that specialize in heart valve therapy.
- Adam's Heart Valve Blog - Get the latest medical news and patient updates from our award-winning blog.
- Educational Videos - Watch over 100 educational videos filmed by the Heart-ValveSurgery.com film crew about heart valve surgery.