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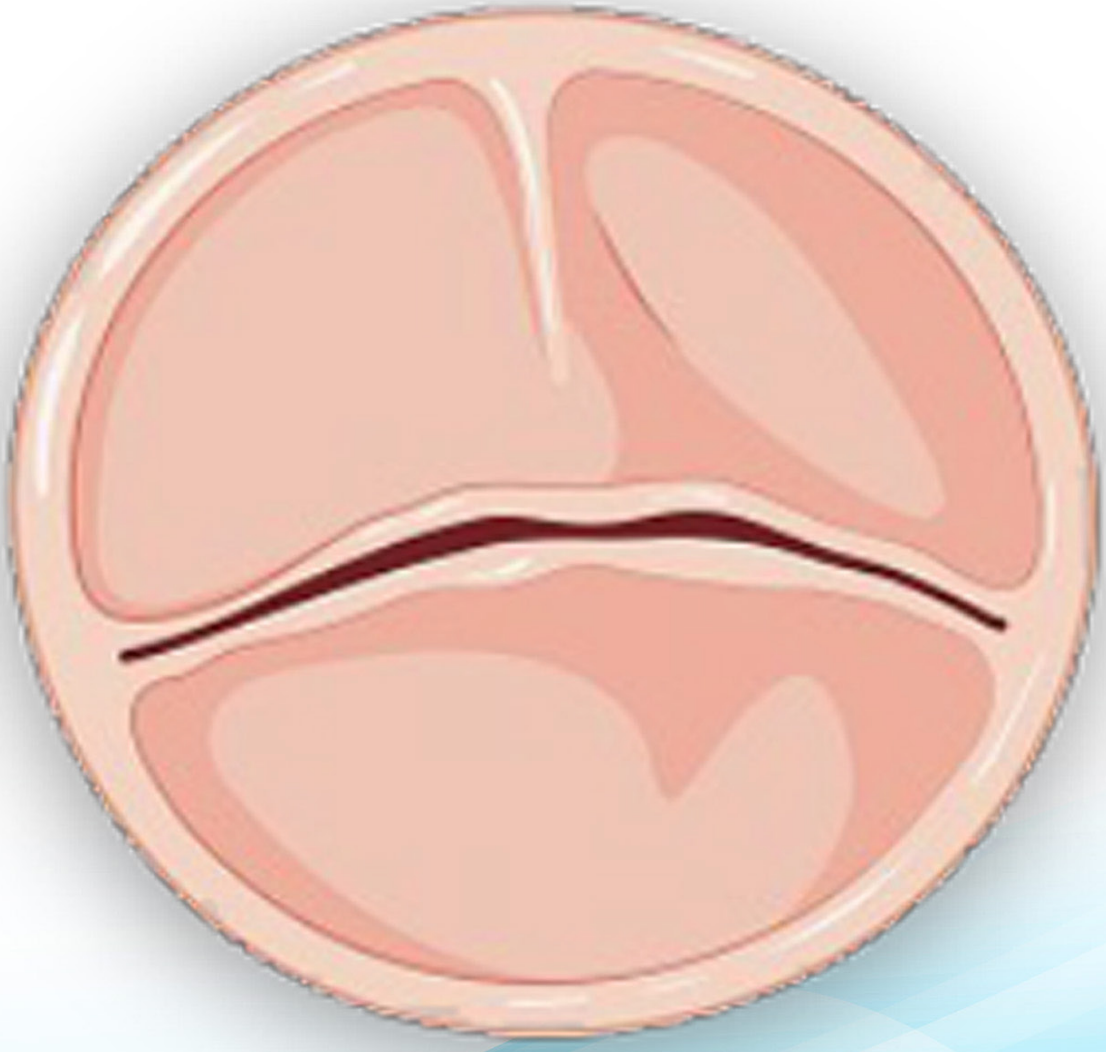
ADVANCES IN BICUSPID AORTIC VALVE THERAPY



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Authors

Dr. Kristen Sell-Dottin

Cardiac Surgeon
Mayo Clinic Arizona (Phoenix)
(480) 741-1876
Learn More.

Dr. Bryan Barrus

Cardiac Surgeon
Mayo Clinic Arizona (Phoenix)
(480) 637-3291
Learn More.

Dr. Jack Haney

Cardiac Surgeon
Mayo Clinic Florida (Jacksonville)
(904) 664-6338
Learn More.

Adam Pick

Patient & Website Founder
HeartValveSurgery.com
(888) 725-4133
Learn More.

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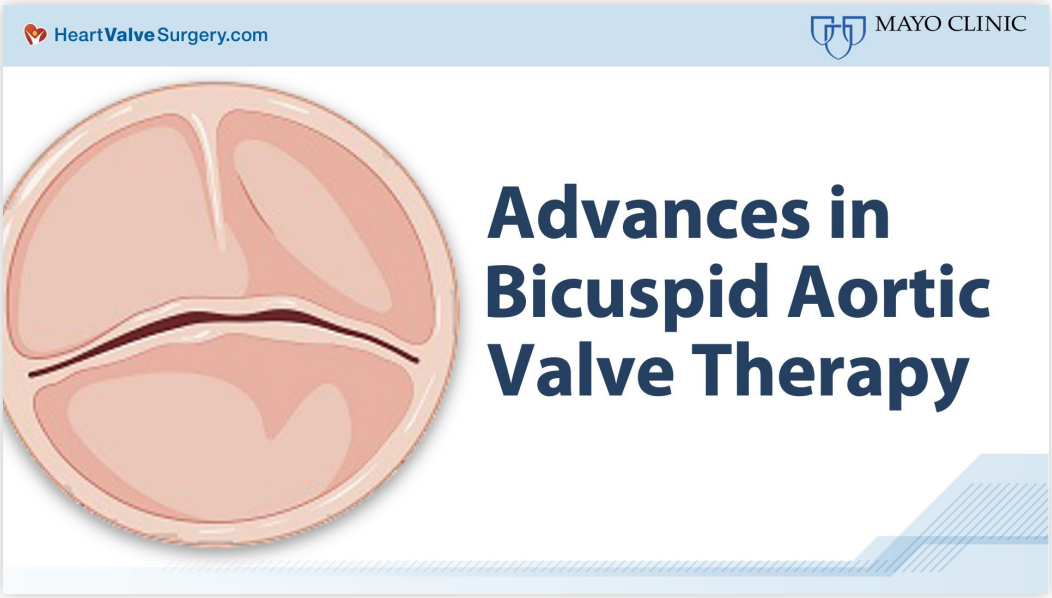
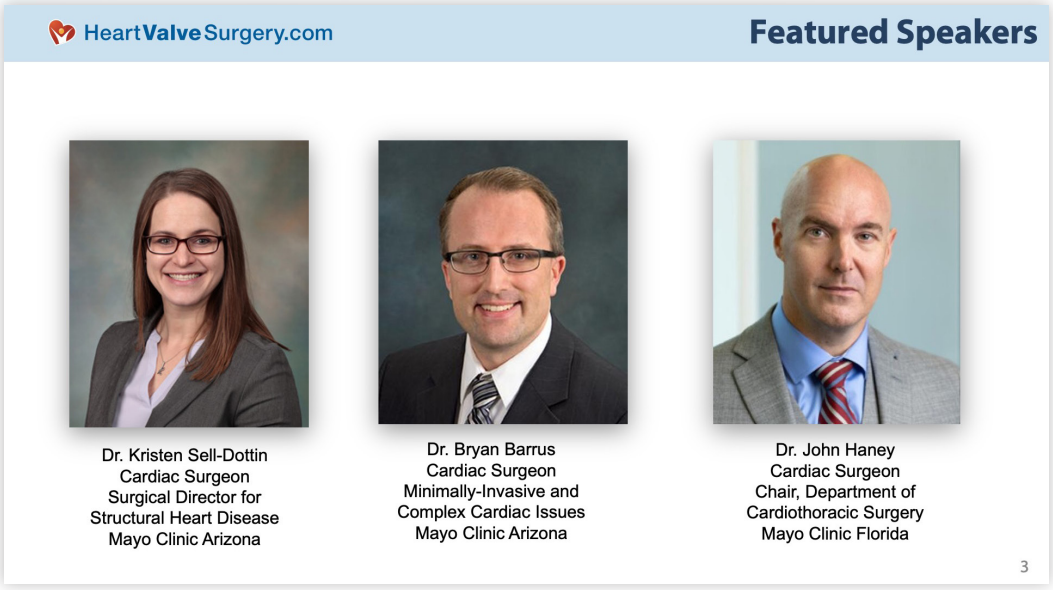
Introduction



Adam Pick: Hi, everybody. My name is Adam Pick, and I'd like to welcome you to the webinar titled, "Advances in Bicuspid Aortic Valve Therapy". If I have yet to meet you, I'm the patient, the bicuspid aortic valve patient, who started HeartValveSurgery.com all the way back in 2006. The mission of our website is really simple. We want to educate and empower patients just like you. And this webinar, which has had over 500 registrations from patients in countries all over the world, was designed to support that mission.

Now, throughout the webinar, you're going to be in what's known as "listen-only" mode, but I'd encourage you to submit your questions in the control panel on your screen. Let's look at the webinar agenda for today. I'm going to introduce the featured speakers; we're going to have a great, deep-dive discussion about bicuspid aortic valve disease and its anatomy. We're going to talk about the treatment options being both surgical approaches and transcatheter approaches. We're then going to launch into a very interactive question-and-answer session, and lastly, I'm going to ask you to complete a very quick five-question survey.



When it comes to the featured speakers, I am humbled and I'm honored that they are taking time away from their very busy practices at Mayo Clinic. I'd submit to you that we have an "All-Star Team" with us today when it comes to valves as they have performed not 1,000, not 2,000 but over 3,000 heart valve procedures. So who are they? Well, we're very happy to be joined by Dr. Kristen Sell-Dottin, who's a cardiac surgeon. She's also the surgical director for structural heart disease at Mayo Clinic Arizona in Phoenix. Dr. Sell-Dottin, thanks for being with us today.

Dr. Sell-Dottin: Happy to be here.

Adam Pick: And we also have from Arizona as well, Dr. Bryan Barrus, who's a cardiac surgeon, and his focus is on the minimally invasive treatment of tricuspid aortic valves and complex cardiac issues. Dr. Barrus, great to have you here.

Dr. Barrus: Thank you for having us.

Adam Pick: And then on the other side of the country at Mayo Clinic Jacksonville in Jacksonville, Florida, we are honored to have with us Dr. John Haney, who is a cardiac surgeon. He's also the chair of the department of cardiothoracic surgery. Thanks for being with us today.

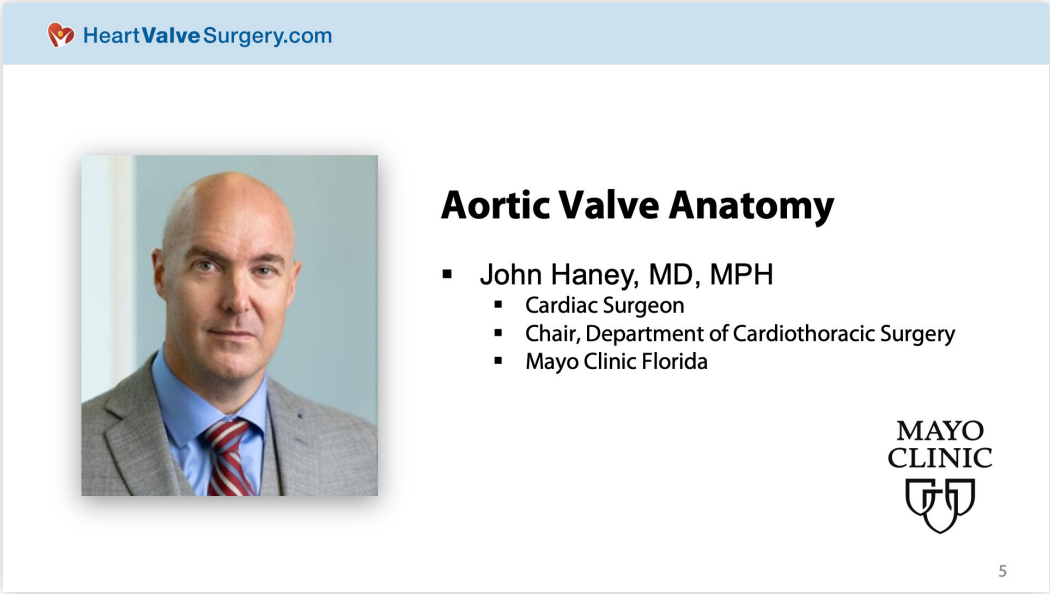
Dr. Haney: Absolutely, thank you.

Mayo Clinic Patient Success Stories

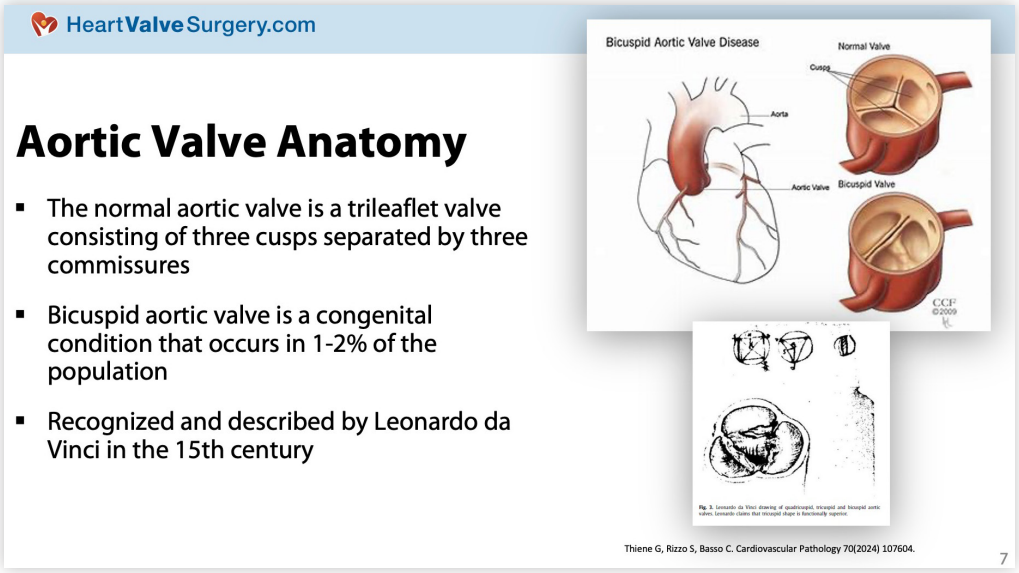
Adam Pick: I could go on-and-on about the achievements, the accolades, the research by these incredible surgeons. What I'd like to do, though, is, given our agenda is jam-packed, I just want to show you this, the smiling faces of patients from the HeartValveSurgery.com community who have gone to Mayo Clinic and had very successful heart valve procedures; Cheryl Mann, Scott Kinghorn, Gary Stanko, Wes Eden, Herman Kanter, and one of my favorite stories is that of Rosemary and Tom Rice, a husband and wife who both needed what? Heart valve surgery and got successful operations at Mayo Clinic.

With that being said, we're going to turn it over to Dr. John Haney for a discussion about aortic valve anatomy and bicuspid aortic valve disease.

Bicuspid Aortic Valve Anatomy

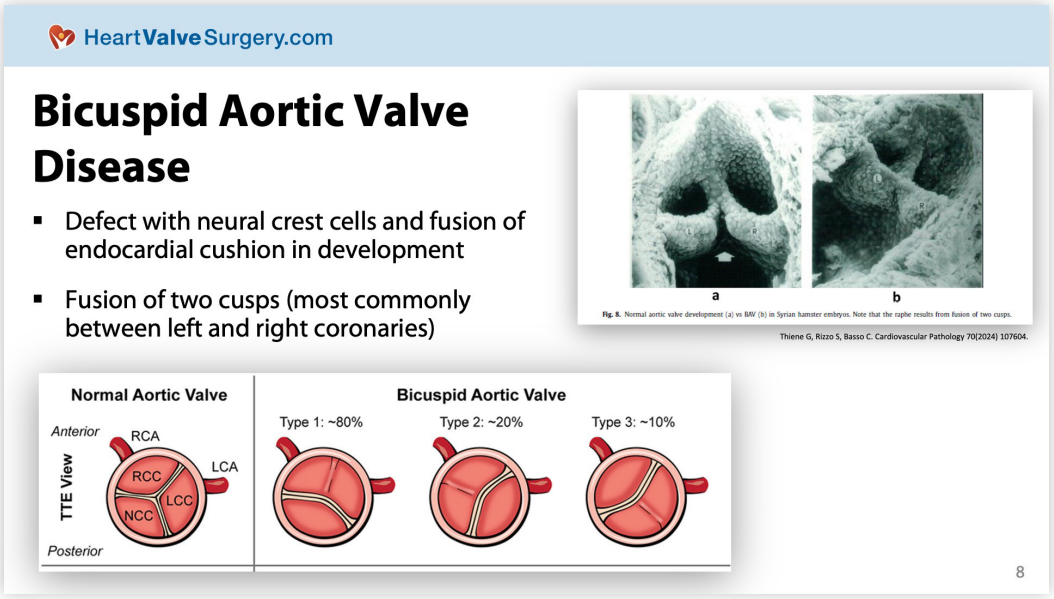


Dr. Haney: Great, thanks. Adam, thank you for putting this together and having us. I'm going to go over a few things today. First, we're going to have a review, and I think many of you are well-educated, have educated yourselves about these conditions, but we're going to review the pathophysiology of bicuspid aortic valves, what's wrong with them. And then my colleagues are going to discuss the roles of surgical intervention and various options including transcatheter and surgical approaches.



So just to review the basic anatomy, the aortic valve is usually a three-leaflet swinging door valve that exists at the root of the aorta, as the aorta meets the left ventricle and allows blood to leave the ventricle by opening widely, and then it closes to prevent blood from leaking back into the ventricle as it's trying to fill. So normally, those three leaflets are separated by little pieces of tissue called commissures. In about 1 to 2% of the population, one of those commissures does not fully separate during development, and so we have what is called a bicuspid aortic valve. Classically, this is not actually truly a two-cusp valve. Usually it's actually a tricuspid valve where one of the two hasn't separated. And this is something that's been around for a long time. It was even described by Da Vinci in the 15th century, describing the mechanics of a tri-leaflet or a bi-leaflet valve.

Bicuspid Aortic Valve Disease

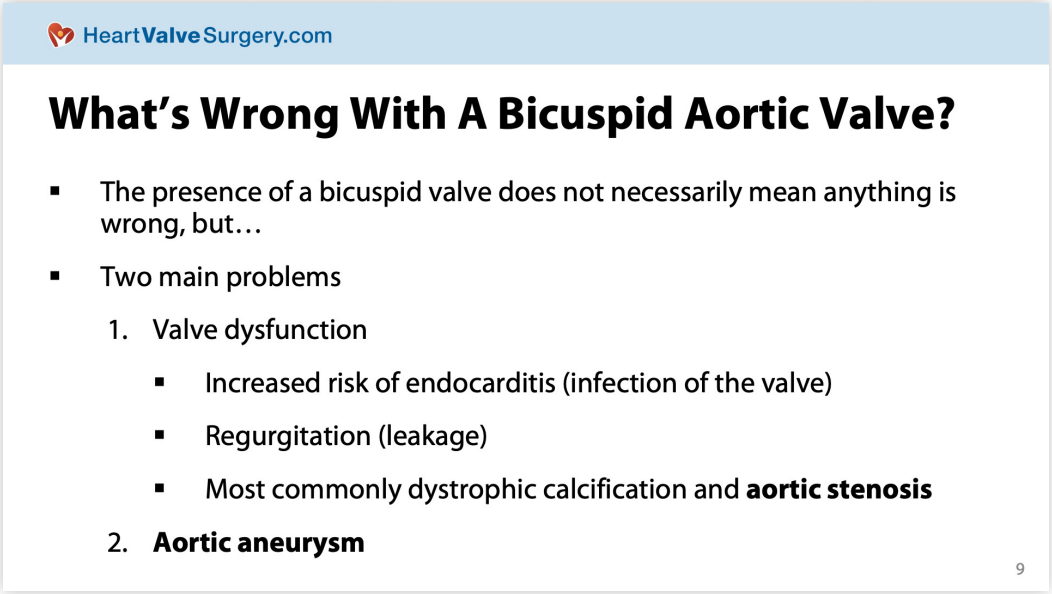


Dr. Haney: So this has been researched in, of all things, Syrian hamster embryos, and you can see some electron microscopy there on the right side where it shows the fusion on the right of these cusps, but it has something to do with neural crest cells and these endocardial cushion defects in development. Again, most commonly, fusion of two cusps, although there are patients who have, as one of the questions mentioned, uni-cusp valves or people who have true bicuspid valves where they truly do not have an additional raphe that's fused. Most commonly, it's actually fusion of one of the two or two of the leaflets together, and this most commonly occurs in the cusps between the left and the right coronary artery.

Adam Pick: Dr. Haney, just real quick, for patients who may've just been diagnosed yesterday with a bicuspid aortic valve, you mentioned the word raphe. Can you share with the community what exactly that means?

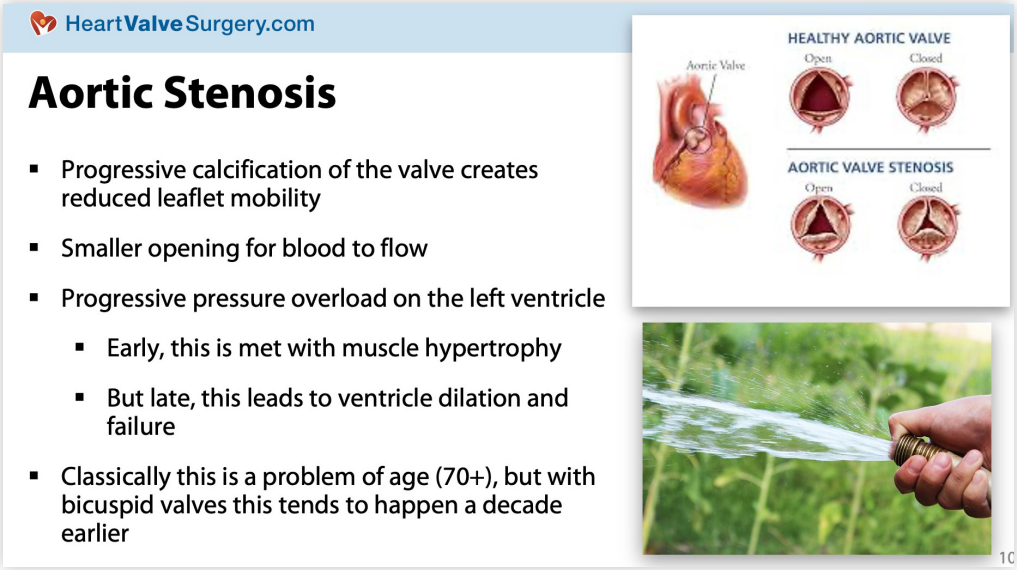
Dr. Haney: So that's that piece of tissue there that you see between the cusps right there, the sort of alignment of the two right where there should be a commissure, a meeting of the two leaflets.

Adam Pick: Thank you.



Dr. Haney: So what's the problem with the bicuspid aortic valve? Well, the first thing is it doesn't necessarily mean anything has to be done. There are a lots and lots of patients walking around with a bicuspid valve that works perfectly okay. So, the presence of a bicuspid valve by itself does not mean that anything has to be done with it. But realistically, there are two main groups of problems that happen. The first is that the valve is at increased risk for dysfunction. These valves are at slightly higher risk of getting infection in the heart valve, probably because the blood swirls and eddies through this abnormal configuration slightly differently, and it leads to slightly increased risk in any bacteria in the bloodstream setting up shop on those abnormal leaflets. But, then the more common thing is that the valves can either leak or regurgitate, so leak blood back into the ventricle. Or, the most common thing is that they can get calcification, or hardening of those leaflets, and they can basically get arthritic and cause aortic stenosis or narrowing of the valve, so valve dysfunction. The second is that there's an association with something called aortic aneurysm or enlargement of the aorta, and we'll talk about that as well.

Aortic Stenosis

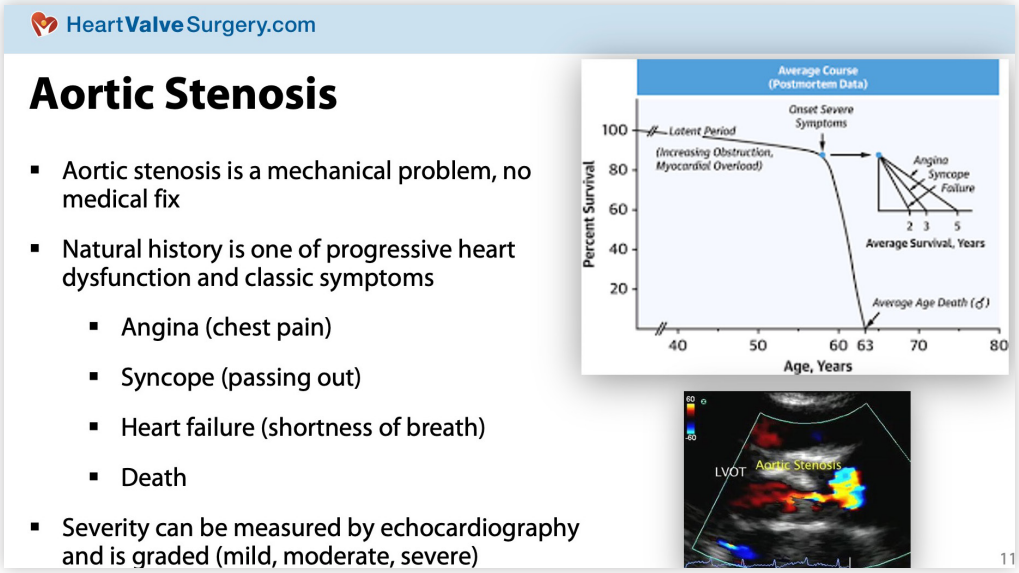


Dr. Haney: So the classic scenario for a bicuspid aortic valve is aortic stenosis.

So aortic stenosis is where valve leaflets get progressively hardened and calcified and those leaflets no longer open fully. It creates a smaller opening for the blood to flow. It's like putting your thumb over a garden hose.

Now, what happens then for aortic stenosis is you get pressure overload of the ventricle. The ventricle has to squeeze the blood through a smaller opening. Early, that leads to the heart muscling up and getting stronger, right, just like a weightlifter gets stronger over time. But over time, that pressure overload starts to stress the ventricle and eventually, it leads to ventricular failure. The ventricle stops being able to push against this very high pressure and the ventricle starts to weaken, and dilate, and you go into heart failure.

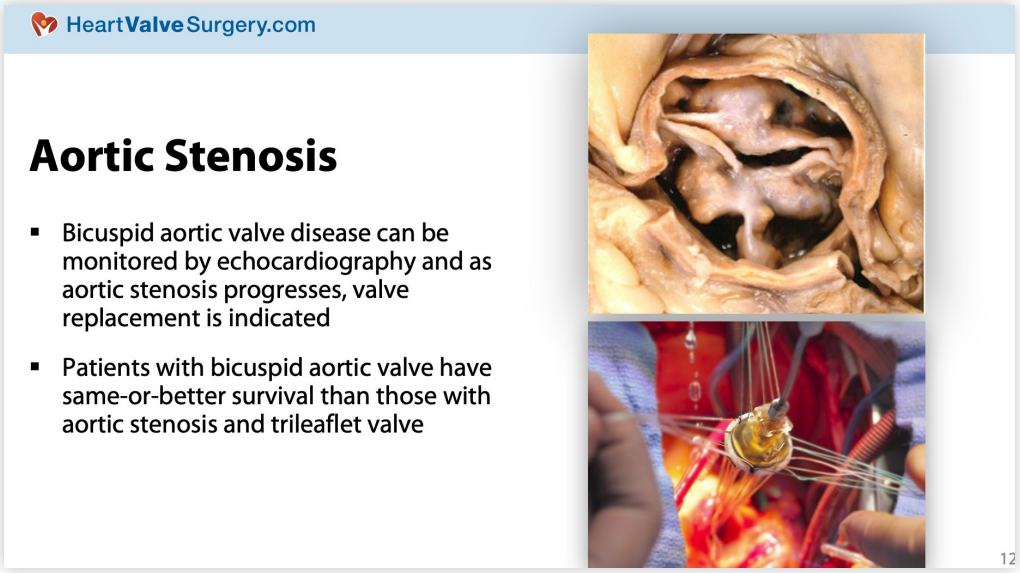
Aortic stenosis is something that can happen to lots-and-lots of people who have tri-leaflet valves, but it classically happens to us as we get older, so in our 70s and up. With bicuspid aortic valves, this definitely happens at an earlier rate, up to 10 to 15 years beforehand. We will not infrequently see patients in their mid-30s with degrees of aortic stenosis.



Dr. Haney: Aortic stenosis is a mechanical problem, so there's not a medical fix, right? You can't put WD-40 on there and loosen the valve up. And the natural history is one of progressive dysfunction. So to the audience's question about being followed, this is really the critical aspect. And if you see there that graph on the right, this is, of course, for classic tricuspid valve, but there's a long latent period right where your heart has some degree of stenosis but is doing fine and is tolerating that degree of stress.

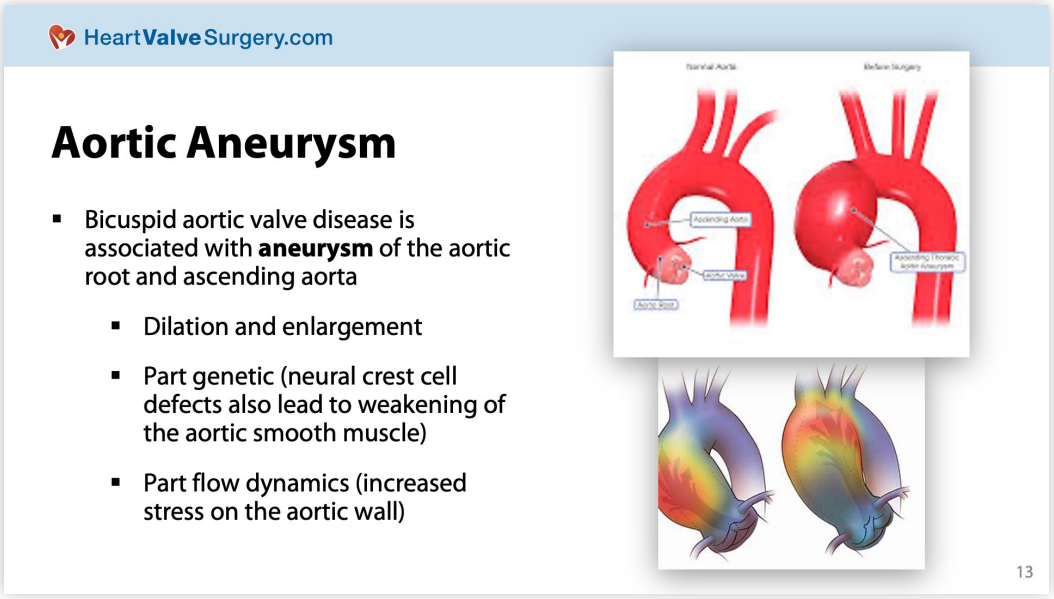
But at some point, there's a tipping point, inflection point, and then your heart function starts to drop off and your survival of the patient starts to drop dramatically. And that is heralded by the onset of symptoms, classically. So, the symptoms include chest pain where the blood flow into your coronary arteries is limited. It can be syncope or pre-syncope, so people passing out or feeling like you're going to pass out as that blood pressure drops. And then ultimately, fundamentally as the heart starts to weaken, you get heart failure; you get short of breath walking.

Now, we can follow these, and I didn't go into great detail, but the classic way to follow a valve and evaluate the degree of stenosis and the progression is with echocardiography - usually a transthoracic echocardiogram, right, so chest wall echo. We can look at the valve; we can look at the blood flow through it. We can measure velocities and we can calculate things like valve area and gradients across the valve. We can basically follow the progression of the disease from what we would call a mild case all the way through moderate and then severe stenosis.

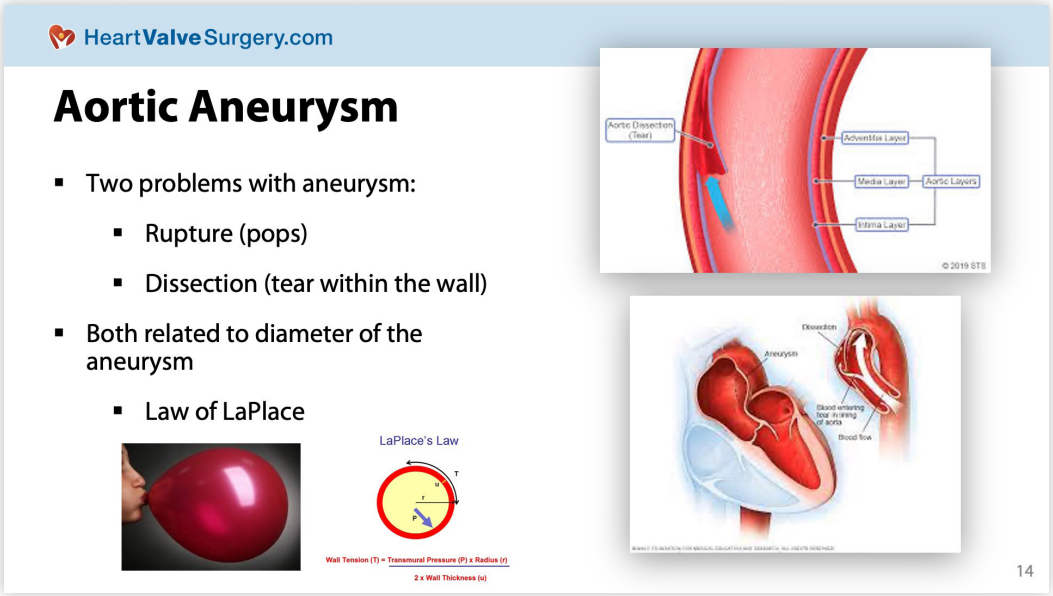


As we said then, bicuspid valves can be followed by echo and then valve replacement can be recommended before we start to get people into trouble and before we hit that inflection point where the ventricle starts weakening. The "good news" is patients with bicuspid aortic valve actually have the same, if not slightly better, survival numbers than patients with tri-leaflet aortic stenosis. This is a fixable problem with a surgical intervention.

Aortic Aneurysms



Dr. Haney: So the other condition I mentioned was aortic aneurysm. Aortic aneurysm is an enlargement, a weakening, and a dilation of the blood vessel, the aorta that takes blood to the body and in bicuspid valve, this is an enlargement of what we call the ascending part of the aorta. So, if you look at the candy cane shape of the aorta, it's the first part of the curve as the blood goes up towards the head vessels. This is due to two things. Part of it is genetic. So, the neural crest cells that cause that problem with the fusion of the leaflets are also involved in the aortic wall development. There are studies that show that there's some differences in the smooth muscle of the aortic wall and people with bicuspid valve disease. But a lot of it is actually probably because of flow dynamics and the way the blood flows through this bicuspid valve and puts stress on the ascending aorta. Patients with bicuspid aortic disease almost always get aneurysm of the ascending only. They do not get aneurysms all over their body, which suggests that again, there's not a big fundamental weakness in their blood vessel tissue.



There's two problems with the aortic aneurysm, and if you imagine as a wall of a blood vessel increases, just like blowing up a balloon, the wall stress gets bigger. And this is described in terms of physics by the Law of LaPlace, which says that the wall stress, the wall tension, is directly proportional to the diameter of the aneurysm. So again, think about the balloon as it gets bigger.

The two big problems related to wall stress are either, one, rupture, which you can imagine is bad. People die. And then the other one is a tear in the wall, so a partial tear, a partial rupture, and the wall of the aorta is laminated and the inner lining can tear and the blood can jet into the middle of the wall and split it apart. And both of those, again, are related to -- the risk of those is related to the size of the aneurysm.

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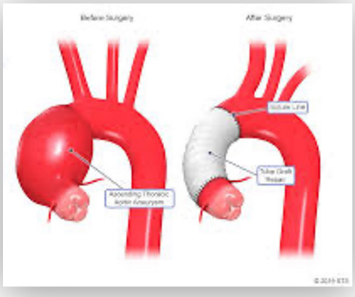
Aortic Aneurysm

- Medical therapy involves keeping blood pressure controlled (less pressure pushing out)
- Surgery involves removal of the aneurysm and replacement with a cloth tube
  - All surgery involves risk (bleeding, stroke, etc)
- The risks posed by the aneurysm increase with aneurysm size, so…
  - There is a size threshold at which the risk of doing NOTHING exceeds the risks of doing SOMETHING



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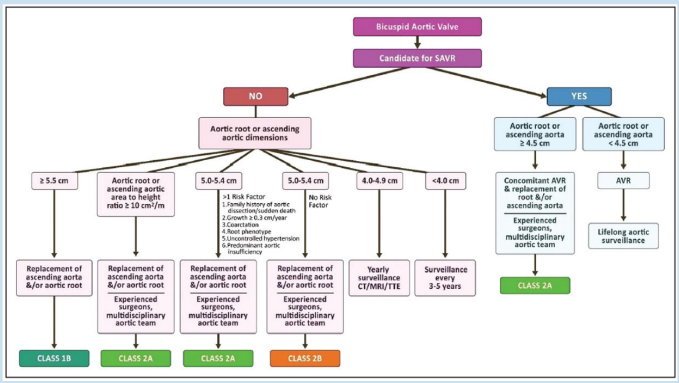
Treating aortic aneurysm can be a little bit medical therapy. If you imagine the blood inside a weakened enlarged aneurysm like a hammer, the fewer times it hits per minute and the lower the pressure that it hits, the reduced risk. So, blood pressure control. But fundamentally, ultimately this is also a mechanical problem that often leads to then surgery.

When we do surgery, we talk about repairing it. We don't really repair it; we replace it. We cut it out and we put in a cloth tube that doesn't expand. When we do a replacement, whether we're doing something else to the valve or whether it's the only reason to go in for the surgery, obviously all surgery involves risk. Well, if aneurysms have risk that increases with size, we can imagine that fundamentally, there's a size threshold at which the risk of doing nothing and allowing the natural history of the aneurysm to exist versus the risk of doing something and incurring the risk of the procedures, those two lines cross. As aneurysms enlarge, there becomes a point in which time it makes more sense to take a risk of doing something because that's lower than the risk of sitting and watching it.

Aortic Aneurysm In Bicuspid Valve Disease

- IF the valve is ok, the threshold for replacement is **5-5.5cm** depending on several variables (valve leakage, family history, etc)
- IF the valve requires intervention, the threshold for ALSO replacing the aorta is **4.5cm**



Verma R et al. Curr Opin Cardiol 2023, 38:61-67.

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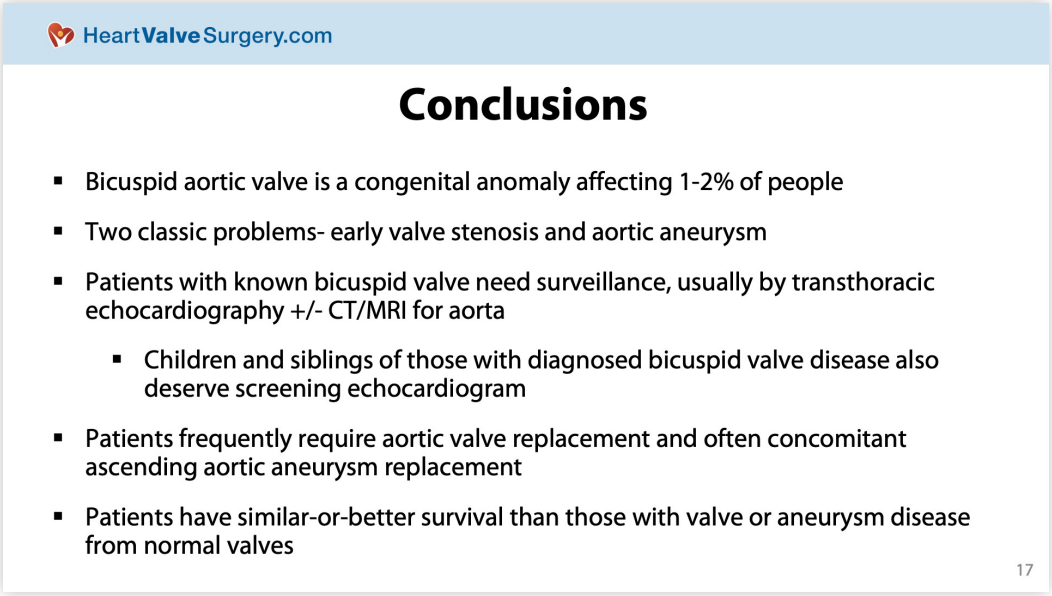
This leads us to a very complicated chart about aortic aneurysm in bicuspid valve disease. And now, what I didn't talk about, which we can talk about down the road, is what are the indications for interventions in the valve. Typically, that's for stenosis when people have severe aortic stenosis. And again, I mentioned before, we turn an inflection point where the valve starts hurting the ventricle; similarly with regurgitation where leakage become severe and people start having symptoms and try to intervene before the ventricle gets damaged.

But aortic aneurysm then is also something where we think about this idea of when is it time to intervene? The first answer is it depends on if you're doing something with the valve. So, if people have a valve that needs surgery, you can imagine you're already incurring lots of the risk of being there for a surgery. So, we're going to replace that aneurysm when it's slightly smaller. And the answer, the short answer to it is if the aorta is 4.5 centimeters wide and you're there for the valve intervention, it makes the most sense to already replace that piece of the aorta.

If your valve is fine, then we don't assume those risks until the risk from the aneurysm itself is slightly higher, and that number classically is more like 5 to 5.5 centimeters. That indication is slightly lower than someone with a normal tri-leaflet valve. That number, with no connective tissue disease, no valve abnormality like bicuspid disease, is really over 5.5 centimeters. But, in some patients with bicuspid valve disease, especially with some other risks, we will typically reduce that number slightly and say if it's somewhere over 5 centimeters, we'll often advise that the patient gets a surgery for their aneurysm.

So the bottom line is... If you have bicuspid aortic valve disease, you get surveillance. You get surveillance both for aneurysm and you get surveillance for valve dysfunction. And at some point as those things get worse, whether the aneurysm enlarges or the valve gets more dysfunctional, you have indications for doing an intervention.

Bicuspid Aortic Valve Anatomy Conclusion



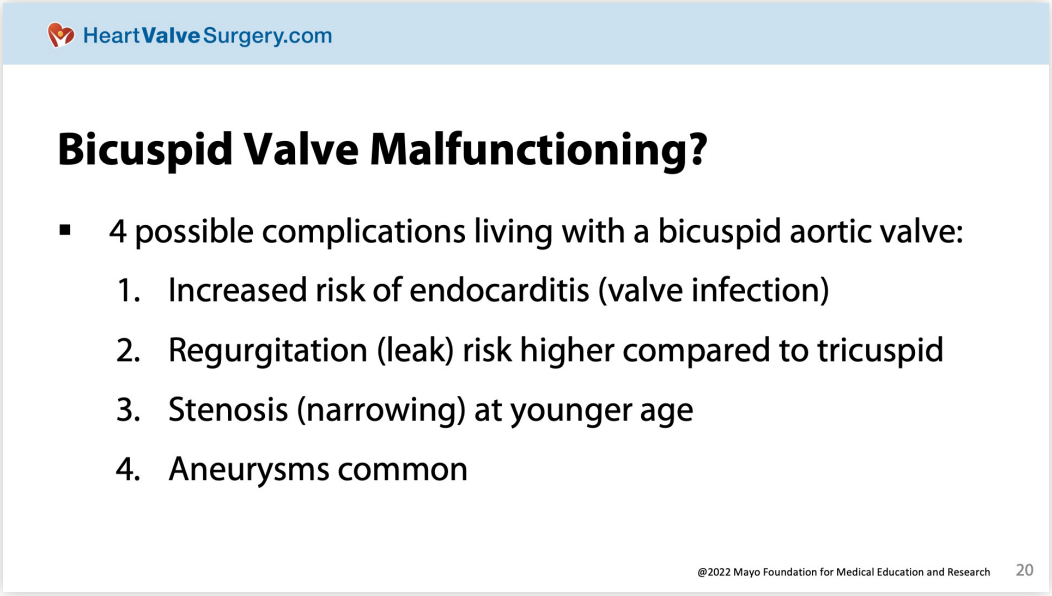
Dr. Haney: In conclusion, bicuspid aortic valve is, while not a large percentage of the population, you can imagine 1 to 2% of people, this is a lot of patients with bicuspid valve. The classic problems involve both aneurysm and early valve dysfunction, most commonly stenosis. People who have bicuspid valve need surveillance, usually by echo, often times then at some point with cross-sectional imaging like CT scan to look at their aorta.

One thing that is important to understand for everyone on this call who may have a bicuspid valve is that people with bicuspid valve should alert their first degree relatives and specifically if you have children, those children should get a screening echo to see if they have a bicuspid valve. It's not classic Mendelian genetics where everyone that you have -- 25% of your children will have a bicuspid valve but it's certainly a higher risk. And that screening, there's no great perfect evidence of when that screening happens, but I think in general, they don't need screening when they're 10 years old; they need screening when they're getting closer to between 25 and 30 years old.

Surgical Bicuspid Aortic Valve Therapy

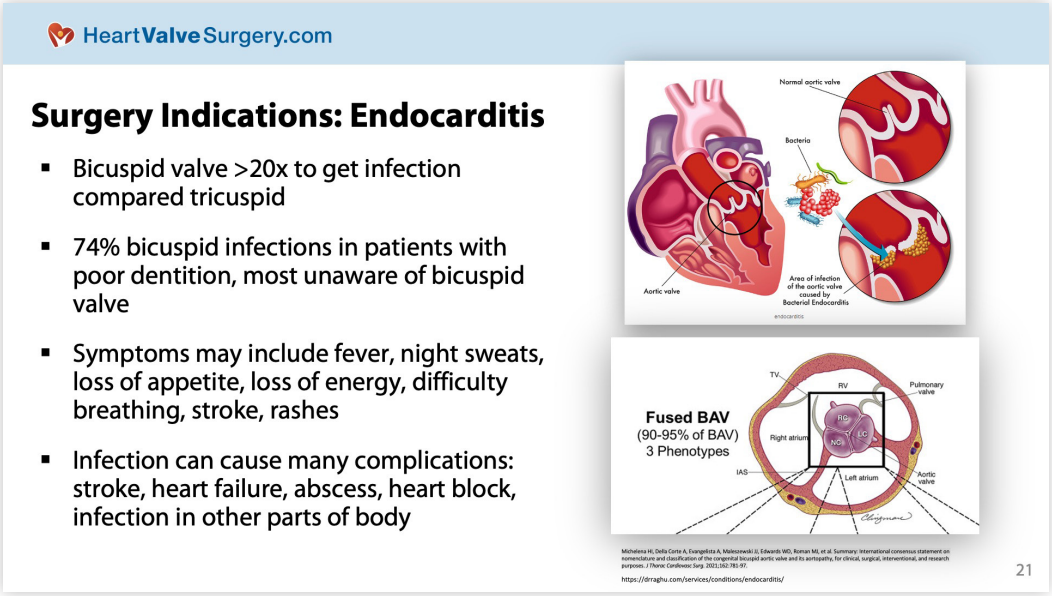
Dr. Barrus: As Dr. Haney was just speaking, there's just the fact that you do have a bicuspid valve does not necessarily mean there's a problem. The question is, of course, it malfunctions, which today I'd like to discuss potential complications that you need to be aware of.

Bicuspid Valve Malfunctioning



Dr. Barrus: First one would be that you are at increased risk of having endocarditis, which is an infection of the heart valve, higher risk of having a regurgitation or a leak compared to those who have a tricuspid valve, and also the valve can tend to get a little more narrow at a younger age than those who have tricuspid valves. And then the aneurysms are more common.

Endocarditis



Dr. Barrus: Bicuspid valve in some of the studies has shown to be approximately 20 times more likely to get infected compared to the tricuspid valve. The issue with this is unless you had an ultrasound screening by a cardiologist or family member, as Dr. Haney was saying, who has bicuspid aortic valve disease, most people don't even know that they have it. So, 74% of the infections that have happened in people who do have a bicuspid valve is because they have poor dentition. They're not taking good care of their teeth. And it's not until later when they've had a tooth abscess or that they find that they become ill. And those symptoms can sometimes masquerade and be difficult for different doctors to diagnose because they can be subtle. Sometimes, they are not so subtle, but they can include night sweats, fevers, losing your appetite, a loss of energy, difficulty breathing, and it can be as severe as strokes. People can also see rashes develop in different places.

Now we've put on the picture in this slide, if you were to take the heart and cut it in half there, the bicuspid aortic valve sits, or excuse me, the valve itself sits right in the middle. It's next to all of the other valves within the heart. And so the type of symptoms you may have depends on if this infection eats away and the different areas of the heart tissue and does it spread.

One of the questions that I always ask when I'm asked to see somebody with an infected heart valve is what is the collateral damage; what is going on with this person; has it caused a piece of bacteria infection or clot even to go to the brain and cause a stroke; or is there abnormal blood flow within the heart leading to heart failure; is there an abscess formed in that heart?

The electrical system is very close to this valve; did the person go into heart block where they might need a pacemaker? And again, is there an infection because all your blood is going through this valve; has that infection traveled to other parts of your body?

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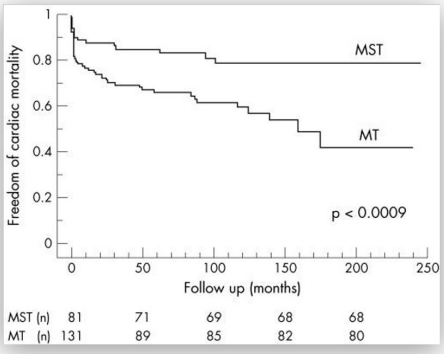
Surgery Indications: Endocarditis

- In hospital mortality about 20%
- Requires long term antibiotics and often surgery
- All infected tissue must be removed and valve be replaced
- TAVR is not an option



Netzer RO, Altwegg SC, Zollinger E, Täuber M, Carrel T, Seiler C. Infective endocarditis: determinants of long term outcome. Heart. 2002 Jul;88(1):61-6.

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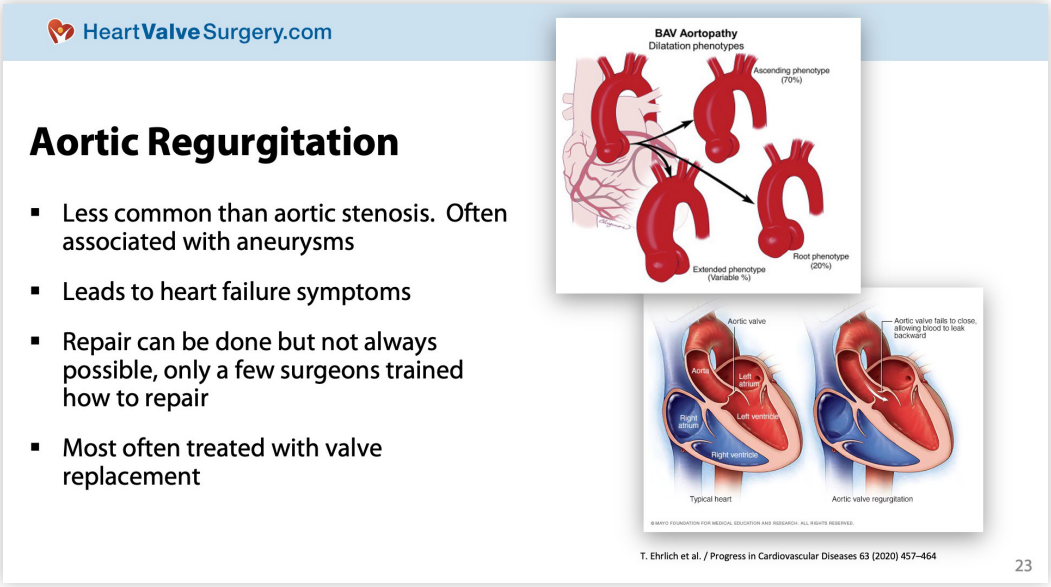
This can be a very serious condition. So the in-hospital mortality or the chance of dying can be up to 20%. Sometimes people go to the hospital and they may not be feeling well and they may be told maybe you have a cold or pneumonia, and they get treated for that, or maybe it's just depression or there's a whole myriad of diagnoses that have been made when it's not as obvious.

The treatment of this then requires long-term antibiotics for everybody. Typically it's in the range of, depending on the type of bacteria, it can be anywhere from four to eight weeks. Often times, it does require surgery and depending on how quickly you get to the surgery the outcomes with that with the antibiotics and surgery are very good and survival is very good.

In order to cure this, the less invasive techniques, particularly the catheter-based valve replacement, is really not an option because you do need to get all that infected tissue removed and replace the valve and repair any damage that had happened to the heart. If we were to put a catheter-based valve into an infected area like that, that new valve will absolutely become infected. So, that is not an option. And of course, to get rid of that infection in that scenario is very difficult.

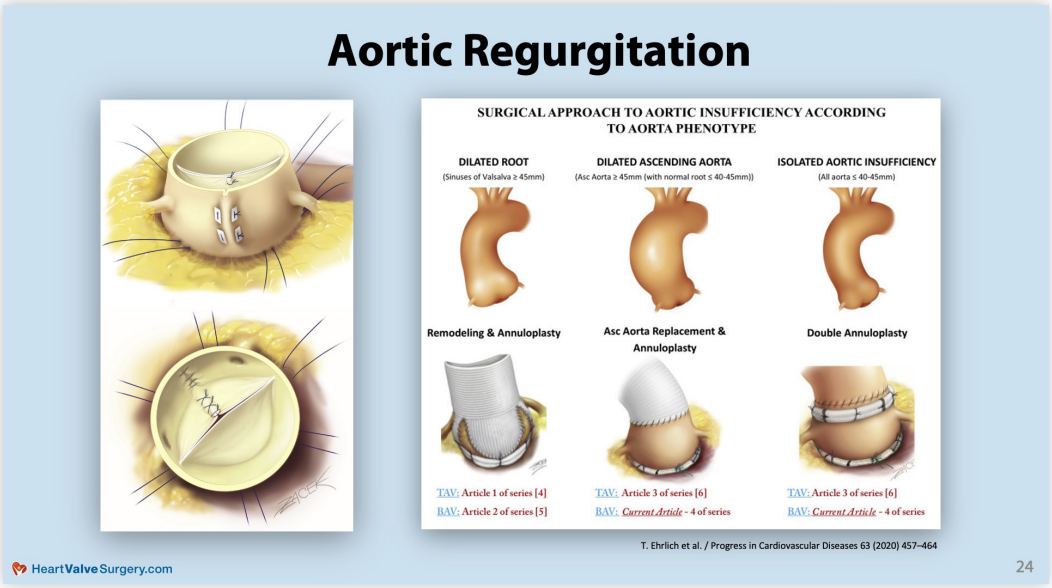
Aortic Regurgitation



Dr. Barrus: Moving onto the next issue that we might dealing with is one called aortic regurgitation. This is a little less common than aortic stenosis but we definitely see it. It's often associated with aneurysms. Couple of things with this… First of all, why does the leak even occur? A leak can occur for multiple reasons. It can be by holes within the valve tissue itself. If you imagine a goalpost and having the valve stretched between -- tissue between two posts, you have an aneurysm in the aorta. It's as if these goalposts are starting to be stretched and pulled apart. And all that tissue is being stretched, so it no longer can close and touch in the middle and no longer create a seal, which then creates that leak.

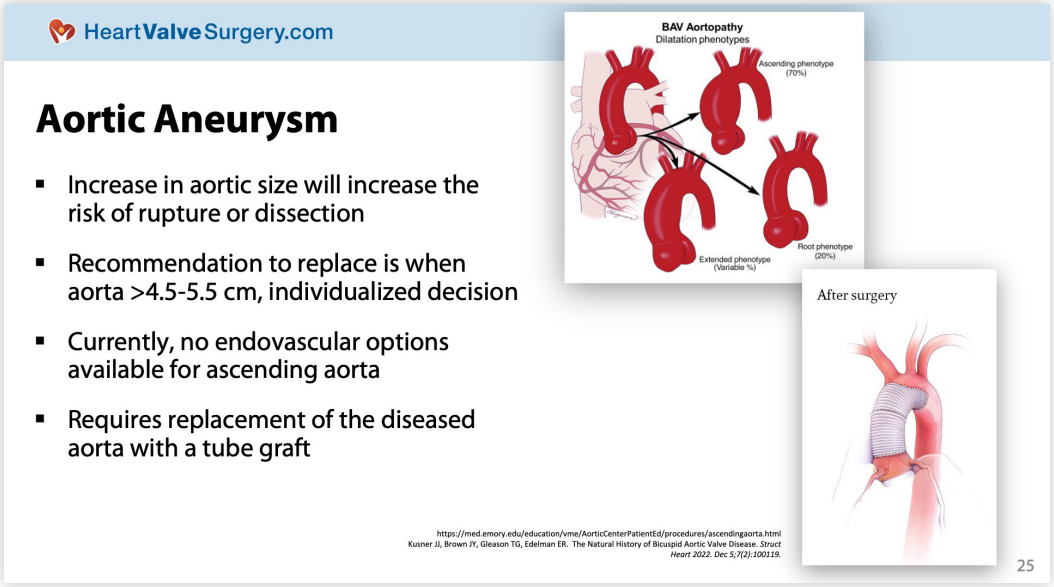
The ventricle -- one of the other issues that happens with these valves is they leak over time. The body's amazing in that it can tolerate a leak for quite some time. But, as it becomes more severe, imagine that now that left ventricle is receiving all of the blood, the good oxygenated blood from the lungs, and then it has to take on an additional amount of blood from the aorta. That increase in the volume over time can start to stretch the heart out; it enlarges your heart over time. That leads to heart failure.

Fixing this is most commonly is done by replacing the aortic valve. But, there are places that do repairs of the valve.



Aortic valve repair is still a newer technique that is being learned and taught but is still starting -- still working through some of the nuances with this. So it is aimed at trying to correct the underlying problem. The picture on the left there shows this bicuspid aortic valve. It's not hardened; it's not calcified. It probably had too much thinned-out tissue, this redundant tissue. So the surgeon in this case can put pleats, almost like on your pants with small folds in the valve, kind of take out that excess tissue, and again, put proper alignment in the valve. There's other techniques there that are aimed at trying to fix any aneurysm size with the goal, of course, of trying to preserve a person's valve.

Aortic Aneurysms



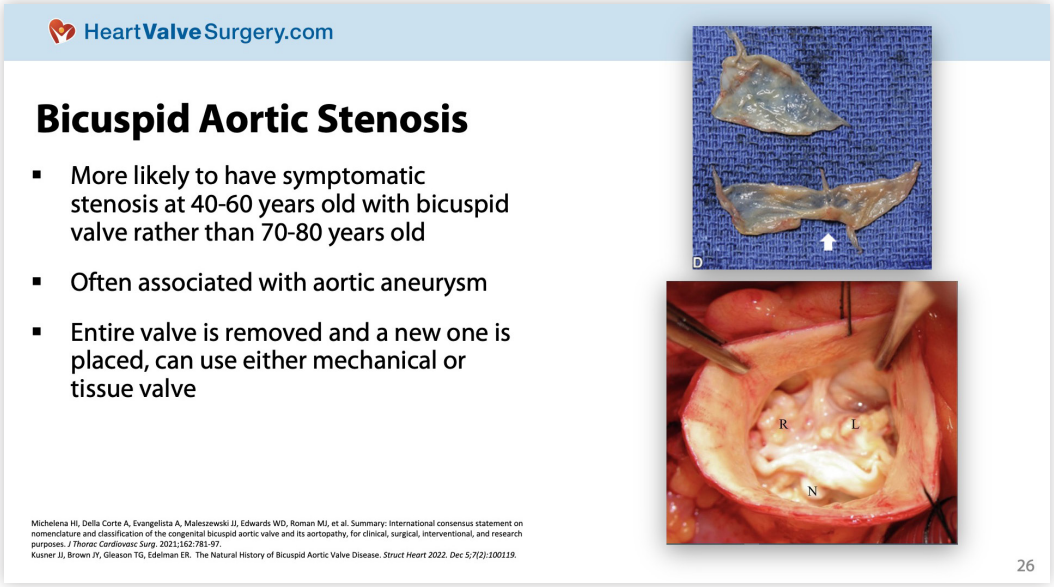
Dr. Barrus: Aneurysms, so there is a genetic component with the aorta and these bicuspid valves and as Dr. Haney said, the jet of flow coming out also seems to affect the size of this, the aorta. As it comes out the aorta, these aneurysms can be in multiple different places. It can be at the very bottom where the valve is. It can also be in the ascending portion, so as the aorta is dilated, it's like a balloon. As the balloon stretches, so does the wall of the aorta. It becomes thin and allows it more likely to have a potential problem with bursting or rupture, or creating a tear in the aorta called an aortic dissection and that flap or tear can start at the beginning part of the aorta and tear all the way down and around, all the way down to the legs.

That tear then can cut the blood supply off, not allow blood flow to everything in your body from your brain to the kidneys to the liver. When it blocks the flow to your brain, that becomes a stroke. Those who get blockage of blood flow to the kidneys could lose a kidney and need dialysis. We have, unfortunately, even seen people who have lost a leg or an arm from this disease process. So it

definitely becomes a life-threatening issue.

This is replaced with a full open heart surgery here and we cut out the diseased portion of the aorta, the aneurysm portion. And you replace it with a cloth tube. The cloth tube is durable. It no longer can't dilate or become aneurysmal and then effectively takes care of that aneurysm. The size, as Dr. Haney pointed out earlier, also depends on what else is going on. This is a topic that is in flux, and so the size has to be individualized to the patient in discussion with the surgeon, but typically, it's around 4.5 to 5 centimeters. In some areas, you may be recommended to wait until 5.5 centimeter but again, it's a discussion between the patient and the surgeon as when would be the most appropriate time.

Bicuspid Aortic Stenosis

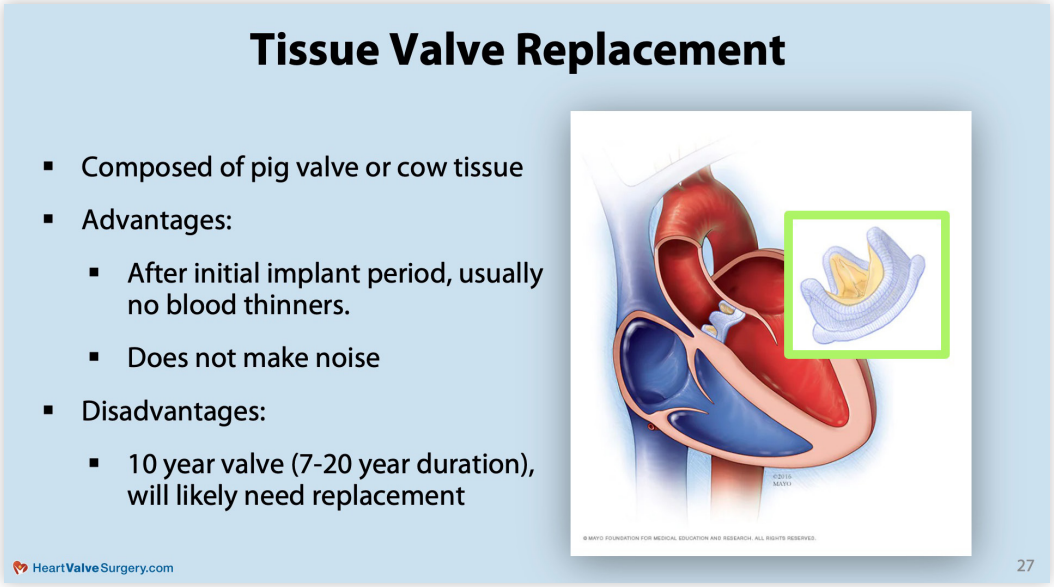


Dr. Barrus: This is something that we frequently see with the aortic valve now becoming more narrow at the other end of the spectrum. People who are born with a bicuspid valve are more likely to have symptomatic narrowing or stenosis at a younger age, the 40 to 60 year old. This is also included with those that have a uni-cuspid valve. We will see that at a younger age. People who have a tricuspid valve typically have narrowing of the valve at an older age, 70 to 80, 90 years old.

Again, often associated aneurysms and if you look at the picture there, the top of the picture there is a fairly normal valve where the tissue itself is very thin and almost translucent. When it becomes stenotic, as the bottom picture shows, it becomes very lumpy and the calcium gets built into it. Best analogy that I can give to help people understand.... I just moved here back to the Southwest where we eat a lot of Mexican food -- is if people are familiar with tortillas, it's nice, soft, and pliable as it moves. But if you throw it in the fryer, it changes the chemical structure, and you can then create a hard shell. And so it's chemically different; it's changed. I've been asked before, why can't people just -- why can't we just scrape off all the calcium like someone does at a dentist? We can take off the plaque or the tartar. And the answer is just simply because the valve itself, the calcium's within the valve. It's chemically different and changed.

In these scenarios, the surgical treatment of this is to remove the entire valve and sew a new one in its place, whether that be a tissue type valve or a mechanical valve.

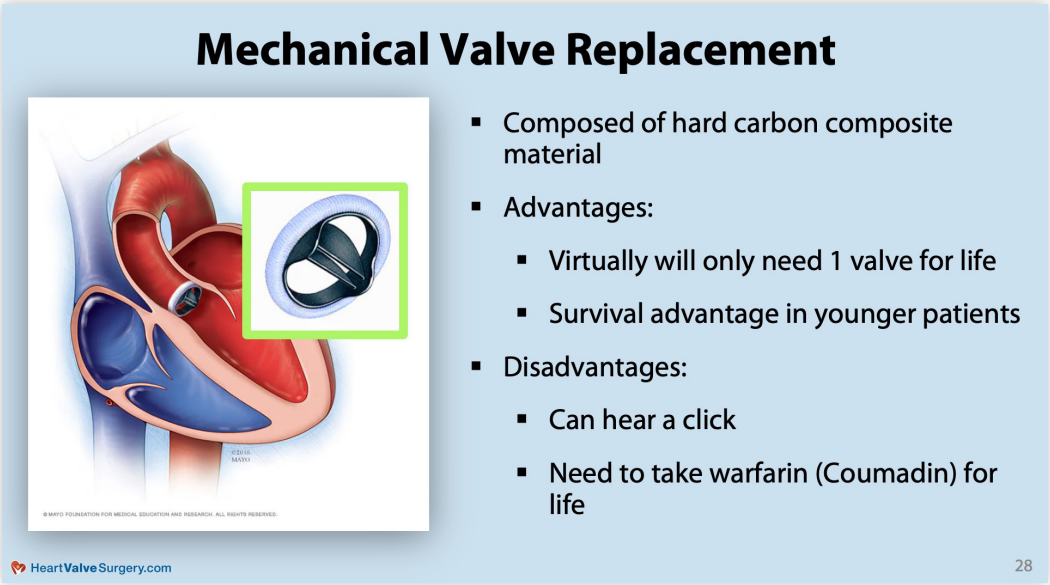
Tissue Valve Replacement



Dr. Barrus: So now we're going to talk about a hot topic in surgical valve replacement. What type of valve are we going to use? There are two different main types of valve replacement. This tissue valve is composed of either a pig valve or cow tissue. The advantage of this are that after the initial implant period, we, at least in the Mayo Clinic in Phoenix here, we do put people on blood thinners for approximately three months, but they do not need life-long blood thinners. It's a quiet valve; you don't hear it moving.

The disadvantage, though, is that -- and we tend to think of these as around a ten-year valve, plus or minus several years. The older you are, the longer the valves tend to last. The younger you are, they tend to seem to wear out a lot quicker. At some point then, you're going to need another -- if you're younger, you will likely need another valve at some point. That can either be done -- and my partner here, Dr. Sell-Dottin, will be talking about the catheter-based replacements, so it can be done within these valves when they wear out. However, the TAVR procedure can be done in these valves. Or, you can go back and have open heart surgery again and have that valve taken out and a brand new one put into its place.

Mechanical Valve Replacement



Dr. Barrus: So on the mechanical valves side, couple of things. So they are composed of this hard carbon almost as if, similar to a metal material. So the advantages of this valve, you virtually would only need one valve for the rest of your life. We tend to think they are not necessarily a forever valve, but they generally don't break down. There is a slight survival advantage for people who are younger. The flow through the valve seems to be a little better, and the main thing for that is because hopefully, you should not need another valve replacement as long as you have this in place. The disadvantages, however, of this valve is that you can -- people often do hear it clicking with every heartbeat, particularly if it's a quiet room. The second thing is you have to take a blood thinner the rest of your life. So this valve, for many, many years, has been -- for decades has been the workhorse for aortic valve replacement, particularly in younger patients.

The blood thinner issue is an important one because if these valves -- there's a cloth sewing ring and also on the valve leaflets itself, your body can form a blood clot on there. And if a clot were -- it can cause two issues. One, it can prevent those leaflets from opening and closing again, and the second issue is if a clot were to break off and start floating in the bloodstream, one of the first places that it can go, the first stop is the blood vessels that go up to your brain and it can cause a stroke. Taking the blood thinners is incredibly important for your life and for its safety.

What's The Big Deal with Warfarin?

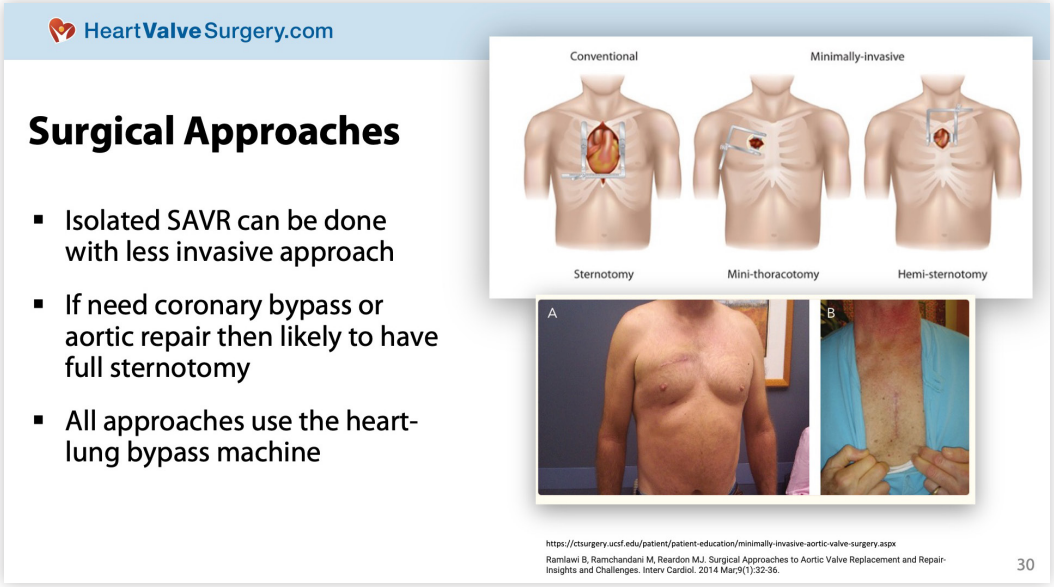
Dr. Barrus: So what is the big deal with or big issue with Coumadin or warfarin? Well, first, to understand warfarin was designed to work against one of the vitamins, one of the essential nutritional elements that we all need. So Vitamin K, when we take that in our diet, and that's found often in leafy green vegetables such as kale and spinach. Your body will take that and use it to form clotting proteins to help your body form clots when you get cut or bruise yourself, for example. So the warfarin is designed, it stops Vitamin K from working. And Vitamin K and warfarin are in this constant back-and-forth battle. So too much Vitamin K, your body is going to lean more towards making more clots; too little Vitamin K, you're more likely to bleed. Too much warfarin, you could bleed to death or have a bleeding issue; too little warfarin, you're not going to be protected from clots forming on this new valve.

The way that we monitor that is you have to get frequent blood tests. This is a test called the INR, which stands for the international normalized ratio, and this tell us how thin the blood is. There is home testing available; that varies across the country, also depending on insurance, if they will cover the cost of that device. There is a half to a 1% yearly risk of severe life-threatening bleeding associated with the blood thinners. This is the only blood thinner currently FDA-approved for these valves. There are trials going on to see if we can get away from this valve and use the newer blood thinners but currently, that is not an option.

The older mechanical valves, they require your INR to be between two and three or twice to three times as thin. So for reference there, most people will take about 30 seconds for their blood to clot, so a goal of two, your blood would stop bleeding, a cut would stop bleeding at 60 seconds. The goal of three, it would stop bleeding around 90 seconds.

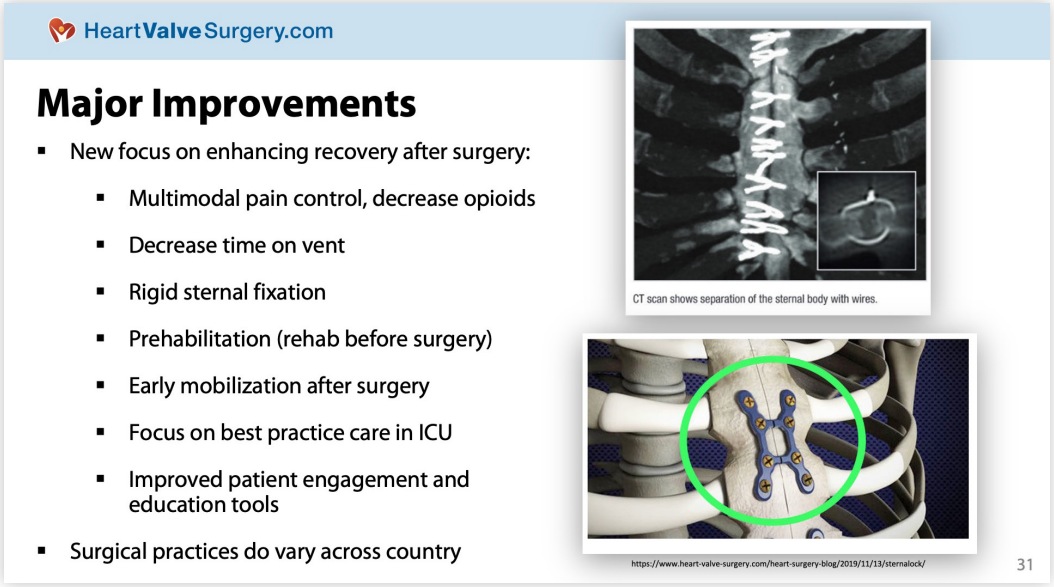
The newer valves, and I know this is something that was brought up in the chatroom, is with the Onyx valve. After three months, the FDA has now approved that you can decrease the goal of the INR from two to three to one and a half to 1.9, which does make taking warfarin a lot easier.

Surgical Approaches



Dr. Barrus: As far as the approaches and how we get to the aortic valve, most surgical aortic valves throughout the country are done through a full sternotomy and the reason for that is this gives the surgeon full access and control to allow for a safe surgery. If other procedures need to be done at the same time, such as bypassing the heart arteries or fixing another valve, that can all be done. Less invasive techniques are available now where it can be done through a small incision in the right chest or opening the top portion of the breastbone but not all the way. And those can be done, of course, when the aortic valve alone is replaced. It's a determination of which technique to use depends on your surgeon's skill or comfort level, the person's anatomy, and again, if other procedures are needed.

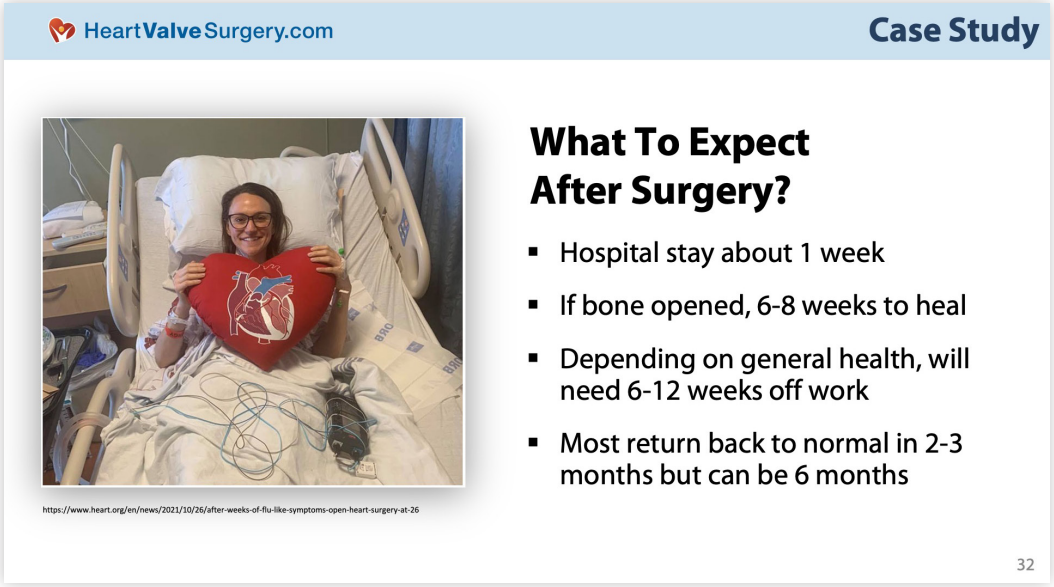
Major Surgical Improvements



Dr. Barrus: Some of the major improvements that have happened over the years is that there is a new focus. For a long time, people were focusing on how can we do this less invasively; how can we make this safer? There's now a focus on looking at enhancing the recovery after surgery for patients, and that goes and entails that using multi-modal, meaning different methods of pain control, so nerve blocks, different pain medicines to try to decreases the opioids, the number of narcotics that patients are needing afterwards. We're looking for ways to decrease the time on the ventilator. One thing is taking the person off the ventilator in the operating room before they even get to the ICU. The way that the breastbone is closed has been changing. It is still standard of care. You can see in the top right corner that stainless steel wires are used to wrap around or through the breastbone to bring the bone back together. Currently, this is one technique. We're using titanium plates and screws to try and bring the bone together a little tighter. The practice varies across the country and you can ask your surgeon which technique they use.

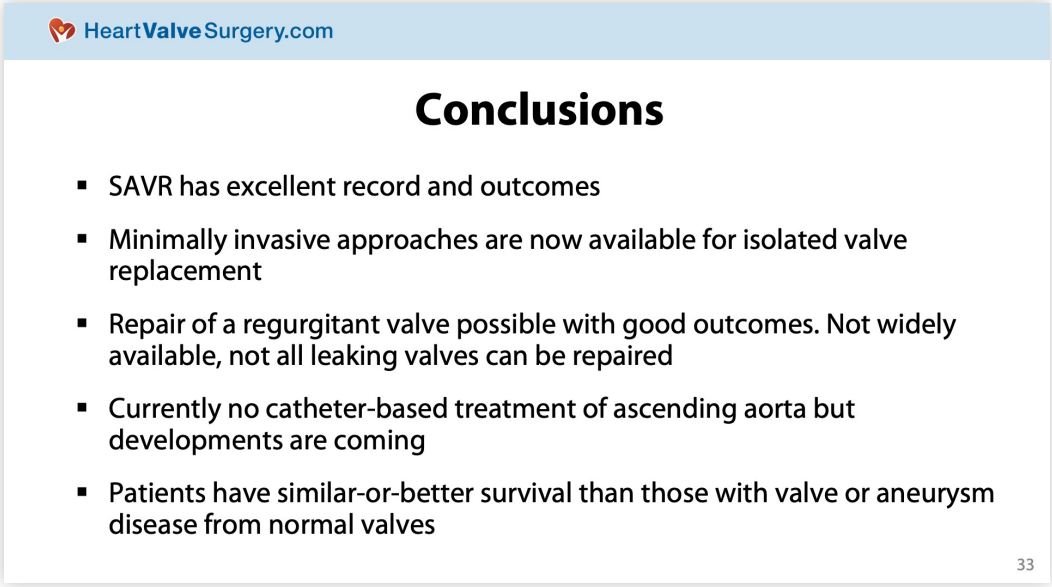
Trying to get a person rehabilitated before surgery because the better shape you are going into an operation, it's a lot easier to get through it. Trying to mobilize or get the people walking as early as possible after operation, focusing on the best practices in the ICU, and improving engagement with patients through technology now through apps on your phone, portals through the computer so when questions do come up, we can nip problems early in the bud rather than waiting for something to develop into a serious complication. Again, this is all currently in development. Practices do vary.

What To Expect After Surgery



Dr. Barrus: What to expect after surgery? Generally speaking, you're in the hospital for approximately one week. If the bone is open, it does take between six to eight weeks to heal. There is a little bit of, depending on the person and their health, there might be a little less time in the hospital with less invasive techniques which can be four to six days, but I absolutely have discharged patients with full sternotomies in three or four days. That's not necessarily a limiting factor. Depending on your health, you generally will need somewhere around 6 to 12 weeks off of work, but most people return back to normal within two to three months. Again, the sicker you are going into this, it can take even longer, can take up to six months.

Bicuspid Aortic Valve Surgery Conclusions

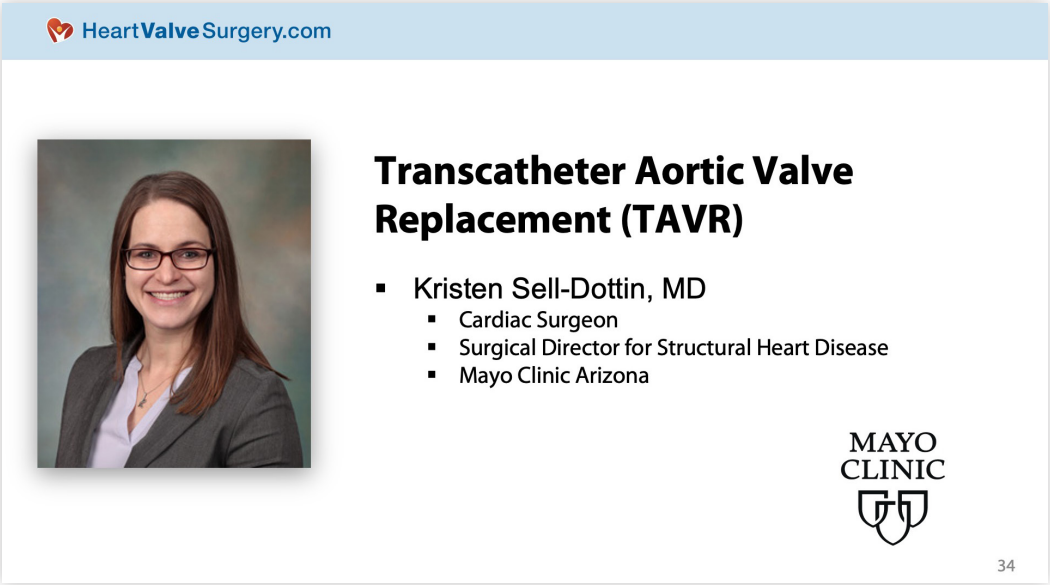


Dr. Barrus: Just in conclusion here, that surgical aortic valve, that's what SAVR is, surgical aortic valve has this excellent record and outcomes. We do have good data on how long these valves, the tissue valves, will last, the mechanical valves. It's a little bit more predictable. There is now minimally invasive approaches. We were talking earlier about robotic techniques that's something that's still considered at this point in the experimental phase. There are places and centers using the robot to try and replace the aortic valve. It will take a little bit of time and it has more to do with suture management with having all the stitches come out as part of the technique and how we replace these, which is a little more complicated with a robot.

The repair of a valve can be done in certain cases, particularly for the leaky valves, with very good outcomes. Again, not widely available, it's a newer technique that is still being taught. Not all leaky valves, of course, can be repaired. Currently, for leaky valves, most of the surgeons across the country are doing replacements.

There is no catheter-based option at this point of treating an aneurysm in the ascending aorta or the root. There is investigation going on but we are not there yet. Then patients, again, do have similar or better survival than those with tricuspid valves or aneurysm disease when you compare the two between the bicuspid and the tricuspid valves.

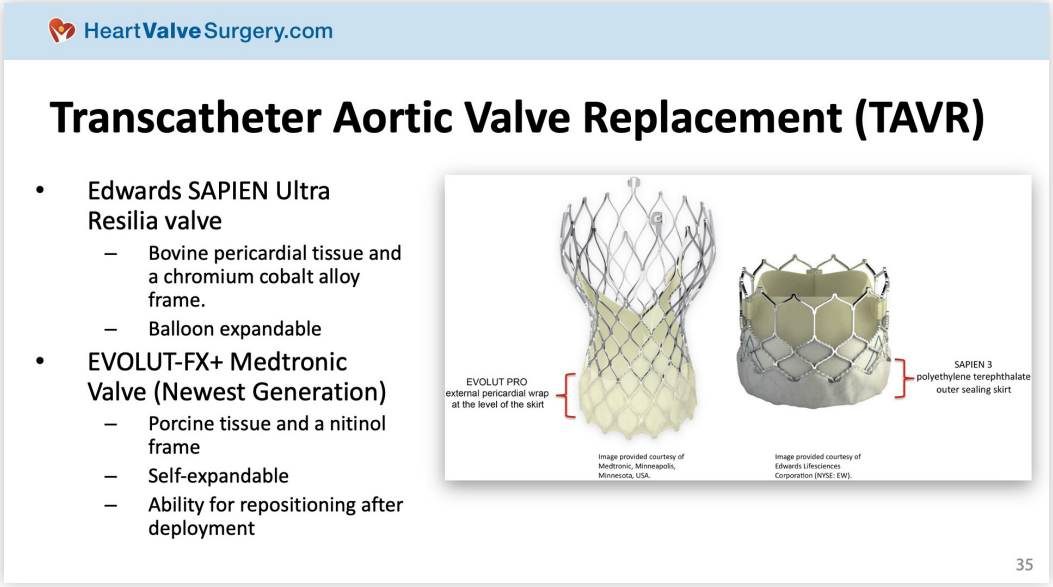
Transcatheter Aortic Valve Replacement (TAVR)



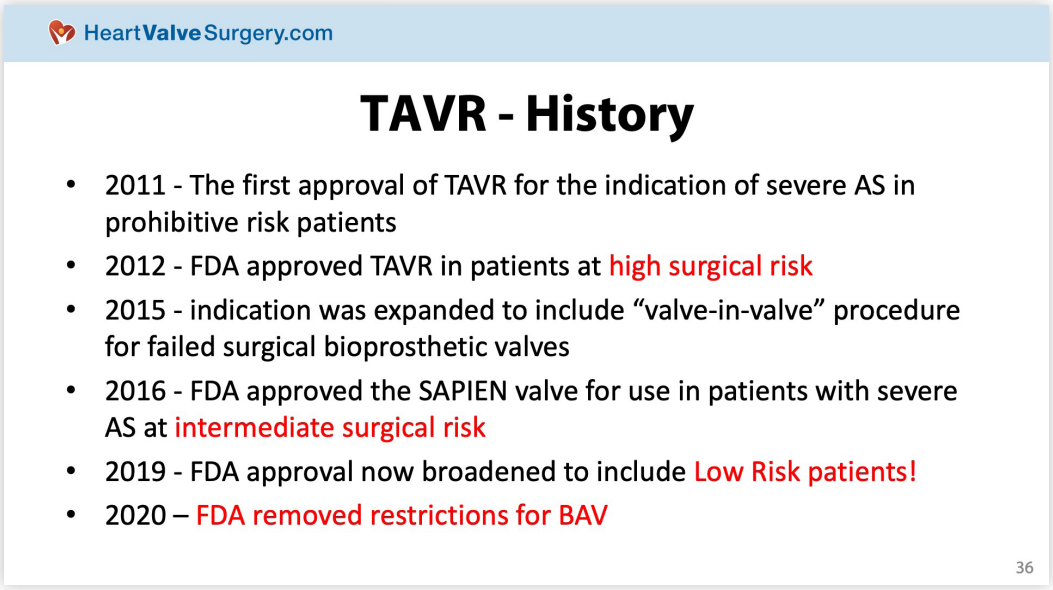
Dr. Sell-Dottin: I'm going to try to fly through some of this material so that hopefully we can have some time for discussion and answering some question at the end.

I do a lot of TAVR and I obviously also do a lot of surgical valve so hopefully I can give you a good perspective on both.

History of TAVR

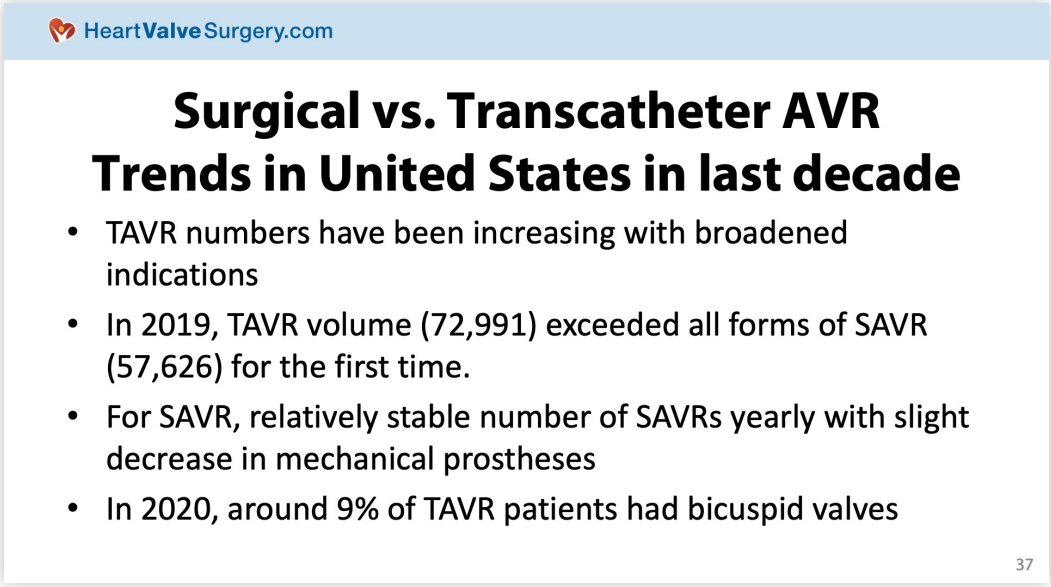


Dr. Sell-Dottin: We're going to start with the history of TAVR. This is a picture of the two different mainstream TAVR valves that are available in the United States. There are some subtle differences between the two, but the idea behind a TAVR is that you have a valve inside of a metal stent or a metal cage that is placed inside of your aortic valve. This is all done in the catheter lab.



This is a relatively new procedure. The first approval for this was in 2011. That was in first approval as an indication. In 2012, it was approved for high-risk patients. We skip down a few lines. In 2016, it was approved for intermediate-risk patients, in 2019 for low-risk patients, and then in 2020 is where the bicuspid valve patients are relevant. That's when the restrictions for use of TAVR in bicuspid valve disease was formally removed. We'll talk about why that's relevant as we move forward. Surgical trends versus transcatheter aortic valve replacement trends, TAVR numbers have certainly been increasing as our FDA approval for this procedure has broadened.

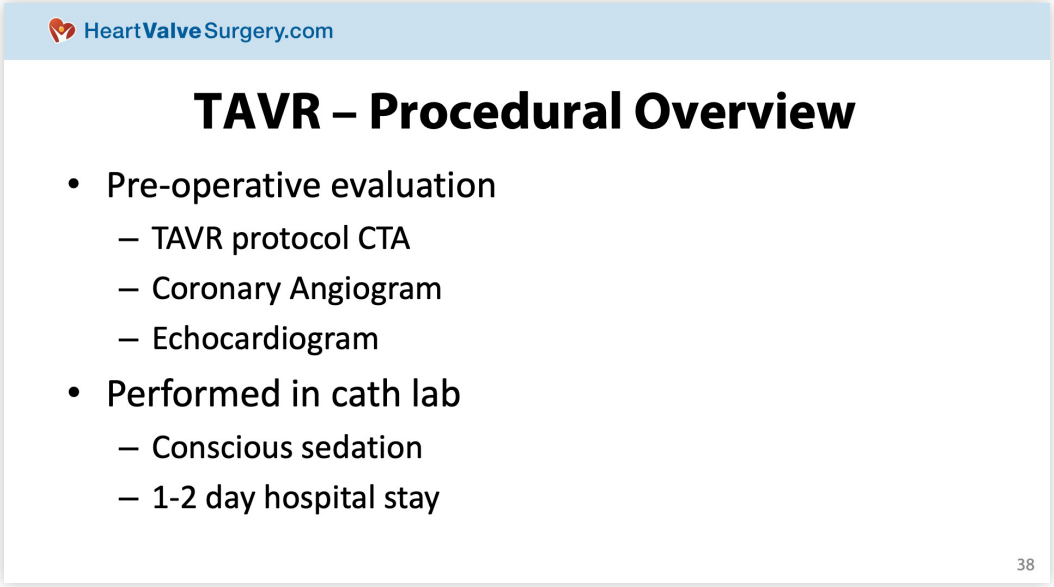
TAVR Growth



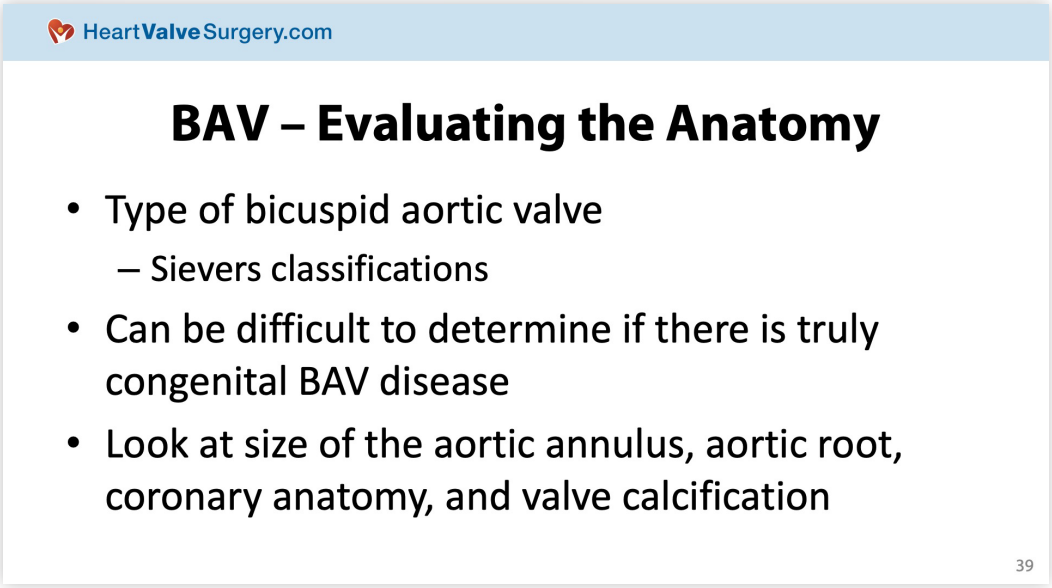
Dr. Sell-Dottin: In 2019, the TAVR volume exceeded all forms of surgical aortic valve replacement and there so far has been no looking back. Both of these are now very big mainstream procedures. For SAVR, there's been relatively stable numbers of these, but a slight decrease in the use of mechanical valves. I think that this is in large part due to the development of TAVR and knowing that putting a TAVR valve inside of a dysfunctional surgical tissue valve is now a very viable option for people. In 2020, around 9% of TAVR patients had bicuspid valves. That really was the most recent statistic that I could get you or find that was published.

I will say that's probably in line with what we're seeing here at Mayo Clinic Arizona is that it's probably around 10%. It also, as I think Dr. Haney highlighted in the beginning, it can be tough to tell. We don't always know 100% whether it's bicuspid or tricuspid. The most important thing is we treat the valve dysfunction.

TAVR Procedure Overview

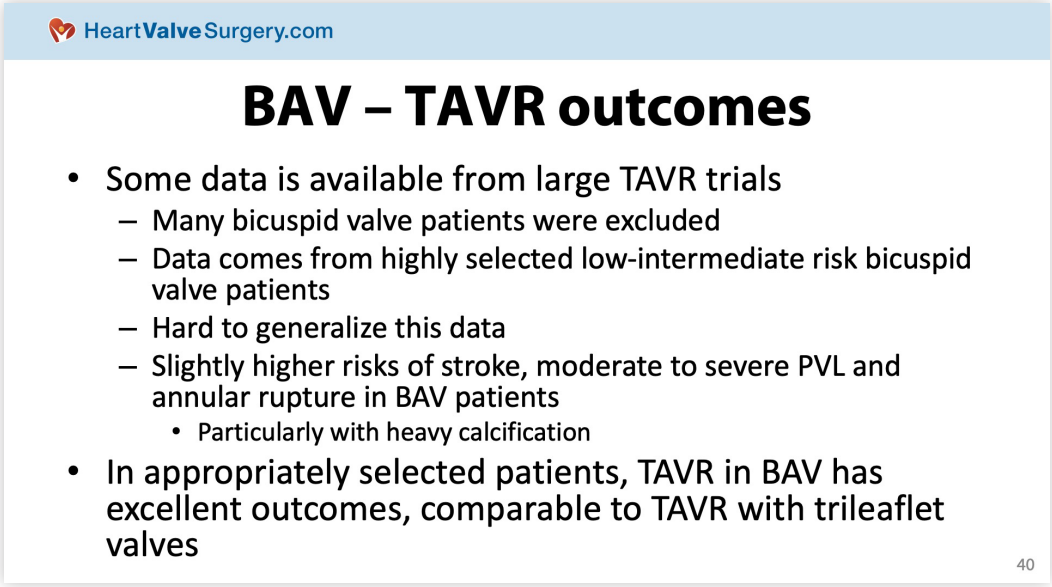


Dr. Sell-Dottin: Procedural overview, we're not going to get into the weeds about TAVR. We do a TAVR protocol CT scan on everybody. We look at the coronary arteries on everybody, and of course, everybody is going to get an echo. These procedures are performed in the catheter lab usually under conscious sedation. You're in the hospital for one to two days. In the world of heart problems and heart surgery, it's "easy peasy" which is great.



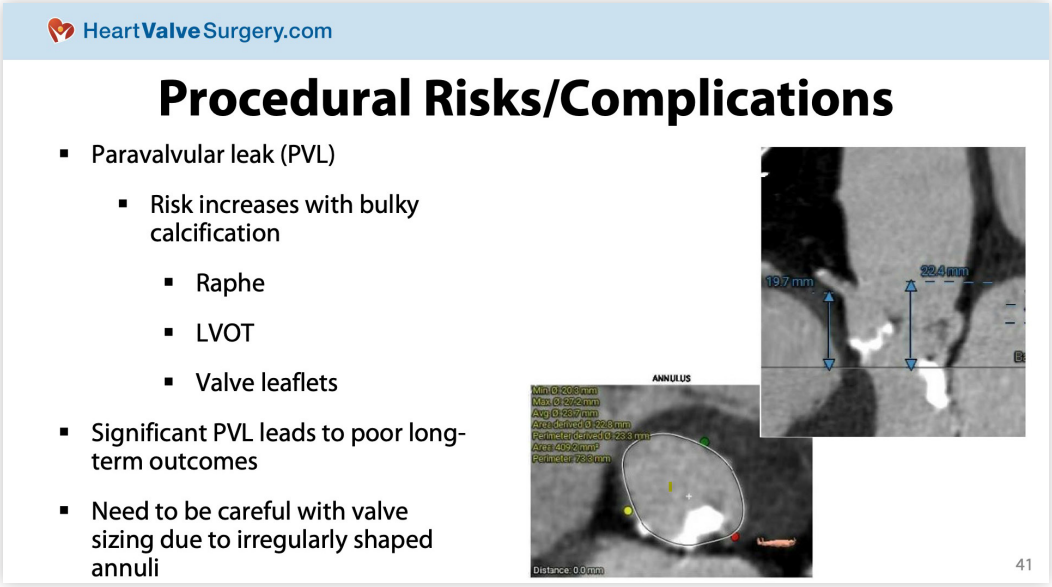
We do some careful evaluation of the anatomy, particularly relevant to bicuspid valve. We look at the Sievers classifications. Again, think back to what Dr. Haney laid out to you in terms of the anatomy. It can be difficult to determine this, but we look at the size of the valve. We look at the relationship with the coronary arteries to the valve. We look at exactly where that calcification is.

TAVR Outcomes for Bicuspid Aortic Valves

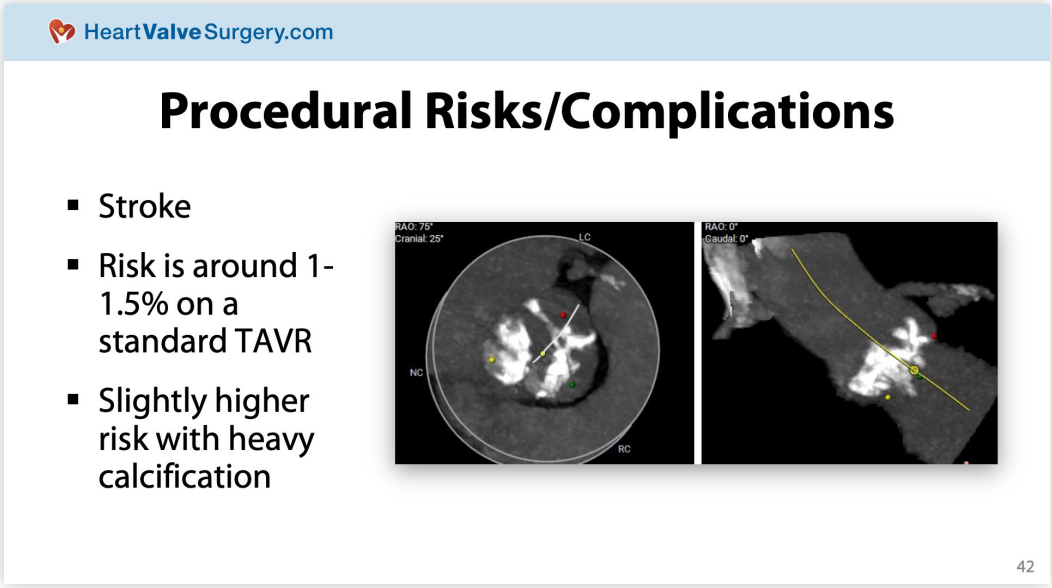


Dr. Sell-Dottin: There is some data available from the large TAVR trials about bicuspid aortic valve disease and TAVR. By and large, what we are finding is that the published data would say that the overall survival is similar between the two groups, bicuspid or tricuspid valves. There is, in that fourth bullet point, slightly higher risk of stroke, slightly higher risk of PVL, which is paravalvular leak, we'll visit that in the next slide, and slightly higher risk of annular rupture in bicuspid valve patients. This is particularly true when there is heavy calcification present along the valve. In short, the bottom line there is, in appropriately selected patients, TAVR in a bicuspid aortic valve has excellent outcomes comparable to that of tri-leaflet valves.

TAVR Risks & Complications

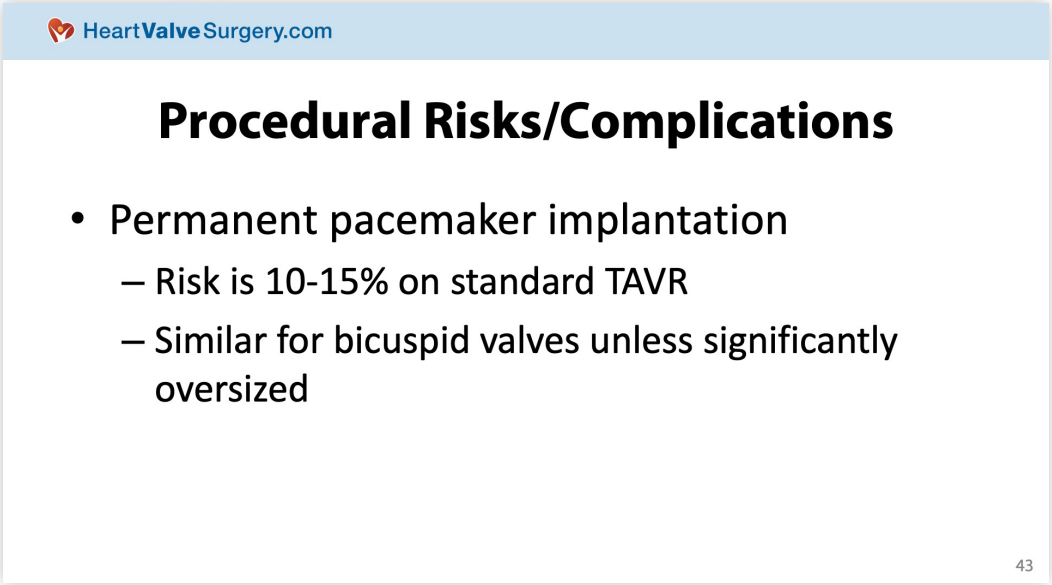


Dr. Sell-Dottin: There are some procedural risks and complications that we worry about. Really, what I want my take home to be from these next three slides that we talk about is that this really is a "heart team" discussion. By and large, if your heart team is telling us as a bicuspid valve patient that they have concerns about their ability to safely perform a TAVR procedure, I would listen to them, right? We understand that people don't want to go through open heart surgery, but these are the real reasons why you may be told that that's not the best choice for you. The first of those you see on this slide which is paravalvular leak. That would mean that there's a leak between your native aortic valve leaflets and that stented valve that we saw a picture of a few moments ago.

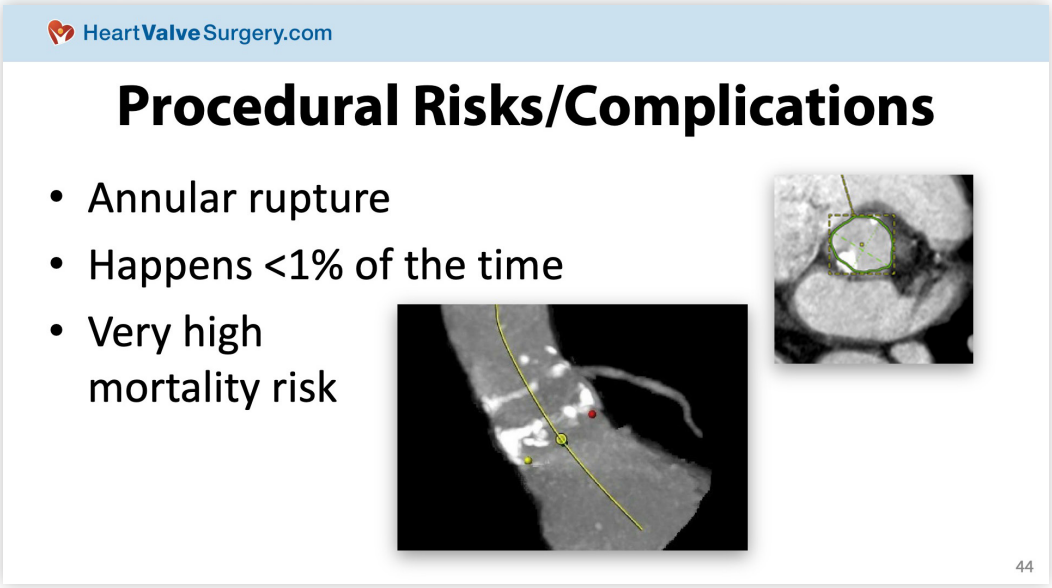


This risk increases when there's big bulky calcium. You see the two pictures I put over here, all the pictures, by the way, are from patients that I've seen in the last six months. You can see all the bright white stuff there in the picture is calcium that's present. That's a valve leaflet and now we're in the left ventricular outflow tractus where the arrow is now. A significant leak cause by bulky calcium leads to poor long-term outcomes. We do need to be careful with valve sizing as well as just deciding to do a TAVR because of the irregular shape that you get. All the TAVR valves are made are circular but if you look at the picture more on the left of the screen here that with that calcium sitting in there, it's not really a circle that we're trying to fit that valve to. That's why it's of concern.

Stroke, of course, is always a concern. Risk is around 1% to 1.5% on a standard TAVR. If really heavy calcification, then the number is going to be closer to 2% to 3%. Overall, not a huge statistical difference between the two.

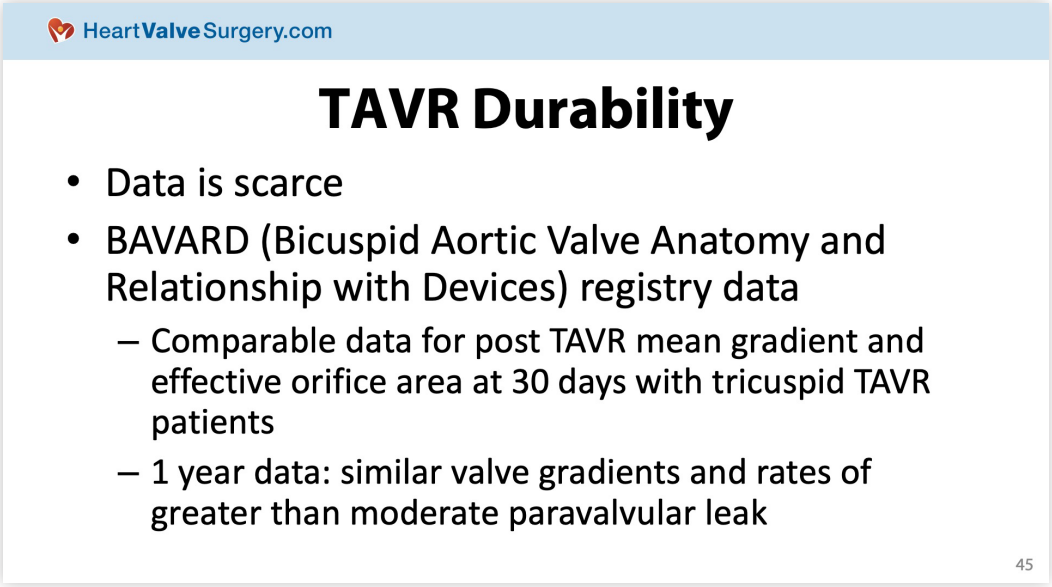


Permanent pacemaker implantation, this is honestly similar regardless of valve morphology it's around 10% to 15% on a standard TAVR.



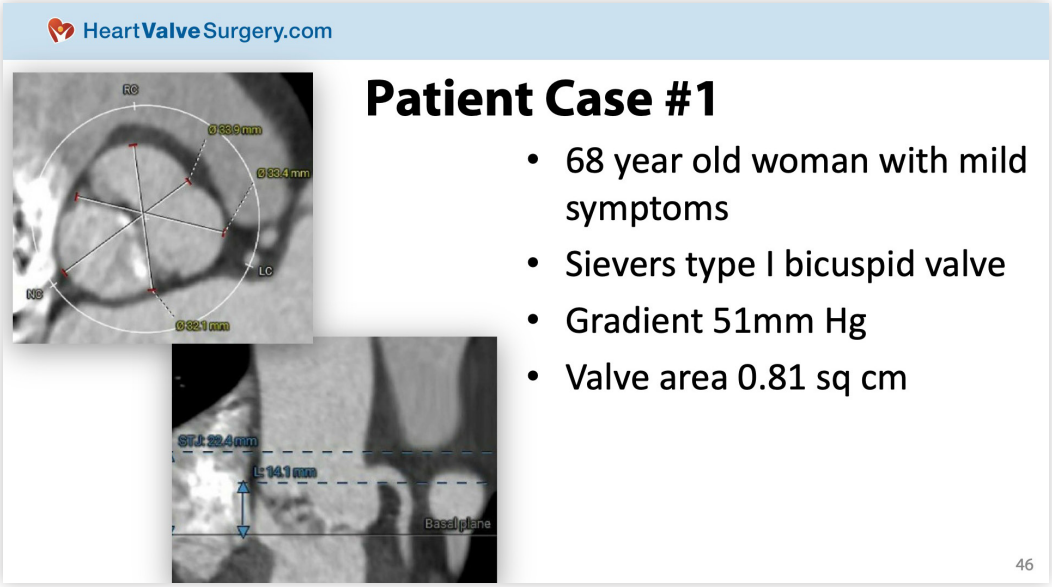
Annular rupture would mean that where the valve is actually seated or where it makes contact and seals inside your body, that that area actually ruptures. That happens very rarely, less than 1% of the time, but is almost uniformly fatal. This is a picture, again, of one of my patients who has, you can see, very heavy amounts of calcium, both of the level of the annulus, which is the bottom ring of calcium, as well as the sinotubular junction, which is the second ring. The same patient has bulky calcification along the side. If you look to the picture on the right, you can see that not only is there calcium around the whole circle where this valve is, but also there are bulky calcium within it.

TAVR Durability



Dr. Sell-Dottin: TAVR durability data is scarce. We're starting to look at this and in the short-term data is showing comparable gradients and durability of these TAVR valves in a bicuspid aortic valve situation. We're going to need a lot more data and honestly time in order to really have the answer to this one.

Bicuspid Aortic Valve TAVR Case Studies

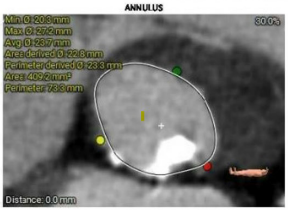


Dr. Sell-Dottin: I thought I would illustrate this with a couple of brief cases. Here is the first one. It is a 68-year-old woman with very mild symptoms. It's a Sievers Type 1 valve. Her gradient is 51 with a valve area of 0.8. You see some representative pictures here on the side. In short, I'm just going to tell you what we did. We performed a TAVR for this patient. She did very well. She doesn't have any malignant appearing calcium. She had a wonderful uncomplicated postop course.

HeartValveSurgery.com

Patient Case #2

- 73 year old man
- Coronary artery bypass grafting in 2012
- Valve gradient 33mm Hg (underestimated)
- Aortic valve area 0.87 sq cm



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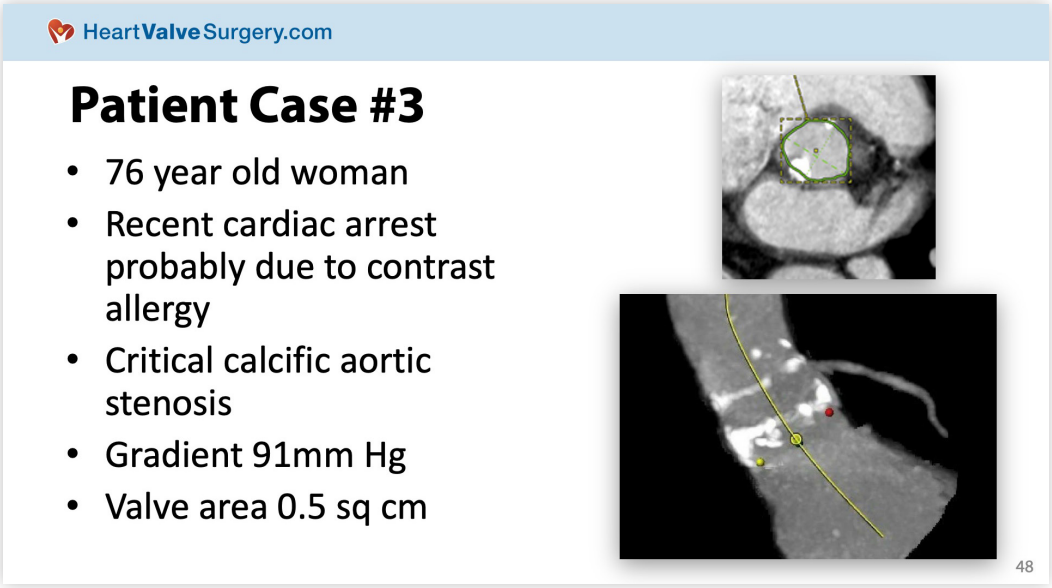
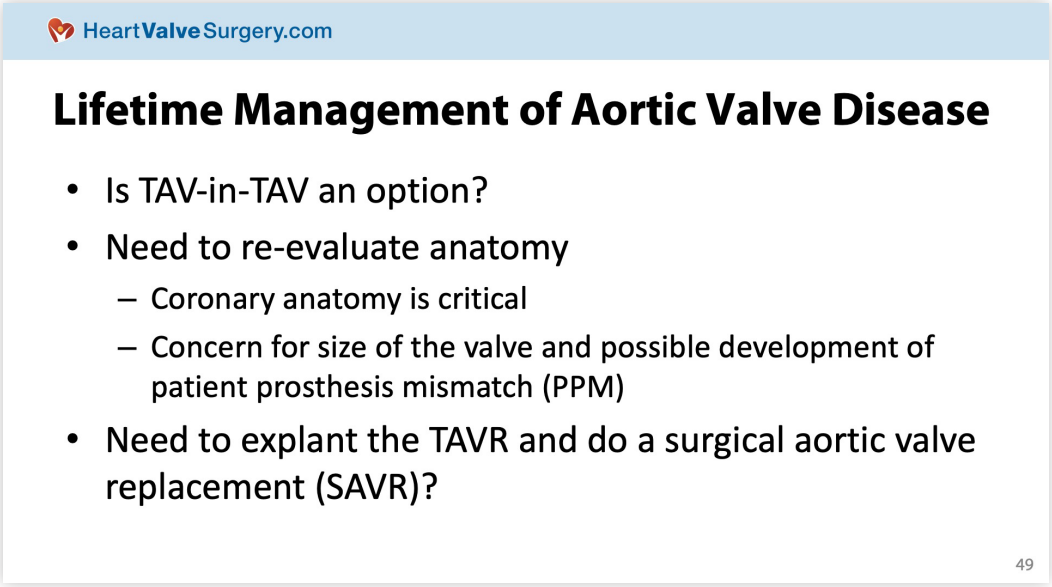
Case Number 2, so 73-year-old man, he had prior coronary artery bypass grafting and has severe aortic stenosis. If you look at the two pictures there on the right, you'll see these are actually pictures from when the previous slides that we had up and you can see some bulky calcium. After looking at everything and realizing most of that calcium is down below the level of the annulus, we actually also TAVR'ed this patient. He did very well. He does not have a significant leak, no stroke, or anything like that, uncomplicated course.

MAYO CLINIC



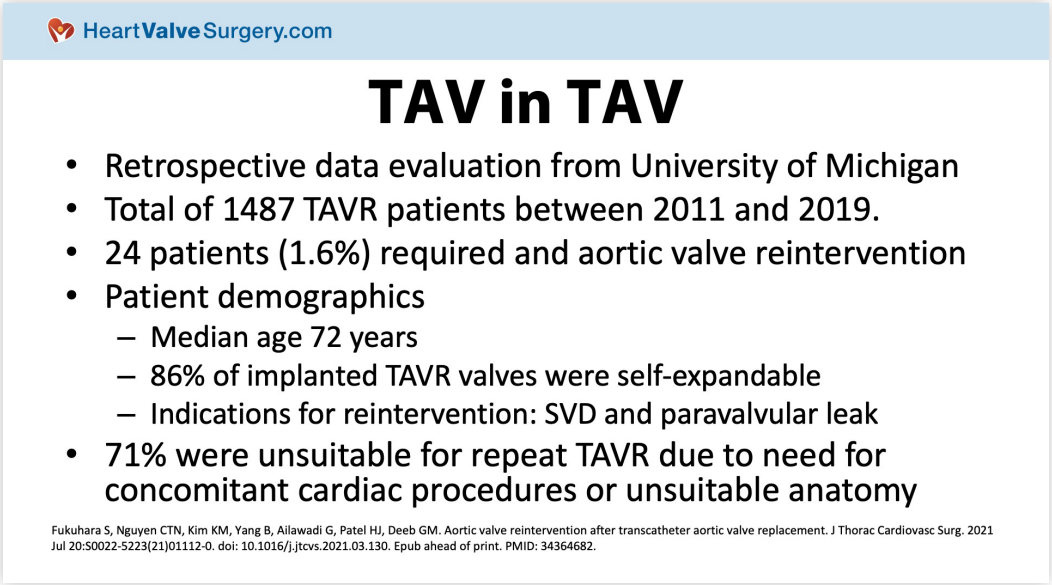
The third case that I'll present, this is a 76-year-old woman. She had a recent cardiac arrest, which is attributed to a contrast allergy, has critical aortic stenosis with a gradient of almost 90, and again, a picture that you've seen before with very heavy calcification. Due to the very small size of this aortic root as well as the amount of calcium present, I had advised her that she should undergo surgery for this. She was also turned down at another center for TAVR for the same reason. She is scheduled for surgery with me next month.

Lifetime Management of Bicuspid Aortic Valve Disease



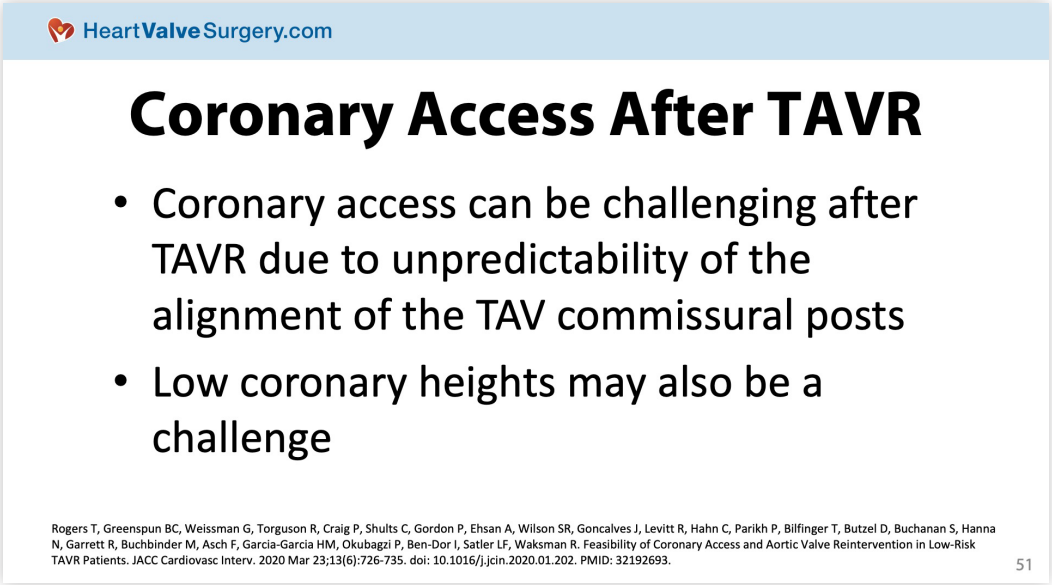
Dr. Sell-Dottin: Lifetime management, I think this is where a lot of the questions are starting to get to in the chat. Okay, fine, we're talking about our first valve. What comes next? Is TAV in TAV an option? Can you put a second TAVR inside of that? The short answer, we need to reevaluate. Coronary anatomy is critical. We worry about the overall size of the valve. If you think about this, we're creating a Russian doll effect where eventually things will get too small and that can be a problem. Ultimately, there can be a need to actually explant, remove the TAVR, and do a surgical valve replacement.

TAV in TAV

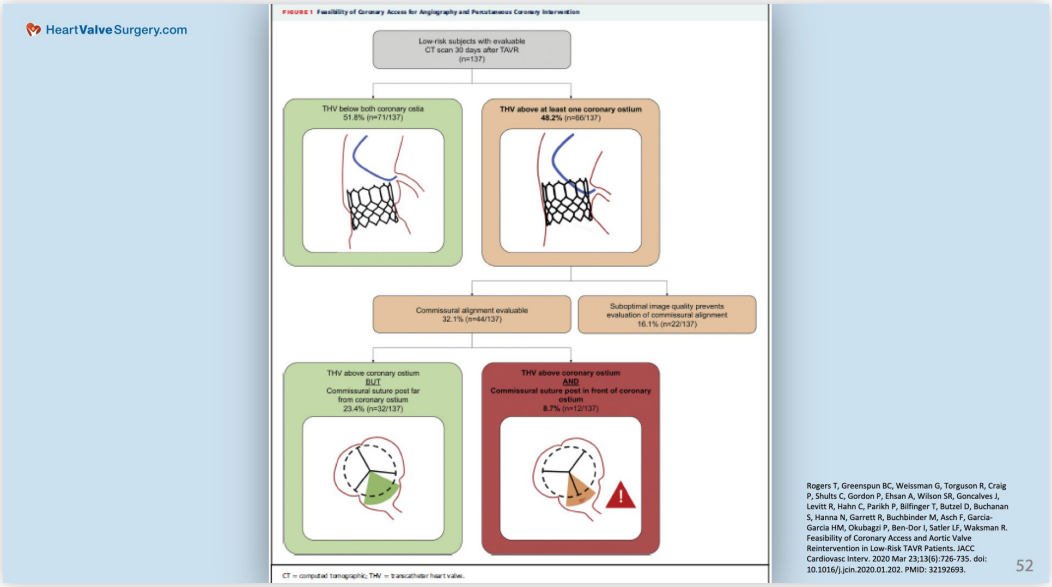


Dr. Sell-Dottin: TAV in TAV, there are a number of these cases that have been done. This is looking at data from around 2019. A good number of patients, but look at the very bottom line here. About 71% of patients who were evaluated were unsuitable for repeat TAVR. This is an area of ongoing conversation where we're starting to talk about at the time of the index procedure the initial TAVR implant. How should we go about this? What type of valve should we put in to really set you up for success and future options and good outcomes?

Coronary Access After TAVR

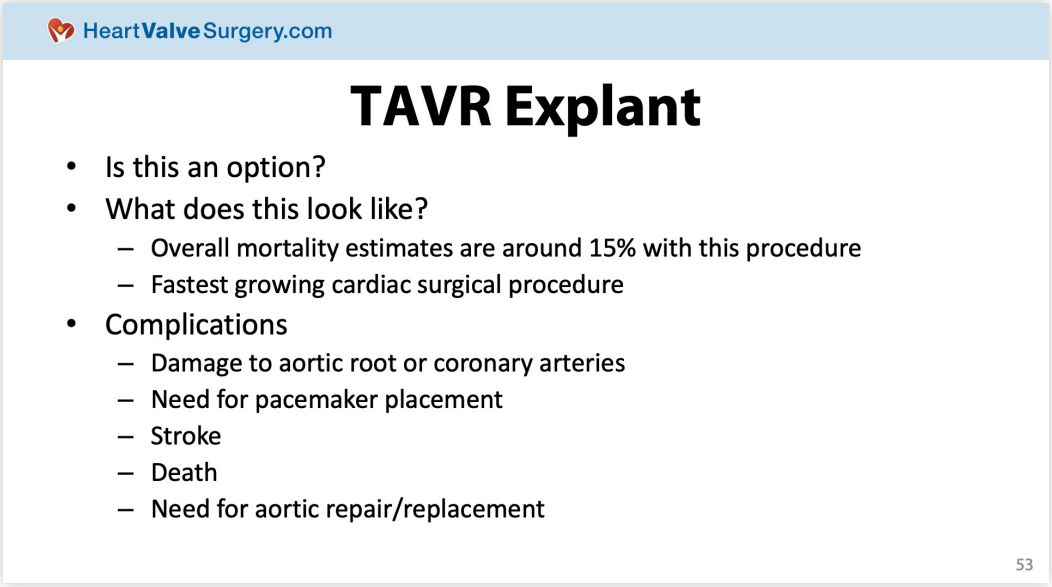


Dr. Sell-Dottin: Coronary access, like I said, this could be one of the reasons that you're not a candidate for a TAVR. Low coronary heights in particular may be a challenge.

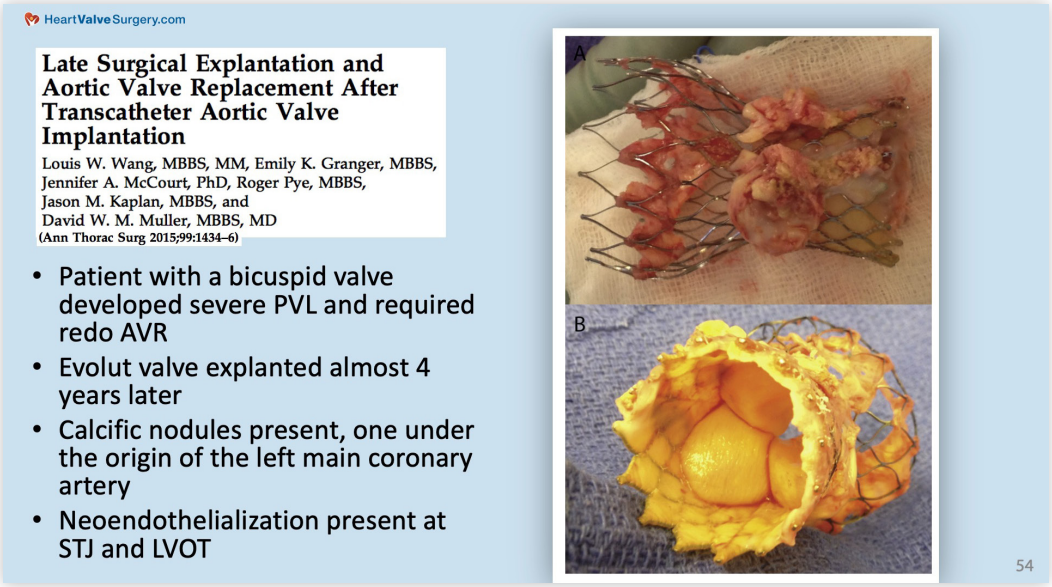


The top two pictures will be showing you two different scenarios in terms of accessing a coronary artery. This may be important if you need to have a stent put in or something like that. You can see the picture on the top left, it's a much easier process and procedure than the one on the top right. Similarly, if we put a second valve inside of that, you can see where that would further complicate your ability to access the coronaries. Down on the bottom, this is a little harder to visualize, but the way that the valve is in there or which way it's rotated is also important to whether or not you would be a candidate. These are all things we're looking at on your imaging.

TAVR Explant

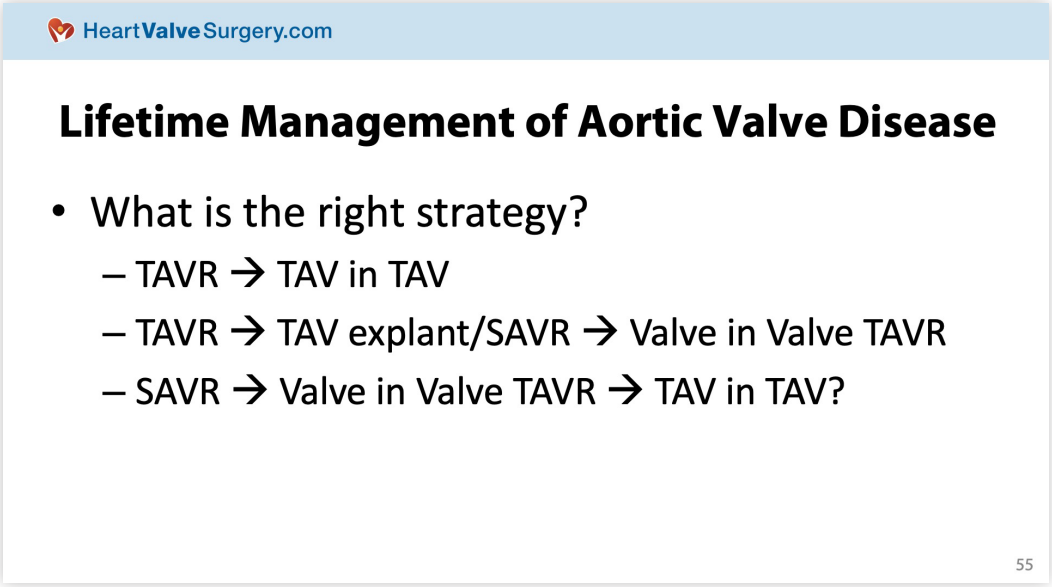


Dr. Sell-Dottin: TAVR explant, is this an option? Maybe, so overall, mortality estimates of this are that it is around 10%. It is the fastest growing surgical procedure in the United States, but there are things we worry about. We worry about damage to the aortic root, the coronary arteries, need for pacemaker, stroke, death. All of these things are the reasons for that mortality percentage.



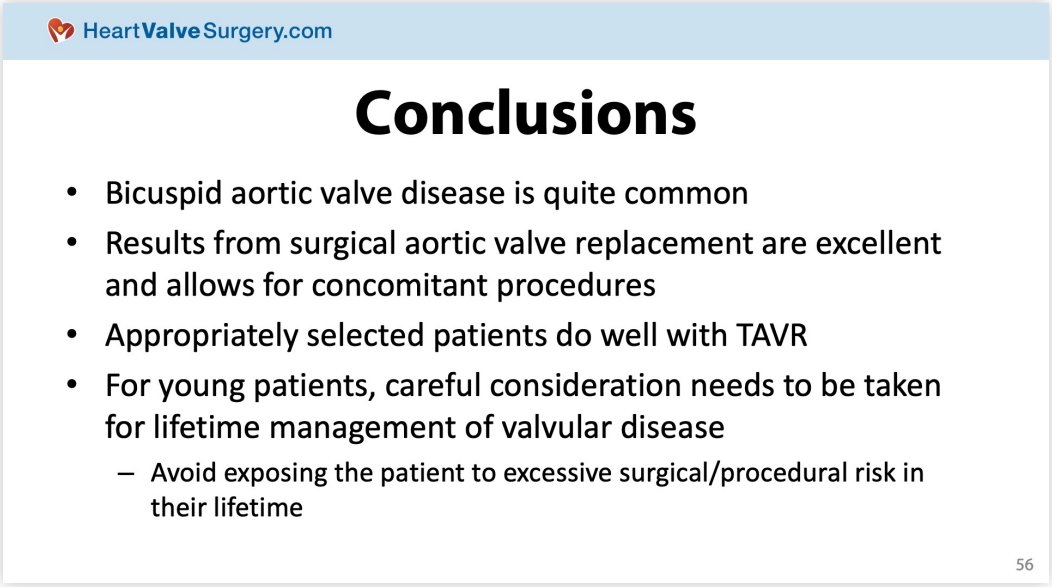
I put in this is a case report but just wanted to show you this picture of what one of these valves look like when it comes out. You can see just a significant amount of calcium and in growth around this valve which is really what makes it challenging to take these out and then do a surgical valve. The reason I put this in is to say explanting a TAVR is not a straightforward thing. To count on that as your next step is maybe not the best life decision.

Strategies for Lifetime Management



Dr. Sell-Dottin: Lifetime management of aortic valve disease, what is the right strategy? We don't have a black and white answer to this. It's something that is really being discussed in the field. I put out a couple of different options here. Let's say you do TAVR first. Do you follow that with a TAV in TAV? If you do TAVR first, do you then do TAVR explant and SAVR and then get a valve in valve down the road? Do you start with your surgical valve when you're young and healthy, follow it with a valve in valve TAVR? Then who knows? Maybe we'll put more valves in there. These are really some of the intriguing questions within the field.

TAVR Conclusions

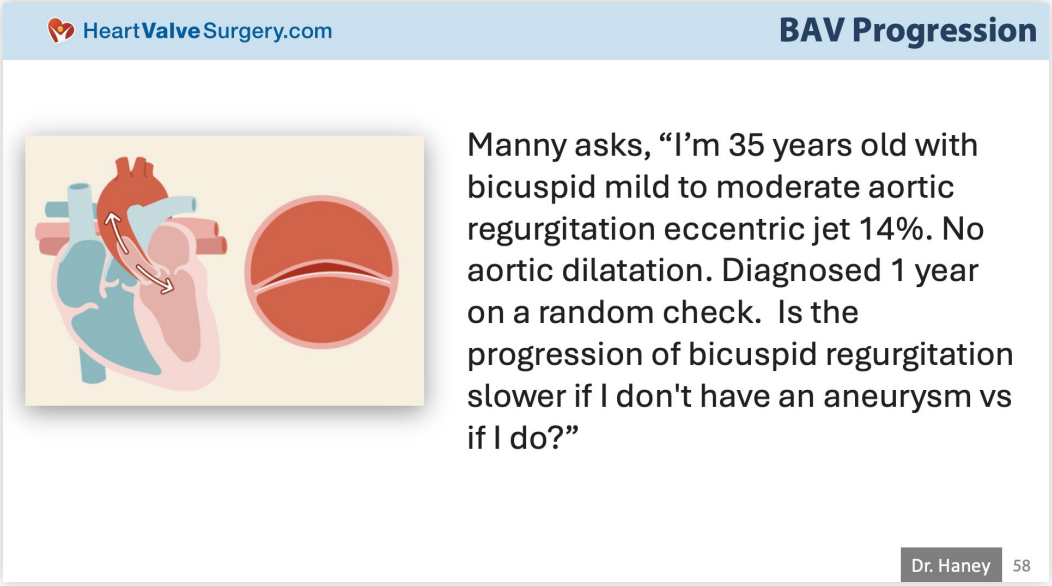


Dr. Sell-Dottin: Conclusions, bicuspid aortic valve disease is common. The results from surgical aortic valve replacements are excellent. Appropriately selected patients do extremely well with TAVR. For young patients, we really need to be careful about making decisions that will serve them well for a lifetime. With that, I think we are open for questions.

Questions and Answers

Adam: I cannot thank you enough, Dr. Haney, Dr. Barrus, and Dr. Sell-Dottin, for the flow of this webinar, starting from the anatomy to the surgical considerations to TAVR. Then for everybody on the line, I think it really comes home at the end with the discussion about the lifetime management of your valve disease. The nuances of taking care of yourself and your heart as someone once said to me, there's no perfect valve replacement. I think that comes out bright here today.

Let's continue on with a rapid-fire question and answer session. I know there's been now 61 questions already answered. Thank you, Dr. Haney, Dr. Sell-Dottin, Dr. Barrus, for doing that. Let's see some other questions that came in.

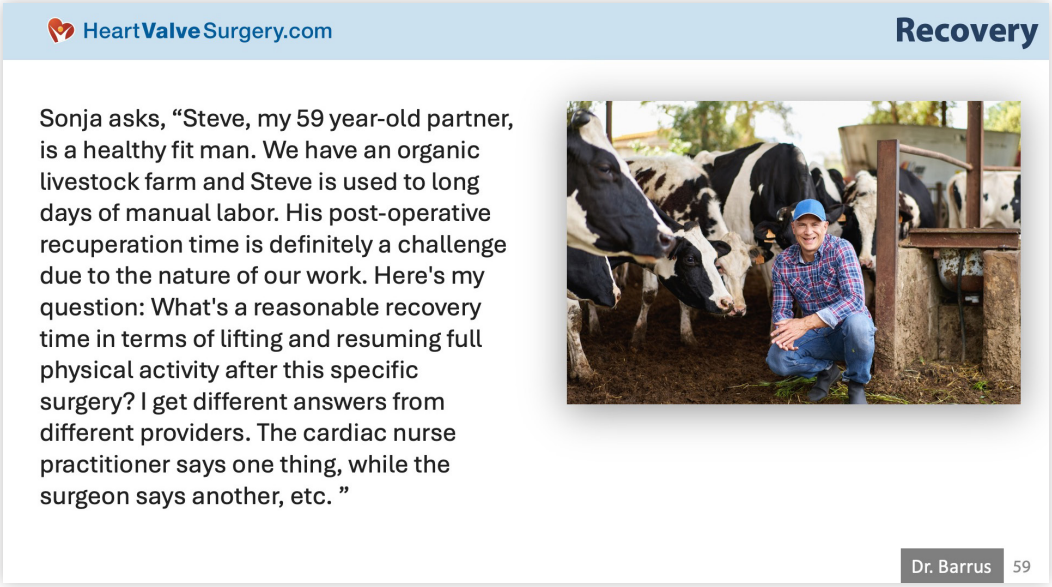


Bicuspid aortic valve progression, this is from Manny who says, “I’m 35 years old with bicuspid mild to moderate aortic regurgitation and an eccentric jet at 14%. No dilation, diagnosed a year ago. Is the progression of a bicuspid regurgitation slower if I don’t have an aneurysm versus if I do?”

Dr. Haney: I think this gets to the question of – it’s a little of the chicken or the egg phenomenon. One of the problems, one of the reasons that people get aortic regurgitation, whether it’s actually tricuspid valve or bicuspid valve, with aneurysm is that as the aorta, specifically we’re talking about the root as the root dilates, that valve could be basically pulled apart and so the leakage and it distorts the anatomy of the valve and so it can increase the degree of regurgitation. With aneurysm, your regurgitation, we would expect it to be

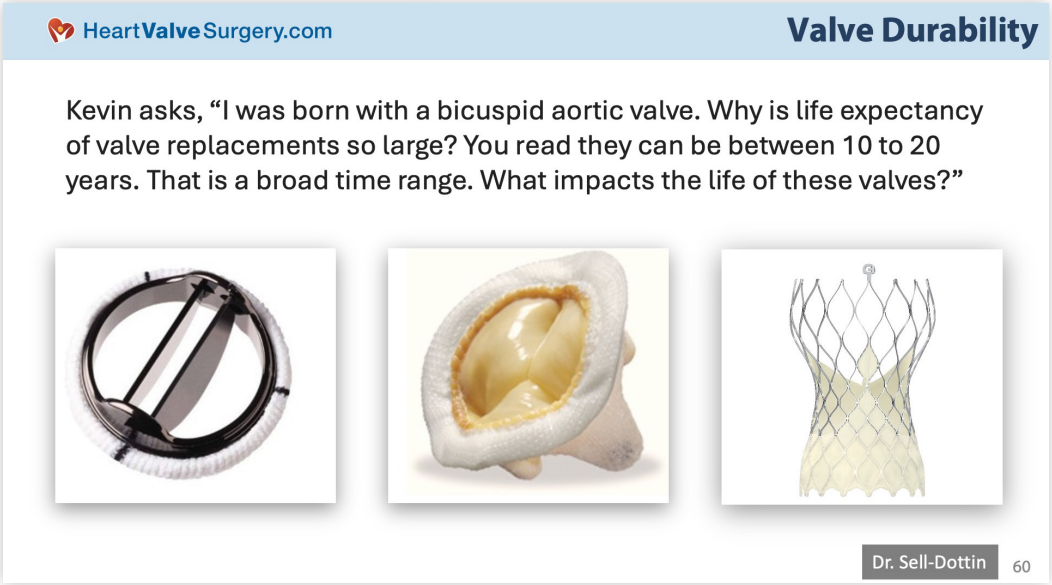
bigger.

Furthermore, bicuspid valve patients with aneurysm and regurgitation are at higher risk for the complications that were mentioned, specifically this section. If you do not have aneurysm, yes, on some level, we could say you'd be less – we would expect your regurgitation to progress less dramatic than if you did. On the other hand, you're still going to ultimately need to have surveillance because there's lots of things at play and your regurgitation, everyone's a little bit different. We would still say you need to have your regurgitation followed.



Adam: This comes in from Sonja about her partner Steve who runs a livestock farm. The question is, “What’s a reasonable recovery time in terms of lifting and resuming full physical activity after a surgery? I get different answers from different providers.” Dr. Barrus, what would you say?

Dr. Barrus: That’s a very common question. If you had a full sternotomy, again, it takes between six to eight weeks for that bone to heal. Practices vary so it depends on how the health and quality of the bone, the tissue, the person’s health overall general, any other health issues they may have. Typically, we can start increasing activity and lifting after three or four weeks. However, I absolutely would say I would refer back to the surgeon who did the surgery who was there and knows in depth the things that were going on as far as when he can get back to full labor.



Adam: Dr. Sell-Dottin, I get this question probably 40 times a week. "I was born with a bicuspid aortic valve. Why is the life expectancy of valve replacement so large? You read they can be between 10 to 20 years. That is a broad time range. What impacts the life of these valves?"

Dr. Sell-Dottin: There's not really a short answer to this. Mechanical valves should last forever, right? With the bioprosthetic valves, there are a number of things that impact it. We are finding out that things like Lipoprotein(a) which is one of the lab markers we can check, that can affect it. Certain medications can affect how long these valves last. We know that our age at the time of implant affects how long these valves last. Unfortunately, the younger we are when we get the new valve put in, the less time it tends to last. The older we are, the more likely we are to live with it forever. This is certainly an area of ongoing evaluation.

I will also say that the valves have changed, right? The valve companies continue to make improvements and adjustments. For example, there are new anti-calcification treatments that are present on some of these valves that we think are going to have an impact. We don't have all of the long-term data from that but it's a complex topic.

Adam: Well, thank you so much for sharing that. We're going to wrap up the webinar, but please don't hang up just yet. I want to take a very quick minute and thank Dr. Sell-Dottin, Dr. Barrus, and Dr. Haney for all of the remarks, all the education, and all of the empowerment for patients in our community. Thank you for being here today. I want to thank you, all the patients on the line. When we get together like this as a community, it helps us best manage and get the best treatment and ultimately the best outcomes of valvular disease, including bicuspid aortic valve.

On that note, I also want to thank you. Survey is going to be coming up on your screen. It's real quick. It's just five questions as we wrap up, but again, thanks so much, Dr. Sell-Dottin, Dr. Barrus, Dr. Haney, and thanks to all the members of our community for being here today. Thanks so much.

Patient Resources

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

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

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