GARY GERSHONY: Welcome to our monthly cardiovascular grand round series. We have something a little bit different today, which I'm very excited about, and I'm sure you will be, too. Today's topic is a very important new area, in which John Muir Health is a leader, both regionally and, here, in our community.

And the topic of the presentation today is "Advances in the Percutaneous and Transcatheter Treatment of Severe Mitral Regurgitation." And what we're going to be doing differently is we're going to reflect the fact that this, like several other programs that are ongoing now at John Muir, are part of a team effort, a heart team effort.

This is the new catch term in cardiovascular medicine, around the country and around the world. And these new treatments really require the expertise and the collaboration across different disciplines, including cardiology, both interventional cardiology and imaging cardiology, cardiovascular surgery, and technical staff in the cardiac catheterization laboratories.

So today, we're actually going to have the team present, on behalf of this new program. And I'm going to turn the microphone over to one of the team members, Dr. Faizul Haque.

[APPLAUSE]

FAIZUL HAQUE: Thanks, Gary. Thanks for the opportunity for us to be able to talk about this as a team. I think it's a really important discussion to have, to get the word out.

Let's talk a little bit about what we're trying to achieve during the course of this presentation. Number one-- give you a framework on how to look at evaluating mitral regurgitation, looking at the anatomy, the pathophysiology, the diagnostic methods. Understand the indications we have for mitral valve replacement, repair, and management, surgical versus percutaneous.

Give you an understanding of the benefits and the limitations of percutaneous mitral valve repair. Give you an idea of the steps that are involving the MitraClip percutaneous mitral valve repair procedure, and then give you a little bit of information about possible future considerations.

And to move things along, let me introduce Dr. Jat Dhillon, who is going to talk a little bit about anatomy and pathophysiology. [INAUDIBLE]

JATINDER DHILLON: Great. Thank you. So I was just going to talk about mitral valve anatomy. Actually, it was Vesalius, back in the mid-16th century, who first gave the name "mitre" to the mitral valve, which was similar to the Episcopal mitre.

He was, in fact, an anatomist, who wrote the first book on human anatomy and went on to become the chief physician for the king of Spain, who was the last emperor-pope. Somewhat interesting.

The mitral valve really consists of the leaflets, the chordae, and the papillary muscles. And the annulus is formed where the-- the bit that's attached to the left ventricle. So you can see, here are the pathway muscles. Here is the anterior leaflets of the mitral valve, the posterior leaflets of the mitral valve. The chordae come from both the papillary muscles to the both of the two leaflets.

But also, there's a continuity of the anterior leaflet of the mitral valve with the aortic valve apparatus. That's a very important anatomical relationship, which becomes important when you're trying to repair these valves.

However, the other components of the complex is the left ventricle and the left atrium. So as you know, functional MI is really disease of the ventricle. And so it will cause the mitral regurgitations. So the whole complex has to be looked at as one.

The [INAUDIBLE] leaflets were described by Carpentier as A1, A2, and A3, posterior leaflet P1, P2, and P3. And the posterior leaflets also have slits, which are important, sometimes, when we try to repair these valves. Yacoub had his own, and Duran had his own.

So that just summarizes what the anterior leaflet looks like and posterior of the relationship with the aortic valve, and the right fibrous trigone and the left fibrous trigone. These are important when we put the rings in, because you have to anchor the ring here. That's part of the skeleton of the heart.

The marginal chordae are the primary chordae, which attach at the free margin. And this will cause prolapse, when they're ruptured or they're elongated. The intermediate chordae or the secondary chordae attach to the ventricular surface.

And the basal chordae are actually very important, particularly the [INAUDIBLE] leaf that has a huge strut chordae, which preserves the ventricular shape and function.

The annulus is actually saddle-shaped as you can see here. Its function is really to support the leaflet attachment. It's a sphincter-like function. When it is in systole, its area is reduced by 26%, apparently.

And the saddle-shape, itself, reduces the leaflet stresses and strains. So that's why we like to use a flexible ring rather than a rigid ring in most of these repairs.

The echocardiographer has become the surgeon's best friend. As you can see, from here, when we have to repair the valve, we actually know exactly where the problem is going be. And indeed, we find it. So usually, the [INAUDIBLE] tells me what to do before I open it.

In terms of the pathology, first, you have to understand what the anatomic problem is. And Carpentier's classification is what we use. Type I is when the leaflet motion is normal, but the annulus is dilating like a cardiomyopathy. Type II, of course, are the ruptured chordae, the ones with degenerative mitral valve.

Type III is the rheumatic heart disease, mainly, where the commissures are fused, the leaflets are thickened. And Type IV is a diastolic leaflet restriction, usually [INAUDIBLE] cardiomyopathy.

This is the Type II, which is the degenerative or primary, some people call it. FED is Fibroelastic Deficiency. The leaflets are somewhat think but they're not redundant. And then you get on to the Barlow's, which is huge leaflets folded over each other, very difficult to repair.

And this is the Type IIIA, mitral stenosis, which we've talked about. And then ischemic MR, where you get wall motion abnormality, left ventricle can dilate. You can get displacement of the posterior-medial-- here it is. And then this causes restriction of the posterior leaflet then eccentric P3. Usually, you got the P3 level jacked.

As you can see, functional MR really has a very bad prognosis, where you get dysfunction of the left ventricle, which causes dilation of the left ventricle, increasing mitral regurgitation, which increases damage to the heart muscle. One-year mortality is up to 57%.

And then you could classify MR into two types, into the anatomic abnormality of the mitral valve leaflets, subvalvular apparatus, chordae-like degenerative mitral valve disease and, of course, secondary, where you get the left ventricle dilation because of ischemic heart disease or cardiomyopathy. And that's it. Before we go further, we should do no harm.

GARY GERSHONY: Our next speaker is Dr. Perkin Shiu, who's director of the non-evasive cardiovascular laboratory on the Walnut Creek campus. And as you can see here, clearly, this multi-disciplinary effort requires the expertise of imagining cardiologists as well as the proceduralists.

PERKIN SHIU: Thank you, Gary. Well thank you, everyone, for being here. So I'm going to pick up a little bit from where Dr. Dhillon left off and talk a little bit more specifically about the clinical presentation, the diagnosis of the severe mitral regurgitation [INAUDIBLE] the valve.

And then specifically, my goal is to give you a framework in terms of when to refer a patient, when is an appropriate time for [INAUDIBLE] and hopefully convince you all that earlier is better. So that's the goal.

So pretty typical history and presentation, increasing shortness of breath, fatigue. I think the key point is exercise intolerance. I think especially for many of our older patients, it's somewhat difficult to discern whether or not intolerance is due to age or due to valvular issues.

We typically try not to catch them when they do have CHF symptoms, orthopnea, PND, [INAUDIBLE], and all that stuff. We would like to try to catch them a little bit earlier. And the earlier we catch them and intervene, the better these patients do.

You want to try to catch them before they develop any sequelae and severe MR, systemic embolization due to atrial fibrillation, recurrent heart failure, et cetera. There are a few presentations where acute mitral regurgitation is quite sudden. And it leads to sudden respiratory failure, hemodynamic embarrassment. That is really a medical emergency.

The physical examination can run the gamut from relative hypotension to frank cardiogenic shock. You see the lateral displays apex, changes to the S1 due to the mitral valve closing at different times and [INAUDIBLE] flow.

And [INAUDIBLE] S3 would be compensation, because of all of the sudden volume overload and heart failure. A typical pansystolic, a very coarse, loud murmur, that can radiate to the axilla and all the way to the back. You can hear it in patient's left, posterior lung fields.

EKG may show biventricular hypertrophy, left atrial enlargement, and atrial fibrillation. And you see sort of classic chest x-ray signs of the large left ventricle, left atrium, and hilar shadows, as well as pulmonary vascular markings.

I'm going to go kind of quickly, here, through these indications, because, for most of us, this will be review. But for acute MR, due to a failed leaflet and ruptured chordae, infective endocarditis causing structural damage, myocardial infarction leading to more papillary muscle rupture.

The Treatment really, here, is surgical. It is an emergency. We can offer them nitrates, offload reduction, inotropes, in the form of pressors, as well as balloon pump stuff. All of these are just temporizing measures until we get them to an operating room for primary repair.

What we're focusing on here is sort of chronic mitral regurgitation, specifically degenerative origin. But other causes for chronic mitral regurgitation include mitral valve prolapse, rheumatic heart disease, pulmonary disease, endocarditis, drugs, collagen vascular disease, as well as functional, due to the dilated left ventricle. As Dr. Dhillon said, that is a disease of the left ventricle.

Medical therapy for chronic severe MR-- there's some data for offloading therapy and really monitoring closely for symptoms and signs of any sort of change of left ventricle performance. And that is via echocardiography, typically transthoracic.

Diagnosis can be also verified with catheterization, because sometimes echo, depending on the hemodynamics of the patient, may not show the severity of the mitral regurgitation. That's truth for both transthoracic and less so for transesophogeal.

Patients can remain compensated for many years, until symptoms develop. And the goal, again, not to overstate it, is to intervene prior to development of any advanced left ventricular decompensation, so if EFS is 60%, and systolic volume dimension is greater than 40.

And, remember, that these patients typically do have typodynamic left ventricular function. Because they can squeeze, even after the valves close, into a closed left atrium.

For the purposes of our talk, we've spoken a lot on mitral valve prolapse. We would just remind [INAUDIBLE] of the diagnostic definition here is only the parasternal long axis or the apical 3, 2 millimeters of systolic billowing of 1 or both leaflets.

It's seen in about 1% to 2 1/2% of the population and, typically, autosomal familial or primary nonfamilial associated with connective tissue disease. Sudden death is rare. There is some potential increased risk for endocarditis. Prophylaxis is currently not recommended and controversial.

And we'll see some more images and go more into the echo assessment with Dr. Whirter's presentation. But qualitatively, we look for the area of regurgitant jet, which is very similar to how we grade [INAUDIBLE] patients by cath, with left ventriculogram, looking for, essentially, how much of the left atrial area is filled by the mitral regurgitant jet.

Look for an intensive signal on doppler, on echo. The duration of the signal and the velocity peak gives you a better sense about the amount of flow that's going backwards. Also, look for downstream [INAUDIBLE] effects of the mitral regurgitation with systolic flow reversal in pulmonary veins. And that is affected by the four pulmonary veins, which direction the jet is going.

Some quantitative things that we can measure on echo to help us guide therapy. It is important to follow the patient longitudinally, to kind of get a sense of at what point is this getting worse and worse, and help us, of course, determine when therapy or intervention with the valve is indicated. More specific, here, is effective regurgitant orifice area of greater than 0.4 square sonometers.

So won't go through all of that. Here's some just typical Kaplan-Meir's graphs here. The key point is reduced survival of medical management with severe mitral regurgitation. So here in the first panel, slide A, you see just purely a natural history of patients with mitral valve prolapse with severe margin flail leaflets.

And you can demonstrate that, essentially, as compared to age matched controls. I mean, this is what I've observed. These are patients, here, that have asymptomatic mitral valve prolapse. And this is more typical of moderate to severe MR or EF less than 50%.

Essentially, this is when they have both of those problems, either moderate to severe MR and P of less than 50%. They do much worse than if the MR is not as bad or EF is better. And this is one of the gross factors. And that's out of [INAUDIBLE].

And in asymptomatic severe MR, we would quantify it, by transthoracic echo, essentially, worse ERO, which is analogous to the flow, and watch what these patients do. ERO greater than 40, they do much worse than ERO less than 20.

We need to look directly at-- and this is for patients, here, in path A. This is mitral valve prolapse, severe mitral regurgitation, versus intervening early with surgery, versus medical management, watching.

Patients who get intervention earlier do much better than patients who kind of wait and watch. And the same here, if we follow them out for a much longer period of time. And this is probably one of the best natural history or direct comparison of medical therapy versus surgery that we have.

So now the question is when to intervene? And obviously, I hope, at this point, you're convinced that earlier is better. In general, surgical mitral valve repair is always preferable to replacement, especially with degenerative MR. These valves, as Dr. Dhillon pointed out, are typically very repairable and with wonderful results, with wonderful long-term durability.

You definitely want to catch them when they're symptomatic and EF's hopefully greater than 30%. If the EF is too low, there's certainly the point beyond which you cannot come back, where the left ventricle actually does not tolerate the repair. So you definitely want to catch them before that point.

And the key point, I want to highlight, here, is that, given the patient is symptomatic at one point, so therapy [INAUDIBLE] and given a [INAUDIBLE] offload [INAUDIBLE] therapy, and they become asymptomatic, that's still is the time. Hey, it's still early in the disease process. Let's consider fixing this valve before it gets worse, and we miss the boat.

And we're going to talk a little bit more specific about the MitraClip procedure. This is really indicated with patients with high risk STS scores above 12%, severe symptomatic MR, with NYHA Class III to IV symptoms. And hopefully, with their therapy, they're doing better than that.

But the key point's, once they've achieved these markers, it's time to consider fixing something. And you want to have reasonable life expectancy. And currently, only approved for degenerative primary mitral regurgitation and not functional MR. And that's in studies. We'll talk more about that down the road.

So there is surgery. Surgery is more durable, tends to provide more complete MR reduction. But transcatheter repair is lower risk. And there is a definite measurable clinical benefit in terms of improvement of the remodeled and functional class. And the results are durable after four years. And 80% of the patients are free from surgery after four years.

This is just a one-year follow-up, from the Everest II study, where, essentially, this is freedom from all cause mortality as well as re-operation. And actually, this is straight, all cause mortality. Essentially, 77% of patients were alive at 1 year. And this is in comparison to what you saw earlier, in those medical therapy or watchful waiting slides. This is a better survival curve.

In terms of the severity of mitral regurgitation, at baseline, [INAUDIBLE] patients at 3 to 4-plus mitral regurgitation. And at 12 months, the result is still, for the most part, durable. And a very small amount have 3-plus MR out to a year.

This is some of the specific metrics that improve even with MitraClip. You see, specifically, the left ventricular volume does get smaller, both in diastolic and then systolic. The ejection fraction tends to stay about the same, again, highlighting the point that there is a point where the left ventricle does not get better and heal. So you do want to catch these patients early to try to prevent long-term cardiomyopathy.

And that's it.

GARY GERSHONY: Thank you, Dr. Shiu. The next part of this talk will be presented by one of the actual implanters in our transcatheter mitral valve repair program, Dr. Faizul Haque.

FAIZUL HAQUE: Great. So let's talk about the procedure, itself, give us a little bit of an impression on exactly what we do. Once again, to recap what was so eloquently [INAUDIBLE] by Perkin, let's talk a little bit about the indications for what the MitraClip is intended for.

It's for degenerative MR. Remember, we talked about functional versus degenerative. We talked about people who do have significant mitral regurgitation, 3-plus to 4-plus. We talked about people who were symptomatic. We talked about people who are at higher risk for surgery. And other things that would make them a high risk for surgery are all included in the table.

The procedural overview of this, I want you to take away four points from this slide. Number one is create the vertical line of coaptation, which results in two owl-eyed, double-orifice visualizations. It's a beating heart procedure. That means there is no cardiopulmonary bypass that's involved with this.

It allows for ongoing, real time positioning and repositioning. That's key. It affords us the time that we need to make sure this is done right. And it allows for preservation of possible future surgical considerations. That means, after we've done something, if something needs to be done later on, surgically, it can be. It doesn't prohibit that from happening.

This is what the device looks at the right. But let's take a look at it in a little more detail. Here are the components of the device anatomy and what this is. Up top, it's a 24 french steerable catheter, which means most PCIs that we do are through a 6 French. It's four times that size. But it's in the venous anatomy not the arterial.

It contains the implant. It's highly maneuverable, giving us the ability to be able to position it where we want it to be, with all the controls at the proximal and outside the body. And it's made of cobalt-chromium construction. There's a polyester cover designed to promote tissue growth. And it's MRI compatible. That's important for the patients you send for this procedure.

Let's talk about sizing. the MitraClip is about 15 millimeters long, horizontally, in length. And it's about 5 millimeters in width, once it's closed. I want you to pay attention to the middle diagram that shows the grippers, because that will be important for different phases of the actual procedure that we'll talk about shortly.

Procedural consideration-- the things that happen at the time of the procedure. They get a transesophageal echo probe. It will be in place for an extended period of time. That's important for the procedure, itself. You require intubation under general anesthesia.

It's a 24 French in the femoral vein, once again. There's usually a bladder urinary catheter in place. It's full therapeutic anticoagulation involving heparinization with a target ACT of more than 250.

And the entire system is tested and de-errored before it gets introduced into the body. So it's a team effort in terms of doing this safely.

The first step is getting into the left atrium. As all of you know, venous access gives us positioning into the right atrium. Using a transseptal procedure is key in terms of finding the right spots to enter the left atrium, which is why we spend a great amount of time, under TEE guidance, to find the right place to cross the septum.

So one, we have the ability to be able to angle the device southward towards the valve. And two, make sure, once we're committed, we have all the things possible at our disposal to be able to position this appropriately.

The Steerable Guide Catheter, or what we'll refer to as the GUIDE, along with the dilator, is carefully advanced into the left atrium, over a wire, usually positioned in the left upper pulmonary vein. And then once we have access to the left atrium, both the dilator and the wire are retracted, and we have, essentially, this catheter that's sitting in the left atrium giving us position to be able to put the device in.

The CDS or the Clip Delivery System is advanced through the GUIDE into the left atrium. And you can see that, right here. This We aorta, sitting in front. Here's the GUIDE catheter across the septum, behind it, giving us access to the left atrium. And here is the actual device that's traversing through the GUIDE, giving us position toward the mitral valve.

The fluoro-guided and echo positioning is actually intended to allow us to align the clip perpendicular to the mitral valve plane and allow us to actually put the MitraClip arms perpendicular to the line of coaptation.

Once we're at that point, right above the valve, we're able to actually advance the device. Once again, the device coming through the guider, perpendicular to the plane of the valve. We advance into the left ventricle. And we actually proceed with grasping.

Grasping involves careful positioning and determining the degree of MR reduction. And once again, going back to the fact as we have the time to be able to adjust this. This is not something we deploy and walk away from. It's something we sit there and do meticulous changing during the course of the procedure to make sure that our actual product is efficacious.

After the leaflets are inserted, the hemodynamic and echocardiographic evaluations is completed to determine efficacy. Have we caused a problem? Have we induced mitral stenosis in the setting of creating two orifices versus one? Are we sure that the MR reduction is what we want it to be? And the pressure gradients are assessed to confirm that.

Once the clip is determined to be appropriate, it's released using a standard procedural technique, with careful manipulation to safely remove the system. Once again, GUIDE in the left atrium, the device is now unhooked from the clip, which essentially looks like a clothesline bringing the two leaflets together.

And they're actually carefully removed from the left atrium, as you can imagine, under TEE guidance, to avoid any kind of disruption.

Mitral regurgitation now has been reduced with the advent of putting the actual clip in. This is what it looks like echocardiographically, but I'll let Paul talk more about the actual real time imaging.

Consideration for a second clip possible. Over 50% of the time, we may have a situation where we decide, you know, the first clip is not enough. Putting a second clip in is absolutely appropriate and may be needed.

And the final closure of the device, from the venous standpoint, is with a pre-close technique, which means a perclose suture. It's excellent to do in venous anatomy. And that's what this institution promotes.

GARY GERSHONY: Thank you, Dr. Haque. The next presentation will be Dr. Paul McWhirter, who is the medical director of noninvasive cardiology, here, on the Concord campus, and, also, is part of our transcatheter aortic valve replacement team. And he'll be talking about all the important imaging considerations.

PAUL MCWHIRTER: Thank you. Good morning. I wore my teddy bear suit, because it was so cold this morning. And I don't look quite as prestigious as my academic colleagues. But I want to kind of give you a gee whiz look at this, because the images do that.

And there's lot of academics behind the images. I want to assure you of that. But they are so beautiful and not just mine. But all of the images that we generate from these echo machines are just fabulous. And they look very much like the cartoons that Dr. Haque just showed you.

So we're going to do two things. I'm going to very quickly go through echo criteria for severe MR, because it's literally a multi day experience to talk about all of those aspects. And then we're going to go through a little bit of the TEE guidance of MitraClip deployment.

So mitral regurgitation usually, as Dr. Shiu described, we oftentimes pick it up in the clinic by symptoms of the patient or the physical exam. And that usually then prompts a transthoracic echocardiogram.

The transthoracic echocardiogram then will show us some valvular abnormality and some indications that there might be very highly moderate or severe mitral regurgitation that's symptomatic for the patient. And that will then prompt the TEE.

Now, you would think coming through the esophagus, the other side, maybe criteria are different. But they're really not. We use the same criteria for the transthoracic echoes that we do for TEE. So they're very much the same.

We use both quantitative calculations to see how much mitral regurgitation there is. And Dr. Shiu mentioned the effective regurgitation orifice. Who knows it? Does anyone know what ERO is? A few people do, I'm sure.

But it's a quantitative calculation. And we're not going to go into it today. I won't bore you with that. And we also use qualitative criteria as everyone talked about. So the left atrium enlarges, because you have this huge jet blowing back into the left atrium and tremendous pressures, and it dilates over time.

The left ventricle, oftentimes, gets decreased and develops a cardiomyopathy because of the regurgitant lesion and/or the regurgitant lesion can be caused by a cardiomyopathy and the left ventricular dysfunction of the venous.

So we look at, also, the chamber sizes. And the we look at a color dopplers, spectral doppler, the valve morphology, itself. All there flail segments? Are there prolapsing segments? Chamber sizes, as we talked about, and then a concept called PISA, which, again, I'm not going to really go into.

I'm just going to tell you that we use it. It's a very useful concept. And it tells us, qualitatively, how to calculate that effective regurgitant orifice. So this is one of my favorite pictures, because it shows a lot of stuff here.

So here is a mitral jet. So you're seeing a large amount of color. Now we can change this just by changing our parameters on the color. But by using certain parameters, we can see how much color goes into the left atrium. And that gives us some kind of a qualitative indication of how much regurgitation is.

We can look at the-- it's called the vena contracto, which is the width of the jet or the hole through the mitral valve from two-dimensional views. We can look at the PISA, which is flow convergence. That's basically just how the flow comes through the hole.

And you can see the color has a very definitive change from yellow to blue, which is right at the aliasing marks of the color here. And that distance, we can use to calculate how big this hole is, believe it or not. It gives us a very effective evaluation of that valve size or the hole leak.

And then we look at the valve architecture. Are there flail segments or pieces of the leaflet that are coacting correctly, as Dr. Dhillon talked about? And beautifully, now, we can look at this, not only in the 2D, which is a little abstract, really, right? You'll look at that 2D, and you're just seeing it kind of on edge. And it's hard to see the whole valve in your mind.

But now, we have this incredible 3D imaging that allows us to turn the valve around and make it look just like the cartoons that you just saw from Dr. Haque.

We also use spectral. So we do this quite a bit. And there's many areas that we can look at the spectral, actually, in the jet, itself. But one of the things we can do is, because this jet is blowing into the left atrium, insistently, it actually reverses the normal S-wave and D-wave coming out of the pulses, out of the pulmonary veins.

And those will reverse, because the systolic jet, from the mitral regurgitation, actually pushes the flow backwards. So this reversal, in the pulmonary veins, which we can see by spectral, is very important. And we use it post-procedure to look and see what's going on, besides all the other things we just talked about.

So we're going to talk about imaging by TEE, because that's what we do. So here is the view. This is kind of the surgeon's view of the heart. So we're looking, here, as Dr. Dhillon showed. Here is the mitral valve. This is the lateral wall over here. Anterior, is the left atrial appendage.

And the Carpentier nomenclature, we have the posterior leaflet, down, posterior on the bottom, towards the spine here, anteriorally flipped, and numbered from lateral to medial, from 1, 2, and 3. And we can take these planes and go through here and look at these valves.

Again, they're a little abstract if you're looking at them in 2D. We have wonderful techniques, now, two techniques. Besides the 3D, we also have something called cross-plane or xPlane. And what that allows us to do is not only look at the plane, this way, but take, immediately, the plane through the valve, in the other direction, at 90 degrees.

And it gives us a beautiful image of whether we're at the posterior or the anterior wall or which scallop or Carpentier segment we're actually looking at.

Just to show you, here's our TEE probe in the esophagus. And here is what we're doing. We're cutting through the planes. Look, you can see the esophagus is right by the heart. So we get these beautiful, crystal-clear planes. And we can rotate that triangle-- or actually, it's a pyramid now, on our new probes-- around, so that we can see whatever we want in that heart.

So here is what we get when we reconstruct in 3D. So I'm going to click this, because it's not looping correctly. But here is the surgeon's view on this side. Let's see if we can get it to stay. Here is the surgeon's view. So P1 is on this side, P2 in the middle, P3.

And you can see, at the end of P2 and between P2 and P3, there's a defect in this one, right in here. And there's a flail segment or there's a little tiny cord, actually, that you'll see coming through here. And the P2 segment is popped up or billowing. And you can see that.

See, this is a little flail segment, right there. And this is the view, actually, on the other side. So looking at it from the ventricle up through the valve. And the computer allows us to render this and give our implanting surgeons these incredible views to guide the clip during the procedure.

So how do we do the imaging for the MitraClip? Well, first we do the valve assessment as we talked about. And we look for severe MR. We look for what the baseline is. Now very interestingly, when we put these patients under sedation, the MR oftentimes is not quite as severe as it was when they're awake and alive in the transthoracic examination in the lab.

And we have to deal with that a little bit. But remember that the architecture, the flail segments or the typing, as Dr. Dhillon talked about, doesn't change. That does not change with anesthesia or changing the pressure very much. So we still can see all of those aspects of it.

So we do a valve assessment. Then we do the imaging for what Dr. Haque talked about. And let me just go through that. So on the valve assessment, we talked about the flail gap, the coaptation depth, and the flail width, as Dr. Haque talked about.

So we like this to be a centimeter or less. The width of the clip has to be within 15 millimeters, so that we can catch it that way, also. Here's the transseptal puncture. So this is the first view that we give them.

And actually, you can see here, here's a shadow of the catheter on the septum. And they're actually tenting the septum. Usually, this is flat. They're pushing in here. And the very first thing we do is we try and help them guide this tenting to be as high as we can, at least 3.5 to 4 centimeters, into the top of the ventricle.

Remember, they have to have room to curve these complex curves of the guide, so that we can actually direct the MitraClip. So we'll take measurements for them, from the annulus to the coaptation point, from the tip of the puncture site. And we will give them distances, right on the spot, during the procedure, so that they know where to go.

So then the guide gets punctured and pushed through. And this is what it looks like in 2D. It's kind of hard to tell, is that touching anything up there? But when we turn 3D on, it's really pretty amazing. We can see all kinds of stuff.

And I don't know what's going on. I think I clicked too much. There we go.

So you can actually see the sheath coming through. You can see, actually, the orifice of the sheath, and that it's not touching any of the other tissue in the left atrium, and give the operators confidence and, really, as I said, a cartoon view of the ventricle. It's almost as if you're there in real time.

So now, we take that guide that crossed. As Dr. Haque said, we put the clip through the guide. And you can see the clip here. And it kind of gives you an idea of what it looks like. As Dr. Haque showed you, here it is, here, folded up. And we're aligning it over the annulus.

And we're advancing the slide. There we go.

And we align it over the MR jet in the 2D.

Why does PowerPoint in video always do this? There we go.

And then we can give them actually these really amazing cartoon views. So look at this. You can see the clip. You can see, in the 3D, that-- remember, we wanted to go a little bit more onto this side. And we're pointing a little bit more to the wrong way. We're pointing more to the P1 area.

And we want to move that clip. So we can just tell our operators or show them the picture. We don't have to tell them really much of anything, they're so excellent. They just move it themselves. But we can show them the images, and they know what to do. So here's a little bit better. There's the clip to lateral.

And let's go to the next one.

So now we can show them. We've come a little bit more towards P3. But now you can see that the clip's not really lined up with coaptation point the way we want it. See, we want it really straight up and down, perpendicular to that coaptation point.

So we can tell them, turn it a little bit, give us a little bit more turn. We can do the 2D and get a better positioning with that. And now, we have a better position. We have more perpendicularity. And we're in a better position.

So now, we can proceed to deploy. Push the clip across the valve. And we're now going to look at the jet. And we want to split that jet, right down the middle. We're trying to split that jet. And then we want to advance the device across the valve.

I'm sorry these won't move. We don't want to be there yet.

We want to ensure that the leaflets are on the clip. So we want to see those leaflets nicely sitting on clip before we deploy it. And then, we deploy the clip. And now that really torrential regurgitation, that we had before, is now just a few little puffs on the side.

And then we detach the clip. Now it's sitting by itself. And now you see, with the clip detached, there's really not much mitral regurgitation, which would be the jet going into the atrium, right? Now we're seeing some flow and aliasing coming through the valve, because now we've actually, effectively given the patient a small amount of mitral stenosis, right?

So we have a little bit of aliasing around the clip. And if we look now in the 3D view, we have, as Dr. Haque described, owl's eyes. We can see our clip now.

And we have actually two holes that we've created, hopefully a smaller hole on the P3 side, and a hole on the P1, P2 side. But that flail segment, now, is pretty much gone, that we were seeing before.

So now our pulmonary veins have gone from systolic reversal. And, immediately, when we look at them, after the procedure, we see, now, an upright wave, consistently, which gives us a very good idea that that big jet, that was pushing the waves backward before, is now relieved.

And we can take Swan-Ganz measurements, too. After the sheath is removed, we do have a small ASD. But this heals very quickly in about four weeks. And it's really not an issue.

So the imaging, in conclusion, is very fun and exciting for us, for Perkin and I, as echocardiographers. And we feel honored to be a part of the procedure.

[APPLAUSE]

GARY GERSHONY: Thank you for [INAUDIBLE]. Implanters are the hands on the steering wheel. And the imaging cardiologists are truly the eyes of this procedure. The final speaker in this talk is Dr. Andrew Dublin. He's an interventional cardiologist, one of the implanters on the MitraClip team.

And he is going to talk about exciting new developments, because MitraClip is really just the beginning of transcatheter repair for the mitral valve.

ANDREW DUBLIN: Thanks for having me. So in the interests of time, so you guys can get some questions in before the conference ends, I'm going to go a little bit faster than I planned to.

So I'm not going to tell my witty anecdotes about *Back to the Future II* and Passover. I've got a lot of them. But I'm going to skip them. We're going to talk a little bit about future options. But just Google *Back to the Future II* and 30-year predictions. It's interesting.

So MitraClip for functional MR is going to be something we'll talk about, because, right now, it's only degenerative. MR. And then a lot of the techniques coming into the future are really base around annuloplasty and annular extension and tightening. And there's several new devices coming out for that. And then, finally, percutaneous mitral valve replacement, which is the next horizon.

So I think one of the reasons we're all so excited about this is that we're really at the dawn of a brand new field. And MitraClip is really just the first device to market. But over the next decade, there's going to be several more. And we'll really have a lot of different modalities on how to treat this. So it's very exciting for us.

So the trial, right now, Everest was for degenerative MR, and COAPT is the trial for functional MR, which is a schema for LV dilated. It's currently enrolling. We're not one of the enrolling centers, but we do have contacts with the enrollment centers. Stanford and UC Davis are probably the closest.

And so, every once in a while, we'll get a patient through the [INAUDIBLE] Clinic that actually has functional MR and not degenerative. And we want to do right by the patient. We want to do right by the technology. So we'll facilitate getting them to an enrollment center. And if they qualify, then they can actually be enrolled somewhere else for this really important trial.

It randomly assigns high-risk patients, one-to-one, to receive MitraClip versus standard of care, which, because these are surgically prohibited patients, doesn't include surgery. It's, right now, trying to get up to 430 patients, in 85 medical centers, in the US and Canada.

So that's all I'm going to say about that. It's currently enrolling. So we are trying to get patients for functional, so you can send them to the clinic, also, and we can take care of them.

Mitralign is the first device I'll talk about, which is an annular repair. And if you remember Dr. Dhillon's slide, the annulus is very important. Surgeons put in an annular ring, oftentimes, and so to have a percutaneous option for an annular ring is pretty exciting.

Two pledgets are delivered across the annulus over a wire on both sides of the valve. And then the pledgets are plicated, basically like little cotton swabs that you can put on. And they're plicated or pulled together and then locked in place. And it reduces the circumference of the annulus. And then that takes care of the symptoms of the regurgitation.

It's a study going on in Europe, CE Mark, 64 patients. At 30 days, the MACE was 15.9%, with 3 patients dying and 2 patients having tamponade. But they did have a substantial improvement in NYHA class and MR grade. So high-risk patients, they do have complications. But the thought is it's better than the alternative, which is nothing.

So you can see this cartoon on the left is the before picture. And then, up on the top, up here, these are the pledgets, on one side, and pledgets, on the other side, those little white swabs. And it basically just tightens around the annulus.

The next device is called Carillon. It's a mitral contour system. It has a proximal anchor and a distal anchor, with a shaping ribbon. It utilizes the heart's natural structures. And again, this one's for functional MR, just like the one before. It's transvenous delivery.

The 30-day data was excellent in regards to safety, with no device-related deaths, MI, perforation, or embolization, or needing surgery. There were a few trials that are looking at this.

In one of the trials, the TITAN trials, the end diastolic and end systolic diameters were both significantly decreased over a year. And long-term data showed six-minute walk and NYHA class improved, by one month, and were sustained out for several years.

This one is called Encorsq. It's a nitinal annuloplasty ring that's surgically implanted. The exciting thing about this one is, because it's nitinal, you can actually hear radio frequency after implantation. And it can change the shape of the band. So if you don't get a good result before, you can, a year later, go back and modify it.

They've modified nine patients, and three of them had improvement in mitral regurgitation. Six of them didn't. Obviously, this is still an emerging technology. They have a long way to go with before it's standard.

This one's called the Cardioband. A lot of these, again, they're all annuloplasty techniques, so they're all pretty similar, transseptal, multiple anchors. This device looked at high-risk patients, with mean STS scores of 7%, and there overall rate of death was 7% at 30 days. But none of the major adverse events were considered to be device-related, for what its worth. And they did have a substantial improvement in MR grade at discharge as well as sustained at six months.

So all these are small data, small trials, but give data. So hopefully, we'll see some of these devices. And there's another one called Accucinch, which is an LV remodeling system. It anchors around the subvalvular space. And then the circumference and tenting of annulus is reduced, which leads to decreased MR.

So those are the annuloplasty devices. The next thing that is coming to market. And at [INAUDIBLE], they had their first live case of a mitral valve implant, mitral valve replacement through percutaneous.

These are transapical approaches not transseptal. There is a transseptal component to it. But the device is actually going in transapical, and that's because you have to get alignment with the mitral valve, so that you can be in the correct position.

There was a greater than 10% mortality rate in these medium to high-risk patients in the early trials. These devices are clearly at the very beginning of their life. There's a lot of them, EndoValve, Tendyne, CardiAQ, Neovasc, Tiara, Fortis. So there's a lot of them. Tiara and Fortis had their first in human implants just last year. So these are really brand new.

This is what CardiAQ looks like. It was a acquired by Edwards, which is obviously a big valve company. It's self-positioning, with the native valve annulus, anchored to the annulus, without radial force. And they did their first implant in 2012.

Fortis is also Edwards. This trial was halted this year because of valve stenosis issues. So it just goes to show that just because it's conceptually a good device, until you put it in patients, you don't know what's going to happen.

So in conclusion, please send us any of your referrals. We're happy to see the patient after the TTE before the transesophageal echo, after the trans. We can make these things happen. And you can call the High Risk Valve Clinic at the number listed.

Allison and Kristin, can you guys wave to everybody? These are our valve coordinators. They do an amazing job. They follow the patients from first referral till well after the procedure is done. The patients feel very close and connected. And they really are what allows us to maintain the practice outside of mitral valve repair and also they'll be involved in the program.

Thank you.

[APPLAUSE]