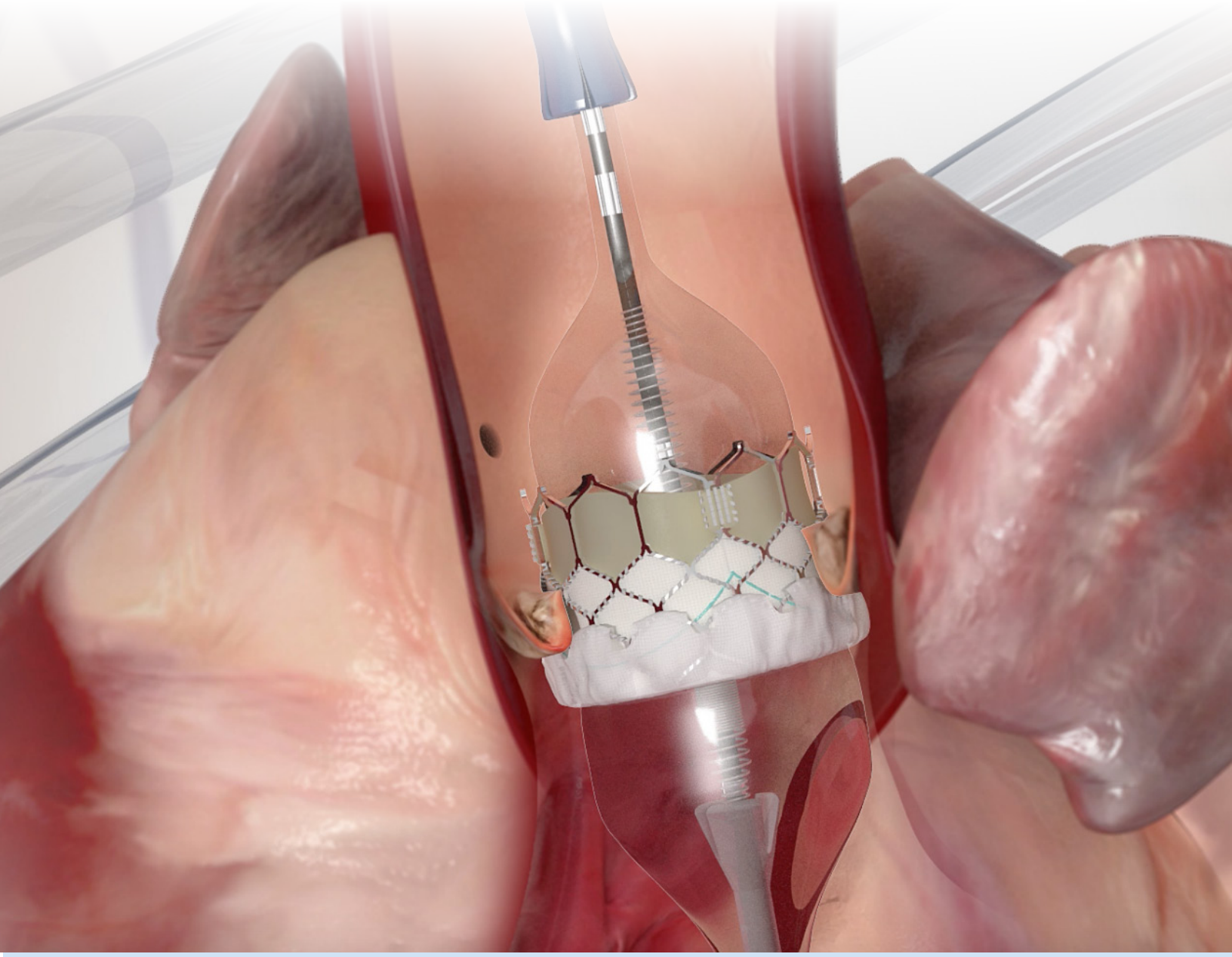
Advances in Transcatheter Heart Valve Therapy



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Introduction from Adam Pick, HeartValveSurgery.com founder

Dear Patients & Caregivers,

During the past 10 years, a revolution in heart valve therapy has occurred. Today, in select patient populations, new minimally-invasive devices are used to treat valvular disease without open heart surgery. To educate you about these "transcatheter" therapies that require no incision to the patient's sternum, Northwestern Medicine and HeartValveSurgery.com held a live, online webinar titled, "Advances in Transcatheter Heart Valve Therapy", on November 9, 2016.

During this live event, Drs. McCarthy, Davidson and Malaisrie, a leading heart team from Northwestern Medicine, and myself shared critical information about transcatheter devices.

The webinar was an overwhelming success -- with over 350 patient and caregiver registrations and over 150 attendees from all over the world. For those patients and caregivers who were unable to attend this event, I prepared this eBook for you.

If you have any questions, please email me at adam@heartvalvesurgery.com.

Keep on tickin!

Adam Pick

Patient, Author & HeartValveSurgery.com Founder

P.S. If you would prefer to watch the video playback of this webinar, click here.

Featured Webinar Speakers

The featured speakers for the webinar were:

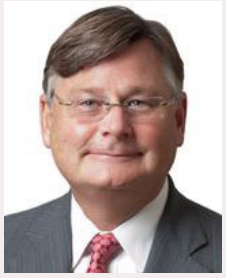

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Table Of Contents

Written Transcript & Presentation Slides

In addition to providing you the written transcript of the "*Advances in Transcatheter Valve Therapy*" webinar, we will also provide you (i) the presentation slides and (ii) hyperlinks to watch the videos shared during the online event.

Webinar Introduction

Adam Pick: Hi, everybody. My name is Adam Pick, and I'd like to welcome you to the webinar titled, "Advances in Transcatheter Heart Valve Therapy". If I have yet to meet you, I am heart valve patient. I also founded HeartValveSurgery.com about 10 years ago. Our mission at the website is really simple. We want to educate and empower patients who have heart valve disease. This webinar, which has had over 350 registrations, from patients in countries all over the world, was designed to support that mission.

During the webinar, all the participants will be in "Listen Only" mode. That being said, you may submit questions during the webinar. You might notice in the up-

per right-hand side of your screen, there is a control panel. That's where you can submit your questions. We will do our best to answer your questions during the Q&A section of the webinar.

Now, let's get to the webinar. I am thrilled to introduce to the featured speakers for this session. Dr. Patrick McCarthy is the executive director of the Bluhm Cardiovascular Institute and the chief of cardiac surgery at Northwestern Medicine in Chicago. Dr. McCarthy has achieved national and international recognition in the field of complex adult cardiac surgery including valve repair and valve replacement and atrial fibrillation. He has performed over 10,000 heart operations, of which more than 4,000 of those involved valve therapy.

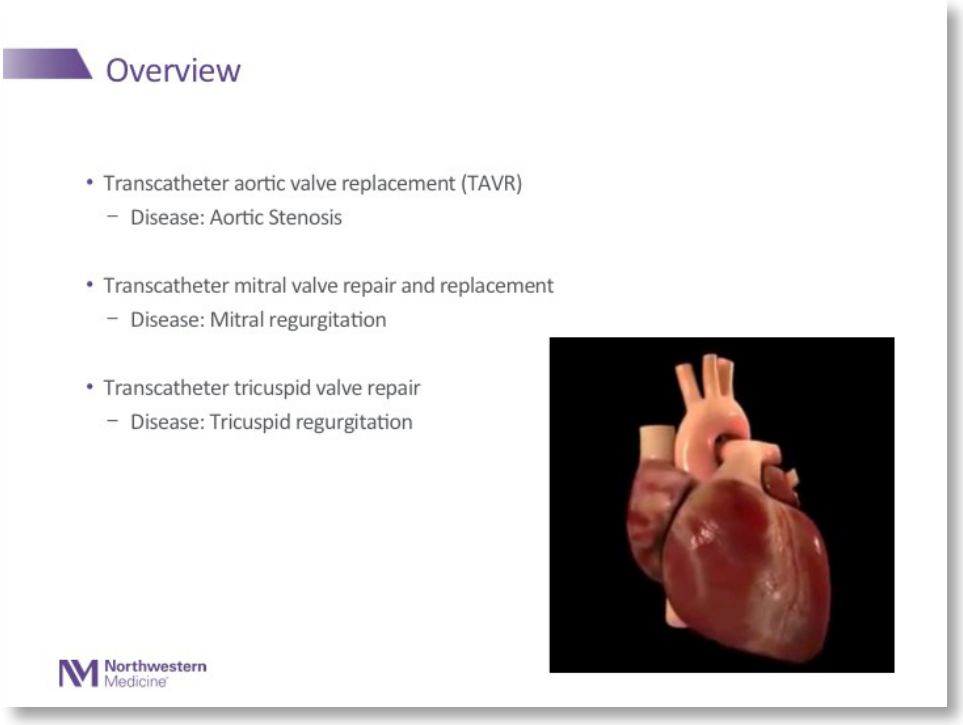
Dr. Charles Davidson is the medical director of the Bluhm Cardiovascular Institute, and he's the clinical chief of cardiology at Northwestern Medicine. Dr. Davidson has several areas of expertise including valvular heart disease, coronary angioplasty, and adult congenital heart disease.

Dr. Chris Malaisrie is an attending cardiac surgeon at Northwestern Medicine and associate director of the Center for Heart Valve Disease. Dr. Malaisrie's clinical interests include aortic valve replacement, bicuspid aortic valve disease, valve-sparing aortic root replacement, and aortic arch reconstruction.

I could go on and on about the careers and the achievements of Dr. McCarthy, Dr. Davidson, and Dr. Malaisrie. Instead, what I want to share with you from the heart is that this team is celebrated by our community, and it's for very good reason. Since launching this website, Northwestern has successfully treated over 100 patients from our community. Those folks include people like Robert Winter, Sara Bloomfield, Ron Rovin, Gene Cook, Sharon Knickerbocker, Lisa Woods, Mark Kroto, John Difazio, Carole Rice, Charlotte Hartzell and Debbie Cross.

Personally, I am humbled that Dr. McCarthy, Dr. Davidson, and Dr. Malaisrie are taking time away from their very busy practices at Northwestern to share their experiences and clinical research during this educational webinar. To start, I'd like to introduce you to Dr. Patrick McCarthy.

Dr. McCarthy: Thank you, Adam. First of all, I want to thank you and all the people that are involved at heartvalvesurgery.com because it's such a great reference for our patients. You really take the time to get it right, and I know they really appreciate it. It's great for me to see the pictures of our old patients that we know so well from Northwestern.



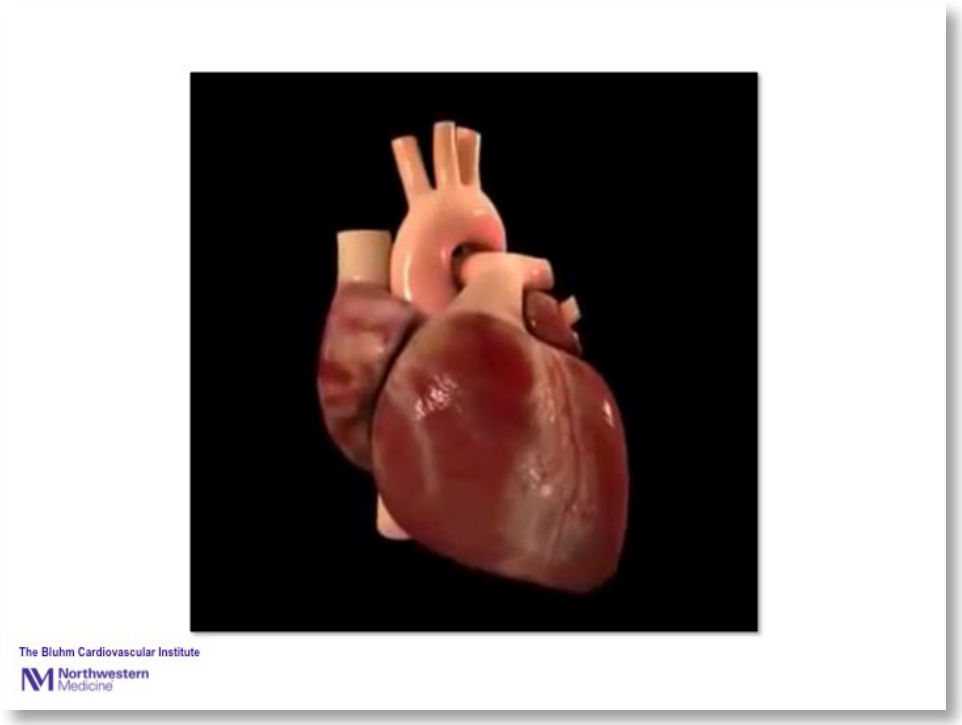
Today, we want to focus on one of the most revolutionary areas in heart disease that I've seen in my entire career that spans decades now. Ten years ago, the topics of replacing heart valves without surgery, transcatheter mitral valve repair, and tricuspid valve repair were not really even talked about. They weren't at our meetings. We weren't considering it for patients. It wasn't anything that we discussed.

In the past 10 years, there's been this revolution. As you'll hear from Dr. Davidson and Dr. Malaisrie... Now, we have commercially approved options and then a variety of new devices that are undergoing early experimental work. With that, my partners, Dr. Malaisrie and Dr. Davidson, are going to walk us through some of those newer options for patients.

Dr. Davidson: Thank you, Pat.

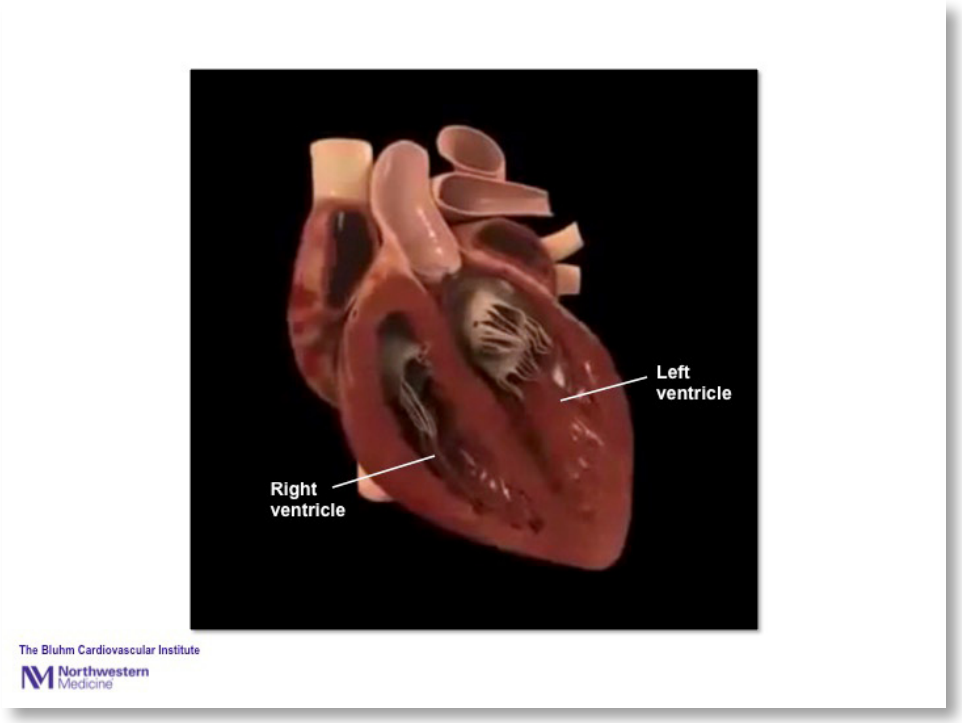
Dr. McCarthy: Can we have the next slide?

Anatomy of the Heart

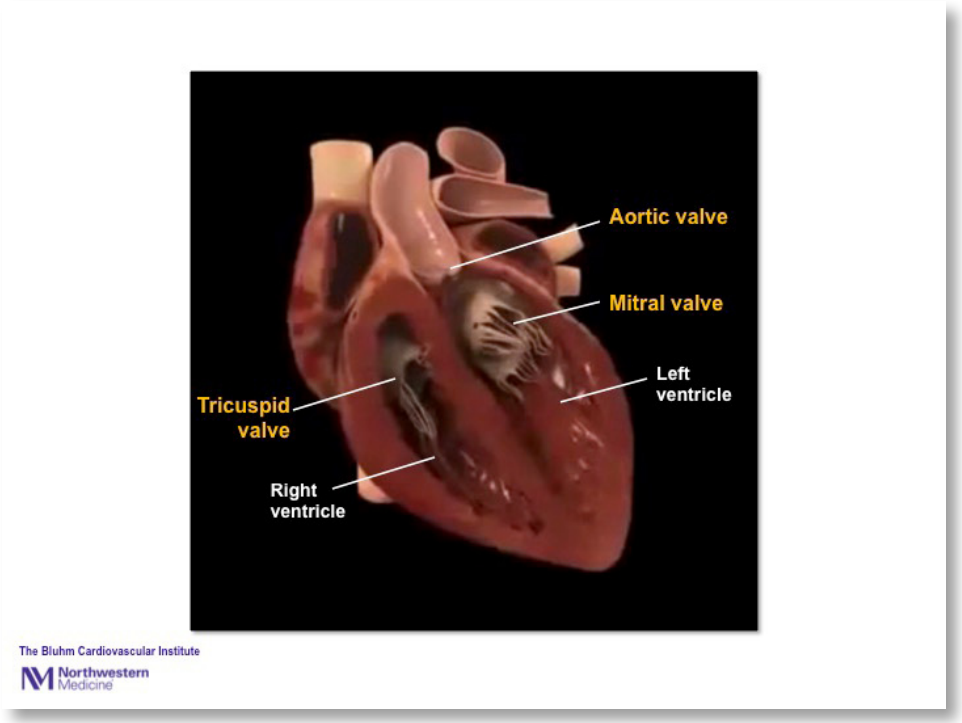


Dr. Davidson: Thank you, Pat, and thanks, Adam, for hosting this today. It's a good opportunity to start the session with some basic anatomy to educate the audience here. The heart is basically a large pump or large muscle, if you will, in the body that pumps blood out through the aorta to the rest of the body and receives blood from the head, and neck, and the rest of the body up through the right side of the heart.

Here you can see a nice cross-section of the heart and shows what the inside of the heart looks like. As you can see, the red part of it is primarily the muscle. Right down the middle is the septum that divides the right side of the heart from the left side of the heart. The white structures are the valves.



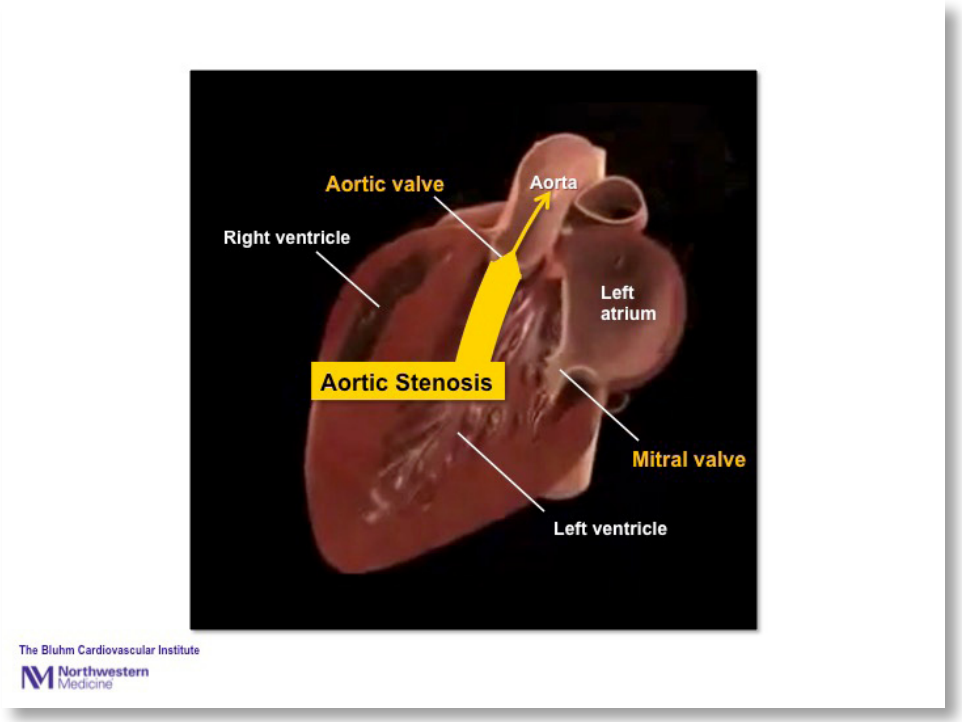
On the next slide, you see the left ventricle. That's responsible for the main pumping chamber of the heart, which pumps blood out then through the aorta, through the aortic valve. Then the right side of the heart, that's where the blood is received from the rest of the body and is responsible for returning blood to the lungs to get oxygen to then come back to the heart.



The next slide gives a little more detail. In order to regulate the blood flow throughout the heart, the heart has a series of valves that open and close in order to regulate the flow from the top part of the heart to the bottom part of the heart and then out to the lungs, then back from the lungs into the top part of the left side of the heart to the left ventricle and then out through the aorta.

What we're going to discuss today are primarily the aortic valve, the mitral valve, and the tricuspid valve. The tricuspid regulates the right atrium to the right ventricle; the mitral valve, from the left atrium to the left ventricle; then the aortic valve, from the left ventricle out through the rest of the body.

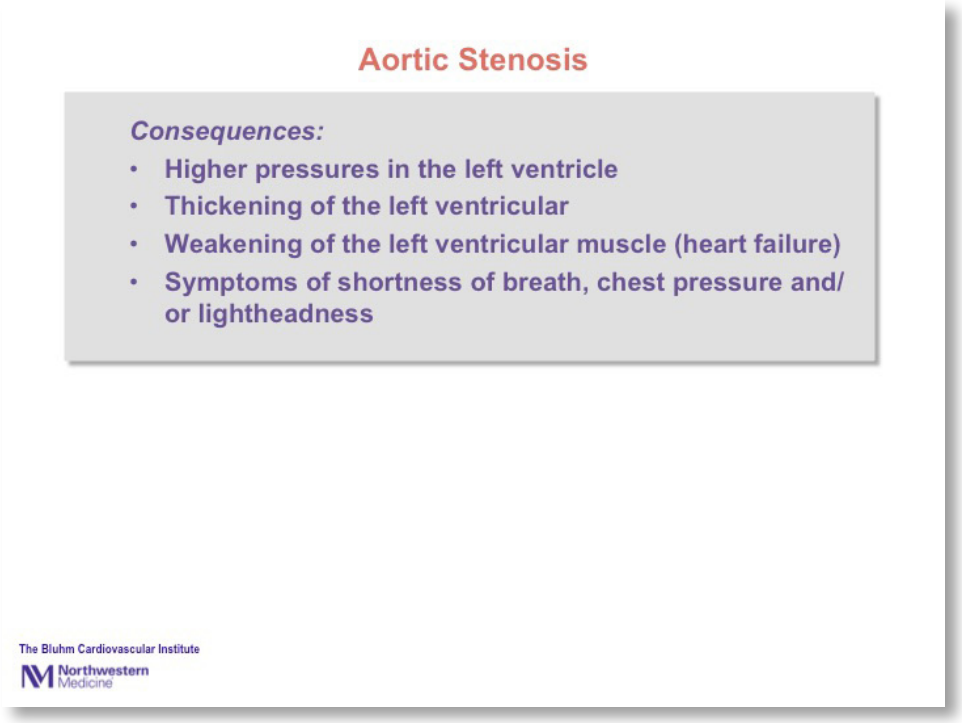
About Aortic Stenosis



Dr. Davidson: Traditionally, open heart surgery was the only way to take care of patients who had degeneration of their aortic valve, typically called aortic stenosis. Approximately 8 years ago in the United States and about 10 to 12 years outside the United States, there was a revolution in therapy, which allowed replacement of the aortic valve with catheter-based therapies. It most often can be done through an artery in the leg.

Aortic stenosis involves blocking of the aortic valve, which regulates the flow from the left ventricle to the rest of the body. This blockage is typically caused by a calcium build-up. It's really not related to your lifestyle. It's not related to your cholesterol levels. It really is just "wear and tear" of the valve over time where calcium builds up and then obstructs flow out through the heart.

We do know that without treatment that this can be a fatal condition. Medications are only partially effective as they relieve the symptoms, but don't actually relieve the obstruction that can lead to problems with heart failure and eventually death.



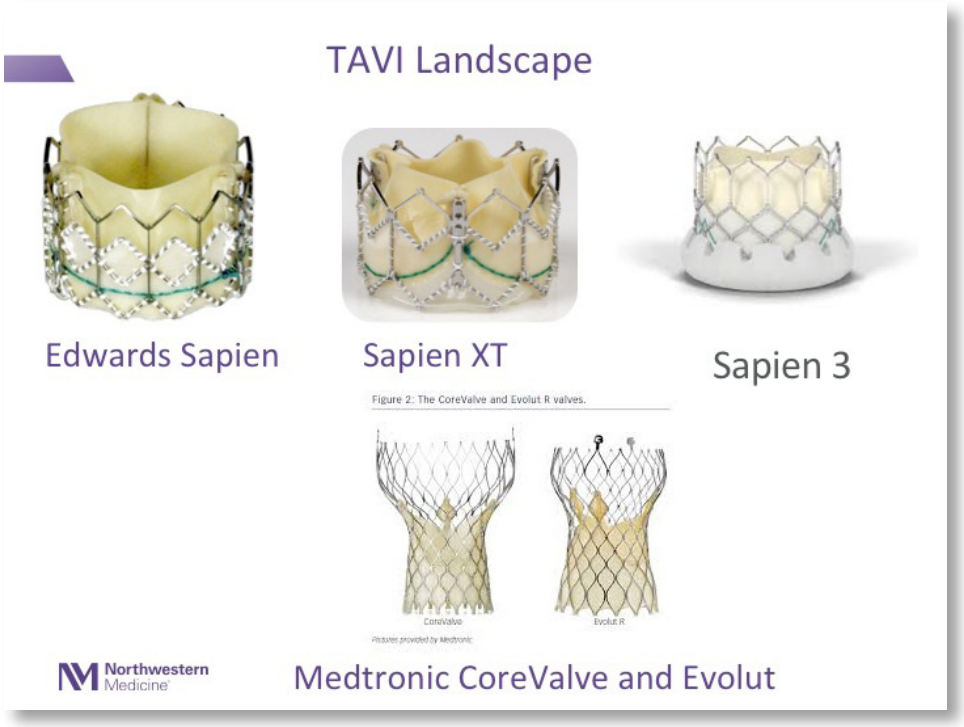
What are the problems with aortic stenosis? Again, this is a lot like plumbing if you think about it. You can use Drano, which is the medications for a while, but after a while, that doesn't work, and you have to do an aortic valve replacement. What happens? You develop high pressures in the left ventricle, the main pumping chamber. That causes blood to back up throughout and into the lungs causing things like:

- Heart failure
- Shortness of breath
- Breathing problems
- Edema
- Chest discomfort
- Passing out

Aortic stenosis also causes thickening of the left ventricle. The ventricle becomes what we call hypertrophied because of the extra pressure it's having to exert to eject blood. Over time, the muscle cannot thicken any further, and the heart begins to weaken and dilate, and that's when we see even more symptoms of heart failure develop.

The heart doesn't actually have to weaken to even cause the heart failure. Even the thick muscle has trouble dealing the extra load against the heart. As I said, the symptoms mostly commonly reflected are shortness of breath, chest discomfort, and light-headedness, or true passing out, which we call syncope.

Transcatheter Aortic Valve Replacement (TAVR)



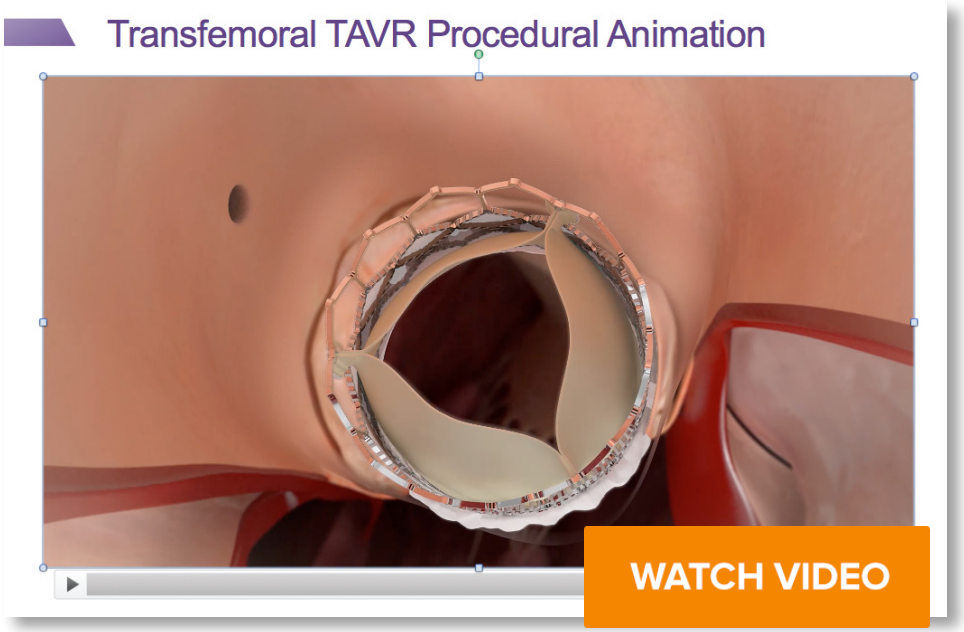
Dr. Davidson: These transcatheter heart valves were developed to, again, try to treat patients initially that were not candidates for surgery. We'll talk about how that's changed. Now, we've moved into more intermediate-risk patients and now into low-risk patients. Chris will speak to the low-risk population. As you can see, there's been an evolution in these heart valves.

Initially, the first one transcatheter valve was the Edwards SAPIEN valve. It was a fairly high-profile valve, but it was a good chance to show that these can be used, and were feasible, and were effective, and did save lives for patients. As we moved across the spectrum, we're now into our third generation of the SAPIEN 3 valve, which really has some unique characteristics. Down near the bottom where you see the white there in the SAPIEN 3, it actually has a skirt that assures that we get a good sealing around the valve when it is placed into the body.

The other advantage of this is it's made of a cobalt chromium metal rather than stainless steel so that it's lower profile and therefore uses a smaller hole and is easier to deliver. It makes the procedure go more smoothly, and has helped in reducing complications from the procedure, and improving outcomes long-term.

Down at the bottom, you can see the evolution of the Medtronic CoreValve, which is a nitinol-framed device. This is a porcine valve (a pig valve). The SAPIEN is a cow valve. We can talk about those differences a little bit later on. This is a self-expanding valve, so kind of a different technology, but both have been shown to be safe and effective in patients with intermediate and high risk for surgery. Again, the low-risk trials are ongoing for both devices right now.

TAVR Video Animation



Dr. Davidson: We're going to show this animated video. This highlights how we perform these procedures. This animated video will be shown using the SAPIEN 3, but it's fairly similar for the CoreValve, at least some of the aspects. There's a sheath or a plastic tube placed into the groin, through the femoral artery. Then a wire that's been put across the stenotic aortic valve is in the left ventricle, and then a balloon is inflated. That gives us some partial opening in the valve that allows us to do the valve implantation. This is kind of a preparation of the valve in order to do the actual valve implantation.

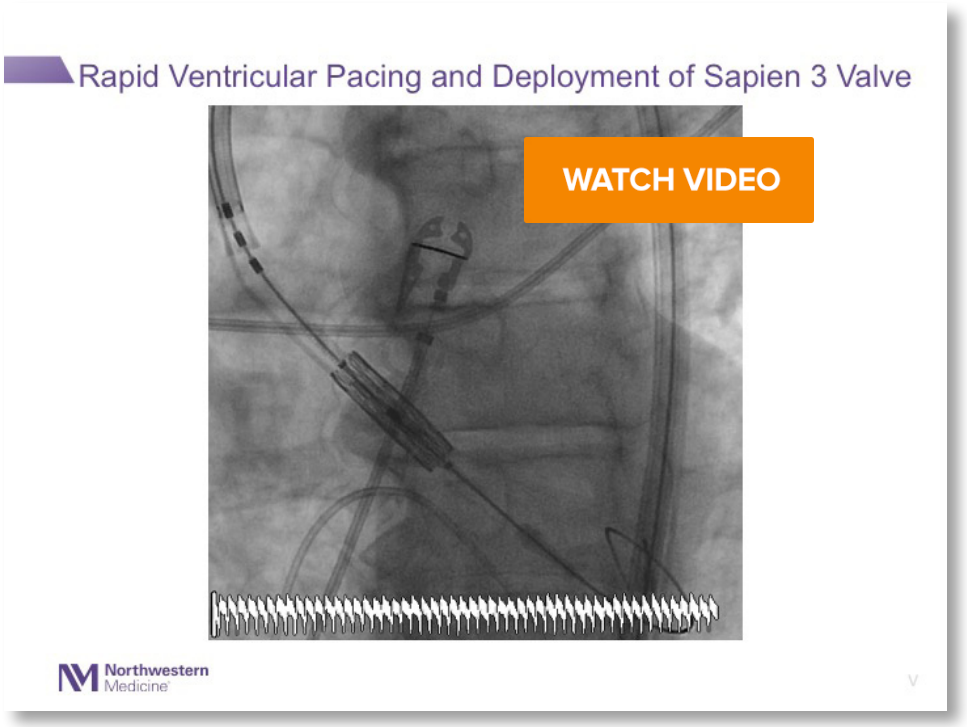
That balloon is then withdrawn over that same wire. Then going through that same plastic tube, we bring in the delivery system for the stented valve, this one being the SAPIEN 3 valve. When we put it into the descending aorta, as it is here, we mount it over the balloon. That's the preparation of the valve. Some of it is done outside the body, and some of it is done inside the body, as you can see here.

Once we have it placed over the balloon, we bring it over the same guide wire, across the aortic arch, and place this across the stenotic aortic valve. You can see this valve has some calcium deposits, as shown in the cartoon. It comes down across very nicely now. In the early days, when they were larger profile, it was a little more challenging to get across. Then we unsheath it. So then, we now we have this valve mounted on the balloon.

We get the heart pumping at a fairly rapid rate so that the blood pressure goes a little bit lower in the body and this allows us to very precisely position this valve. We want to put it to the exact location where we can get maximum valve function and also prevent any leaking around the valve. Then this has been inflated, and the valve is implanted in across the old valve.

This is all done under x-ray guidance. At Northwestern, we do most of our patients today with conscious sedation. They don't even require general anesthesia anymore. It's done in collaboration with cardiac surgery and interventional cardiology. We've done over 600 of these now with excellent outcomes and even more importantly, with great collaboration among the specialties, trying to design the best therapy for the patients.

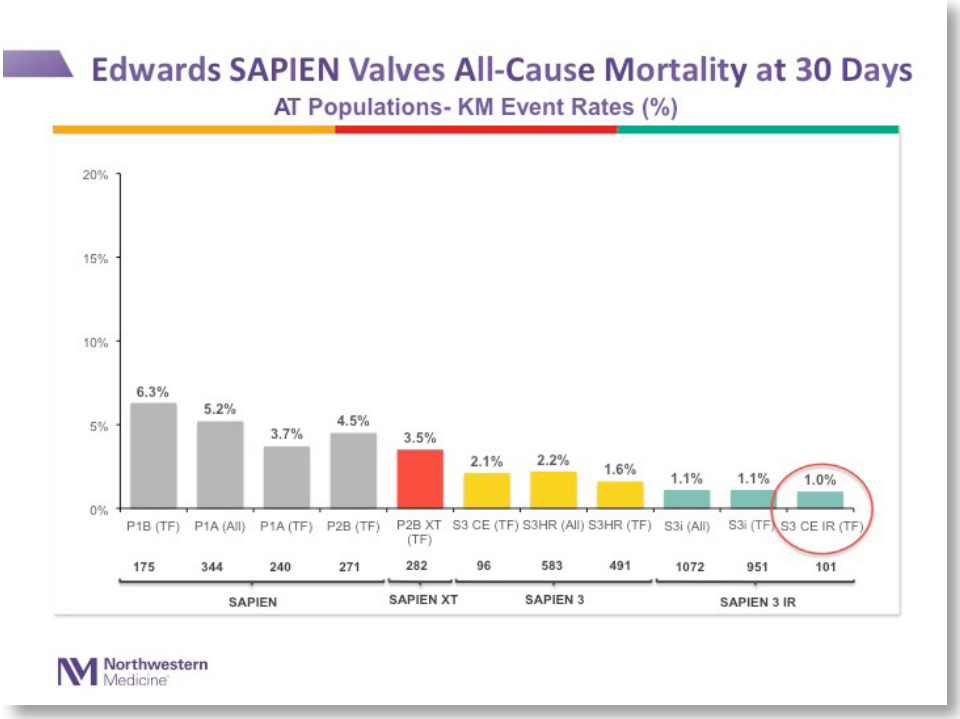
After implant, the valve becomes immediately functional and blood flow is regulated by that new valve. The old valve has been pressed aside. At that point, the sheaths are withdrawn from the body, and we use some stitches to close the artery. About 90% of people can be done from the femoral artery. About 10%, because of smaller arteries, will have the valve placed in a different way, usually through an artery in the armpit area.



This video is showing you an actual procedure. This is now under fluoroscopic guidance, x-ray guidance. We do an aortogram. That was a little puff of black there. Now you can see the balloon being inflated and the valve being positioned permanent in its location across the native aortic valve, again, all done under x-ray guidance. That's the valve being implanted.

This is typically how it looks after it's been implanted. We then do an aortogram with some contrast dye to evaluate to make sure the valve is functioning properly and there's no leaking around the valve. If there is some leaking, we can inflate it a little bit larger as needed. We also do a transthoracic echo, meaning an echocardiogram on the chest wall to verify that the valve is functioning properly. We get two assessments of the valve before we leave the room to make sure everything's okay.

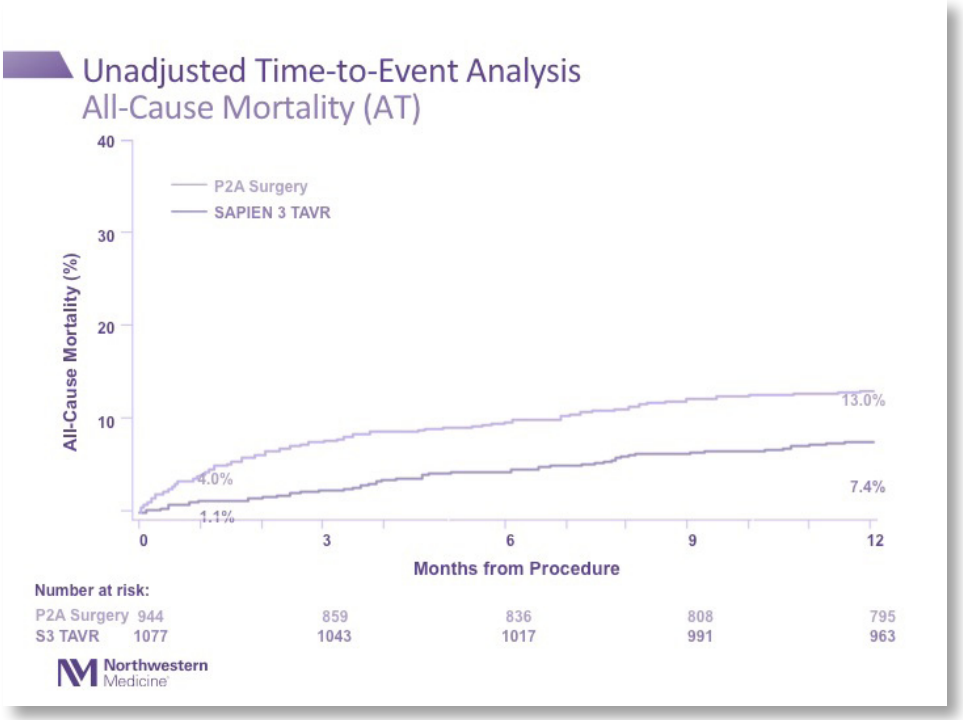
TAVR Procedure Outcomes



Dr. Davidson: How does this valve perform? Like everything, nothing's perfect, but I think this is really exciting. You can see that in the early going, mortality at 30 days was a bit higher. It was 6%. Remember, these were patients that were extreme-risk. They were essentially not eligible for surgery. They really had no option, and so we thought that was good, but we want to do better than that. The exciting part, I think, for all of us that have been involved with this technology, as we move to the right side of the graph, you'll see that mortality rates have now dipped into the 1% rate. Now we have both a durable treatment and a safe treatment for patients.

What we recently demonstrated in one of the studies that we participated was the PARTNER 2A Trial, which looked at patients in intermediate risk. That means their surgical risk was calculated to be between 4% and 8%. The risk of dying within 30 days based on a calculated risk was 4% to 8%. Patients were randomized to surgical aortic valve replacement or transcatheter valve replacement.

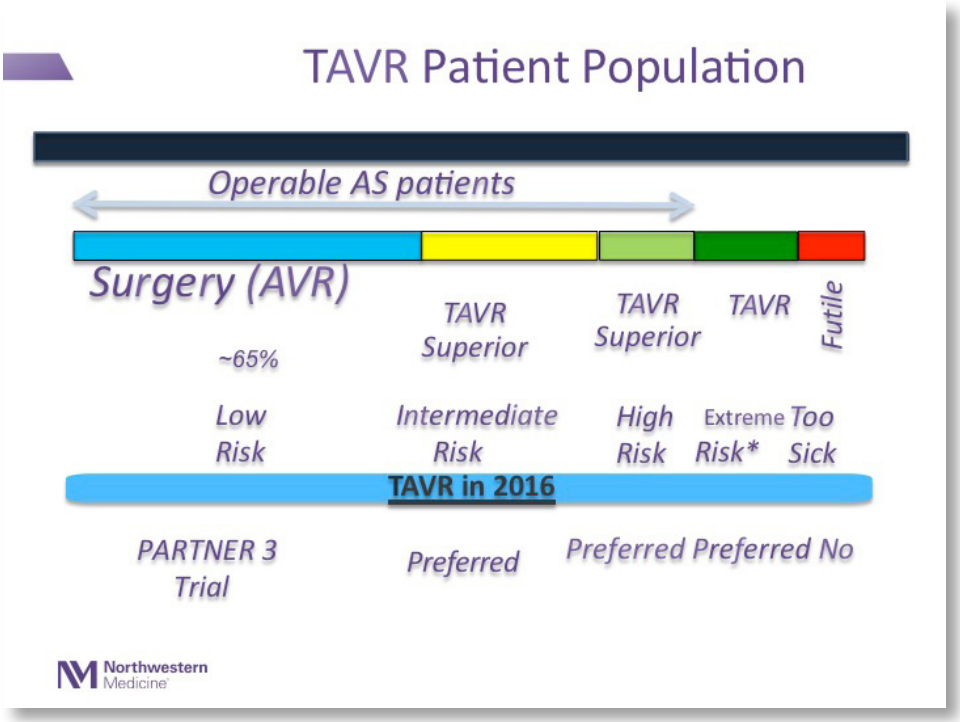
These are data points that were published in The Lancet, which is one of our most prestigious medical journals, showing mortality all the way out to 12 months. If you looked at the surgery groups, shown in the light purple, it was 13%, and if you looked at the valve in patients that got the transcatheter valve replacement, it was 7.5%. These, I think, were fairly impressive data.



Even if you look at the 30-day data, again, earlier, left side of the slide, it was 4% for surgery versus, as I showed you earlier, 1% with transcatheter valve. Both early and late mortality seem to be benefited by the use of the transcatheter valve in this intermediate-risk population.

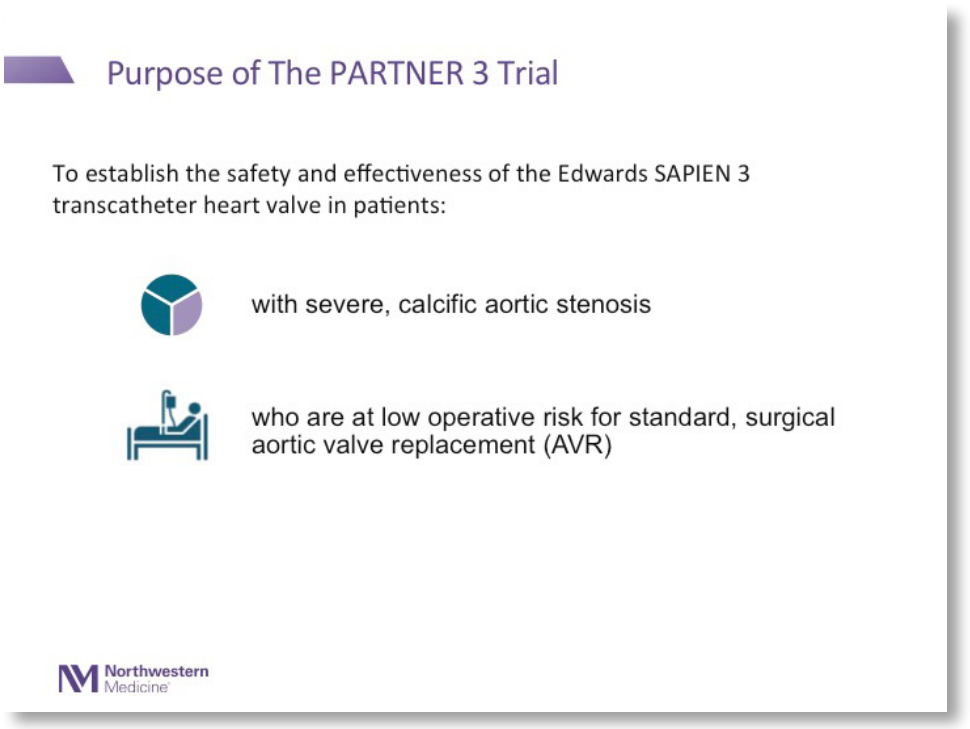
Obviously, this begs the question how will this perform in a low-risk population, patients who have a calculated surgical risk that's less than 4? That's where I'm going to turn it over to my colleague, Dr. Malaisrie, to go through what we have to offer that population right now.

Low Risk TAVR Clinical Trial (PARTNER 3)



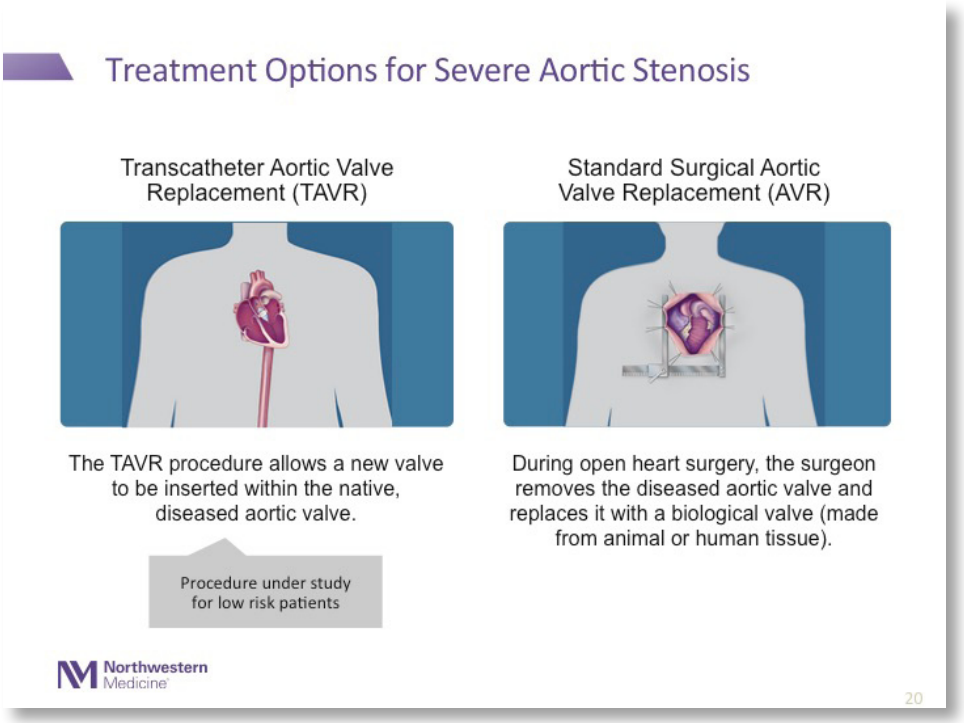
Dr. Malaisrie: Thanks, Dr. Davidson. Adam, thanks so much for having this webinar for our patients. I'd like to start by telling this group about a very exciting group of trials that are coming up and ongoing at this point. Given that TAVR is a standard of care and commercially available for very high-risk patients, what about the vast majority of patients that are low-risk? This is the basis of two ongoing trials in the United States studying TAVR for low-risk patients. What does this mean for the average patient?

If you're a low-risk patient with aortic stenosis who would otherwise just go ahead and have aortic valve surgery, which is a great option, you may be a candidate for enrolling in this trial and possibly getting a TAVR procedure. The purpose of the PARTNER 3 trial, a trial that we're enrolling here at the Bluhm Cardiovascular Institute at Northwestern Medicine, is to find patients with severe calcific aortic stenosis. Secondly, these patients should be low operative risk for standard surgical aortic valve replacement.



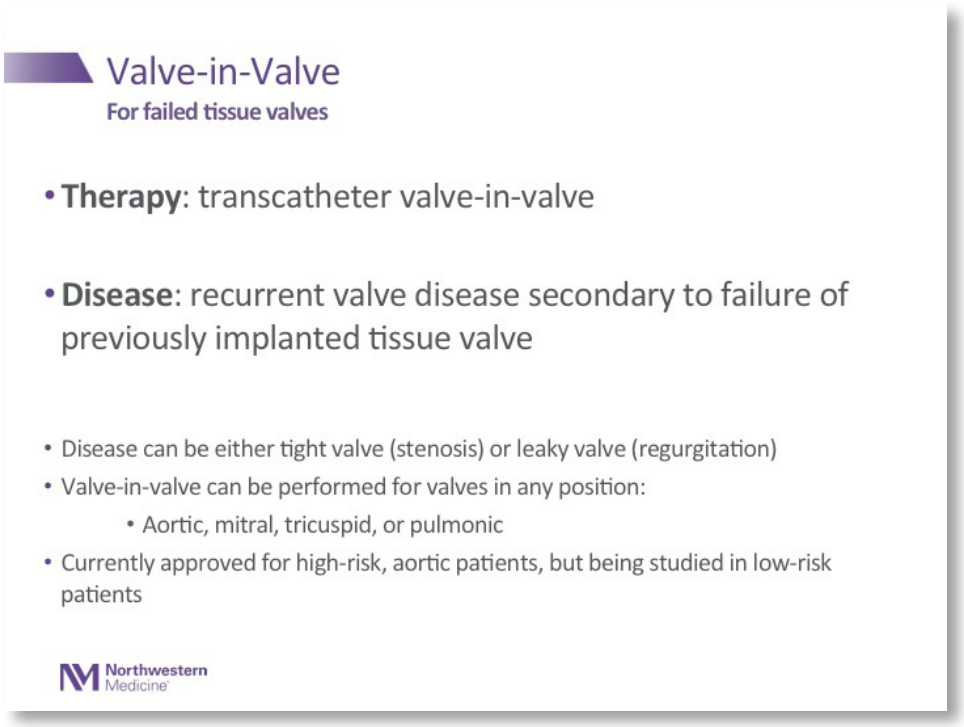
Now, patients that are candidates for this trial will get one of two therapies. The first is standard aortic valve replacement, seen to the right here. The other will be the transcatheter aortic valve replacement, or a TAVR. This procedure is under study for low-risk patients.

If you randomize in a group that gets aortic valve replacement, this is an excellent operation for patients who are low risk for aortic stenosis. For most centers, including ours, this could be done through a minimally invasive approach through a keyhole incision with a cosmetically appealing scar.



The study group is the TAVR group, the transcatheter aortic valve replacement group. This is the procedure that Dr. Davidson had previous described to you in high-risk patients now being studied for patients with a low risk for aortic valve replacement. This procedure can either be performed to the groin, which we're seeing on the animation, or it can be done through a transapical procedure through a small incision below the left breast, or through a transaortic procedure also through a small incision through the upper right chest.

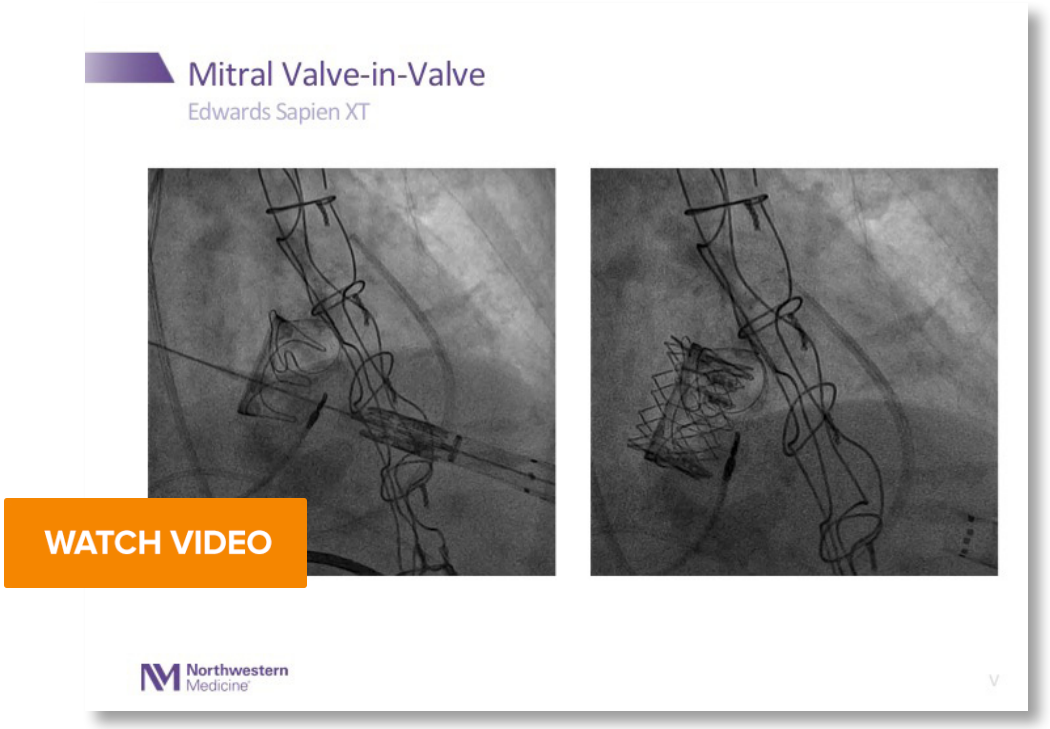
Transcatheter Valve-in-Valve Procedures



Dr. Malaisrie: In addition to the low risk trial, we're also studying very specific subsets of patients. This procedure called transcatheter valve-in-valve procedure, is meant for patients who have recurrent valve disease secondary to failure of a previously implanted tissue valve. When patients have an aortic valve replacement, we certainly hope that they will have a durable replacement for a long time. However, some patients do outlive their tissue valves, so this therapy is meant for that group of patients.

It's interesting to note that we can do a valve-in-valve procedure in a previous surgical valve that is either too tight or too leaky, and this video shows what we see in real life when we implant a Medtronic valve in a patient who had a previous aortic valve replacement. Currently, this procedure is approved for patients who have previous surgical aortic valve replacement who now need a new aortic valve.

What's currently under investigation is whether or not this therapy will also be good for patients who've had previous mitral valve replacement who now need a new mitral valve. This is currently being performed in select centers in an off-label approach, meaning that the FDA has not specifically approved this device for this procedure but has been shown to have very good outcomes in select patients.


Mitral Valve-in-Valve
Edwards Sapien XT
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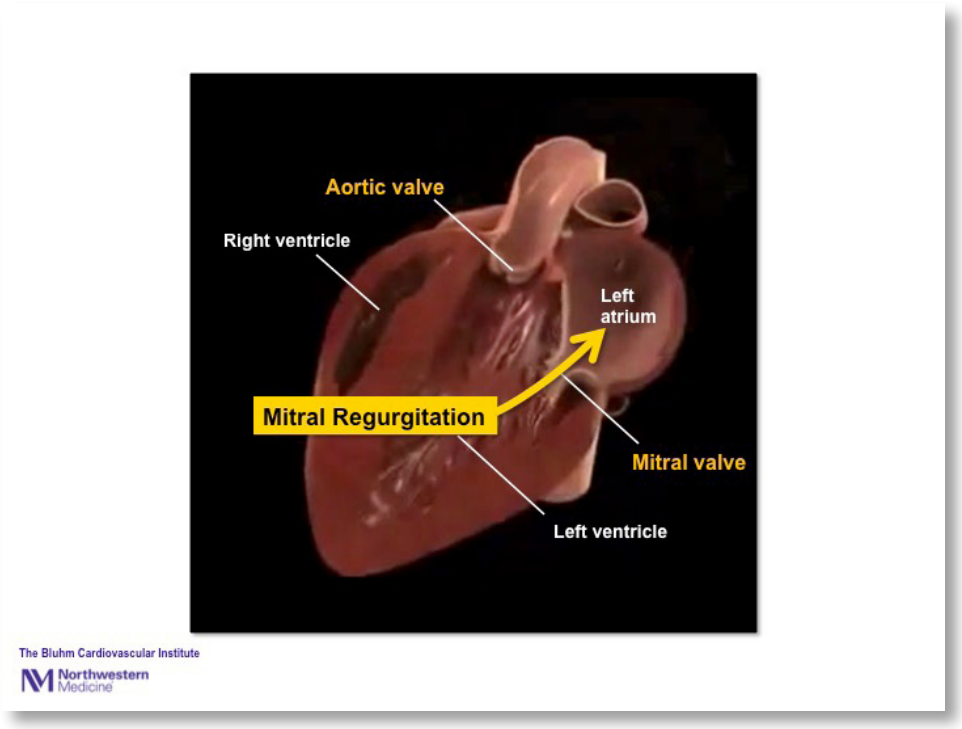
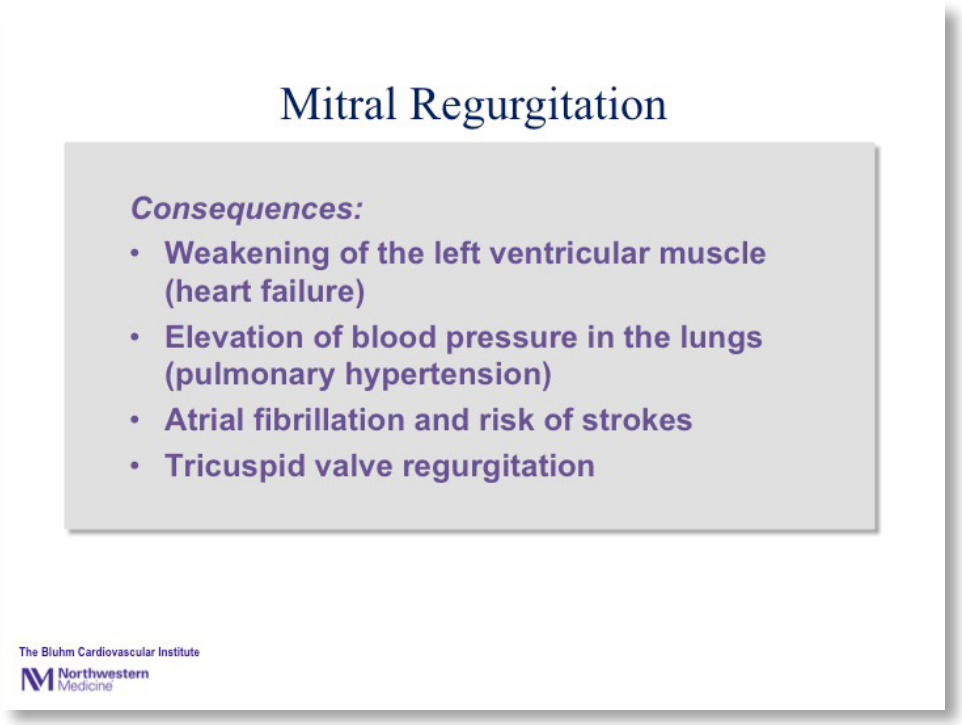
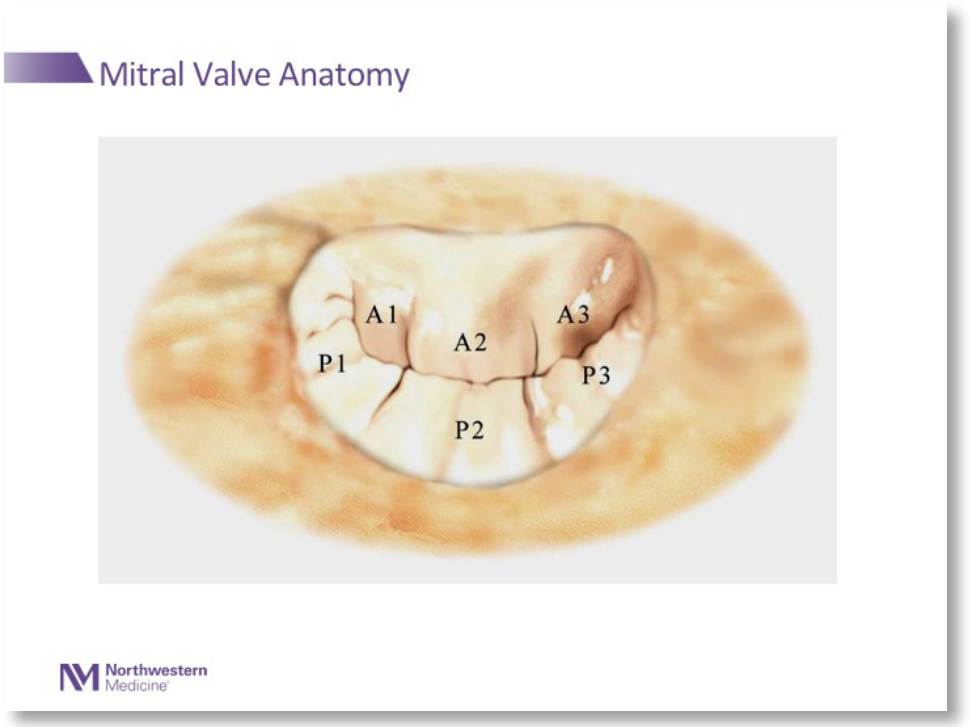
About Mitral Valve Disease



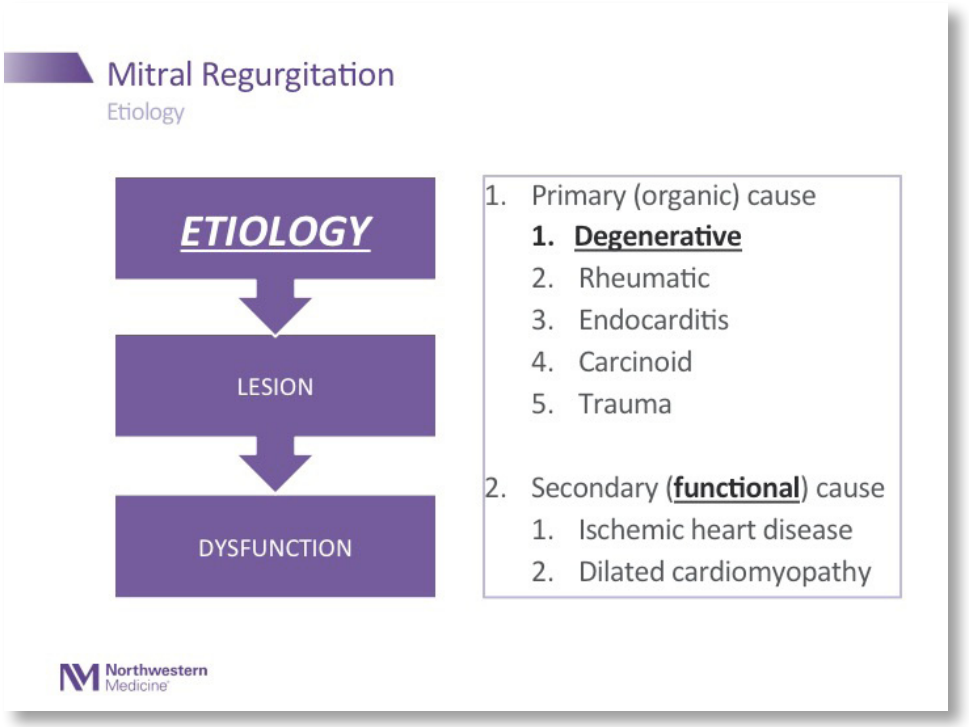
Dr. Malaisrie: Now, let's talk about the mitral valve and discuss transcatheter mitral valve repair and replacement. This is for the group of patients who have mitral regurgitation or a leaky mitral valve. Mitral valve regurgitation happens when the mitral valve leaks and the heart beats. Instead of the blood going forward into the body, it goes backwards towards the lungs. This causes symptoms secondary to the weakening of the left ventricular muscle, otherwise known as heart failure, elevation of blood pressure in the lungs, also known as pulmonary hypertension, atrial fibrillation and the risk of strokes, and also tricuspid valve regurgitation.



This is what we see in surgery when we look at the mitral valve. It's a valve with two leaflets. Why do patients have mitral regurgitation? We broadly classify mitral regurgitation in two very large groups. The first group is the group of patients that have a primary problem with their mitral valve.



We call this primary or organic etiology, and the majority of these patients have what we call degenerative mitral valve disease or mitral valve prolapse, in common language. The second group of patients has mitral regurgitation not because of the mitral valve but secondary to heart failure, and this is what we call functional mitral valve regurgitation.



Traditionally, we will repair mitral regurgitation secondary to degenerative mitral valve disease with excellent results, complete resolution of mitral regurgitation, through a sternotomy. Occasionally, we can do these procedures through a minimally invasive approach through the right chest. As you can see, this patient has a small incision tucked below her right breast, which is also very cosmetically appealing.

Minimally-invasive Mitral Valve Repair

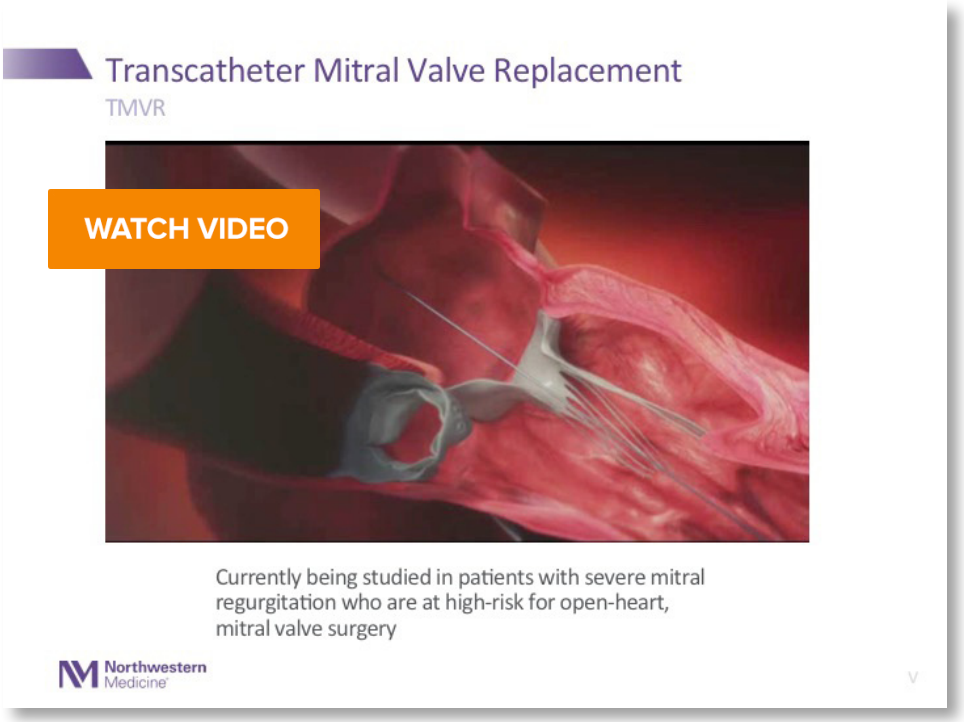
Mini-MVR

Northwestern Medicine

The MitraClip for Mitral Valve Repair

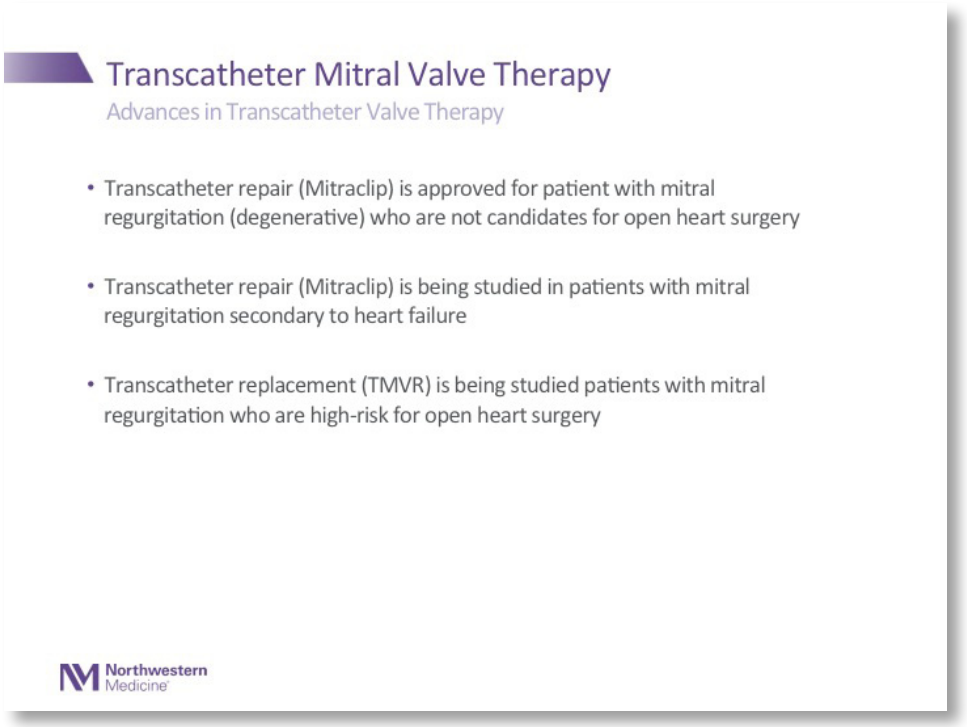
Dr. Malaisrie: There are a group of patients who will not tolerate open mitral valve surgery, so this is a great application for transcatheter procedure. This is a device called the Abbott MitraClip. It uses a procedure that is used also in open heart surgery, and it's meant for patients who are not candidates for open heart surgery. In this video, you can see a catheter within the heart. The MitraClip is loaded on the end of this tube and with careful positioning under echocardiography and x-ray, we can advance this clip into a position right between the two leaflets. Here, the cartoon is showing you how the mitral valve is leaking backwards. Once we advance the clip into the left ventricle, this clip can then grasp the two leaflets right down the center. We don't like this position, we can always release and re-grasp the mitral valve in order to get the perfect position with the most reduction in leakiness of the mitral valve. This is a completed MitraClip procedure with a clip right down the center between the two leaflets, successfully reducing the mitral regurgitation.

Transcatheter Mitral Valve Replacement



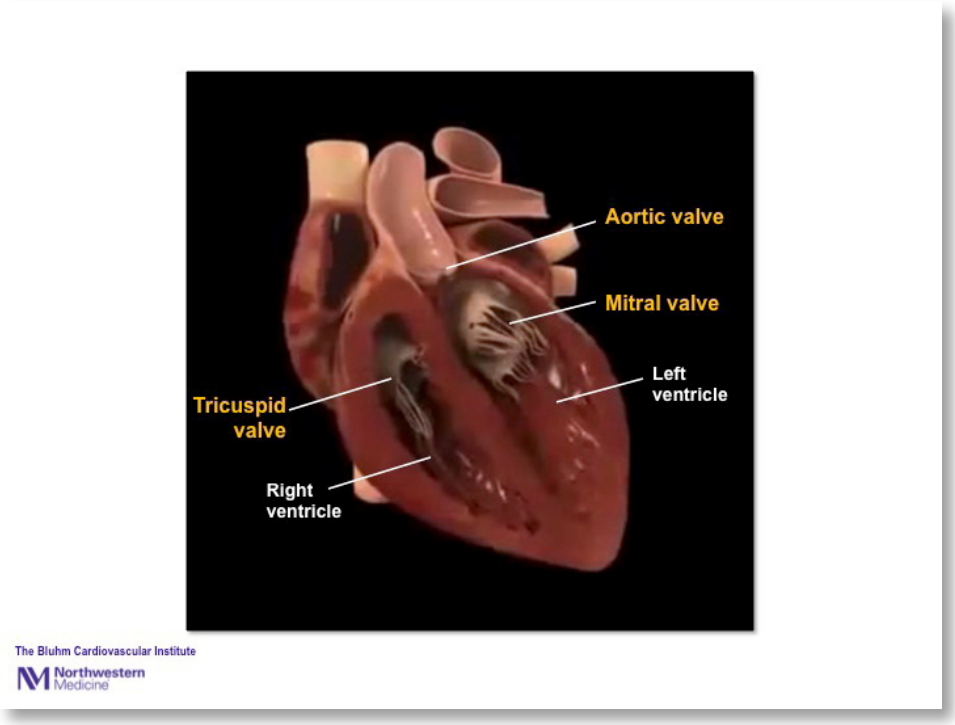
Dr. Malaisrie: A final very exciting group of procedures that can be done with the transcatheter approach is a complete mitral valve replacement without open heart surgery. Currently, these devices are under investigation, meaning they are not FDA-approved. We have had the opportunity to participate in this trial and deploy this device with very good success. Play the video.

Again, this procedure is done all within the heart and the vessels. This particular device has a valve inside a plastic tube, very similar to the TAVR procedure but meant for the mitral valve. This valve is asymmetric, meaning it is a D-shaped valve. We have to position it in the perfect position in order to make this work. This is done under echocardiography as well as x-ray. Once this valve is in position, we can deploy the valve where it becomes immediately functional, completely abolishing the leakiness of the mitral valve.



In summary, the transcatheter mitral valve therapy, is the therapy meant for patients with mitral regurgitation or leaky mitral valve. Most patients will do very well with open heart surgery. Occasionally minimally mitral valve surgery would be an option for some of these patients. For patients who are too high risk, we have transcatheter therapies available. The one that is currently commercially available and FDA-approved is the MitraClip procedure for leaky mitral valves. We are currently investigating trials using a complete transcatheter mitral valve replacement, which is a very exciting therapy we hope to see in the next several years.

About Tricuspid Valve Disease

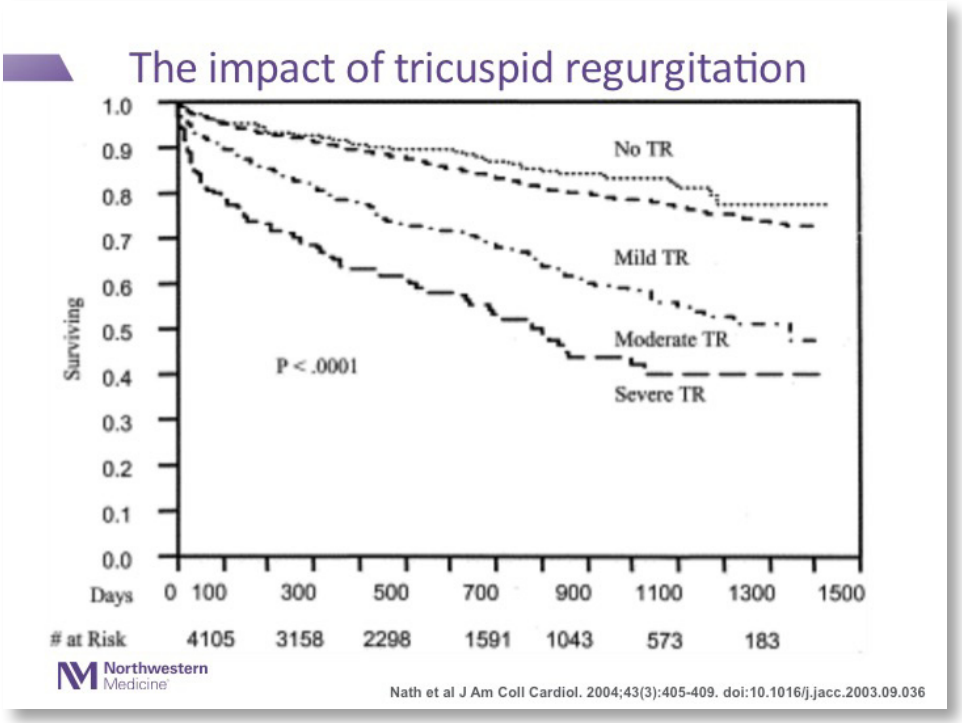


Dr. Davidson: I know we're hitting you with a lot of rapid-fire technologies and treatments, but we want to try to cover the breadth of therapies that are involving with transcatheter approaches to valvular heart disease. The next one to cover is the transcatheter tricuspid valve repair. To refresh your memory from the earlier anatomy lesson, the tricuspid valve regulates blood flow on the right side of the heart between the right atrium and right ventricle. Once again, if there is leakiness in this valve, it causes blood to accumulate primarily in the extremities and causes problems with fatigue, shortness of breath, heart failure. It can also lead to right ventricular failure if it dilates too much, as well, and can cause symptoms that can eventually lead to survival issues with the patients.

This is a valve that some people have called the “forgotten valve” because it’s more on the right side. It typically causes a lot of symptoms often managed by medication. Surgery is not often offered as a sole therapy for this valve. Most of the surgery that’s done with the tricuspid valve is done in relation to a mitral valve, let’s say, mitral repair and a tricuspid repair at the same time or aortic and tricuspid at the same time. It’s done in combination, but as a sole therapy, not often performed. The people that have had previous mitral valve therapy and the tricuspid was not addressed at that time; over time, that valve may become diseased.

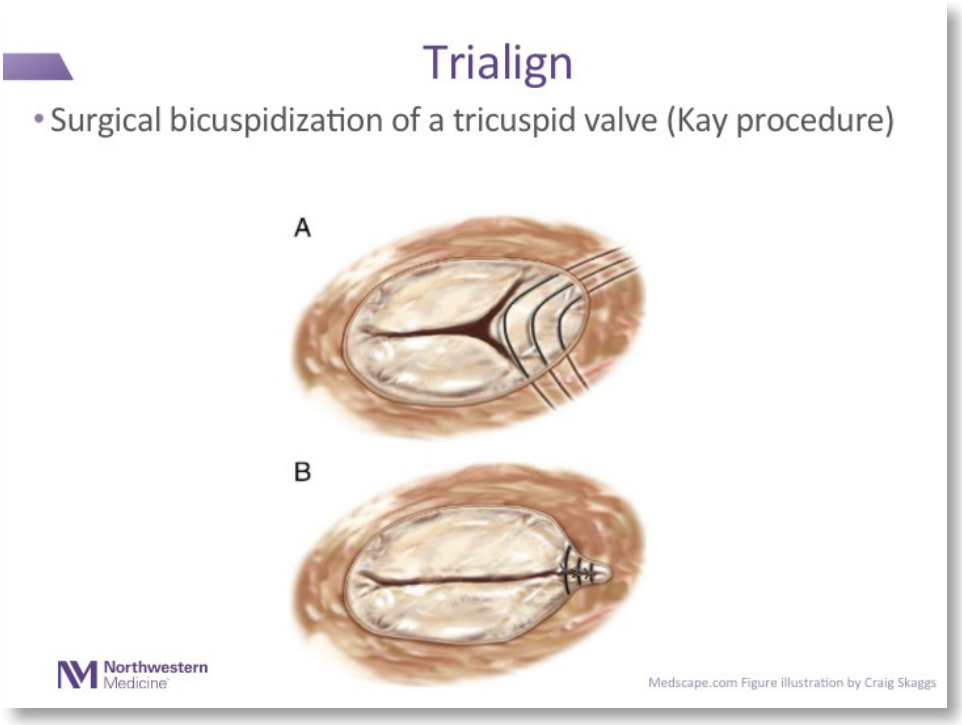
What are the symptoms? We talk about functional tricuspid regurgitation, it’s a lot like Dr. Malaisrie was explaining with mitral regurgitation. There are several mechanisms and functional means that the heart has dilated to the some degree, and the three leaflets of the valve are not coapting well, and so there’s leakiness. This causes the pulmonary disease and right ventricular dysfunction that we talked about. This makes up about 80% of patients with tricuspid regurgitation. These are some of the other causes, just for your understanding; chronic atrial fibrillation, prolapse, rheumatic heart disease, leaflet restriction from ventricular pacing leads, endocarditis, and the very special group of patients have had cardiac transplantation in multiple right ventricular biopsies.

This shows you what happens with tricuspid regurgitation over time. These are called Kaplan-Meier curves. As physicians, these are how we assess therapies, we assess outcomes from medical treatment, and understand disease states. The top graph where it says no tricuspid regurgitation we are looking at patients who have no tricuspid regurgitation and what is the survival? Up to 1500 days, approximately 5 years, which is very high survival.



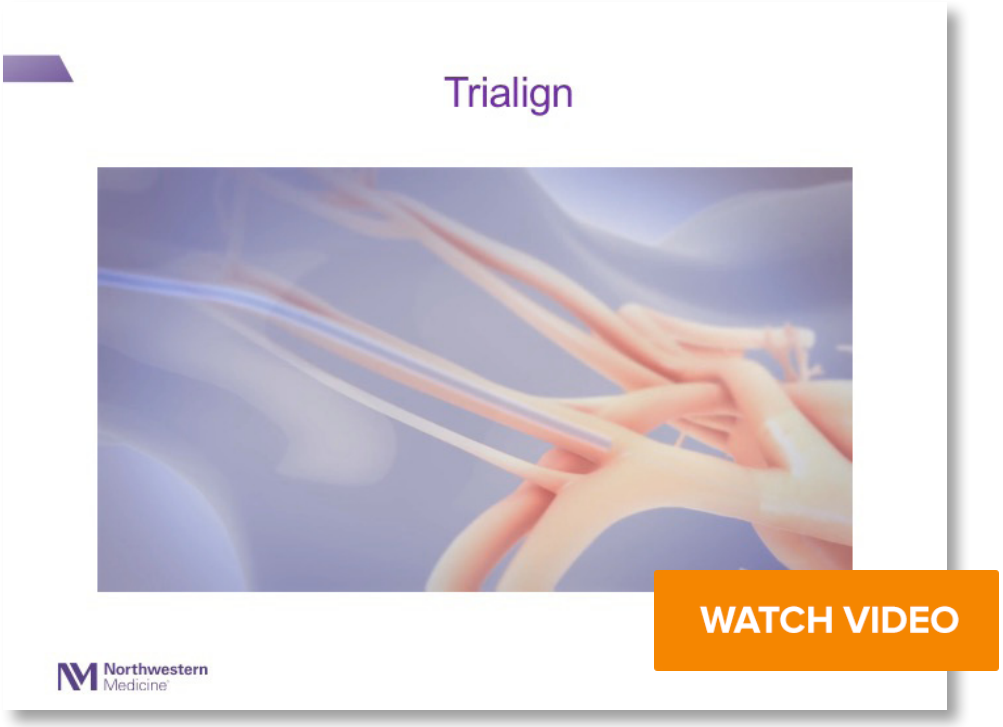
I think what's important here is you drill down to mild, moderate, and then on the very bottom graph, people with severe tricuspid regurgitation. You can see that their life expectancy is markedly diminished by almost 50% when they have severe tricuspid regurgitation. It doesn't just have consequences regarding symptoms but may also have prognostic consequences as far as survival quality.

Transcatheter Tricuspid Valve Repair



Dr. Davidson: What has been recently developed are some transcatheter approaches to treat severe tricuspid regurgitation. The one we've had experience with and the one that's been most widely studied at this point in the United States and elsewhere is called the Trialign device. What this does is puts some sutures into the tricuspid valve very much mirroring a surgical technique called the Kay Procedure. The tricuspid valve essentially becomes a bicuspid valve. Therefore, it decreases the regurgitation by providing better coaptation of the leaflets.

We've had the opportunity to be one of the first in the US and the fourth in the world to do this. This is done through a neck vein. As you can in this video, the catheter gets placed down across the tricuspid valve. A wire then goes through the tricuspid annulus, and then two pledgets are placed down; one on the ventricular side of the annulus and then one on the atrial side. This is a procedure that's guided also by fluoroscopy and echocardiography. Then a second pledget is placed into the posterior annulus and on both sides of the annulus. It's drawn together, pulled together, which we call blanketing the pledget, and then the suture is tied off with a staple and removed from the body.

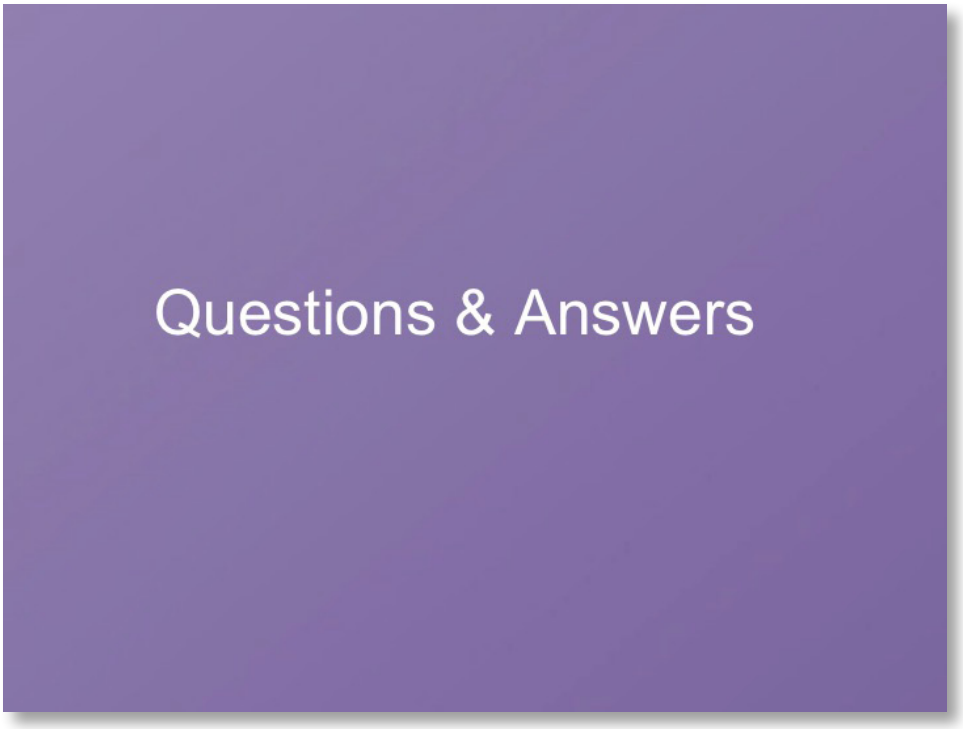


What you can see is this created a bicuspid valve from a tricuspid valve and improved the coaptation. We can assess this at the time of the procedures, and the nice part about this procedure is it does allow for some customization. Much like the MitraClip, if one suture doesn't work, you can potentially put a second one in, and we have had the opportunity to do that. Again, in that situation, we're the first seven in the US to do two pairs of pledgets for tricuspid regurgitation.

This is also investigational. It's being done in a non-randomized registry in the United States right now in what's called a feasibility trial. The randomized trial will be beginning at some point but right now, any patient with this disease that is not doing well with medical therapy can be at least considered. There are certainly anatomic characteristics that we're looking for in order to assure good success for the patient, but we can evaluate based on an echocardiogram for that patient.

I think that takes us through most of our prepared remarks. Now, let's begin the question and answers section of the webinar.

Live Questions & Answers:



Adam Pick: As we being the live Q&A, I want to thank the entire Northwestern team for sharing all of this incredible information. I am just blown away by all the technologies that you've been working on, your collaboration with the various medical manufacturers and the device teams, to come up with these transcatheter approaches. It really is amazing to see.

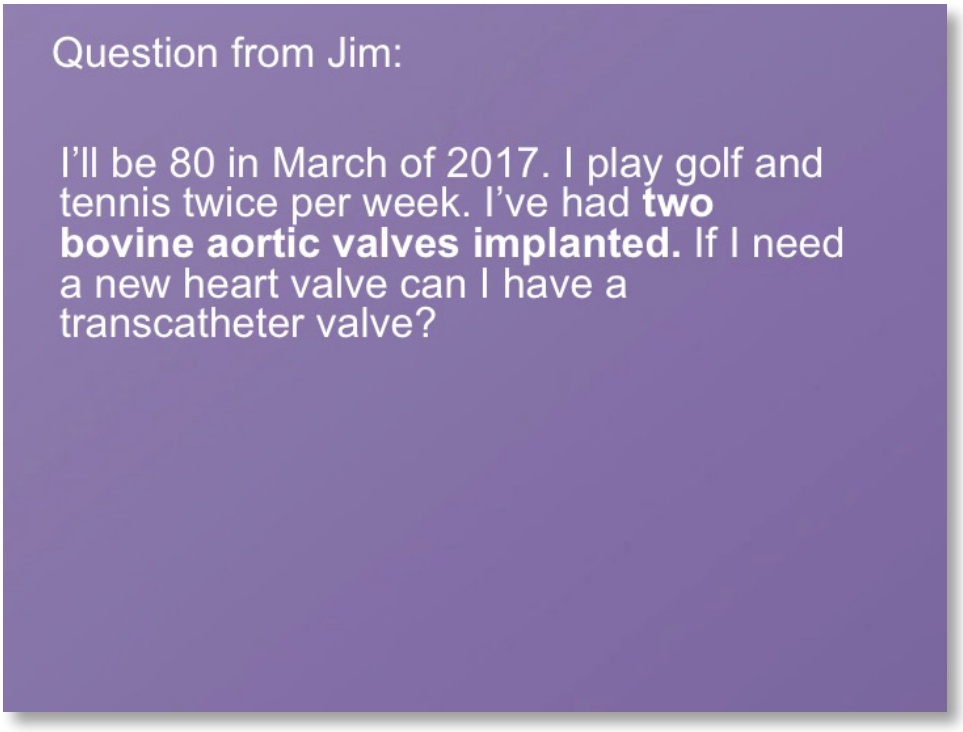
Dr. McCarthy: Just before you move on, I just want to make a very high-level comment for the patients back home, and it's apropos this year in particular. Many years ago, I saw a patient with heart failure who really needed to be treated for aortic stenosis. Turns out she was 101 years old, and so surgery, obviously, would've been very high risk. She had a TAVR, and I'm pleased to report that in August this year, she turned 108. That's a remarkable story. It also happened to be 108 years since the Cubs have won the World Series. She's seen it all.

Adam Pick: That is a wonderful story.

Dr. Davidson: When they were down three games to one, I was saying I don't know how many more years we can expect out of her, so I'm counting on the Cubs to pull through this time for her because she's 108 years old.

Adam Pick: Congratulations to you and your city on the patient success story and the Cubs. Getting to the Q&A section again, we've received many questions for this webinar. So, let's get into it.

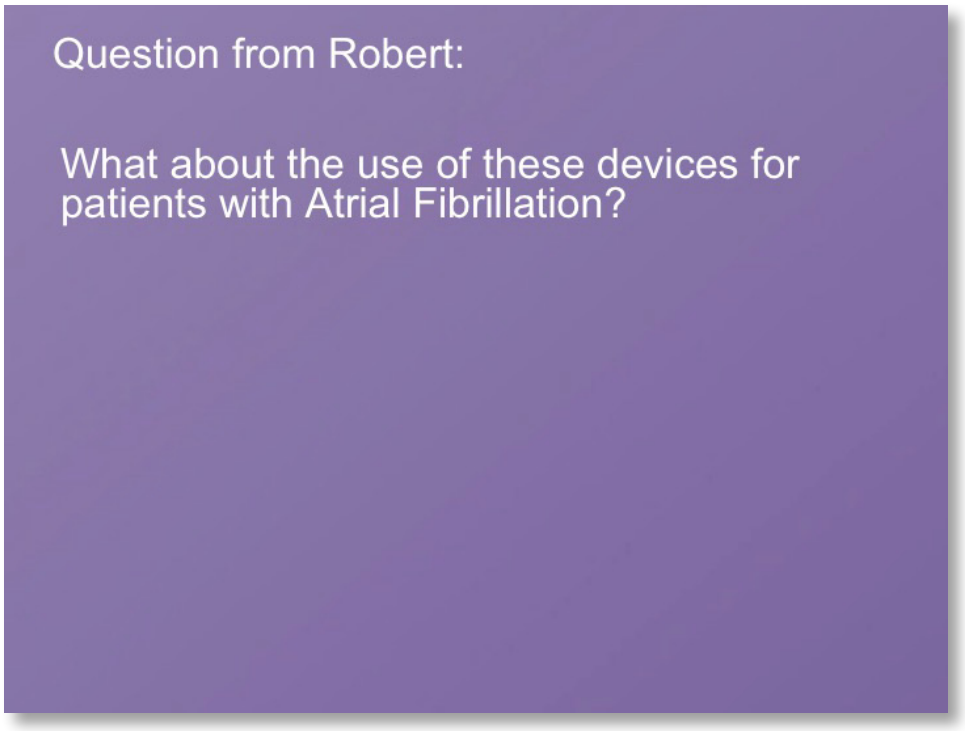
The first question comes from Jim. He writes, "I'll be 80 in March. I play golf and tennis twice per week. I've had two bovine aortic valves implanted. If I need a new heart valve... Can I have a transcatheter valve?"



Dr. Malaisrie: This is a great question. This is Chris Malaisrie. Congratulations on playing golf at the age of 80. We certainly hope that your new bovine aortic valve will last you for the rest of your life. The question is whether or not we can do something about it if you happen to outlive that valve. I think for this particular case, if the valve fails over time, this would be a great case to do an aortic valve-in-valve procedure. Aortic valve-in-valve procedure is a transcatheter procedure, TAVR procedure. The good news is it is commercially approved for high risk patients, so I think someone who is 80-years old with two previous cardiac operations would certainly qualify. I think you'll be able to enjoy good life out of your second valve but if it does go bad, the aortic valve-in-valve procedure would be an excellent procedure for this patient.

Adam: Dr. Malaisrie, for the patients on the line... Could talk about the different experiences, from a patient perspective, of surgical procedures and transcatheter procedure like a valve-in-valve?

Dr. Malaisrie: Correct, Adam. I think the most striking feature of the TAVR procedure is the very short recovery time. Patients who have a TAVR procedure, in this case an aortic valve, can expect to have this procedure with no general anesthesia. Average length of stay in the hospital, about three days. Majority of these patients go directly home, do not need to go to rehab, and would likely, for this patient, be able to start playing golf again in about four weeks. This is compared to open heart surgery where we'd expect maybe about five days in the hospital and about six weeks of recovery time for the sternum to heal.



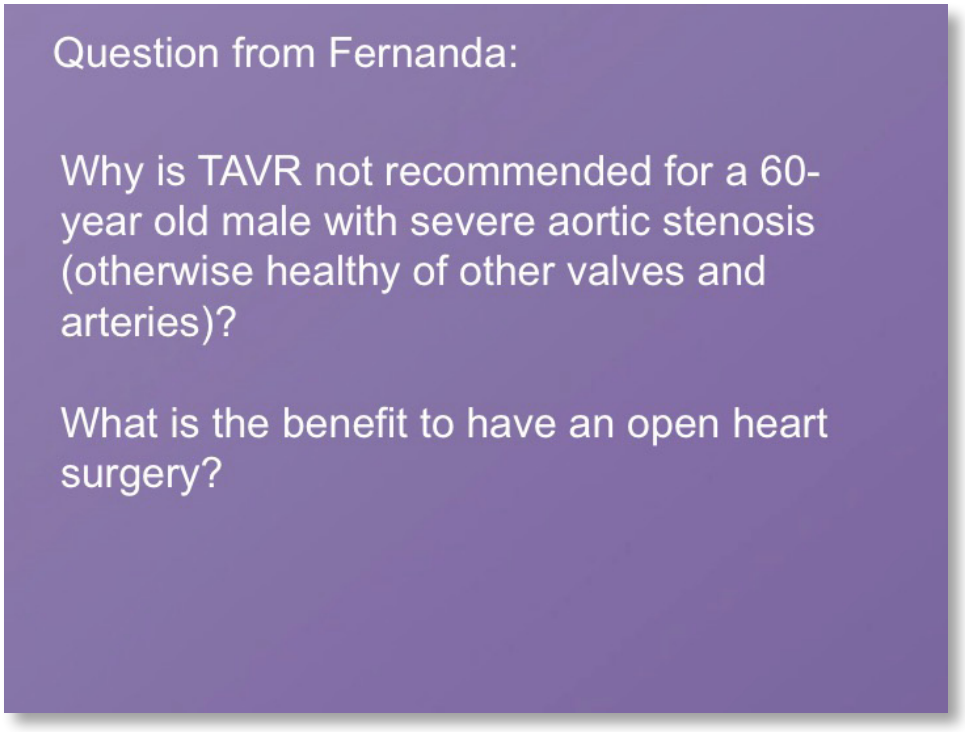
Adam Pick: Great. The next question is from Robert. This is a real interesting one because many, many, many patients in our community have abnormal heart rhythms or atrial fibrillation. Robert asks, "What about the use of these types of devices for patients with AFib?"

Dr. McCarthy: I think it was last year that our webinar focused on mitral valve disease and atrial fibrillation. When we're there to do mitral valve surgery, we also treat the atrial fibrillation. It's a little like plumbing and electrical problems, though. They're different, so these devices themselves do not treat the electrical problem, which is the atrial fibrillation. When we're there at surgery, we treat both the plumbing and the electrical problem, but most of these would not preclude the idea that someone could have the plumbing fixed, and then there's different ways of treating atrial fibrillation with a catheter. They could still work hand-in-hand.

Adam Pick: I understand it right, Dr. McCarthy, there could be a double catheter procedure; one operation for the valve and also one operation for the AFib?

Dr. McCarthy: You would fix the valve with one procedure and then treat the

patient for a while and at a different procedure, they could potentially be candidates for a catheter-based ablation of the Afib.

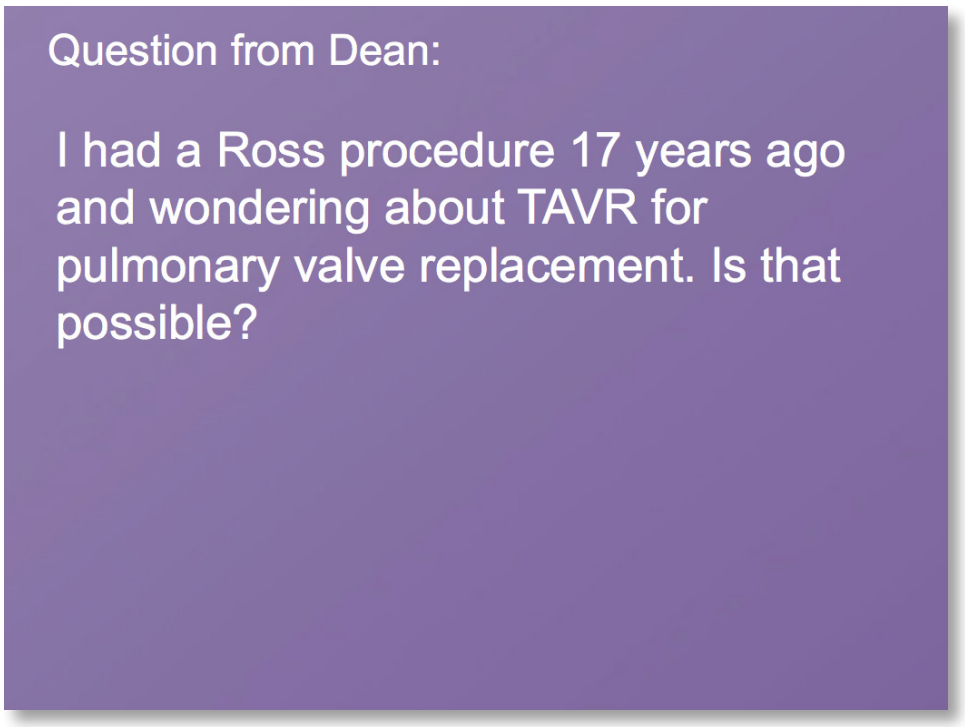


Adam Pick: The next question is from Fernanda is, "Why is TAVR not recommended for a 60 year old male with severe aortic stenosis who is otherwise healthy?"

Dr. Malaisrie: This is another very pertinent question for 2016. Currently, devices that are approved are approved for high-risk patients in this first or second generation devices. Now only recently have third generation devices become available, which we think are going to be good enough for low risk patients such as this 60-year old male with severe aortic stenosis. This is the basis of the low risk trials that are going on currently, Edward SAPIEN 3 valve and the Medtronic Core Valve Evolut-R.

Now it's important to note that aortic stenosis is not aortic stenosis in every pa-

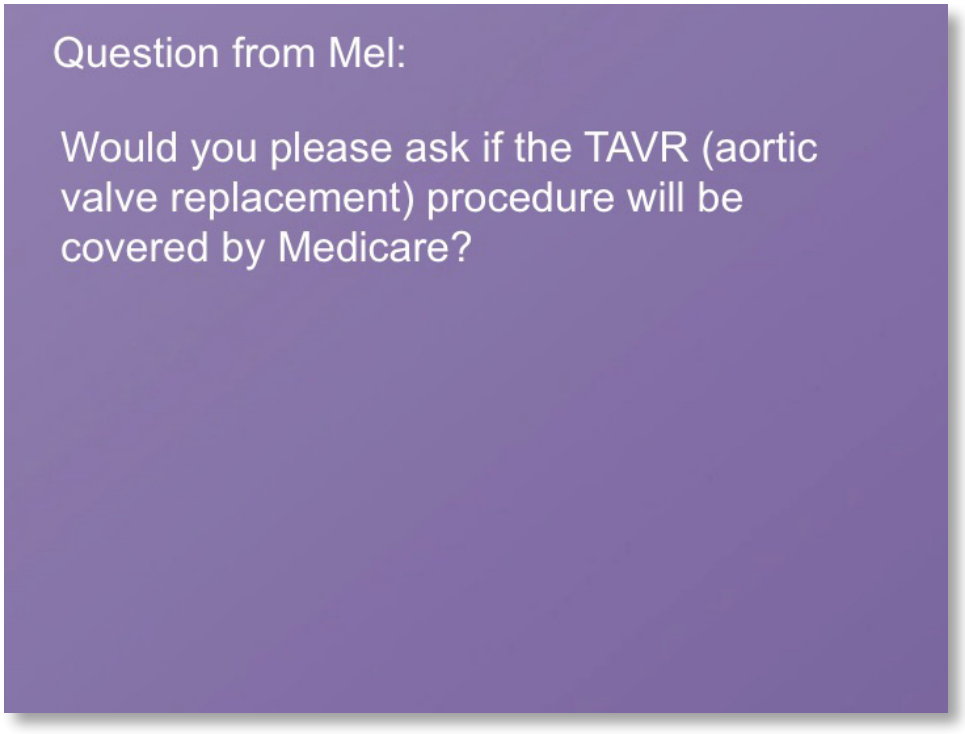
tient. Some patients have aortic stenosis because they have a congenital problem which they were born with. The most important to think about is bicuspid aortic valve. In this particular patient, it'd be very important to know whether or not the patient has a bicuspid valve because up to about 50% of patients with bicuspid aortic valve will also have a coexisting aneurysm. In these particular cases, open heart surgery would be a better procedure to address both the aortic stenosis and the aortic aneurysm at the same time.



Adam Pick : The next question is very near and dear to my heart considering I had a Ross procedure. Dean writes in, "I had a Ross procedure 17 years ago and wondering about TAVR for pulmonary valve replacement. Is that possible?"

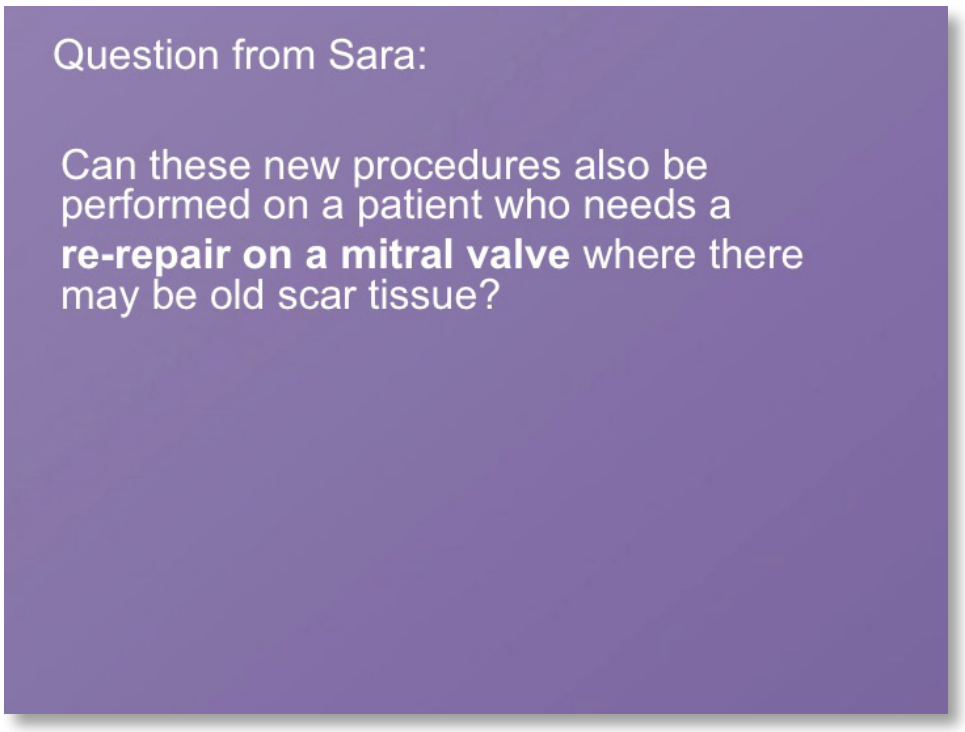
Dr. Davidson: This is Charles Davidson again. In fact, it's a great question because that has just recently been approved by the FDA for homograft in the pulmonary artery and also for pulmonic valve degeneration from a prosthetic valve. It seems to be a good option. I would say that the body of data, because this is a less frequently diseased valve, is less than we have from the aortic valve disease population but seems to be also a fairly safe procedure with the durability data we have thus far; it seems to be excellent and can be also done transcatheter. It's usually done from a vein in the leg; can be done from a vein in the neck. It's placed across the existing homograft or bioprosthetic valve. Some of that depends on the dimensions, make sure we have the right size valves and all. It is an option, should you need valve replacement, to be explored.

With a good heart team like we have here at Northwestern we really try to customize the therapy for what's best for the patient. Something I didn't get a chance to emphasize is all of the decisions on whether we use a transcatheter or open-heart surgery with a patient is really decided by the team and what's best for that particular patient. There's not one treatment that's necessarily going to be ideal and applied to everybody. We obviously like to favor the not invasive or less invasive method, but on the other hand that may not be the best answer for all patients.



Adam Pick: Great, and let's keep moving. Here comes a question from Mel, which is, "Would you please ask if the TAVR procedure will be covered by Medicare?"

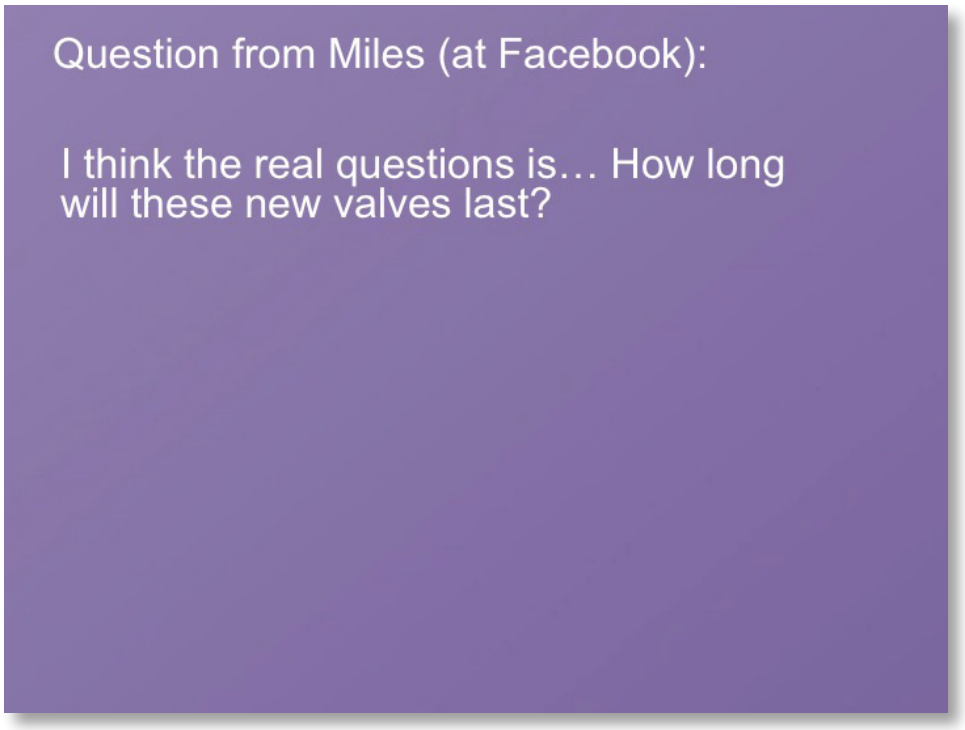
Dr. Davidson: Well, there's some good news here, and that's that CMS / Medicare does cover TAVR procedures, both the commercially approved indications and also the ones that are involved in clinical trials. This low risk population right now is being covered by CMS or Medicare, and obviously in patients with intermediate or higher risk are also covered. The same thing is true for the MitraClip procedure. Any investigational IDE trial that we've talked about today, including the Trialign, would also be covered by Medicare.



Adam Pick: Sara asks, "Can these new procedures also be performed on a patient who needs a re-repair on a mitral valve where there may be old scar tissue?"

Dr. McCarthy: So I would say that's a maybe. It's going to depend on the age of

the patient and other medical conditions, and what the status is on that mitral valve. Theoretically, it's possible. It's not always necessarily the best choices, however. If it's a very young patient with a valve that could be re-repaired, then that's probably going to be the safest and most durable procedure. The TAVR procedure was really the last ten years that it rapidly developed. The next ten years, you'll actually see or hear about a lot more developments in mitral surgery, but it's still pretty early developing transcatheter treatment of mitral valves. Theoretically for some patients, there is definitely a possibility instead of a second operation.

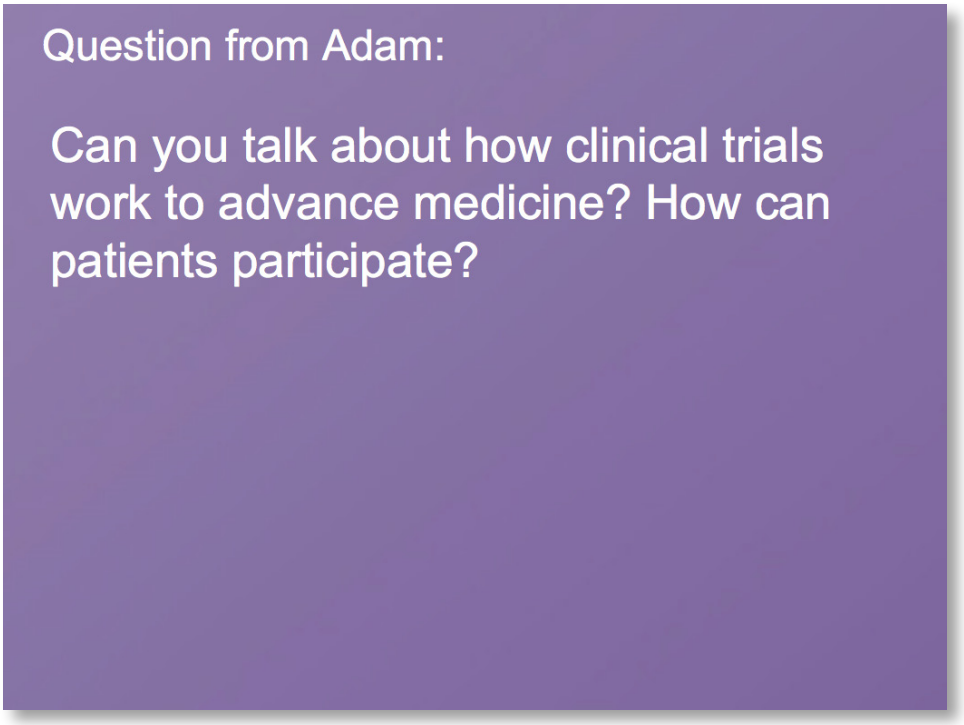


Adam Pick: Great. I hope that helped you, Sara. Let's move on to a question from Miles over at Facebook, who asks, "I think the real question is... How long will these new valves last?

Dr. Davidson: That's an outstanding question. I'm going to answer it in several

ways. There is the cow valve that's being used; at least the valve itself is very similar to the surgical valves. However, it is being mounted on a stent rather than a surgical ring. What we've tried to do is try to understand what the durability is and to date, we have some seven and even some early ten-year data that are comparing head-to-head with surgery that seem to show a similar durability.

Having said that, though, we did not have really good long, 15-year data, 20-year data that we do have on surgical valves. I think some of this is unanswered. It looks favorable at this point in time, but we don't have that direct head-to-head comparison. Those studies are ongoing and as we continue to collect data, it seems to be indicating similar durability, at least at this point in time.



Adam Pick: To follow that question up... We've talked a lot about clinical trials today. For some of the patients who are on the line they may not have known what a clinical trial is. Could you maybe spend a minute or two talking about what a clinical trial actually is and how it's used to learn about these technologies?

Dr. Davidson: Clinical trials are ways in which we try to understand whether new technologies or new drug treatments are either benefiting or not benefiting patients. Typically most of the ones in the US, not all but many, are done through

industry-sponsored trials because they're trying to test whether their device or their medication is of benefit compared to traditional therapy

What happens at that point is that they work with the FDA to design a study that would help prove either the benefit and safety and efficacy of the device. Those are the typical endpoints we looked at. In these studies, we'll look at one-year or two-year follow-up of patients who are randomized to the standard therapy, versus the patients treated with the new investigational therapy. Then we look at what their outcomes are in the short-term and in the long-term.

Sometimes, studies are done as a clinical trial registry, which we talked about some of this valve-in-valve type work, for example, where the FDA has agreed that if you can show safety and efficacy without randomizing to a control group that they would also potentially be willing to approve it. Once all of the data is collected on this, the clinical outcomes, how the patients have done, safety and efficacy, that's presented back to the FDA. The data is then reviewed with a group of experts and decides whether the therapy has met the expectation, that it can be approved for general use and commercial use in the United States.

That's kind of your general, industry-sponsored clinical trial. There are some studies that are also sponsored by the government, which we call NIH trials, National Institute of Health. They're done in similar ways but have a different sponsorship compared to an industry-sponsored trial.

Adam Pick: Great, and with that response, we're going to go ahead and conclude the Q&A section of the webinar, but please, please don't exit the webinar just yet. On behalf of the entire community at heartvalvesurgery.com and all the patients with valve disease around the world, I would like to extend an extraordinary thank-you to you, Dr. McCarthy, to you, Dr. Davidson, to you, Dr. Malaisrie, for sharing all of the work that you're doing, your expertise, with us today. As we end this webinar, I'd like to thank all the attendees on the call. You are part of our community. It's been great getting to know you, many of you recently and many of you, over the years. I just want to thank you for being a part of this community.

Lastly... As we always say here at heartvalvesurgery.com... Keep on tickin!!!

HeartValveSurgery.com Resources for Patients

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