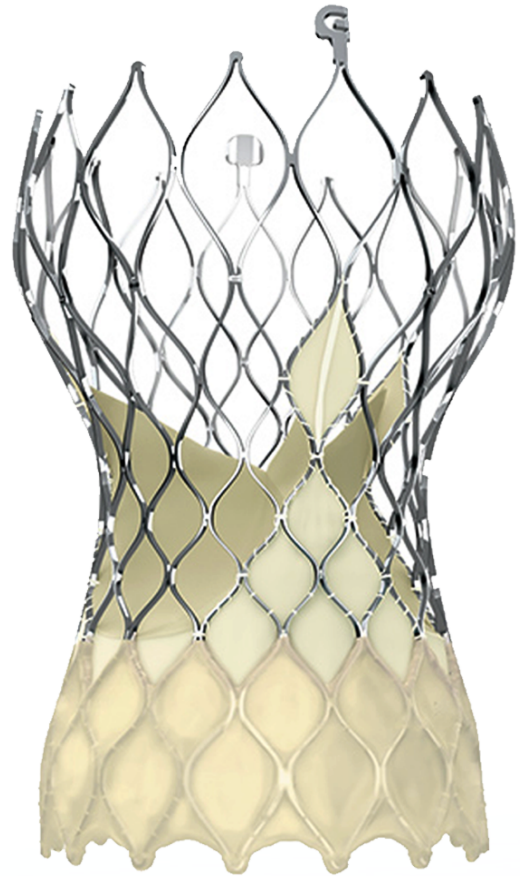
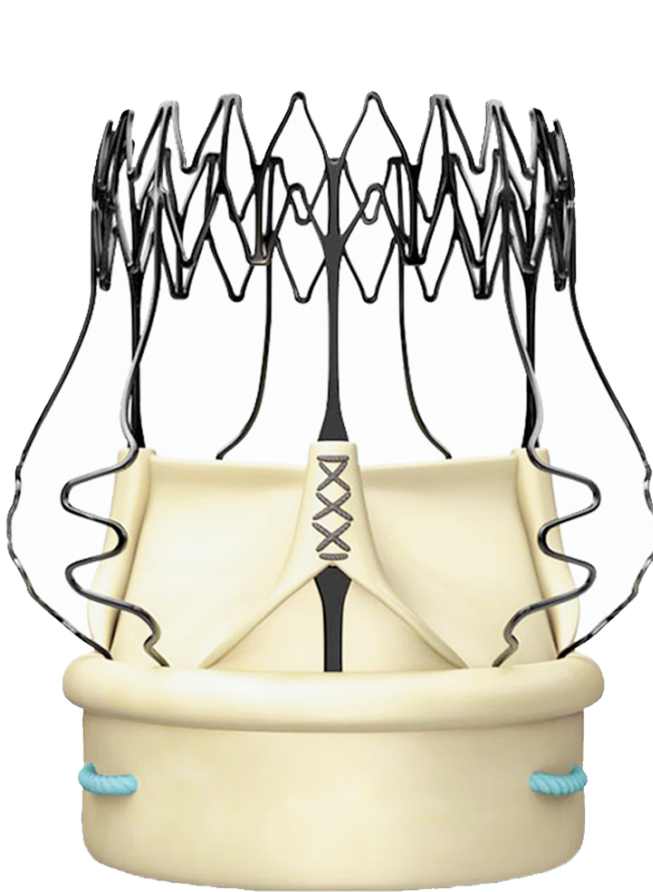
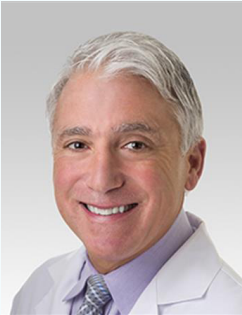


SAVR vs. TAVR

What Should Aortic Valve Patients Know?



Featured Speakers



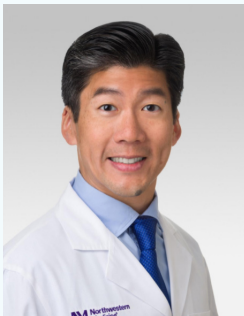
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Adam Pick

Patient, Author & Website Founder

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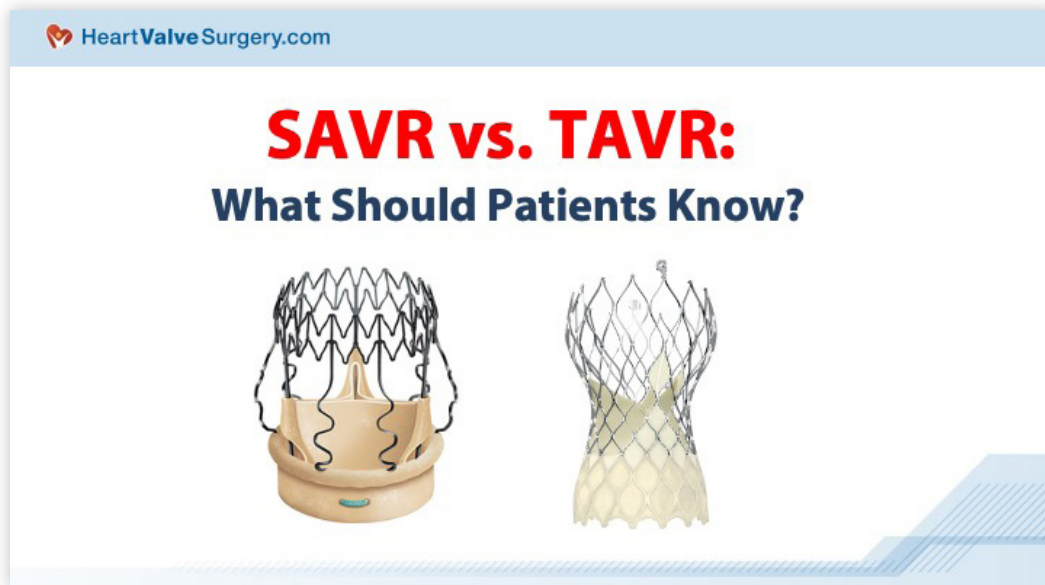
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Introduction




Adam Pick: Hi, everybody. My name is Adam Pick, and if I have yet to meet you, I'm the patient who started HeartValveSurgery.com all the way back in 2006. Today, we have a very special webinar which is SAVR, surgical aortic valve replacement, versus TAVR, transcatheter aortic valve replacement: What Should Patients Know?

Our mission at HeartValveSurgery.com is to educate and empower patients. This webinar, which has had registrations from 550 patients is designed to support that mission.

We have a great agenda for today's webinar. I'm going to introduce the featured speakers. We're going to talk about aortic valve disease, have a meaningful conversation about SAVR and TAVR, answer your questions, and then as we wrap up the webinar, I'm going to ask you to complete a very quick five-question survey to help us enhance these community events in the future.

 HeartValveSurgery.com

Dr. Charles Davidson




- Professor of Medicine
Clinical Chief, Division of Cardiology
Northwestern University Feinberg
School of Medicine
- Medical Director, Bluhm
Cardiovascular Institute,
Northwestern Memorial Hospital
- Clinical trial specialist for PARTNER,
EVOQUE, EARLY TAVR, PASCAL, REPAIR MR
and more.
- Consultant to and receives grant support
from Edwards Lifesciences and Abbott

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Now for the introductions...

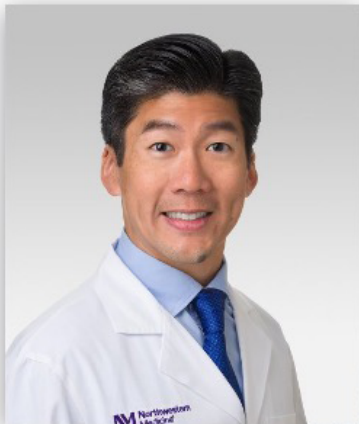
I would submit to you that we have on the line with us today really a dynamic duo or aortic valve replacement. We have [Dr. Charles Davidson](#) on the line who's the Professor of Medicine, Clinical Chief, Division of Cardiology, at Northwestern University Feinberg School of Medicine. He's also the Medical Director at Bluhm Cardiovascular Institute at Northwestern Memorial Hospital in Chicago.

One thing I know about Dr. Davidson is that he is one of the leaders when it comes to clinical trial research. I know of his work on the PARTNER trial, EVOQUE, EARLY TAVR, PASCAL, REPAIR MR and many more. He is a consultant to and he receives grant support from Edward Lifesciences and Abbott.

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Dr. Chris Malaisrie

- Professor of Surgery, Division of Cardiac Surgery
Northwestern University Feinberg
School of Medicine
- Program Director, Thoracic Surgery Residency
and Fellowship, Bluhm Cardiovascular Institute,
Northwestern Memorial Hospital
- Specializes in minimally invasive, complex valve
surgery including valve-sparing aortic root
replacement and the Ross Procedure
- Clinical trial specialist for Edwards PARTNER 3
Valve-in-Valve Trial, Medtronic Apollo Trial,
Cryolife PROACT Xa Trial
- Consultant to and receives grant support from
Edwards Lifesciences



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We also have another, really big member of the heart team, which is [Dr. Chris Malaisrie](#) who is a Professor of Surgery at the Division of Cardiac Surgery at Northwestern University Feinberg School of Medicine. He's the program director of thoracic surgery residence and fellowship at Bluhm Cardiovascular Institute and Northwestern Memorial Hospital.

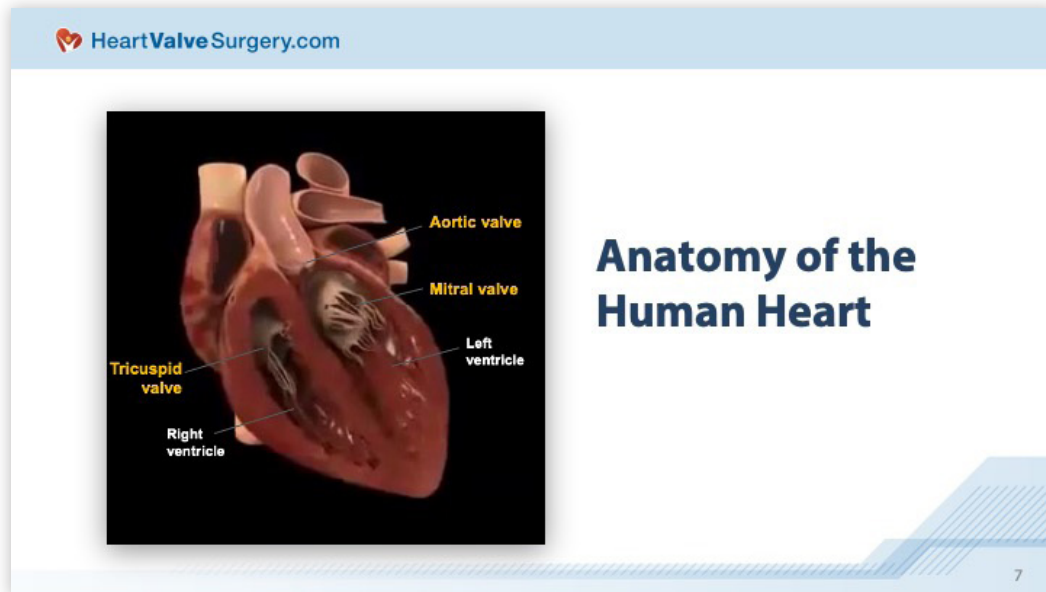
As you may have seen over the years in all of his education videos, Dr. Malaisrie specializes in minimally invasive and very complex valve surgery including valve sparing aortic root replacement and the Ross Procedure. Like Dr. Davidson, Dr. Malaisrie is a clinical trial specialist and right now he's working on several trials including PARTNER 3 Valve-in-Valve, the Medtronic Apollo Trial, and the Cryolife PROACT Xa Trial that has gotten a lot of attention recently. He is a consultant to and receives grant support from Edwards Lifesciences.



In addition to all of these incredible credentials for both Dr. Davidson and Dr. Malaisrie, what I know after seeing these two physicians in the operating rooms at Northwestern and seeing them in the cath lab and seeing them in the hybrid operating suite, I know what really drives these two men. It's not the credentials. Instead, it's the success and the health of their patients. Over the years that we have partnered with Northwestern Medicine, several hundred patients have found their way to Northwestern and had extraordinary results.

Whether it's Paul Powers, Jesse McBride, Jean Frank, Janis Kielbasa, Jim Whitney, the list goes on and on. With that, I can do nothing but thank Dr. Davidson and Dr. Malaisrie for all their past work with patients and all the future work they're going to be doing to help folks just like you and me. With that said, I'm going to turn this webinar over to Dr. Charles Davidson and Dr. Chris Malaisrie.

Human Heart Anatomy



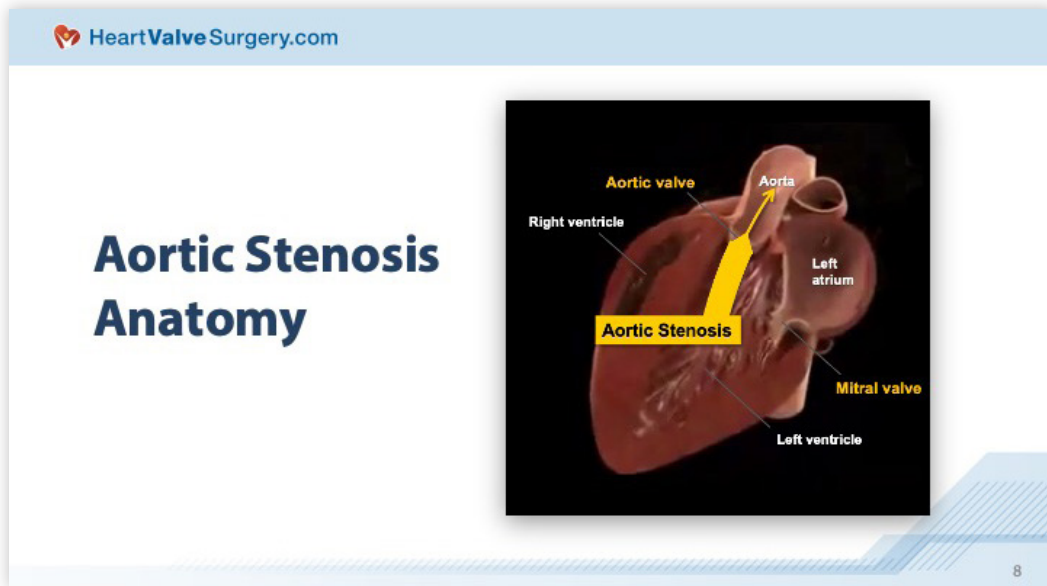
Dr. Davidson: It's really a pleasure to be on the webinar and to be able to speak about transcatheter aortic valve replacement, which has had really a transformation in the last couple years. When we were putting together this talk, Dr. Malaisrie and I, it's amazing how much it's changed in just a short period of time. First of all, it's been an absolute honor, privilege, and just a ton of fun working with Dr. Malaisrie over the years. I think we've been at this for 15 years together. Dr. Malaisrie remarked the other day I think I know your next move before you make it. I said I think the same thing with you.

It's really the type of partnership that we've developed that's led to what we wake up for in the morning, which is getting great patient outcomes. Hopefully the clinical trials help move that forward, and that's what we're going to try to present with you today is what's going on today with transcatheter aortic valve replacement.

For those that want an anatomy of the human heart, how does it all occur, you look at how blood gets into the heart. It gets in from the superior vena cava and inferior vena cava, the big veins in the body, to the right atrium, goes through the tricuspid valve, goes through the right ventricle, goes out to the lungs, gets its oxygen, comes back to the left atrium, then goes through the mitral valve and then what we call the main pumping chamber of the heart, the left ventricle, and then out through the aortic valve.

Today we're going to focus on that aortic valve because it can both block up, what we call [stenosis](#), or it can cause leaking, which we call aortic [regurgitation](#). It's the final exit point of the heart and the blood to the rest of the body.

Aortic Stenosis Causes & Symptoms



Dr. Davidson: As I gave you the information of how blood gets through the heart, aortic stenosis is generally calcified blockage of the valve. There are other causes of blocking up the aortic valve, but far and away it's calcific aortic stenosis. This is not something that occurs because of bad diet or not a lack of exercise or even other factors that we might think about with coronary artery disease, high cholesterol. Those aren't clearly related to this. Sometimes, very frequently in younger patients, it's due to a valve that was not properly formed from the day they were born called [bicuspid aortic valve disease](#).

Also, tricuspid aortic valve stenosis, which means it has three leaflets that come together but have now developed calcium over time. This can occur early in life but generally occurs as we get into the 60s and then above, 70s, 80s, 90s.


Dr. Malaisrie and I helped a patient a few years back who was 101. She lived until she was 110 and did not die of her aortic valve. She was a really sharp

person.

Aortic stenosis develops blockage in the aortic valve. Therefore, the pressure in the ventricle, the left ventricle, has to increase in order to get blood out there. That puts a strain on the left ventricle, and therefore, you get a thickening of the heart muscle, and over time, that heart just can't generate that increased thickness.

The heart get very stiff or actually dilates, and that's when we start seeing heart failure. Now we could see heart failure with aortic stenosis before it dilates. Clearly, we want to get to it before it dilates. The cardinal symptom that we see in the vast majority of our patients is shortness of breath. Some will present with chest discomfort, almost like angina, and others have light-headedness or passing out spells. Those are very, very ominous signs when they develop passing out spells from aortic stenosis, so something that needs to be treated more quickly. I'd say 80% of patients come in with increasing shortness of breath.

Aortic Disease Indications & Treatment Options



Aortic Disease: Indications & Treatments

Aortic Stenosis (AS)

- Higher pressures in the left ventricle
- Thickening of the left ventricular
- Weakening of the left ventricular muscle (heart failure)
- Symptoms of shortness of breath, chest pressure and/or lightheadedness

Age	Treatment Options
> 75	TAVR Preferred
65-75	TAVR vs. Mini-thoracotomy SAVR Shared Decision between Patient and Heart Team
< 65	Mini-thoracotomy SAVR Preferred
< 50	Mini-thoracotomy AVR with mechanical valve vs. Ross procedure

Aortic Regurgitation (AR)

- Can develop suddenly or over decades; once severe, surgical treatment is often required
- Aortic valve does not close tightly
- Blood pumped out of left ventricle leaks back into it
- Symptoms of shortness of breath, chest pressure and/or lightheadedness

Treatment Options
Surgical valve repair/mini-thoracotomy AVR
TAVR devices in the future?

Dr. Davidson: We're going to talk about treatment options here. This on the right here greater than 75 – this is up for discussion. I think Dr. Malaisrie and I can go on back and forth on this for a long time, but just some general ideas.

Over 75 to 80, TAVR is generally preferred. 65 to 75, TAVR versus mini-thoracotomy – we'll talk about both of those, and this is really where the shared decision making between the patient and the "heart team" comes in.

The heart team is so important here to help really decide what's best for you and that patient. Less than 65, mini-thoracotomies, which is a surgical aortic valve replacement, is preferred, and less than 50, a mini-thoracotomy with mechanical valves or even a Ross procedure, which I think Dr. Malaisrie will go through in a little bit.

For aortic regurgitation, that's a leaking aortic valve, can develop suddenly or over decades. Once severe, that is a surgical treatment.


There are no approved transcatheter treatments available at this point in time for aortic regurgitation. So, if that occurs, that is a surgical treatment.

What is the difference?

A leaking valve doesn't have the calcium in the valve, and the calcium is what anchors that transcatheter valve. The valve's not closing tightly. Blood's pumped out of the ventricle. It leaks back in.

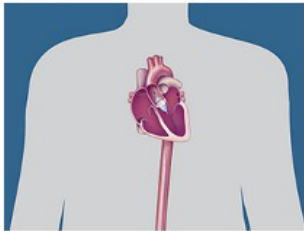
Sometimes with this disease, symptoms don't come on until late in the course of the disease. So, if we detect a murmur and we follow it up with an echo, we need to continue to follow those patients because regurgitant lesions, symptoms are often late onset, and often damage has been done to the heart. Again, no TAVR devices right now. Surgical valve replacement repair, mini-thoracotomies, aortic valve replacement are the hallmark treatment and with excellent results in good hands.

SAVR & TAVR Overview

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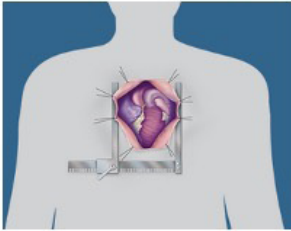
Aortic Stenosis Treatment Options

Transcatheter Aortic Valve Replacement (TAVR)



The TAVR procedure allows a new valve to be inserted within the native, diseased aortic valve.

Standard Surgical Aortic Valve Replacement (SAVR)



During open heart surgery, the surgeon removes the diseased aortic valve and replaces it with a biological valve or mechanical heart valve

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Dr. Malaisrie: Adam, thanks for having Northwestern Medicine back again on the webinar this year. It's really exciting to be talking to your audience, and after 15 years of working with Dr. Davidson, we've accumulated a tremendous amount of knowledge in aortic valve disease. We've been very excited to see the progression in technology and all of the options that are available to our patients with both aortic stenosis and aortic regurgitation.


Here two approaches for patients with aortic stenosis. Those are valves that are calcified too tight. Transcatheter aortic valve replacement, or TAVR for short, has

also progressed over the past ten years.

Before we talked about TAVR for old and elderly patients who were high risk for surgery, sometimes not even a candidate for open-heart surgery. Now TAVI or TAVR is an option for patients who are low risk, so we're looking at TAVR for younger patients.

This is really exciting because with the indication expansion, I think more patients will see this as an option for aortic stenosis. Surgical aortic valve replacement seen on the right here has also progressed. We've had great experience with minimally invasive aortic valve replacement.

Surgical Aortic Valve Replacement


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Surgical Aortic Valve Replacement (SAVR)

Standard surgical aortic valve replacement (an open heart procedure) is the most common treatment for aortic stenosis and has been performed for many years.


Open Heart Surgery - Sternotomy

During open heart surgery, the surgeon will make an incision in the middle of your chest. The surgeon will open the aorta and replace the poorly working aortic valve. The new valve will be stitched into place.



Minimally Invasive Alternatives


Minimally invasive incisions have been shown to be equally safe and even superior to conventional sternotomy. These approaches result in less bleeding, lower rates of atrial fibrillation and pneumonia, and quicker post-operative recovery.



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Dr. Malaisrie: With aortic stenosis patients who need open-heart surgery, patients don't need to have a complete sternotomy. Patients can have minimally invasive cardiac surgery either through a partial sternotomy, seen on the top picture here, and preferably through a miniature thoracotomy – so this gentleman all the way at the bottom here has a small incision. It's a horizontal incision, off to the right. It does not involve splitting the breastbone. This is our favorite approach for AVR for patients who are not candidate for TAVR.

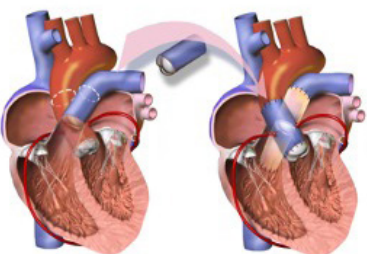
The Ross Procedure

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Ross-Yacoub Procedure

The Ross-Yacoub Procedure is usually performed in patients younger than 50 years old with single-valve disease who want to avoid taking long-term anticoagulant medications after surgery.

During open heart surgery, the surgeon will remove the patient's pulmonary valve and use it to replace the diseased aortic valve. The pulmonary valve is then replaced with a pulmonary homograft. A replacement valve can be more likely to succeed in the pulmonary position because of less demand on this valve.

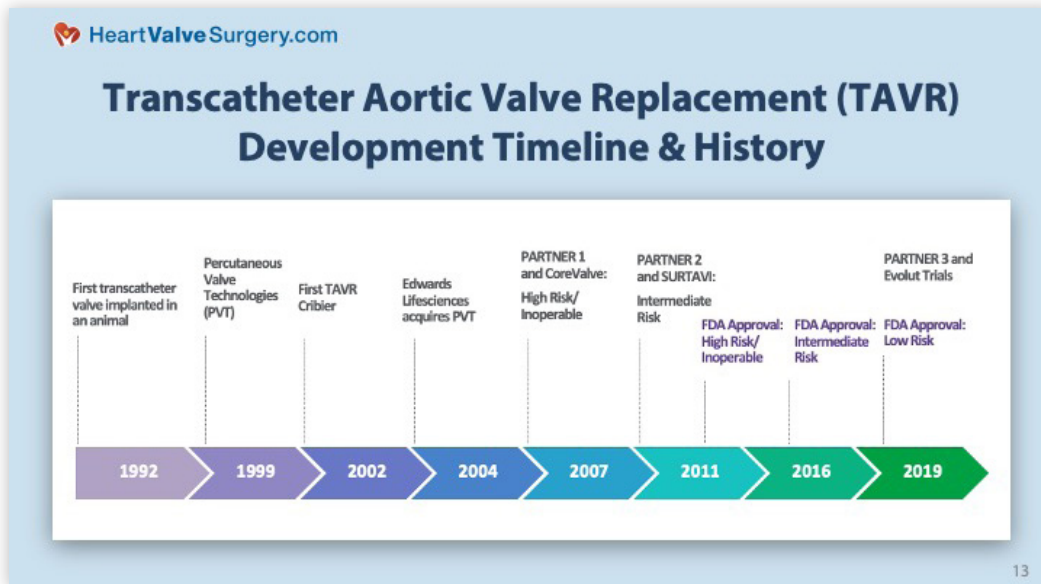


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Dr. Malaisrie: The [Ross Procedure](#) pioneered by Donald Ross and iterated by Magdi Yacoub is a procedure for patients who are less than 50 years old who have aortic stenosis who are considering other options that don't involve an artificial valve.

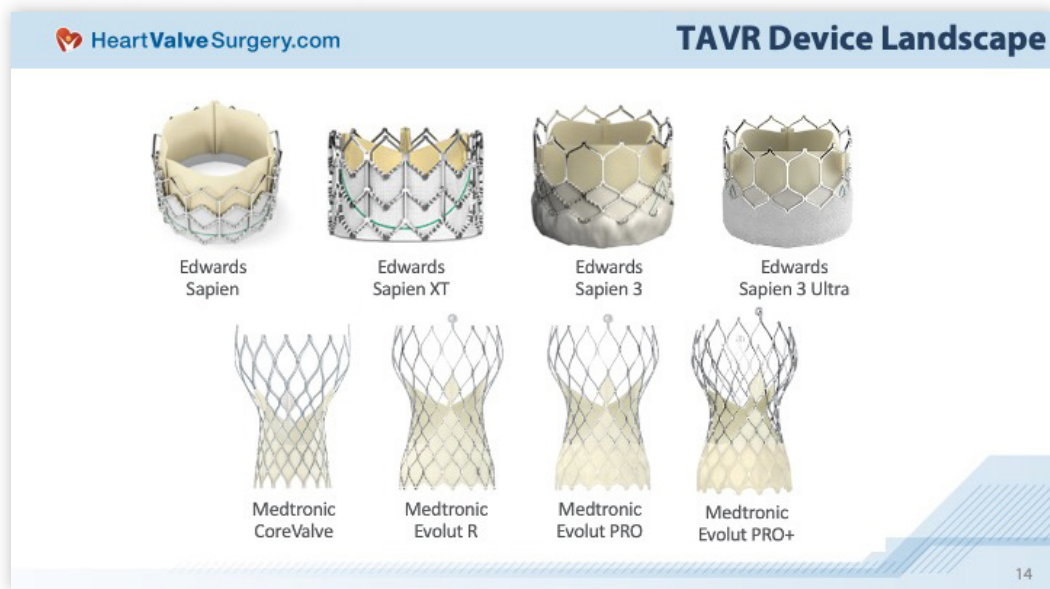
This is a procedure where the aortic valve is removed but replaced by the patient's own pulmonary valve. The pulmonary valve is moved over in the aortic position, and in its place, in the pulmonary place, we use a human pulmonary valve. The human pulmonary valve, also called a homograft, lasts much longer in a pulmonary position because it only sees low pressures from the blue blood that goes to the right ventricle, so this is an exciting option for patients who are less than 50 years old. It offers them an opportunity to have a long-term durable result with likely better survival without the need for anti-coagulation such as Coumadin.

TAVR Development & History




Dr. Malaisrie: TAVR has progressed over the past 15 years. You look all the way to 1992 when the first transcatheter valve was implanted in an animal. Then the first company was founded. It was called PVT. That was back in 1999, and the first TAVR performed by Alain Cribier in 2002 in a human. Edwards acquired this company called PVT and started to work on in-human trials that eventually led to commercial approval. These were through a couple studies. Edwards led the PARTNER study. Medtronic led another study, and by 2007, TAVR was approved with two different valves for high-risk or inoperable patients.

The next iteration of trials came through that looked at TAVR for intermediate or medium-risk patients, and that was approved in 2011. These approvals came through as you see here, and finally, in PARTNER 3 as well as the Medtronic Evolut Trial, these are the low-risk patients, the last group of patients to be studied, and that approval came through in 2019. Dr. Davidson and I are very proud to be leaders in all three of these trials, PARTNER 1, 2, and 3. We've been glad to offer these results to our patients, both in an investigational setting as well in a commercial setting.



Here is an iteration of the valves for both companies. Edwards on the top row and Medtronic on the bottom. What's the same about all these is they're all tissue valves. They are not mechanical valves. These are made out of tissue from an animal. The frame is metal, and that's what allows the valve to be anchored into the heart without coming out. The differences as you move from left to right have to do with the mechanisms that are designed to reduce leaking from around the valve. So, on the top one, you can see a skirt starting at Edwards Sapien 3 where it's been molded to a little bit higher skirt in the Sapien 3 Ultra. Similarly for the Medtronic Evolut, you can see covering on the bottom of the valve, which is also designed to reduce leakage around the valve, which has been iterated in the Medtronic Evolut PRO.

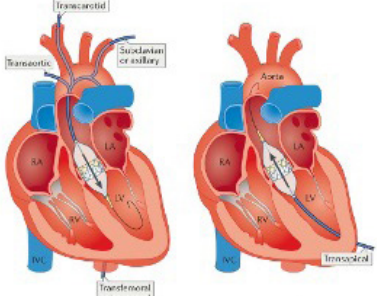
TAVR Approaches



TAVR Operative Approaches

The TAVR procedure uses a catheter to insert the new valve within your diseased aortic valve. The frame will use the leaflets of your diseased valve to secure it in place.

The procedure can be performed through multiple approaches:



Transfemoral (preferred)
Through an incision in the leg

Transcarotid (preferred)
Through an incision in the left carotid artery

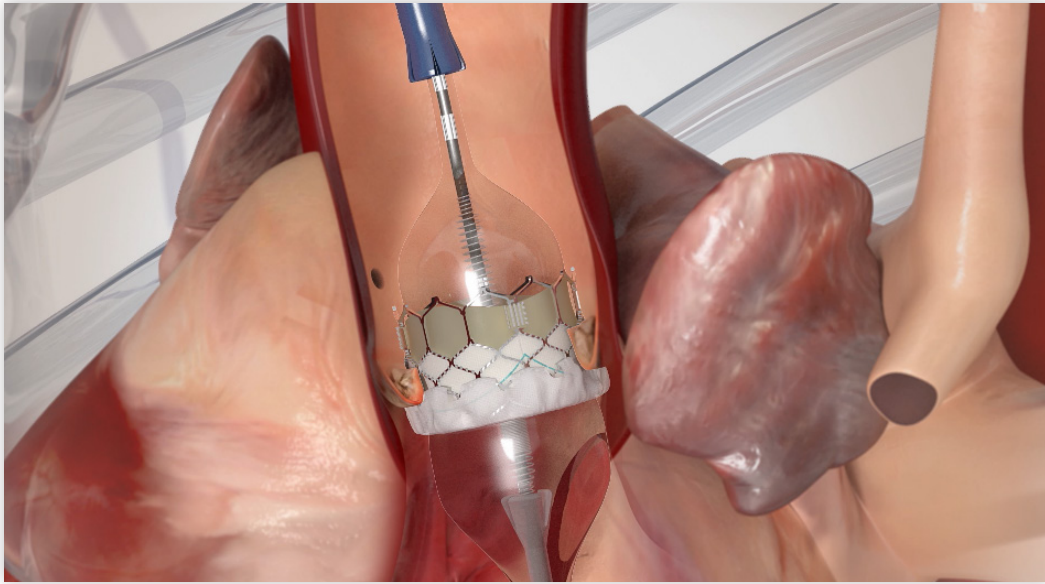
Transapical
Through an incision in the chest between the ribs

Transaortic
Through an incision in the upper chest

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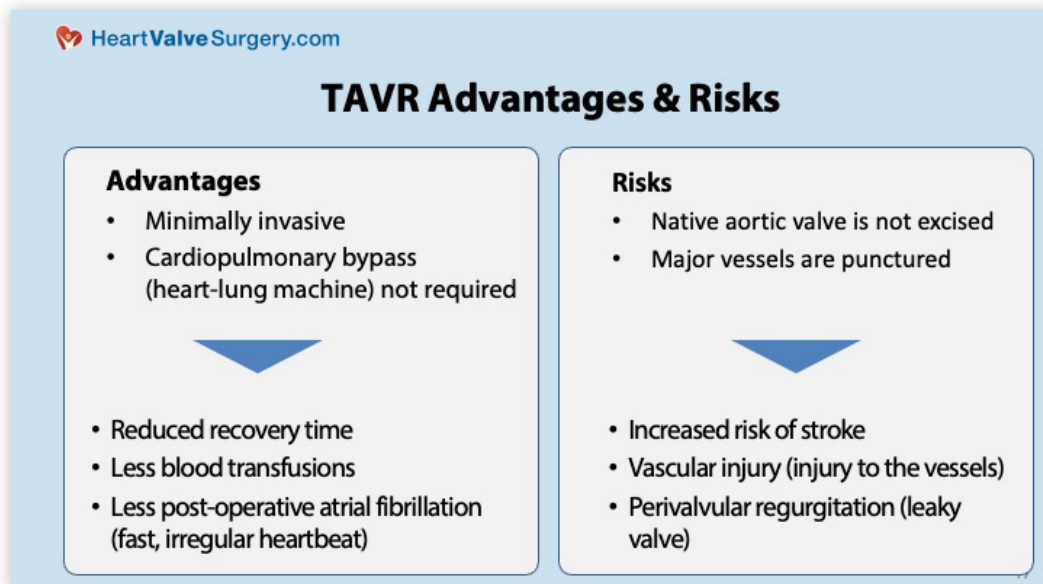
Dr. Malaisrie: Our favorite approach for TAVR is through the groin. So, that's through the femoral artery in the groin through a percutaneous approach. No open incisions. That's what we mean when we say transfemoral preferred. That is the heart all the way on the left. 90 to 95% of patients can have their TAVR procedure through a transfemoral approach. That's most of the patients. A minority, five to ten percent, will need an alternative access. Our preferred alternative access, when the groin is not an option, is through the carotid artery. This is done with general anesthesia through a small incision on the neck, and we can access the carotid artery to deploy the TAVR valve.



Here's a [video of a typical transfemoral TAVR](#) through the groin with an Edwards Sapien 3 valve. After access of the groin without an incision – this is done percutaneously – a balloon is passed over a wire into the aortic arch, past the aortic valve. The balloon is inflated to pre-dilate the aortic valve, which is calcified and tight. This valve is removed from the body and subsequently exchanged for the valve which is mounted on a thin catheter. Here you can see the valve that is crimped down on the catheter in order to allow for it to be passed through the femoral artery. The balloon can be mounted inside the valve, and now the valve is ready to deployed.

The valve is fine adjusted on the balloon and then passed around the aortic arch, over the same wire, into the aortic valve. You'll note that the old aortic valve is not removed in the TAVR procedure. It is left in place and provides a mechanism for anchoring of the new TAVR valve inside the heart. Once the catheter is in position, we can steer the valve to optimize the position. This is done under fluoroscopy. Here the fine tuning is again illustrated here to get the valve in a perfect position. The heart is briefly paced, and a balloon is inflated. The balloon is removed. The valve is left in place that is fully functional. The catheters and sheaths can subsequently be removed from the groin and the small percutaneous access secured. Here's the final video of the functional valve in place.

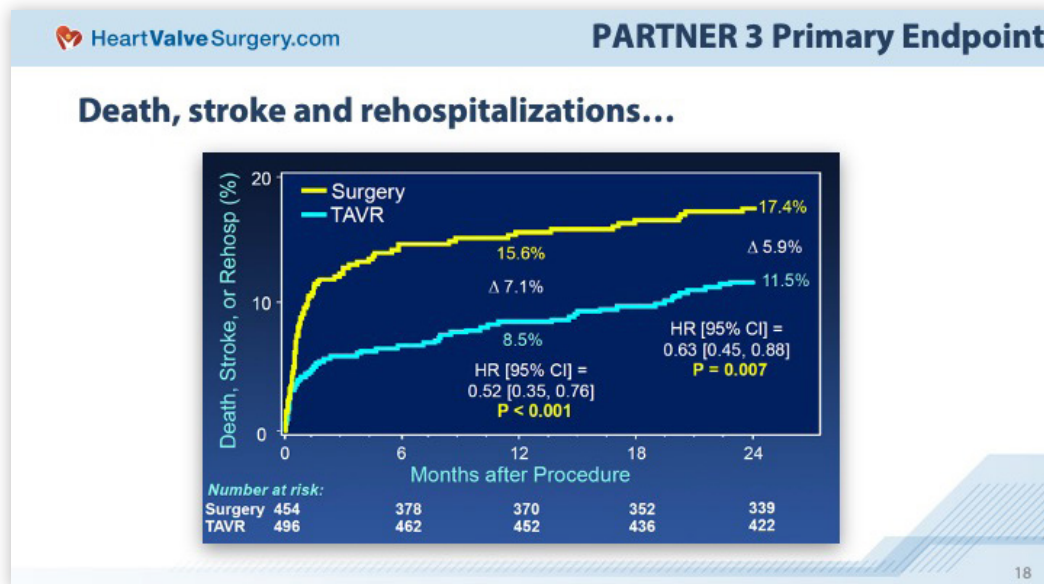
TAVR Advantages & Risks



Dr. Malaisrie: Why do we choose TAVR versus SAVR? There are advantages for TAVR procedures. The biggest advantage is it is minimally invasive or non-invasive. So, for patients who've had cardiac cath in the past to look at coronary artery by angiogram, it is very reminiscent of this procedure. Cardiopulmonary bypass, otherwise known as the heart lung machine, used for open-heart surgery is not required for TAVR. Because of this, recovery time is reduced. Many patients are discharged the day following the procedure, and most are discharged within two days afterwards. There's also less risk of blood loss and therefore less risk of blood transfusions, and post-operative atrial fibrillation has a risk rate in the single digits after TAVR.

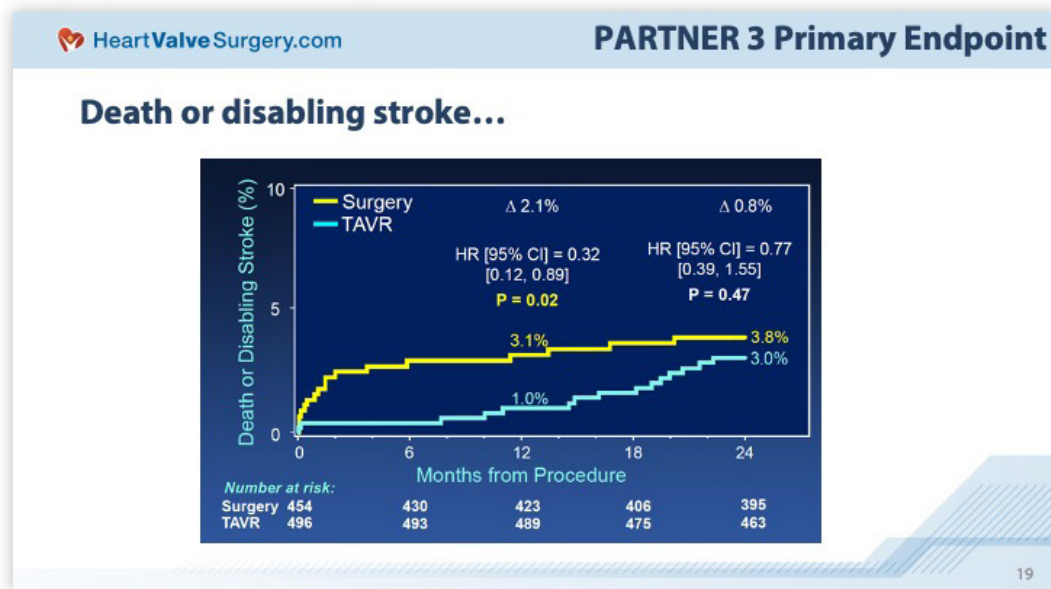
The risks with the TAVR procedure include not being able to take out the aortic valve as we do in open-heart surgery. The aortic valve is left in place, but it does provide an anchor point for the TAVR valve to seat in the heart. Major vessels are accessed, particularly the groin, so these arteries occasionally can be injured but easily repaired. The risk of stroke has decreased significantly with TAVR procedures and are equivalent or even better than open-heart surgery perivalvular regurgitation, which is leakiness around the aortic valve, has similarly gotten better with the valves that have been developed over the past ten years so that we expect almost no one to have any significant leakage around a TAVR valve.

TAVR Clinical Trial Update



Dr. Davidson: Let's go through some of the data that supports the statements that were made on the previous slide. This is data extracted from the PARTNER 3 trial, which as Dr. Malaisrie mentioned is a low-risk trial. It's the most recent one that was done, and I think what's important when you look at TAVR is to look at the fact of now in our fourth generation of valves. Many of the things that plagued the early data with TAVR and why we just did high-risk patients is that we had leaking around the valve, there was large devices so bleeding from the groin was reasonably high, and there was higher stroke and death rates. As we've now moved into the fourth generation and with a lot of operator experience, the data has really flipped, and that's what generated these low-risk trials. What they'll say is can TAVR actually compete with surgery as a viable treatment option in low-risk patients? Not necessarily is it better or worse, but is it even a valid comparison?

These are what we call Kaplan-Meier curves. They're survival curves. They explain event rates. If you look on that vertical axis, you'll see this slide looked at death, stroke, and re-hospitalization. That was what we called the primary endpoint of the trial. It randomized patients to either TAVR or open surgery. What we found in this – and if you look at where it says 12 months after the procedure – is if there was actually less death, stroke, and re-hospitalization in the TAVR group compared to the surgical group. Now, recently, the 24-month data has become available, and it shows a continual improvement compared to surgery in the endpoints of death, stroke, and re-hospitalization. I'm going to drill in a little bit more, and so it was 17% versus 11%.



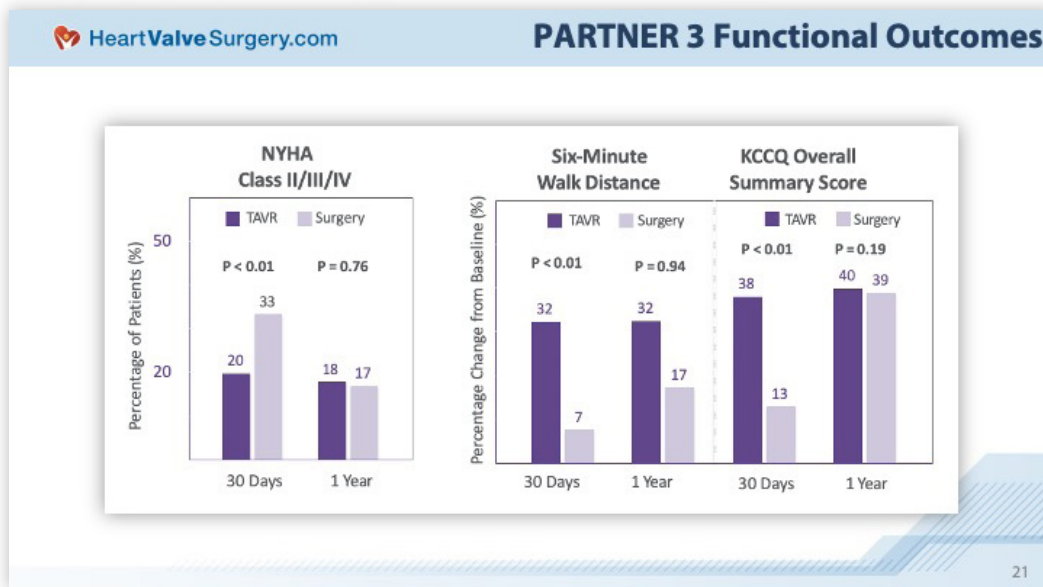
Dr. Davidson: Let's look at just death and stroke. At 12 months, there was 3% death and stroke in the surgical group shown in that yellow line and 1% in the TAVR group, which was a p-value of .02. Anything less than .05 is considered significant, so it was marginally better, but a change of about 2%.

Now out to two years, it looks like the two curves have converged. We're seeing that basically at two years, the incidents of death or stroke are the same for surgery or TAVR, meaning that we have some equipoise here. It really gets back to the shared decision making. How old's the patient? What are some of the comorbidities? What's the patient and family preference? What's the anatomy look like? There's many factors that can go into this decision, but if we have a patient population that was studied in PARTNER 3, we know that we can provide equal death or stroke rates – less re-hospitalization, but equal death or stroke at two years.

HeartValveSurgery.com		PARTNER 3 Secondary Endpoint				
Outcomes	30 Days			1 Year		
	TAVR (N=496)	Surgery (N=454)	P	TAVR N=496	Surgery (N=454)	P-value
Bleeding – Life-threat/Major	3.6% (18)	24.5% (111)	<.001	7.7% (38)	25.9% (117)	<0.001
AKI - stage 2 or 3*	0.4% (2)	1.8% (8)	0.05	0.4% (2)	1.8% (8)	0.05
New PPM (incl baseline)	6.5% (32)	4.0% (18)	0.09	7.3% (36)	5.4% (24)	0.21

Looking at a little bit more of the endpoints, these are ones that came out at one year. Some of the things I do want to highlight is we looked at bleeding was actually higher in the surgical group. Bleeding is really those that require transfusion. It may not have been a – it's counted as a major bleed anytime you get a transfusion, but in my mind, maybe that's maybe a bit of a misnomer, albeit those are the definitions, and it was lower in the TAVR group at 30 days and also at one year. AKI means kidney injury. Was there a problem with the kidneys for some period of time afterwards? In the first 30 days and at one year it was slightly in favor of TAVR, .05 being the p-value, so therefore we'd say it's insignificant, so borderline. As you can see they are low frequency events. Only two in the TAVR group and eight in the surgery group. Once again, we're dealing with small, small percentages. A trial of this size is not really going to detect a difference even if it did occur.


Pacemaker rates is something people talked a lot about with the early TAVR results. Higher pacemaker rates were thought to be occurring with that. Different techniques, different technologies, and with the Elite – with the Edwards valve, the Sapien line of valves, the pacemaker rates in these two trials were identical. Remember, these are not bicuspid valve patients. These are tricuspid aortic valve stenosis, and the results look like they were equivalent in those two populations, surgery compared to TAVR.



Then finally, I wanted to finish out with is functional outcomes. We talk about stroke and death. Obviously, those are the two most important outcomes that we want to monitor, but other things we looked at is functional class. This is a way of measuring how well did patients feel pre-procedure compared to post, and if we looked at people in the TAVR group, they actually appear to get better quicker, as you might expect since it's not an open procedure at 30 days, but by the time they go to one year, they were essentially identical.

We looked at the six-minute walk distance. Again, better at 30 days in the TAVR group, but once you get out to the one-year endpoint, it looks about the same, p-value .94. This is a KCCQ, so it's a quality-of-life measurement based on a questionnaire that patients filled out. Once again, quicker recovery, better feeling at 30 days, but follow it out to one year, about the same. Quicker recovery. Some of the secondary endpoints look a little bit better with TAVR, but when you look at the main input of death and stroke at one year, a little better with TAVR. Same in two years, and if we look, the re-hospitalization, that seemed to be very durable throughout the one- and two-year time frame.

TAVR Valve-in-Valve Procedures

 HeartValveSurgery.com

"Valve-in-Valve" for Failed Tissue Valves

- Disease:** recurrent valve disease secondary to failure of previously implanted tissue valve
 - Over time, usually 10-15 year, tissue (or bioprosthetic) heart valves degenerate and eventually fail
 - Either tight valve (stenosis) or leaky valve (regurgitation)
- Therapy:** transcatheter valve-in-valve
 - A new transcatheter valve is tightly placed into the orifice of the failed surgical valve, pushing the old valve leaflets aside

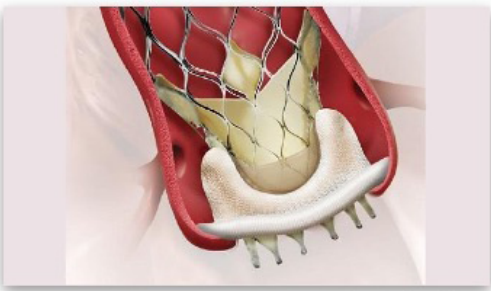



Photo Credit: Medtronic


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Dr. Malaisrie: Thanks, Dr. Davison. I think a lot of the audience have previously heard us talk about the valve-in-valve procedure for failed tissue valves. This is also a TAVR procedure but for a different reason. Previously, patients who had bioprosthetic valves or tissue valves were older patients, and when those valves failed, they either faced reoperative surgery or the valve-in-valve procedure.

We're very excited to bring this online several years back for high-risk and inoperable patients, but now we're glad to lead a low-risk trial that had demonstrated very safe and effective outcomes with a valve-in-valve procedure in patients who were younger and lower risk. This will soon become available for younger patients to get a tissue valve that later go on and have a failed tissue valve. Many patients will not need to see reoperative surgery for failed tissue valves. They can either get an Edwards Sapien 3 valve or Medtronic valve that is shown here. Those results are pending, and currently awaiting approval by FDA.

SAVR Mechanical Valve Clinical Trial Update


PROACT Xa Clinical Trial



- **Hypothesis:** On-X aortic valve and AAP patients can be maintained safely on the Factor Xa inhibitor apixaban (Eliquis) compared to those maintained on warfarin (standard INR)
- **Study Design:** Prospective, multicenter, randomized, open-label, active controlled trial
 - Isolated AVR with the On-X Aortic Valves or On-X AAP
 - 1,000 subjects across approximately 55 sites
 - 2 year follow from last patient enrolled


Study	INR Regimen	Enrolled
Test Group	Eliquis - 5mg BID	≈N=500
Control Group	Coumadin - INR 2.0-3.0	≈N=500

Primary Endpoint: Non-inferiority for thromboembolism and thrombosis

Project Status: Currently enrolling

Patients can transition after having at least 3 months history of standard Coumadin therapy (INR 2.0-3.0)

¹ <https://clinicaltrials.gov/ct2/show/NCT00191525>




VS.

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Dr. Malaisrie: The Achilles heel of mechanical valve on the other hand is anti-coagulation. Here's a picture of an On-X valve that we use for patients who require mechanical AVR. Remember, these valves are extremely durable. We expect these valves to last a lifetime unless they get infected. Patients with mechanical valves must be maintained on an anti-coagulant. Currently the only anti-coagulant that is approved is Coumadin, otherwise known as warfarin.

This is an exciting trial that Dr. Davidson and I are enrolling here at Northwestern. For patients who have an aortic valve replacement with the On-X valve, these patients, three months after surgery can potentially get ELIQUIS, otherwise known as apixaban, as an alternative to Coumadin. This drug has been associated with lower bleeding risks and it's very convenient in that you don't have to test levels for ELIQUIS. We are looking for patients to enroll in this trial, and this could be a potential option for patients who get AVR with mechanical On-X valves.

TAVR Experience at Northwestern Medicine

 HeartValveSurgery.com

Northwestern Medicine TAVR Experience

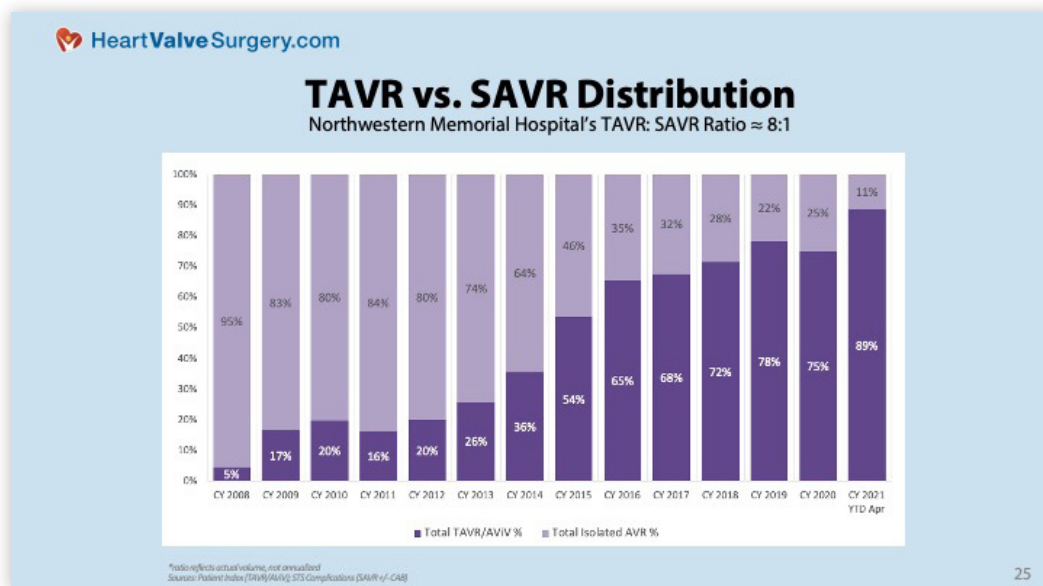
- Started TAVR program at Northwestern Memorial Hospital in 2008
 - Expanded to NM Central DuPage Hospital in 2016
 - Also offer TAVR at NM McHenry Hospital and NM Palos Hospital
- Participated in the initial US FDA pivotal trial and enrolled intermediate risk patients in trials for TAVR with second-generation devices
- Over 2,000 transcatheter valve procedures performed to-date
- Continuing to treat inoperable and high-risk patients, and have expanded distribution of patients to more intermediate and low risk with commercially available TAVR

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Dr. Davidson: We started this program in 2008 with the PARTNER 1 trial. What we've tried to do – we now have the ten-hospital Northwestern network of hospitals and in 2016, we opened this up at our Central DuPage Hospital. We had trained those physicians here. They've now done over 300, actually, with zero mortality, so getting great results out there. We've also extended out to McHenry Hospital and Palos Hospital. We also offer TAVR there as well.

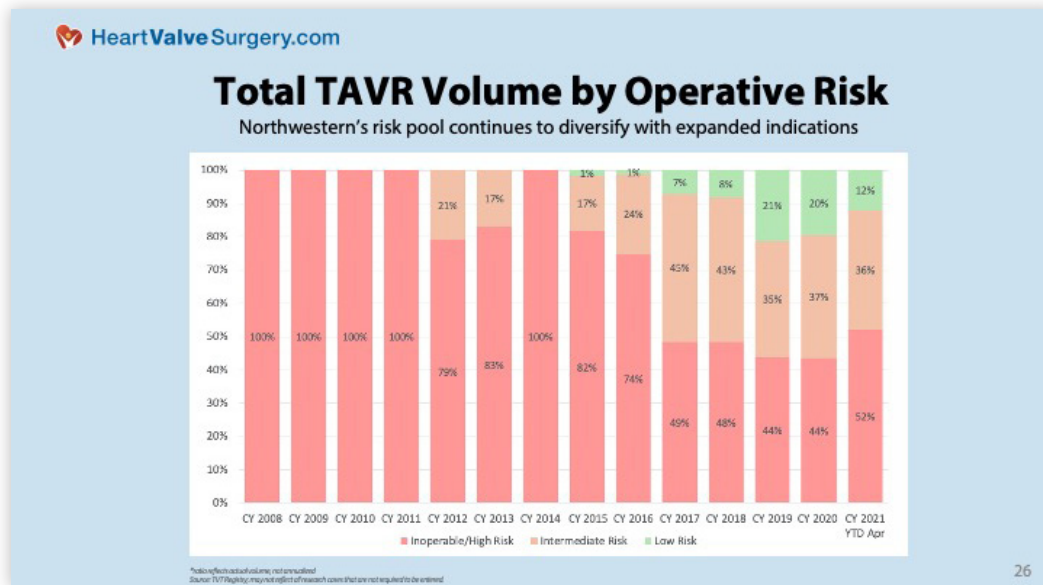
As you know, we participate in the pivotal trial and enrolled intermediate-risk patients. With the second-generation now, we're doing the low-risk patients. We've done over 2,000 transcatheter valve procedures not just in the TAVR arena but also in the mitral and in the tricuspid where we do both repair and replacement, some of those approved technologies and some are investigational and even the early investigational. Dr. Malaisrie and I did the first ever US treatment of a tricuspid valve with a clasp repair a couple years ago. We are continuing to treat inoperable and high-risk patients and have expanded distribution of these patients to more intermediate and low-risk with commercially available TAVR.

TAVR vs SAVR Procedure Distribution: Northwestern's Experience



Dr. Davidson: I think this is, to me, the most astounding slide we'll show here today. Look at where we came in 2008. This is Northwestern data. TAVR, at that point, made up 5% of the aortic valve replacements that were done. Now in 2021, year-to-date, we are almost 90% of these are being done with TAVR. We talked a little bit about bicuspid and other indications for it, but it's really astounding how this field has really flipped in the last 15 years from a surgical-only to a TAVR, but that's not the most important point. The most important point is we're also treating patients that previously could've been inoperable or very high-risk for surgery and may have been turned down at many institutions. Now we have an opportunity to extend those people's lives and improve their quality of life. I think that's the real big story about this slide, not that the field has changed but also that we're addressing populations that may've had limited options in the past or no options.

TAVR Procedures By Operative Risk




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Dr. Davidson: This is just looking at it by operative risk. You look at the far left, you can see basically they were all high-risk patients, inoperable, and once again as it's moved out, you can see that the low-risk population now makes up about 12% of our overall TAVRs, 20% last year, somewhere in that range. Again, this is – many of these people are younger and they need to think about the lifetime management of their valve disease, and I think that's a whole separate discussion but something worth discussing. If someone is, let's say, 60 years old, has severe aortic stenosis, if they get a biological valve, they're likely going to need a second valve somewhere in their lifetime. That's where counseling comes in. Do we want to do a surgical valve this time and then do the TAVR valve inside of that surgical valve like Chris explained when they develop stenosis or regurgitation of that biological valve? Some people say, "I want the TAVR this time and I'll do the surgical next time." This is where we need to discuss this, and that's why I think you'll see this low-risk population will fluctuate at the lower number because they tend to be younger and likely needing a second valve if it's not a mechanical valve the first time through.

Questions & Answers



Adam Pick: Thanks so much Dr. Davidson and Dr. Malaisrie, on behalf your patients and patients all over the country, all over the world who get to benefit from the research that you are doing. We cannot thank you enough for your commitment and Northwestern's dedication to advancing valvular therapy, whether it is a transcatheter approach or a surgical aortic valve approach. Dr. Davidson, I love how you ended talking about the lifetime management of valve disease because that's become an epicenter as our patients – as we all live longer and a lot of our patients need reoperations. That's become front and center to many of the conversations I've been having with patients.

 HeartValveSurgery.com

Aortic Stenosis & Aortic Regurgitation

Wilson asks, “I have both aortic stenosis and aortic regurgitation. Does that impact whether I can have a TAVR or SAVR? What should I do?”

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Adam Pick: Now we’re going to go ahead and shift gears. We’ve been getting lots of questions, and it’s time to open this up to a Q&A session. I’ll just go ahead and read the questions and Dr. Malaisrie and Dr. Davidson, you want to jump in. I’m sure we will all appreciate your responses.

Let’s start with a question from Wilson. He asks, “I have both aortic stenosis and aortic regurgitation. Does that impact whether I can have a TAVR or a SAVR? What should I do?”

Dr. Malaisrie: When you have aortic stenosis and aortic regurgitation – we see that very commonly. We call that mixed aortic valve disease. For patients with mixed aortic disease, they can be treated very similarly as patients with aortic stenosis. If you have mixed aortic disease, Wilson, you can be a candidate for TAVR.

Gregg asks, "At 68, I've been diagnosed with Severe Bicuspid Aortic Valve Stenosis and I'm asymptomatic. Also appears I'm needing a double bypass procedure. My surgeon is recommending full sternotomy with bovine valve replacement. Is TAVR not an option in my situation? Does the surgical team need more "room to work" given the bypass?"

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Adam Pick: Great, I hope that helped you, Wilson. I did not know the answer to that, so thank you, Dr. Malaisrie. Let's go on over to Gregg. As we all know on the line, valve disease is not isolated. A lot of patients will have additional cardiac disorders, whether it's atrial fibrillation, coronary artery disease, or an aneurysm. This question comes in from Gregg. He asks, "At 68, I've been diagnosed with severe bicuspid aortic valve stenosis and I'm asymptomatic. It also appears I'm needing a double bypass procedure." There's that concomitant procedure. "My surgeon is recommending full sternotomy with bovine valve replacement. Is TAVR not an option in my situation? Does the surgical team need more "room to work" given the bypass?"

Dr. Malaisrie: This is an interesting scenario because the patient has both aortic stenosis and coronary artery disease. The treatments for those are aortic valve replacement and coronary artery bypass grafting, so that's what the surgeon is recommending here. That is a perfectly reasonable option and yes, the surgeon needs some room in order to do the bypass depending on where they are. This case would be done with a full sternotomy, not through a mini-thoracotomy approach. However, TAVR can be an option depending on your risk group. If at 68 you're at high risk or have comorbidities that make you inoperable, then TAVR is also an option along with percutaneous coronary intervention, otherwise known as coronary stenting. These are often done in two different settings. Usually the stenting is done first followed by the TAVR procedure. TAVR is an option, but I tend to agree with the surgeon, that if you're an acceptable candidate for open heart surgery, I think bypass with an AVR is probably your best bet.

Dr. Davidson: I always thought that if you're an otherwise reasonably healthy 68 year old with concomitant coronary disease and bicuspid aortic valve, really the first recommendation would be aortic valve replacement by surgery with a coronary artery bypass. That's coming from an interventional cardiologist that does a lot of these, and I – if there were some extenuating circumstances – let's say they had – if they had hepatic disease, renal failure, other things that were not – morbid obesity – there may be things that we – we're not seeing in the slide that could alter this conversation, but the vast majority of people, given what we have in front of us here, would be better served for an open approach.

Adam Pick: Thank you so much. Now maybe Dr. Davidson and Malaisrie, I might throw you a curve ball in terms of Gregg's question. I imagine giving the association of aortic valve disease and aneurysms patients might be on the line having this exact same question. Look, I've got aortic stenosis. I've been told I have an aneurysm. Can that be done using TAVR or some hybrid approach?

Dr. Davidson: This is what Chris does more – probably better than almost anybody, but this is clearly a surgical approach because there's not a catheter-based approach to treat aortopathies and bicuspid aortic valve. I'll let Chris elaborate on the techniques he uses for that.

Dr. Malaisrie: A lot of patients with aortic stenosis, they're caused by bicuspid aortic valve. Those patients often have an associated aneurysm. We estimate about half of those patients would also have an enlarged aneurysm. Currently, there are no TEVAR options. TEVAR is not to be confused with TAVR. TEVAR is a stent graft that is designed to treat the aorta but the aorta and the descending aorta, so that's the aorta that runs along the spine. It's a fantastic option for patients with aneurysms in this area.

However, TEVAR is currently not approved for patients with aneurysms in the ascending aorta. That is the aorta that is next to the aortic valve. These have been done experimentally, including by us, for patients who are extreme risk with perfect anatomy. For the run-of-the-mill patient with bicuspid aortic valve disease with an aortic aneurysm, right now surgery is the best option for you. There has been recent data looking at preemptively influencing the level of inflammation in the body, and there are two things that I found in the literature. This is my own personal hunt. One is patients should always have their influenza vaccine before having heart surgery. The reason I say that is I took that out of the cardiology literature when they saw that patients who had had coronary stents would have a higher incidence of major adverse events if they hadn't had their influenza vaccine, so I dug a little deeper, and I found that once you have your influenza vaccine, it lowers the level of inflammation in your body, so you're set up to tolerate cardiopulmonary bypass better. There's one paper – I don't know if it got published to tell you the truth, but there was one paper that showed that indeed people who had had their influenza vaccine had lower inflammation on cardiopulmonary bypass.

The other thing is we use – even in folks that don’t need them otherwise, we actually put patients on statin drugs coming into operating – before surgery, and we do that because statins also lower the overall level of inflammation and we think might avoid some of this early cognitive impairment. That cognitive impairment appears to be not – it’s not strokes. It’s not stuff going to the brain. It’s this kind of general inflammation in the body that we try to obviate.

The other thing that we do – this is obvious from all the things I’ve said is that we stay away from a lot of medications and things that make people foggy, so we get people snapping to right after surgery. If you’re awake and alert well after surgery and well rested, a lot of that stuff goes away. It’s a multipronged approach, goal directed perfusion being the key element that when you’re on the heart-lung machine, somebody knows how to manage it, and then there’s not being on a heart-lung machine all day, being with a surgeon who can move the operation along and get things done for you. Long answer, but it’s an important question.

Julie asks, "Are there any updates about TAVR approvals for young patients? I'm wondering how/if TAVR might impact female patients with aortic stenosis who want to get pregnant."

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Adam Pick: At HeartValveSurgery.com, we have patients as young as 5 years old to patients as old as 95 years old. This question is for younger folks and in particular, the women on the call. Julie asks, "Are there any updates about TAVR approval for young patients? I'm wondering how/if TAVR might impact female patients with aortic stenosis who want to get pregnant."

Dr. Davidson: Julie, unfortunately there's not a ton of data on the very young patients. The majority of the patients that were enrolled in the PARTNER trial were 65 and older, and much of that is actually predicated by the fact that CMS will reimburse for patients that are in clinical trials that are approved by the FDA. Therefore, less than 65 requires pre-authorization from the commercial payers. We don't have a lot of data on TAVR in very young patients. The fact, though, once an aortic valve replacement's done, whether it be surgical or transcatheter, these patients can go on to have pregnancies and fairly treating them fairly normally as we would. With biological valves, the anti-coagulation for this is really aspirin alone and not really any of the anti-coagulants that we talk about like warfarin or the like.

I think the real question here is mechanical versus biological valves in a very young patient. I think that's, again, a subject for a whole 'nother discussion but those mechanical valves also require anti-coagulation like warfarin that can impact the risk during pregnancy. Those need to be very – managed very carefully and should really be done in a heart center that has a dedicated group looking at women, young women, pregnant women, and how to manage them throughout their pregnancy with congenital heart disease. Chris, you want to add any more to that?

Dr. Malaisrie: I think this question gets to the heart of valve choice for patients and for patients who are considering pregnancy, these are obviously patients who are less than 50 years old, so which valve would you take? The Heart Association and the American College of Cardiology would recommend mechanical valves for most patients less than 50 years old but not for patients who are considering pregnancy. Pregnancy would disfavor mechanical valves and bioprosthetic valves are probably the preferred valve for young patients who are considering getting pregnant.

This also gets to the heart of lifelong planning of aortic valve disease. If you consider that bioprosthetic valves last maybe about 15 to 20 years at best, if a patient is in their 30s and takes a tissue valve, you may be looking at three procedures in your entire lifetime. Planning becomes very important. I suggest that with this complex patient that you talk with your heart team and understand your options clearly and make a decision in conjunction with your physician.

Chris asks, "At 47, I had SAVR. At 55, I had another SAVR given limited data and higher stroke rates of TAVR. I'm going to need another valve in the future. What do the doctors think I should do for the 3rd aortic valve replacement?"

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Adam Pick: Chris' question is a wonderful follow-on to the conversation that we're having about the lifelong management of valve disease. Chris asks, "At 47, I had SAVR. At 55, I had another SAVR given limited data and higher stroke rates of TAVR at that time. I'm going to need another valve in the future. What do the doctors think I should do for the third aortic valve replacement?"


Dr. Davidson: This is an excellent question, and probably we won't do it complete service here in this discussion. Getting back to the heart team, so at 55 – unfortunately 47 to 55 is not what we normally expect for a SAVR. As Chris said, 15 years is the number I usually quote and put some numbers around that, but 8 years is a little bit on the early side.

This is someone – let's hoping that they're going to get to age 70 without

needing another procedure and if they did, that would be to me probably a person we'd think about a valve-in-valve on. Again, it depends also on what the size of the valve is that's in there because if it's a smaller valve, we might do another operation and then talk about a valve-in-valve. If it's a larger valve and we can start stacking TAVR valves, we might think about double valve-in-valves. Having said that, there's not a lot of data, very little, on more than one valve-in-valve procedure. This is a great question, and I hesitate to give too much advice on this because a lot of it will depend on how long this second valve lasts and the size of the valve and then the risk category that you're in at that point in time. How well did you recover from your first two surgeries is another important point that we need to keep in mind.

I'm giving you a 30,000-foot opinion here. Clearly not enough that if I were you, Dr. Malaisrie, that I'd be able to make a decision what to do. You'd start framing the discussion you're going to likely have to have. Dr. Malaisrie, you want to add to that as well?

Dr. Malaisrie: I think all those points are very important For this patient, I think I would go into the mindset of valve-in-valve procedure first unless the anatomy is not suitable for it. This is really important because patients should go to centers that have advanced imaging that can study the anatomy of the aortic valve and the aortic root. Some patients, valve-in-valve are not suitable based solely on anatomy and surgery becomes the only option. For this patient, it's a lot easier than the pregnant patient. I think this would be a valve-in-valve.

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TAVR Lifespan

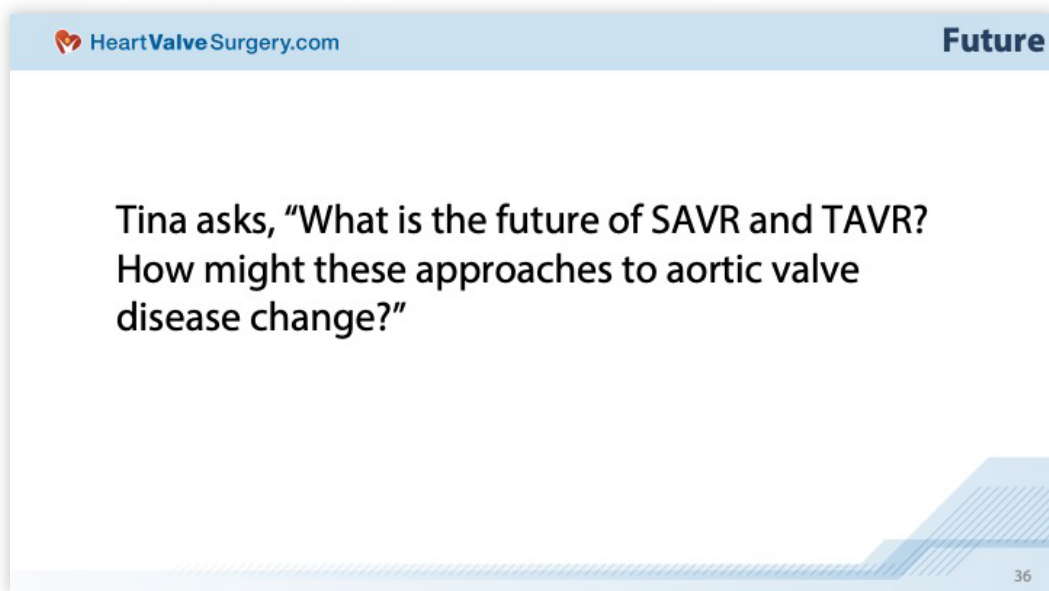
Shannon asks, “Does the TAVR valve last for less time than a valve implanted via surgery? What are the lifespans of the TAVR valves used today?”

32

Adam Pick: I threw you a curve ball earlier. I’m going to throw you one right down the middle because I imagine you get this question all the time about TAVR and its life span. Shannon asks, “Does the TAVR valve last for less time than a valve implanted via surgery? What are the life spans of the TAVR valves used today?”

Dr. Davidson: This is not a straight fastball because we don’t know the answer to this one yet. As we’ve said, we started doing these 15 years ago, and it’s pretty much inoperable high-risk patients. The best data we have at this point are only out between five and ten years, which looks reasonably equivalent, but we don’t really have 15-year comparative data right now that we can cite to know whether these are different. It’s the same [48:19] valve material, whether it be bovine or porcine, made by the same companies that make the surgical valves. They are now – though now they are implanted now on a metal frame,

not on a surgical ring, and so they are done slightly differently. The old valve's not removed. We don't know the answers yet and we're in our fourth generation so even if we looked back and tried to pull out some of the early data, it's a different valve design at that point in time. More to come here and what I tell patients is just what I said here today. The best data we have is they look equivalent, but we do not have 15-year data at this point in time to make a valid comparison.



Adam Pick: Great, and we're getting close to only having time for one more question. I wanted to ask a question that came up from Tina, and I think it's a really important question about the future. You guys are doing a lot of research, a lot of work with your team there. She asks, "What is the future of SAVR and TAVR? How might these approaches to aortic valve disease change?"

Dr. Malaisrie: I think both approaches have changed a bunch in the past several years that I think I'm very hopeful that both procedures will get safer in the future. For SAVR, minimally invasive approach I think will become more available across the country. Probably currently only a handful of surgeons will offer minimally invasive cardiac surgery for a SAVR. In the future, I think that most surgeons will offer minimally invasive cardiac surgery.

TAVR, I think the valves will also continue to get better. I think there's a couple challenges to overcome but not that many. Peri-valvular leak or leakage around the valve I think has been overcome. Pacemaker risk has similarly come down. We're also looking to have TAVR approved for patients not just with aortic stenosis but also with aortic regurgitation. I think the indications will expand for TAVR. We'll get longer term data to prove to the previous patient who asked the question of durability. How long does TAVR last? We'll have that ten years data probably in the next five to ten years

Dr. Davidson: I would agree with everything Chris said. I think that only points I'd want to highlight additional is we don't have really good comparative data on bicuspid aortic valve disease without aortopathy surgery versus TAVR, and I think that's something we will need moving forward so we can advise those patients better. Aortic regurgitation, although less frequently seen without an aortopathy, is an area that seems fruitful for also expanded technologies

I look at this like I did coronary stents and valves [51:21] and drug-eluting stents. We've reached a point now where we're getting to the very tip of refinement. We're making changes that were huge in the beginning and now they're becoming less. I don't see a large change in this technology right now because most of the limitations have been addressed, but I do think we need data, durability bicuspid and some technology to treat aortic regurgitation.

Adam Pick: Great, thanks so much, and with that I need to go ahead and thank everybody on the call today.

HeartValveSurgery.com Resources for Patients

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 dis-ease 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.