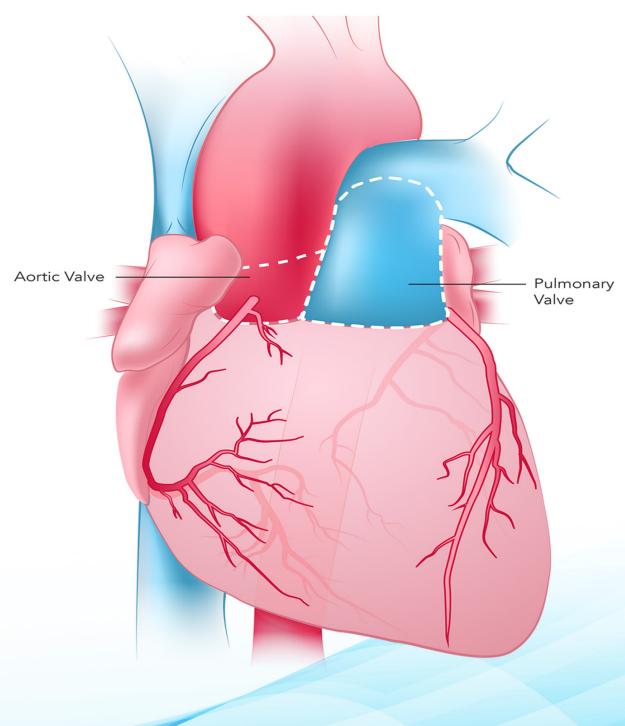


Advantages of The Ross Procedure





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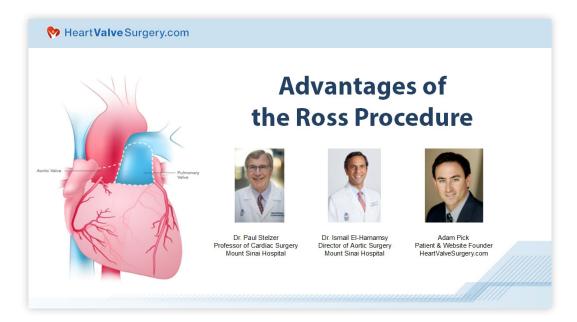


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Introduction



Adam Pick: Hi, everybody. My name is Adam Pick, and I'd like to welcome you to the webinar. If I have yet to meet you, I'm a Ross Procedure patient who started HeartValveSurgery.com all the way back in 2006. The mission of our website is simple. We want to educate and empower patients just like you. This webinar, which has had patient registrations - over 250 in number - from people all over the world, was designed to support that mission.

During the webinar, you're going to be in what's called "Listen Only" mode. I would encourage you to submit your questions in the control panel that's in the upper right part of your screen.





Agenda

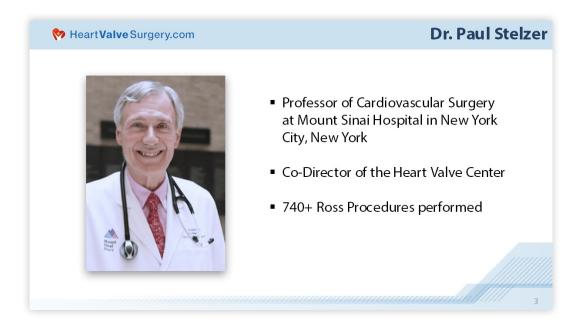


Adam Pick: Let's look at the here for the webinar. I'm going to go introduce our speakers. We're going to talk about aortic valve anatomy and disease, some of the more common treatment options, and then we're going to really focus on this advanced technique for aortic valve replacement known as the <u>Ross Procedure</u>. We're going to have a "Q&A" session and then I'm going to ask you to just complete a quick five-question survey





Dr. Paul Stelzer

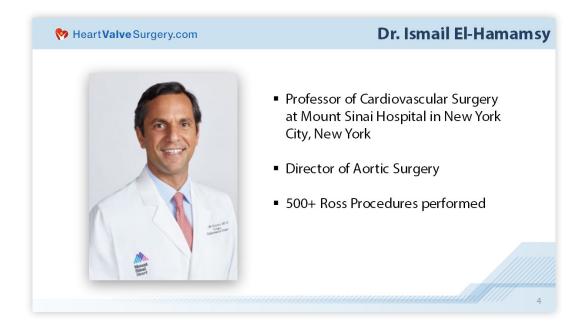


Adam Pick: Let's talk about some of the extraordinary physicians on the line. Dr. Paul Stelzer is a professor of cardiovascular surgery at Mount Sinai Hospital in New York City, New York. He's also the co-director of the Heart Valve Center at Mount Sinai. I have to tell you, when people mention the name Paul Stelzer to me and I realize about all that he's accomplished with aortic valves, aortic aneurysms, and most importantly the Ross Procedure, I'll let you know that I actually call him a "Living Legend" when it comes to the Ross Procedure. The reason being is that he has now performed over 740 Ross Procedures. I could be wrong, but I think he is the leading at Ross Procedure surgeon here in the United States. It is an honor to have Dr. Stelzer on the webinar with us.





Dr. Ismail El-Hamamsy



Adam Pick: Dr. El-Hamamsy is a professor cardiovascular surgery at Mount Sinai Hospital in New York City, New York. He is the director of aortic surgery at Mount Sinai and again another aortic valve and aneurysm specialist. When it comes to the Ross Procedure, we've got a "Living Legend" in Dr. Stelzer, and when it comes to Dr. El-Hamamsy, he doesn't know this, but I actually call him the "Rockstar" of Ross Procedures. He has trained physicians all over this country, all over this world about this special procedure. We've got a Living Legend and we've got a Rockstar on a webinar all about valve treatment. Could it get any better?





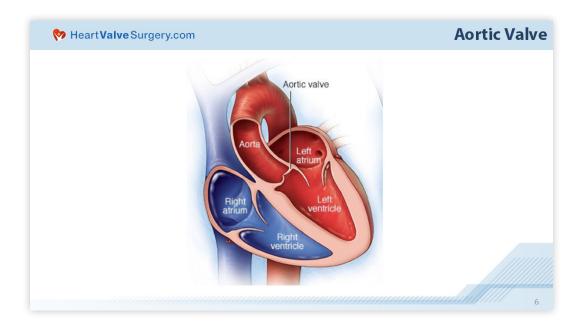
Ross Procedure Patient Success Stories



Adam Pick: Actually, it can. Because what I want to show you is the result of the dedication and the hard work of these two men. It's not just them. It's their entire teams. Here you see Peter Woglom, Jeff Shebovsky, Elizabeth Boylan, Jeannie Sullivan, and Mark Kroto. These are all people who are not just surviving. They are thriving, and it is all because of the commitment to the Ross Procedure, which all of these patients have had. These doctors are celebrated and we, in particular me, I'm honored that Dr. Stelzer and Dr. El-Hamamsy have taken time away from their very busy practice to be with us today. To get things going here, I'm going to turn it over to Dr. El-Hamamsy.



About The Aortic Valve



Dr. Ismail El-Hamamsy: Thank you so much, Adam. Thank you for this wonderful and very generous introduction. Congratulations on all the work that you've been doing over the years. I think what you've done is really tremendous in terms of empowering patients and educating patients and helping them navigate all these very difficult decisions that they have to go through. What you didn't mention is Paul is definitely a Living Legend, and I am the luckiest surgeon out there because I have the opportunity to work with him on a daily basis. I joined Mount Sinai just about nine months ago, and it's been a true privilege to witness him every day interacting with patients and do surgery. He's really a masterful surgeon and an incredible doctor.

What we will try to do together today is really walk you through what aortic valve disease is and what the different options for treating aortic valve disease are but with a specific focus on the Ross Procedure. We won't spend too much time discussing the alternatives but really delving into the specifics of why we believe the Ross is a very appropriate procedure for young and middle-aged adults.



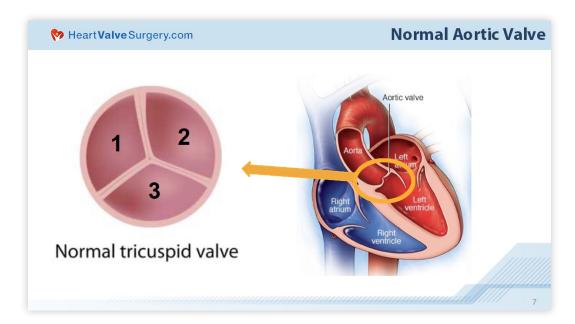


As you all know the – or you may know - the heart basically is a pump, and every time your heart beats, the pump – the muscle just contracts and it squeezes, and it pushes the blood out of the heart into a big vessel called the aorta, which you see here on the screen. Between the pumping chamber of the heart, which we call the left ventricle, and the aorta, lies this little valve which opens and shuts with every heartbeat, over 100,000 times every single day. The function of the aortic valve in simplistic terms is really to open fully to allow the blood to exit without any obstruction and then to close to prevent the blood from falling back into the heart. It really ensures the blood flows in a single direction in every single heartbeat.

Beyond just opening and closing, the aortic valve performs many sophisticated functions within what we call the aortic root, which contribute to the ventricle working as least hard as possible and also ensuring that the flow of blood into the coronary arteries, which are the arteries that feed the heart muscle, is very seamless both at rest and with exercise. It really is a phenomenal piece of architecture, or creation of nature that is in that position.



Aortic Valve Structure

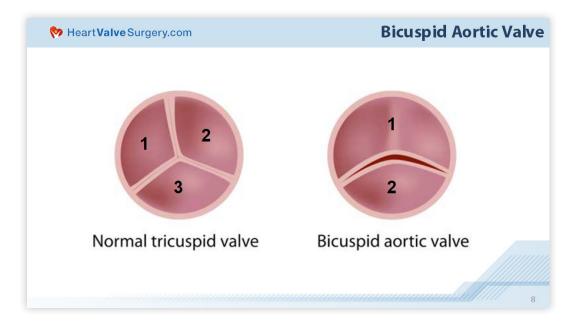


Dr. Ismail El-Hamamsy: If we look at the heart from the top, it looks exactly like this. Next, it has one, two, and three little what we call cusps or leaflets. That's a normal valve. That's why we call it a tricuspid aortic valve. In about one to two percent of the population, instead of having three little cusps on the aortic valve – because a normal aortic valve such as you see here is able to perform its functions for almost 70 to 80 years before it starts showing any signs of fatigue or any signs of calcification on these cusps. But, if we look at the next slide, you'll see a condition call <u>bicuspid aortic valve disease</u>, which affects about one to two percent of the population.



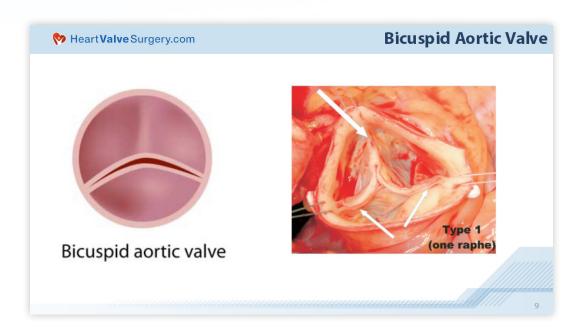


Bicuspid Aortic Valve



Dr. Ismail El-Hamamsy: A bicuspid aortic valve is the most frequent in-born anomaly in the heart, and instead of having these three little cusps, you'll see that you have two leaflets instead of the three in the valve. That's why we call it a bicuspid instead of a tricuspid aortic valve. The issue with bicuspid aortic valves is that, unfortunately, they are not as performant in the long-term as tricuspid aortic valves are. They tend to wear out a little bit sooner, and typically, patients will present in their 30s, 40s, or 50s with a valve that is not functioning normally.



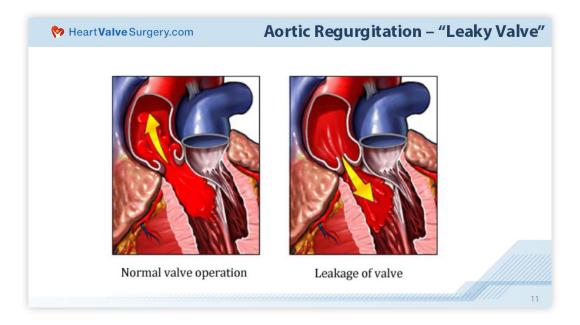


Dr. Ismail El-Hamamsy: There are two ways that a aortic valve can malfunction. If we look at the next slide, you'll see a surgical view of a bicuspid aortic valve. You can see where you see those two traction sutures on the left and the right-hand of the screen is the edge of each of these – the bicuspid aortic valve.





Aortic Valve Regurgitation



Dr. Ismail El-Hamamsy: What is aortic valve disease? You can have one of two things. As I mentioned earlier, the main function of the aortic valve is to open fully and then to close perfectly and to seal perfectly well to prevent blood from seeping back into the heart. In some circumstances, the bicuspid valve can present in a way that it doesn't shut properly well. In such instance, you have a leaky aortic valve, or <u>aortic regurgitation</u>. In other words, instead of touching with every diastole or every time the heart relaxes, the leaflets don't really touch each other, and there's blood that – as you can see on the right-hand of the screen, the blood goes back into the left ventricle. The left ventricle eventually starts enlarging to accommodate this extra volume of blood.

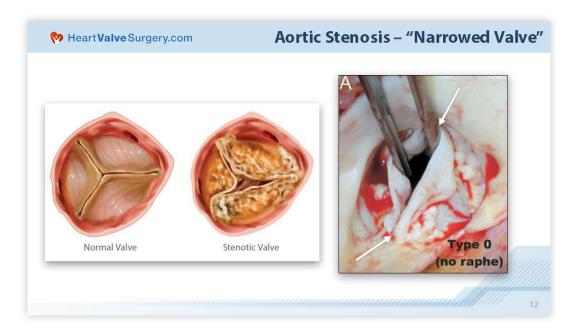


This, as you can imagine, creates a flow of blood that is not very efficient because the blood goes up and down the aortic valve flowing back and forth instead of flowing really in a single direction. With time, we'll discuss what symptoms can appear in these patients. That's one form of aortic valve disease or dysfunction. It typically presents at the younger end of the spectrum in terms of age, so these patients will usually be in their 20s, 30s, or early 40s. A leaky bicuspid aortic valve is typically a valve where we don't see necessarily too much calcium, and these valves can be repaired in a fair number of situations.





Aortic Stenosis



Dr. Ismail El-Hamamsy: The other way that aortic valves can present with a form of disease is what we call <u>aortic stenosis</u> or a narrowed aortic valve. Again, if we go back to what the normal aortic valve does which is simply open and shut with every heartbeat, in some circumstances, particularly with bicuspid aortic valves, around age 50 or so, we start seeing calcium deposits on the aortic valve cusps as you can see on the left-hand side of the screen. That makes these leaflets very rigid, and they don't open quite as well. So, as the calcium deposits increase, the leaflets don't open quite as well. As you can see on the right-hand side of the screen, this is a surgical view of a calcified bicuspid aortic valve. You can see that the forceps is pushed into the opening but really forcing that opening to let that blood out.

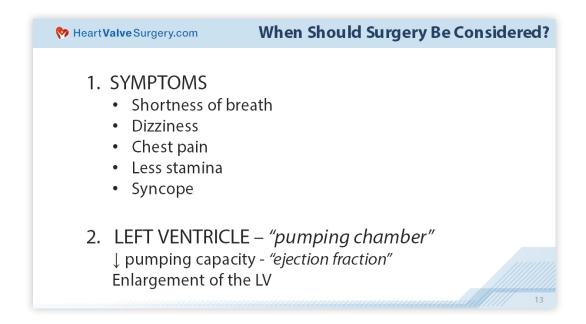


Really in a normal aortic valve, the full area of opening would be the full circle where the valve is sitting right there. I always like to tell patients aortic stenosis is very much like a water hose that you pinch and pinch and pinch more and more and more. You have a lot of pressure on one side, and flow, it becomes weaker and weaker on the other side. These are the two main forms of aortic valve disease that patients can present with. Mainly patients with bicuspid aortic valves are the patients that we're talking about today because that disease presents at an early age in life.





Timing Aortic Valve Surgery



Dr. Ismail El-Hamamsy:One of the questions – or two questions when you're a patient that you will – you always want to ask is first do I need surgery and secondly will be what kind of surgery do I need. The first question is when should surgery be considered. There are mainly two things that we look at or that your cardiologist or primary physician will always be tracking. The first one is looking at symptoms, and the symptoms of aortic valve disease are quite typical in that patients will either present with shortness of breath either at rest or typically with exercise, especially in young patients. Sometimes they can complain of dizziness. Some may complain of chest pain. Some may complain of just decreased stamina. After a long day, patients come home and they're completely wiped. They're very tired, and they need to go straight to bed, whereas a year or two before they would've been able to go for dinner or to do things afterwards. Syncope or "passing out" is the ultimate symptom associated with aortic valve disease and one that we fear a lot because that can be indicative of very severe form of aortic valve disease.

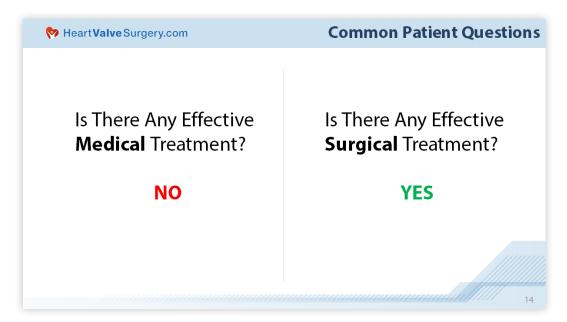


The second thing that we look at and that we consider in terms of whether a patient needs surgery or not is looking at the echocardiogram, the ultrasound that your cardiologist or your physician will do, with a specific look at the left ventricle or the pumping chamber of the heart. There are two things that we look at there. One, is the heart able to squeeze as hard as a normal heart does, and secondly, has the heart enlarged beyond a certain dimension at which point we would definitely consider performing surgery because, really, anything that we do with regards to the aortic valve we're doing to preserve the health of the ventricle, the pumping – of the engine of the heart, which is the pumping chamber. The valve is really there to make the ventricle's life easier. Any time we see signs of distress at the level of the ventricle, we start having a more serious conversation with regards to surgical intervention with a patient.





Common Questions About Medical & Surgical Treatment



Dr. Ismail El-Hamamsy: Some common questions that patients ask are – the first one is a very natural one. Is there any effective medical therapy if I have bicuspid aortic valve disease whether it's a leaky valve or a narrowed valve? The reality is, unfortunately, there is, to this day, really no effective medical treatment. All we can do is just give medication to control blood pressure or to try to minimize fluid retention but nothing that will impact how fast your aortic valve disease will progress or even to eliminate aortic valve disease from appearing. However, on the good news is that there are very effective surgical treatments for aortic valve disease, and that's what we'll be discussing over the next 30 or 40 minutes.





Aortic Valve Replacement Options

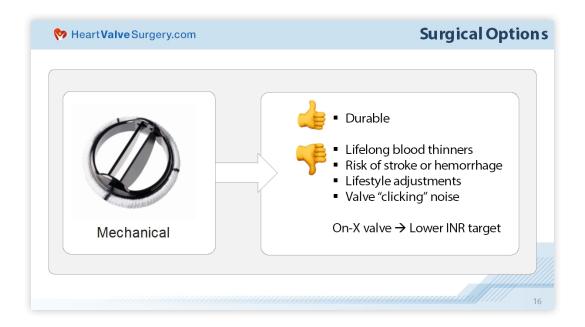


Dr. Ismail El-Hamamsy: These are the three main surgical options that patients have. Any time you go see a surgeon with aortic valve disease or an aortic valve that needs to be replaced. I should mention that as I alluded to earlier, when you have a leaky bicuspid aortic valve, that can be repaired in a fair number of cases, and that will always be our "Plan A" is to consider repairing a bicuspid aortic valve. We have ample experience here doing aortic valve repair procedures, but we really will focus in this case on the situation where we have to replace the aortic valve. A mechanical valve is the first option. The second option is using an animal valve or something we call tissue valve or bioprosthesis. These are valves that are made either out of cow or pig material. The third option is doing the Ross Procedure, which will be the focus – the main focus of this presentation here.





Mechanical Valves



Dr. Ismail El-Hamamsy: Each of these options has advantages and drawbacks. There is no perfect solution for the treatment of aortic valve disease, but as you will see by the end of this webinar, there are different options which are best suited for a given patient. We always try to tailor and individualize the decision or the choices for patients in terms of what we think best suits their lifestyle or life expectancy, what their professional career is, etcetera.

The first option is a mechanical valve, and these are valves that are made with, as you can see here, two little metal clips that will basically open and close every time the heart squeezes, so as long as the heart squeezes, the valve will continue to open The main advantage of a mechanical valve is its durability. Although you may hear oftentimes that a mechanical valve is a one and done solution, the reality is some patients do require a reintervention to re-replace a mechanical valve whether because of an infection or sometimes because of a bit of an inflammatory reaction beneath the valve or sometimes there's a bit of a leak around the valve that can develop, but by in large these are very durable options.



The main issues with a mechanical aortic valve is two-fold. The first – and really all hinges on the need to take blood thinners for the rest of the patient's life, the reason being that if you don't take any blood thinners and you have a mechanical valve in the aortic position, these mechanical valves tend to favor clot formation, and if you do have a clot that forms on the aortic valve, that can go up to the brain and cause a stroke. So, patients need to be on lifelong blood-thinning medication. What that means is that if your blood is too thin, you have a risk of having a serious hemorrhage. If your blood is not thin enough, you have a risk of having a stroke.

When we look at populations of patients with mechanical aortic valves up to 20 years after surgery looking at young adults, the risk of stroke or major bleeding is about 20% at 20 years, so about one in five patients will have something pretty major happen 20 years after surgery. Although it's a very durable option, this is something that always has to be kept in mind is that risk of a stroke or a major bleeding.

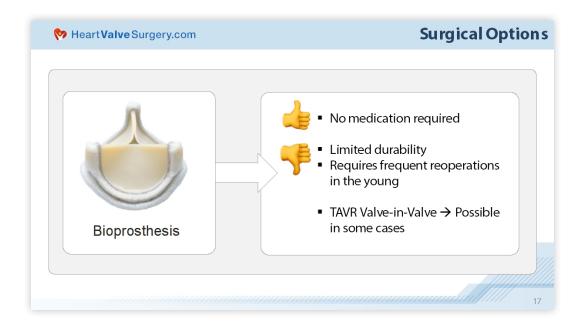
Then the other little element that may in some patients cause a bit of disruption is the noise of the valve. In the majority of patients who hear the ticking of the valve with every heartbeat, most patients get used to that, but some patients actually come back, and I've had patients come back and ask to have that valve removed and replaced just because they really couldn't bear the noise of the valve.

On the upside or in terms of new technologies, there's a new valve that you may have heard about called the On-X valve that allows for lower INR targets. INR is really what we measure in terms of how thin your blood is, and we can aim for having slightly lower thinning of the blood, which is associated with less bleeding in the long-term, but still, it doesn't completely eliminate that risk of stroke or bleeding in the heart





Bioprosthetic Valves



Dr. Ismail El-Hamamsy: The alternative to mechanical valves is putting biological valves, animal valves, cow valves. Their main advantage is that they do not require any medication in the long-term. There's no need for blood thinners. You can go about your normal life on a regular basis, but the main issue with biological valves is that the younger you are at the time of surgery, the faster these valves wear out and need another intervention and another intervention Depending on the age of the patient at the time of surgery, a biological valve may be very suitable, for example, someone in their 70s or even in their 60s, but patients in their 30s, 40s, or 50s, if we put a biological valve in place, we are certain to go back for another intervention.

That span of time between the implantation and the reintervention gets shorter and shorter as the patients get younger and younger. In a 30-year-old, a tissue valve, we would not expect it to last much more than 10 years. In a 50-year-old, we would expect it to last maybe around 12 to 15 years. Frequent reoperations are common for a young person who undergoes a biological valve replacement.



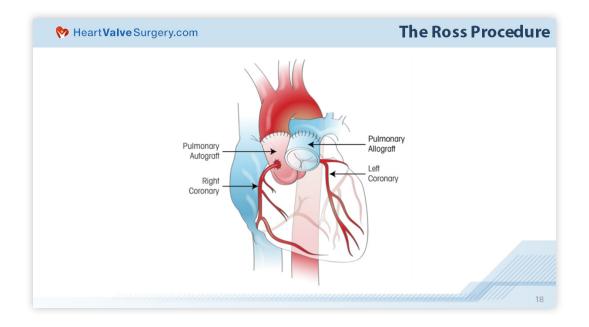
However, looking forward in terms of where the technology and where the advances are – the R&D is happening, TAVR, which I'm sure all of you have heard of, allows in some circumstances to implant a catheter valve through a biological valve that has worn out, that needs replacement, which would eliminate the need for a surgical reintervention, but that has to be said with a lot of caution in the sense that if we looked at the preliminary data of what we call valve and valve technologies, the results are slightly sobering and particularly so in young adults, where we don't have any knowledge about the durability of a TAVR valve, and also in terms of the blood flow characteristics for the valve when we put a TAVR inside of a biological valve and we know we may need to do this on several occasions during a lifetime. It's a bit like a Russian doll principle where there's only so many of these we can do before needing to do another open operation.

The third option then becomes the Ross Procedure, and to talk to you about that, I will pass on the virtual mic to my colleague Paul who will then – who will explain to you all about the Ross Procedures.





Ross Procedure Overview & History



Dr. Paul Stelzer: Thanks very much, Ismail, and thank you, Adam, for this opportunity. This is an anatomical drawing by an artist that shows the close association of these two valves that look very much alike. **Dr. Donald Ross** discovered that when he was trying to find out something to use to replace a diseased aortic valve way back in the early 1960s. The first logical thing that they had was a cadaver aorta complete with its valve, and he put one of those in really early in the 60s, but he thought there might be something better, and he saw that guy sitting right next there, same size, doing about the same amount of work, the pulmonary valve but taking it easy because the pressure of there is like 25/10 compared to 120/80 on the aortic side.



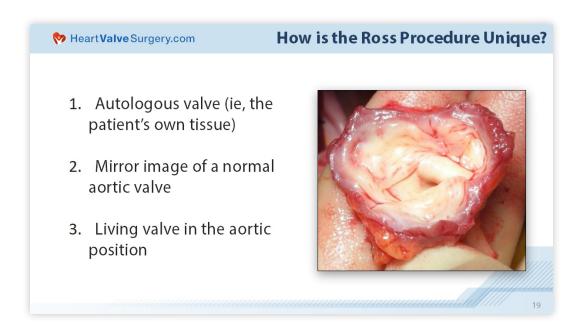
Living on the wild side, he decided to try to make that work by putting that in the position of the aortic valve. Now, he put it on the inside of the aorta when he first put them in, although he did do a number of patients where that was just not going to fit so he replaced the entire root. The aortic root is pictured here in that light pink color as a – first couple centimeters, an inch and a half or so of the aorta, complete with the coronary arteries and the valve. That's really where the machinery is in this part of the aorta, so replacing that entire root with the pulmonary root is a little bit a daunting concept even to experienced surgeons.

This was first done way back in 1966, 1967, so this is a long time. It's not a new thing. It's not experimental. It's been done for a long, long time, and I've had the privilege of doing them now since 1987, so it's been a long journey. As you might imagine, there's a lot of sewing to do, and this is something that you don't just take it out of the box and as long as you put it in, it's going to work. You have to dismantle it from the right ventricle and move it over and sew it in in such a way it not only is now oriented in three dimensions just like the cylinder that it was on the other side of the heart, but it also has to have all those little needle holes stop bleeding by the time you're done and put the coronary arteries back where they belong, so it's a much more complicated thing.





How Is The Ross Procedure Unique?



Dr. Paul Stelzer: What is the concept of the Ross Procedure? Why is this so special? It's special just looking at that picture you get the idea. It's your own valve. We call that autologous. Your own valve, and it has the advantage of being just like the aortic one. It's a mirror image one. This is not made in a factory. This is one of those gifts from heaven kind of things. They lasts for 80 years or more in the vast majority of people. It's amazing technology. We aren't there yet with the artificial stuff by any means. The living valve, one of the things that Dr. El-Hamamsy's a little too humble to tell you, but he's not just an MD, he's a PhD as well. That doctoral thesis that got him that degree, the title of the thesis he wrote was, "The Living Aortic Valve", so he knows about as much about why that's special as anybody in the world.

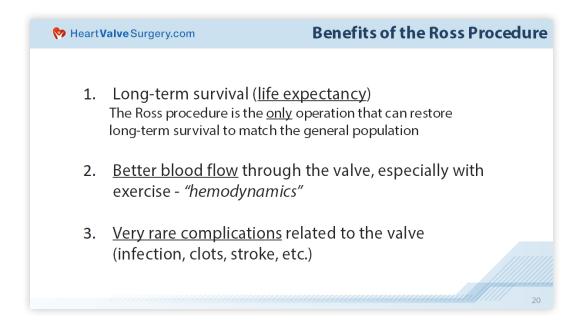


This is a picture of what the pulmonary valve looks like. It looks just like the aortic valve. This is upside down. We're looking at the inflow end, and you see the three leaflets nestled in there with a little bit of muscle around the edges. We flip that around, put that in the aortic position, and it'll do just exactly what the aortic valve does. The difference is that because it's alive, it is going to be submitted to much higher pressures, it's actually going to change. It's going to make itself thicker, stronger, more elastic. Its cells are going to line up in straight lines instead of just all over the place, and they're going to start making some proteins that they've never made before because it's got a different job to do. That's what living things do. They can adapt. Nothing else we put in there can do that.





Ross Procedure Benefits



Dr. Paul Stelzer: Why go through all the trouble? There's got to be something good to come from this. What's been shown in a number of studies way back when, almost 20 years ago, long-term survival benefit was virtually the same as what people had without anything wrong with them, like matching the normal population. That's pretty amazing. The Ross operation is the only thing that can do that, that gets close to that. Others can come close. We'll show you a couple slides in a minute about how they do, but that's why it's worth going to a lot of trouble. It is more trouble for surgeons too, but we think you folks are worth it that need this





surgery done.

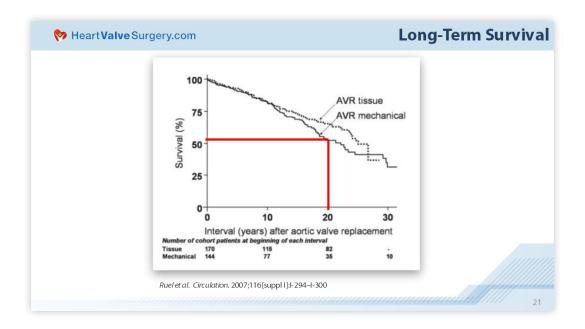
Why is that? Better blood flow. As Dr. El-Hamamsy said, the purpose of the valve isn't to see how little blood you can get through the hole or how much work the heart has to do to get it there. You want it to go through as smoothly as possible without all that extra pressure work or having to do the work over because it came floating back in because the valve didn't close properly. We call that hemodynamics, blood flow characteristics. This has the best blood flow of anything. That's the way God made it in the first place, and it's pretty hard to beat that one.

The other thing is that the complications that come from using this technique are extremely rare in the long-term. This kind of valve is much more resistant to infection, again, because living things are that way, it is resistant to forming clots because those cells in the lining of these leaflets repel that sort of thing. Therefore, the chances of having a stroke are extremely low. Next.



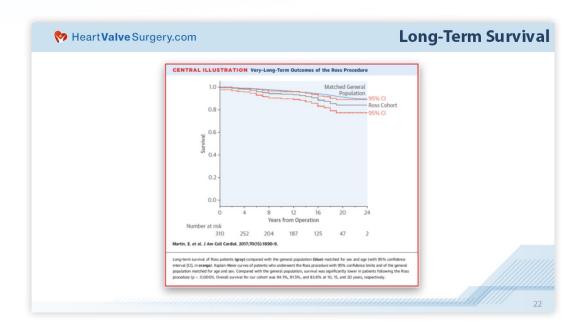


Long-Term Survival of Ross Procedure Patients



Dr. Paul Stelzer: Talking about the long-term survival, this is a picture that I like to show people that comes from Canada. It's about 13 years old now, but it has the advantage of looking at both tissue and mechanical valves. They didn't look at mitral valves too, but this is the aortic one. It looks like everybody survived the operation, so they only looked at the survivors of the surgery, and they watched them for almost 30 years. There are only 10 people alive at that point as you can see at the bottom of the slide, but at 20 years, there's still quite a few people with both tissue and mechanical valves, but the sobering truth comes out when you see the red line on there. Only half of the patients are still alive, and even at 15 years, it's about 70%, so that's not normal survival.

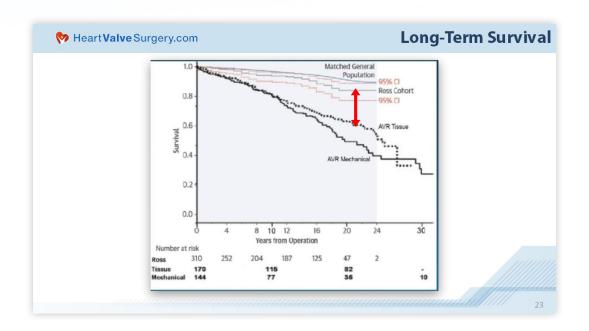




This research also comes from Canada but much more recent, published in 2017, and you can see that the top blue line is hard to see under there. It's called the match general population, same gender, same age, matched with the patients. Then the jagged gray line is the Ross population that they were studying, and the dashed reddish-orange lines, those are what's called confidence intervals, confidence limits. If you think of something as two standard deviations within this or that, that's what 95% confidence limits are. It's a statistical way of saying the chances are that these are really different if these confidence limits don't overlap with the others.

They proved out there by 20 years that they didn't quite match the general population, but then you have to always ask yourself when you read a study, are my patients or am I as a patient like the patients that were studied here? Five of those patients committed suicide. You might not have the same result as long as you don't do that. Let's look for cheerier outcomes and not anticipate that to be the problem. That's not your valve's fault. After you get to 20 years, there's not enough people to really look at. You don't become immortal at 20 years where the line turns straight. Let's put those two together on the next slide.





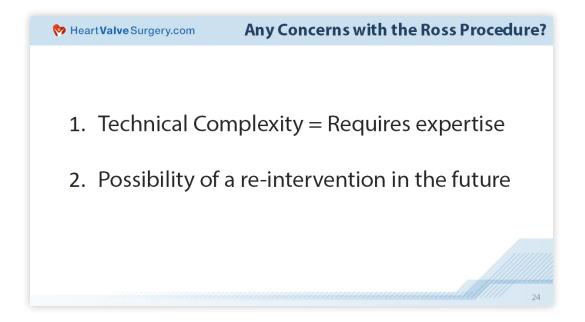
This is done to put them both on the same scale, the two studies, one with the tissue and the mechanical valves and the other with the Ross Procedure. Now you see there are actually four curves because there's the normal population at the top. Then there's the Ross operation and then there's the tissue valve and the mechanical valve. You have to ask yourself okay, if I'm a surgeon, I want to be able to give people the longest life and the best life I can. That certainly looks like a better life and a longer life if we can do this operation.

From the patient's standpoint, it's which curve would you like us to put you on. That often gets a duh comment because I want to be on the best possible survival curve that I can, but it's not as easy as it looks, as you probably concluded at this point, but that's why you go to all this trouble. This kind of normal or near-normal life expectancy out to 20 years is something that's been proven on at least three continents in the last three years, so it's not like we're just telling you stories here. These are real numbers.





Concerns With The Ross Procedure

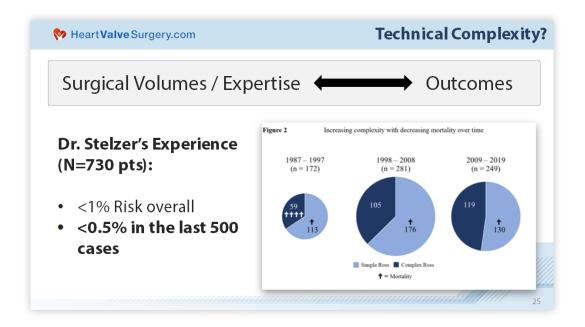


Dr. Paul Stelzer:Are there some concerns about the Ross Procedure? It is a big operation. It requires a lot of expertise. I'll pass it back to Dr. Stelzer to talk about how do we overcome those kind of difficulties, and obviously, there's a possibility of reintervention in the future just as he mentioned with the durability of the animal valves. By 20 years, virtually all of them are going to need to be redone, and by 20 years with a mechanical valve, the number is actually at least 10% are going to need further surgery.





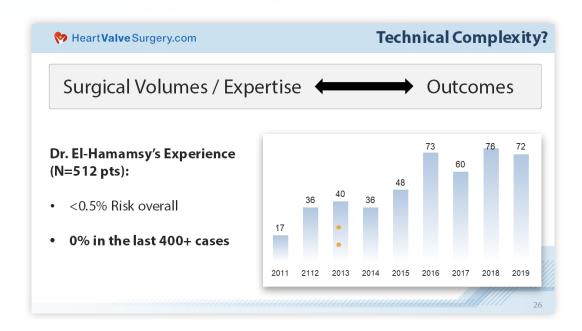
Technical Complexity



Dr. Ismail El-Hamamsy: We'll finish here in five minutes and then take the questions. As I said, so the two elements that Paul mentioned technical complexity and durability. Technical complexity – anything in heart surgery, surgical volumes and expertise correlates really well with outcomes and it does so very, very much with aortic root surgery.

If you look, for example, at Dr. Stelzer's experience with the Ross, you see Dr. Stelzer has done over 730 Ross cases right now, and his overall risk is less than one percent. In fact, if you look at the last 500 patients, the operative risk is less that 0.5%, so particularly safe results, and that graph on the right side shows that actually, the complexity of the cases has increased over the years, and yet the safety has actually improved over the years. There's definitely expertise and outcomes.



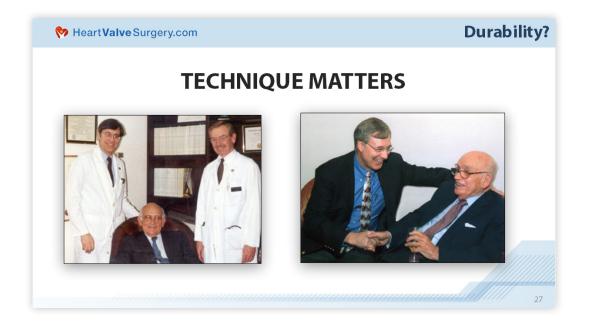


If you look at my own results, I've now performed over 500 Ross Procedures, and the operative risk overall is also less than .5% with 0% mortality in the last 400+ cases that we have done. Combined, I think we really demonstrate the notion that this operation can be performed very safely with equal outcomes to a regular aortic valve procedure.



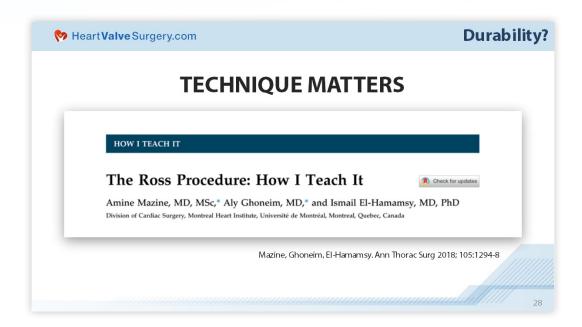


Technique Matters



Dr. Ismail El-Hamamsy: The second point about durability is that when it comes to the Ross operation, technique really matters not just for the safety of the operation but really for the long-term durability and the avoiding reintervention. These are pictures of Dr. Stelzer when he was younger with Donald Ross, and Dr. Stelzer 20 years later with Donald Ross. Just to show you this is an evolutionary tale and the operation has really evolved over the years. Paul will tell you that he's not doing it today like he did 30 years ago because we have learned many things over the years. Whatever we used to do in the 1990s, we did differently in the 2000s, and we're doing slightly differently today because we keep improving on all of that. The good news for you out there is that there's not just Dr. Stelzer and myself doing Rosses.



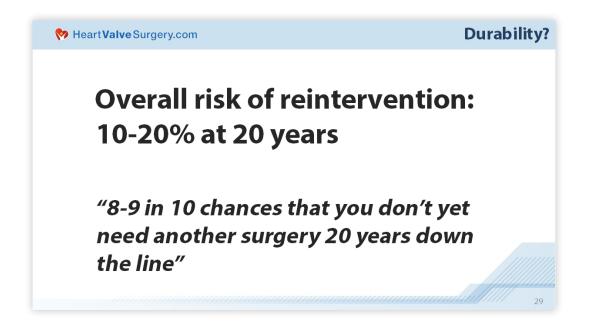


The principles of the Ross have now become really clearly understood, and we're now able to clearly articulate them. As Adam mentioned earlier, there are now many, many groups around the world starting Ross programs with very clear and dedicated aortic surgeons and using a proper technique that will ensure long-term durability of the operations.





Risks of Re-Intervention

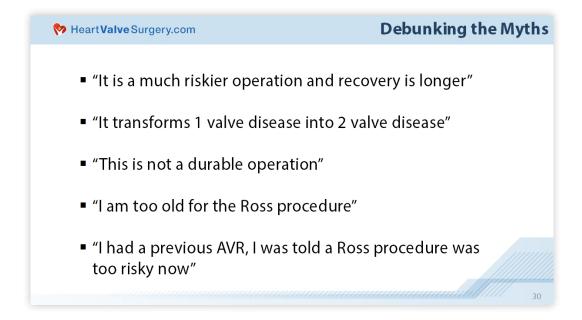


Dr. Ismail El-Hamamsy: By doing all of that, your overall risk of reintervention, particularly in patients with aortic stenosis, is around 10-20% 20 years from the time of surgery. In other words, you have 8-9 in 10 chances that you will not need another surgery 20 years down the line, which I think is pretty significant. Again, it all hinges on the technique. I think, Adam, this really completes the – just a quick overview.





Debunking Ross Procedure Myths



Dr. Ismail El-Hamamsy: These are some of the things that you will hear sometimes around the Ross. We call them myths because although some of them may be based on some realities maybe in the 1990s or many years ago, today I think all of these are – all these notions are a bit overstated, that it's a much riskier operation and recovery is longer. I think we've just shown you some of the results. Another thing you will also hear – next – is that it transforms a single valve disease in two valve disease. That's a very catchy phrase, but the reality is that what you're interested in is what is my survival like and what is my quality of life like, and this is really what we're interested in showing you as well.



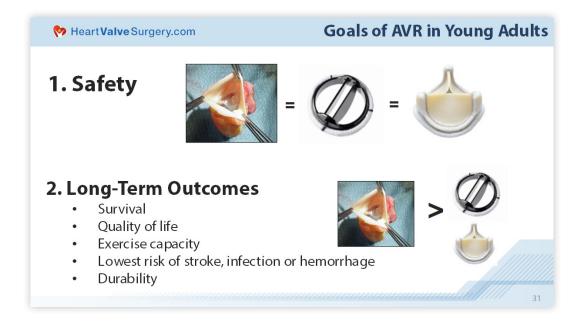


Next is that this is not a durable operation. Again, as I mentioned, it really is intricately related to surgical technique. If you don't do a good Ross operation, yes, it will not a durable operation, and you're probably better off just having a mechanical or a biological valve put in place. You will also perhaps hear sometimes that I'm too old for the Ross Procedure. Again, it really all depends what your biological age is, and that's really what we focus on, Paul and myself, when we meet patients rather than just a number or a number age. Then the last thing that you may hear is I've had a previous AVR or aortic valve replacement, and I was told that the Ross Procedure is too risky now. Again, we can discuss that in more detail.

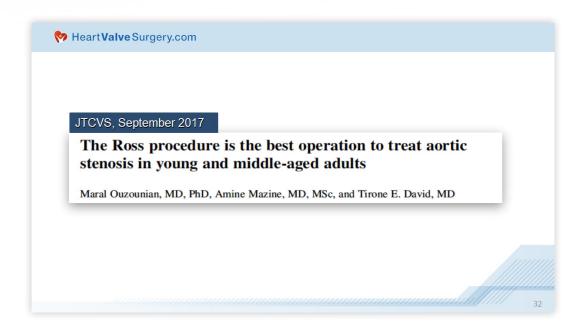




Ross Procedure Goals In Young Adults



Dr. Ismail El-Hamamsy: I think we have one last summary slide with the goals when we approach patients with aortic valve replacement in young adults. One is we absolutely put as our top priority the safety of the patient, and we think that we can do a Ross as safely as a mechanical, as safely as a biological valve. We will never do something that is riskier for a patient. The second point is looking at the long-term outcomes, and I think the younger the patient, the more important the focus on the long game is rather than simply the short game. The long game is – what are the chances that you will still be alive, your quality of life, your exercise capacity, your risk of having a stroke, infection hemorrhage, and obviously the durability of the operation.



Dr. Ismail El-Hamamsy: For all of these things, the evidence over the last ten years or so overwhelmingly supports the notion that having a Ross Procedure will favor these long-term outcomes versus a mechanical or even a biological valve in young adults. Again, Adam, thank you so much for having us today. We could spend a full evening talking about aortic valves, and we won't get tired. So, we'll stop right here.



Questions & Answers:

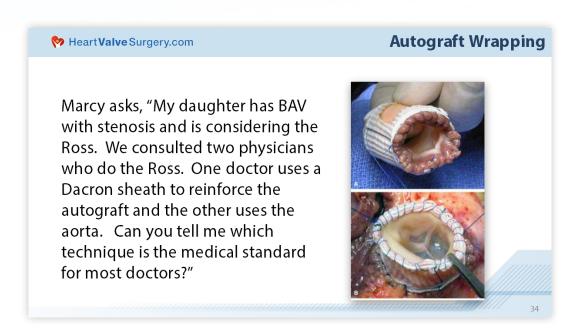


Adam Pick: Dr. Stelzer and Dr. El-Hamamsy, I can't thank you enough for that overview, and I have to tell you I've had the Ross Procedure, and I've never been so interested in it as I am right now for all the reasons that you talk about, the quality of life and the life expectancy for patients. Getting patients as close back to that normal life expectancy given the central impact of valve disease on one's life. I can't thank our community enough for posting your questions during the webinar. We're just going to get into the "Q&A" session and go as long as we can.

Dr. Ismail El-Hamamsy: Let's do it.

Dr. Paul Stelzer: Alright.





Adam Pick: Here's the first question from Marcy. She asks, "My daughter has bicuspid aortic valve disease with stenosis and is considering the Ross. We consulted two physicians who do the Ross. One doctor uses a Dacron sheath to reinforce the autograft, and the other uses the aorta. Can you tell me which technique is the medical standard for most doctors?" I threw in a picture here, Dr. Stelzer, of an autograft that I think you may have worked on.

Dr. Paul Stelzer: I've done a few this way, but the majority of them I have not done that way. This is a technique that has been used to – I call it "Davidizing" the Ross. When you put it inside a cylinder of Dacron, what that's going to do is it's going to prevent it from stretching. The problems come with picking the right size because the autograft isn't always the same size on the bottom as it is on the top, and that can pinch the bottom together too much and stretch the top too much and all those kind of things, so it's really tricky thing when I try to do it. I did maybe 10 of them, 15 that way. I finally quit doing it. I use other ways of supporting it to make sure it wouldn't stretch but still give it some room to actually give a little bit of ballooning of the sinuses, which is one of the ways that it helps coronary blood flow. That's a little bit harder to do in this situation.

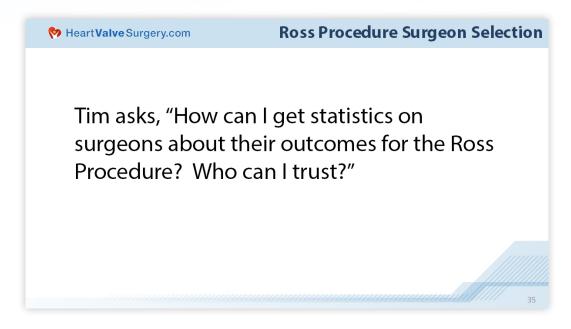


You'll never end up with a hematoma, we call it, where you have a blood clot between that graft and the aorta. Now, the way this is drawn, it's drawn where it's not going to be locking things in. Some people do it where they sew the coronaries in including that outer shell, so then you end up with we call it a dead space in between. Long story short this works. We call it a "Jacketed Ross", fully jacketed Ross, and there are a number of surgeons that I know and respect that are making this work really well. I do it differently. Dr. El-Hamamsy does it differently. There's not just one way to do it right, but there's some concepts, particularly in patients who have aneurysms or patients who have aortic regurgitation or mixed disease where the dilatation potential has already been documented.

Patients with pure aortic stenosis and a normal aorta, you probably don't need any of that. There are other ways of containing the autograft inside the native aorta like Peter Skillington does down in Australia or that Hans Sievers do in Lubeck, Germany, doing the original Donald Ross technique. There are many ways to do it where there is support that keeps it from stretching and maintains its three-dimensional structure. That's what's important to make it work.







Adam Pick: Thanks so much for that Dr. Stelzer, and let's move on to the next question, which is a really important one for patients, and I can remember trying to find the right surgeon for me. Tim asks, "How can I get statistics on surgeons about their outcomes for the Ross Procedure? Who can I trust?" We got another question that came in during the webinar, "What are the types of questions I should ask my potential Ross Procedure surgeon?"

Dr. Paul Stelzer: I think this is a trust kind of proposition. People come into my office every week, and something has to happen in about 30 to 45 minutes, sometimes an hour, that convinces them that it's a reasonable proposition for them to put their life in my hands. That's a big step, a big jump of faith. A lot of them have done some internet research, and there's a lot of good stuff on the internet. You can find out specific information about specific surgeons. There's some in different websites that specifically talk about Ross surgeons like the CryoLife website has.

That's something that – nothing's perfect. What it boils right down to – you need to ask the surgeon what is your experience? How many of these have you done? How many have you done in the last two, three, five years, whatever it might be?

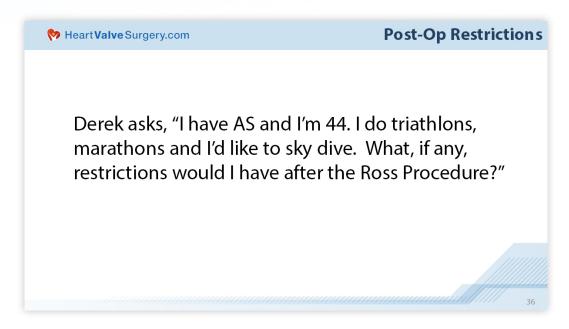


How have your patients done? Could I talk to one of your patients? That kind of thing sometimes gives you a little bit of an insight into it, but it really boils down to if they've only done two or three, then that raises a little bit of a red flag because this is not an operation you can get really good at with the first two or three. How many would you say, Dr. El-Hamamsy, would it take to say you're competent and how many to become an expert?

Dr. Ismail El-Hamamsy: We had done a study actually looking at the learning curve associated with the Ross, and we had determined it's around 75 cases until you get to a level of expertise with the Ross, 75 to 100 cases, but I think 75 total cases is a benchmark towards really having true expertise. Importantly, it's having a regular volume every year. You have to be doing this at least once a month if not more. Paul and I do about – anywhere between 60 to 80 Rosses a year, but if you're doing 15 to 20 Rosses a year, that's a very good volume.

I think asking all these questions to your surgeon, there's nothing wrong with it. It's absolutely normal. You'd do it if you're buying a house or a car. This is your heart. You should be asking all the questions, and as surgeons, we're never uncomfortable answering these questions because we put ourselves in your situation and that's exactly what we'd be doing. Just ask the questions and try to get all the answers you need.

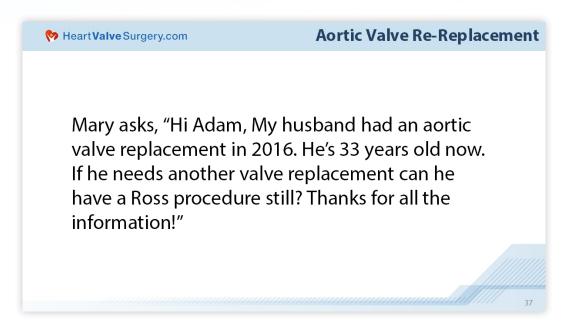




Adam Pick: One thing for the patients out there, I remember writing down all the questions before I came in to see the surgeon for the reason that it can be a little anxious, and you might forget, so don't hesitate to write down and just go one by one to make sure you get your questions answered. Let's move on to post-op restrictions regarding the Ross, and Derek asks, "I have aortic stenosis, and I'm 44. I do triathlons, marathons, and I'd like to sky dive. What, if any, restrictions would I have after the Ross Procedure?"

Dr. Ismail El-Hamamsy: That's a good question. Part of the reason why we're so passionate about the Ross Procedure is really the lifestyle and the quality of life element. All the studies where that has been studied, it has always performed really well because there really are no restrictions or no lifestyle modifications when you have a Ross Procedure. Again, it's a living valve. It adapts really well. The only thing we're very careful with is controlling your blood pressure in the first 6 to 12 months after surgery to allow it to adapt, but really beyond that, you can go on to do anything. I have patients that run marathons, that have done triathlons and Ironman. Paul has jet fighters, and he has a whole army of patients who also have done exceptional – things that are really exceptional after their surgery, so really no limitations. If anything, that is one of the unique elements or aspects of the Ross.





Adam Pick: Great, and moving on to aortic valve re-replacements, I think you talked about this a little bit earlier, but Mary asks, "Hi, Adam. My husband had an aortic valve replacement in 2016. He's 33 years old. If he needs another valve replacement, can he have a Ross Procedure? Thanks for all the information." What are your thoughts there, guys?

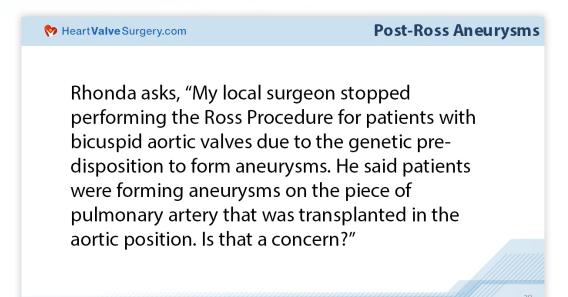
Dr. Paul Stelzer: Absolutely. We do – about 15% of our cases are redo sternotomies that the vast majority of patients had procedures done on their aortic valves. I've got at least 40 that had aortic valve replacements. Eight of them were mechanical valves, I should comment, and a couple of them had homograft root replacements, and those are a real bear to dig out. We can take most anything apart and upgrade that to a Ross, but again, as Ismail pointed out, we're going for safety too. We're not going to do one trick pony things. We're going to go in there and make sure we've got a spectrum of plan A, plan B, and so forth to make sure that we can get this patient safely through this procedure and give them the best long-term prognosis that we can.





That's like the marathon runner that I had that was 54 when he came. He got short of breath when he was running, but that was after he'd done the bike ride and the swim, and so his dream was to be in the Ironman Championship someday. He got his wish when he was 68 years old, 14 years after his Ross. Now he's 80 years old. He got COVID living in retirement in Florida. He managed to get through that, and he was back to riding his bike 100 miles a week when I talked to him a few weeks ago. Yeah, you can go a long time. He's never had anything done to either of those valves, I should add.





Adam Pick: Those are the stories that we love hearing here. Let's keep moving as we go on here. Interesting question Rhonda asks. "My local surgeon stopped performing the Ross Procedure for patients with BAV due to the genetic predisposition to form aneurysms. He said patients were forming aneurysms on the piece of the pulmonary artery that was transplanted in the aortic position. Is that a concern?"

Dr. Ismail El-Hamamsy: That's a good question and something that was a real concern I would – or a topical issue about 20, 25 years ago. There were concerns that patients with bicuspid aortic valves may have some genetic weakness in the wall of the pulmonary artery and therefore may tend to dilate after the Ross and require reintervention, but the reality is, as I said earlier, knowledge has evolved, and we've been following hundreds of patients in cohorts and studies, and that has really not turned out to be quite true. What it really is about is more surgical

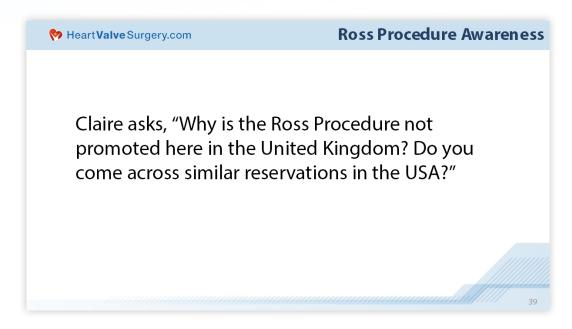




technique than a genetic predisposition to dilatation or to stretching of the pulmonary autograft.

No, if you look at all the cohorts and the studies looking at Ross patients, almost 80% of the patients have bicuspid aortic valves and some degree of aortic enlargement at the time of surgery, and very few of these patients require a reintervention because of stretching of the pulmonary artery in the long-term if the operation is done, again, following clear principles. That goes back to the first question about the wrapping in the – in that Dacron graft, which is one way that some surgeons have chosen to address the problem that both Paul and I think may not be the most suitable way to do it just because the aortic – the autograft is such a dynamic structure that to encase it in such a rigid Dacron tube eliminates some of the benefits of this procedure, particularly when it comes to exercising and how the blood flows for people who want to do skydiving or Ironman or a marathon. There are other ways that we can control that, but the notion, to answer Rhonda's question, of whether bicuspid aortic valve is associated with weakness or predisposition, the answer is a clear and definitive no in today's – with today's data.





Adam Pick: Great. Thank you so much. Let's move on to Claire. She has a really interesting question. I hear it often. She asks, "Why is the Ross Procedure not promoted here in the United Kingdom? Do you come across similar reservations in the USA?" I hear this all the time from folks. What are your thoughts on why a lot of patients have no idea what the Ross Procedure is?

Dr. Ismail El-Hamamsy: I'll let Dr. Stelzer go first. I'll go second for this one.

Dr. Paul Stelzer: I think no surgeon likes to say there's something he can't do or she can't do, so they don't mention it if they don't happen to do it. It's not that good surgeons all do it. There are a lot of good surgeons that just haven't had the experience that Ismail and I have. We've really been very fortunate in our careers to have patients come and more patients come and so forth, but there are some really great surgeons out there that are 55 to 65 years old. It's not the time to start doing them. You're not going to get enough experience. By the time you get good, you're going to be retired.



Even though this was born in the UK, and there are a lot of pediatric surgeons that do Rosses in the UK, or at least certainly enough do the kids that need it, the adult surgeons other than Sir Magdi Yacoub really never got into it. I think part of that was a training – what shall I say – perspective. There was a very much observational approach to teaching people, wouldn't you say, Ismail? You went through that system. The American way is a little bit more hands-on. Little bit by bit, you help people learn to do parts of an operation that are more complicated. Just say hey, watch me here for five years. Then go out there and try it. That doesn't fly. It does work. Why don't you pick up on that, Ismail, and say what your thoughts are, why it's different.

Dr. Ismail El-Hamamsy: Yeah, no, I agree. I think – overall, I think Claire's question is a good point. I think there are reservations, and these are some of the things we mentioned in the slides. You will hear a lot of that. If you go back to the history of the Ross, what happened is in the '90s there was true enthusiasm for the Ross, and a lot of surgeons started doing Ross Procedure right, left, and center. The reality is what we now understand much better is that these are really specialized procedures, and only a handful of dedicated aortic surgeons with understanding of the anatomy, physiology, and all the principles should be doing.

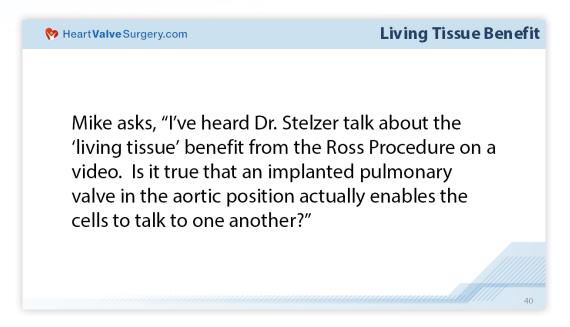
These are all typically young patients undergoing these surgeries where any bad or negative event is really so traumatic to everybody that it really leaves a big, big mark on cardiologists, surgeons, and the community in general. Following that experience and some bad events, I think there was loss of enthusiasm or a lot of people got a little away from the Ross because of that. What we're now seeing in the last 10 years is a real renaissance of the Ross based on all the evidence and the science, which we really didn't delve into in too much detail here, but there is a tsunami of evidence in the last 10 years to show these long-term benefits.



What is now being done in a very proper way is that aortic surgeons who have the expertise or at least the skills to be able to start Ross programs are doing so. If you live in the UK, I'll be happy to tell you that there is a program that is just starting in Liverpool. The surgeons came to visit my program. They saw – they spent a full week with me back when I was in Montreal observing the whole team, and they're actually starting next – they were supposed to start in the summer. I was supposed to be there to help them, but COVID hit, but they're starting next month. There's a team in Bristol that is also starting, so there's definitely a conversation that's picking up in various centers in the UK and around the world as well but in a much more – in a much more thoughtful and a much more organized way that will ensure patient safety and good long-term results.

Adam Pick: I like the way you characterized it as a renaissance. It's almost like for me who's been in the space now for 15 years or so, it feels like there's a reboot of interest. I've never seen so many emails come to me asking questions about the Ross Procedure, and it's great to hear that you're making this fully reproduceable by setting up these other institutes to carry on all the great advantages of the Ross Procedure. This is one of my favorite questions, and I would love to hear an answer on this one. This can be our last question, but it comes in from Mike. He says, "I've heard Dr. Stelzer talk about the 'living tissue' benefit from the Ross Procedure on a video. Is it true that an implanted pulmonary valve in the aortic position actually enables the cells to talk to each other?"





Dr. Paul Stelzer: This is what I was implying and talking about how living things adapt and how they start making proteins that they didn't make when they were in the pulmonary position. They make substances that are capable of communicating, shall we say, for lack of a better way. For instance, nitric oxide is something that certain cells make, and certain cells don't. What does nitric oxide do? It makes vessels dilate, so if you learn how to make nitric oxide, send a little down – you're sitting right there next to it. It makes sense that that might be set up that way. I don't know if that specific example is true, but that's an example of things that cells make to talk to other cells. The body does work this way. It's not just every cell for himself. That may be true in prison, but it's not true in our body cells. Ismail, of course, knows all about the living aortic cells. That's what his PhD's all about. Take it away, Ismail.



Dr. Ismail El-Hamamsy: I'll tell you just one thing to add to that. One time the opportunity – a patient that had had a Ross at the age of 33 in the UK – I was in the UK at the time. This is in 2008, and the patient was now in his 70s. He was 42 years after his Ross. Both valves were still functioning normally, and he unfortunately, passed away, the family called Professor Yacoub, who'd done his surgery, and one of the first Ross patients – or his first Ross patients, and he asked them one thing. Would it be possible to look at the valves under the microscope? The family absolutely agreed. He was family to them, and they really owed him so much, so we took that valve, and we looked at it under the microscope.

Forty-two years after the Ross Procedure, and when we looked at it, the cells were still alive. The trilaminar structure that we see in a normal aortic valve was still present in that pulmonary valve in aortic position. It was a really – it was one of these ah-ha moments where you think wow, this – all of these theoretical benefits actually do translate into reality not just in terms of the viability of the valve in the long-term but also now knowing that that translates into clinical relevance in terms of the other things that we mentioned, survival and exercise capacity, etcetera. It makes a complete story from the very early days where the Ross was invented because of a lack of alternatives to now making this comeback because of the impact in the long-term. It really is quite the 50-year journey, I have to say.







Adam Pick: Amazing to hear that from both of you about the living cells. As I know, Dr. El-Hamamsy, you said you could talk about the Ross Procedure for a long time. I know, Dr. Stelzer, you could go on just as long about how important this procedure has been to you, your life, and your patients. We've gotten a lot of questions here today, but I think it's time as we come to the end of the hour that we're going to wrap this up, unfortunately, but what I'd like to extend to all the people in our community, the folks on the line, the heart valve patients, everybody at heartvalvesurgery.com a tremendous thank you. Getting together with you live at these community events are fantastic.



Please don't exit the webinar just yet because I'd like to have you on the line when we extend a huge thank you to Dr. Stelzer and Dr. El-Hamamsy for their incredible work around this very unique, very advanced treatment for aortic valve disease. They are empowering patients, and we are thrilled to have them on the line today. I know Dr. Stelzer, you mentioned the CryoLife website. I just want to make sure everybody knows there is a website out there called – I believe it's therossprocedure.org. If you can write that down, I think you could learn a lot of information, and the folks at CryoLife were very kind in giving us the opportunity to have some of their images shown today on the webinar.

Lastly, what we're going to do is we are going to put up a quick survey. It's just five questions. If you could take a few minutes to complete it, we would really appreciate it. On that note, I want to extend another thank you to Dr. Stelzer, another thank you to Dr. El-Hamamsy, everybody in the line, and as we approach that time of year, I want to wish everybody a very happy, health, and safe holidays. Thanks so much, and as we always say here keep on ticking everybody.

Dr. Paul Stelzer: Thank you.

Dr. Ismail El-Hamamsy: Thank you.



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- <u>Heart Hospitals Directory</u> Learn about medical centers that have dedicated teams and resources that specialize in heart valve therapy.
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