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[MUSIC PLAYING]

Hi, I'm Hemal Gada. I'm an Interventional Cardiologist, the President of Heart and Vascular Institute, the Medical Director of the Structural Heart Program here at UPMC, Harrisburg. I'm privileged to talk to you today about transcatheter tricuspid valve approaches.

So before we get into the actual technical nuances and the systems that are out there for transcatheter tricuspid valve, repair, and replacement, let's talk about our nomenclature in assessing tricuspid regurgitation. And Becky Hahn obviously has done a lot of work in this particular field. This is a really seminal paper that came out in Jack imaging just in July 2021, looking at a classification scheme for different morphologies of tricuspid valve lesions that would lead to tricuspid regurgitation.

And it's akin to carpentier classification, but a little bit different. The tricuspid valve is not just three leaflets. It's a little bit more complicated than that.

You can have a pseudo division in the posterior-- sorry-- the posterior, anterior, and septal leaflets shown here in this type classification shown in the central illustration. And there are examples shown in the left on IIIDT and IIDT assessments, showing you the various anatomies and morphologies of tricuspid valves that could be seen. The greatest incidence is a type 1 morphology, which is an incomplete fusion between the posterior and anterior leaflets of the tricuspid valve that would then predispose you to developing tricuspid regurgitation.

And so this is ischemia to help you assess the tricuspid valve and assess the type of anatomy that we are talking about. And so what is basically attached to the intraventricular septum, where the leaflets extend out to, or extend from, this is really going to help you identify the leaflet locations, and then off of that, assess the different leaflet morphologies that may exist. And so again, trying to count up the number of leaflets or subleaflets that are apparent in some of these anatomy's I think is crucial in understanding what the type of tricuspid valve you're dealing with is.

And so here's an example of a type IIIB tricuspid valve where there's a division of the posterior leaflet and two scallops almost. And then you can see here the amount of regurgitation that would be apparent in an anatomy like that. Really, a mid esophageal 3D en face view on 3D is going to give you all the anatomic delineation that you would need in order to make this type of assessment. This is shown here on this moving image quite well. And you can see the division in that posterior leaflet.

Really, the transgastric inflow-outflow view or the 0 degree view is the only 2D view where all three leaflets can be imaged simultaneously as shown here. And you can see the path of the T-probe in going to that transgastric inflow-outflow view. The short axis view is going to help you identify the anterior papillary muscle. It's typically fused with the moderator band of the right ventricle. And that is going to be used to identify the anterior leaflet of the tricuspid valve as shown here.

Now, showing the type classification here. Type I as shown here again. The most common type of tricuspid valve would be, again, partial fusion of the anterior and posterior leaflets. Type II here is more of a complete fusion of the anterior-posterior leaflets, as well as a division of the septal leaflet as shown.

Going to our next slide showing a type IIIA, which would be a division of the anterior leaflet and fusion of the posterior and second scallop of the anterior leaflet. And then type IIIB be shown below, which is partial fusion of the scallop of the posterior leaflet and anterior leaflet as shown there.

Type IIIC, partial fusion of the posterior and anterior leaflet with a division of a septal leaflet and then type IV where you have subscallops of the posterior and anterior leaflets with more complete fusion of the posterior and anterior leaflets. So this ischemia gives us an understanding of what is going to be a successful outcome with regard to transcatheter tricuspid repair versus replacement. And it's going to give us an idea of who maybe is better served with replacement versus an annual capacity versus an edge-to-edge repair.

And so this is just an understanding before we get into the modalities of treating tricuspid regurgitation via transcatheter means. This is 129 patients that underwent edge-to-edge tricuspid repair using the Abbott platform. And you can see here that they basically use this classification scheme to understand who had a successful outcome versus who didn't.

And so the co-optation gap was observed more in a four leaflet tricuspid valve again where you have the sub-scalloped anterior-posterior septal leaflet. And then in three leaflet tricuspid valves. Patients with four leaflet tricuspid valve show trends towards larger right ventricular mid diameters and larger co-optation gap. And that would basically influence your repair outcomes.

And so shown here, basically, the technical success was numerically lower in a four leaflet tricuspid valve versus a three leaflet tricuspid valve. Less than moderate TR was achieved in a greater incidence with a three leaflet tricuspid valve with a larger degree of procedural failure with a four leaflet tricuspid valve. And you could see here the procedural success and how it was defined. And it was achieved in a greater number numerically of four leaflet tricuspid valve, which is interesting.

And so looking here, you don't really see any difference in all cause mortality, and then maybe some differences in composite endpoints when you put into account like residual regurgitation. But I think the long term outcomes of lower procedural success are unknown. What this takeaway is for me is that the procedure may be somewhat more difficult with a four leaflet valve. But it doesn't mean that you can't get a good outcome.

And so as far as edge-to-edge is concerned, as we'll discuss, I think that it is a go-to way of repairing the valve. And just because you have a three versus a four leaflet valve doesn't mean that you can't get a good outcome. It just may be harder to do it with a four leaflet valve than a three leaflet valve.

So this is a nice little visual of the current tricuspid technologies. Again, all of these are in research or in the aspect of being devised. As far as clinical research is concerned, really the only commercially available tricuspid repair platform is the clip, which we've used for the mitral for many years now. I think that got commercialized back in 2013 for degenerative MR. And for tricuspid regurgitation, this is really the only commercially available device that we have.

And we have several in clinical trials that UPMC is currently involved with. The tricuspid valve, the limitations of repair, you have imaging limitations. It can be hard to get these transgastric views that are going to identify the leaflets that are going to identify your grasp.

The leaflets can sometimes be restricted or really plastered up against the wall of the right ventricle or septum. And that can create difficulties in grasping leaflets, especially with edge-to-edge. Limitations of replacement, the size of the valve-- unfortunately, the sizing of these valves, these transcatheter valves, were more based for the mitral apparatus.

And of course, the tricuspid apparatus, or the annulus, tends to be much bigger. And so really device companies have to do more in order to create larger valve sizes to accommodate a larger variety or a larger extent of tricuspid regurgitation patients. The impact of replacement on RV function, taking it away that pop-off valve, the short term limitations of that can be quite profound.

Patients may suffer with right ventricular failure for a period of days to even weeks after getting a triscupid valve replacement. The durability of these valves is largely unknown. And the optimal course of anticoagulation, the agents to use, again, and for how long also unknown.

And so when we think about post-operative 3 to 4 plus TR in a variety of surgical repairs, meaning failed repairs, you can see a variety of different techniques that have been used, edge-to-edge techniques, different suture techniques, putting in rings. And you can see the amount of tricuspid regurgitation that is left over. It is not trivial with any form of repair.

There is a good amount of TR left over in a large majority of these procedures, and that's an issue. And so when we think about reducing the annulus, we can think of two ways of doing that, a direct ring annuloplasty or a suture anchor bicuspidization annuloplasty.

So direct ring annuloplasty, the one with the most evidence, I would say, and the most experience worldwide is the cardioband. The cardioband is an annular reduction device. Think about pledgets going around the annular plane from the right atrial side and basically a cinch that is involved to pull in all aspects of that tissue to create a smaller annulus.

So you see here the TEE guidance. We're basically looking at anchored pledgets that basically march around the aspect of the annular plane of the tricuspid valve. In part one of this, TEE guidance is fine. But as we get to other aspects of the tricuspid valve, most notably towards the septum, where TEE imaging becomes more difficult, you could see that using an intracoronary echo or intracardiac echo, ICE guidance, you'll be able to see things much better with regards to placement of these pledged anchors.

Into procedural TEE at the end of this procedure shows a significant reduction in tricuspid regurgitation. Now, keep in mind that many of these procedures will take upwards of 2 and 1/2, 3 hours to do because of the amount of anchors that are involved and the difficulty of imaging. And so this is one of the major limitations of an annular repair like this is just the amount of time that it takes to achieve the result. This is your final 3D TEE assessment shown here. Again, a really great outcome with regards to tricuspid regurgitation.

The cardioband US EFS study, you can see here 30 days post implant for 30 patients followed out to 30 days. That's 27 patients. And you can see the change in septal lateral dimensions, decrease of almost 15% as far as the annular assessed septal lateral dimension is concerned, diameter is concerned. The TR severity definitely improves with use of the cardioband and subsequently NYHA classification and KCCQ scores also improve with this technology in this particular study.

In the US EFS there was a very low rate of adverse outcomes. I would say the most eye popping of these were the severe bleeding outcomes. And this was largely secondary to the caliber of access that was being used in the vein. And obviously, with better venous closure techniques, surgical cut downs, we can expect these severe bleeding events to go down in incidence.

The cardioband US EFS study showed a very marked decrease in TR severity and at least a reduction in heart function in the immediate period after the cardioband placement as we discussed. And so by taking away that pop-off valve, the already weak right ventricle, decides to be a little weaker. Unfortunately, it is in a situation to be a little weaker after some period of time. But we can expect that to improve hopefully with longer term follow up.

So another way of reducing the tricuspid annulus would be a suture anchor system. And this is one particular technique called PASTA, Pledget-assisted Suture Tricuspid Annuloplasty, and basically walking through each of these steps that I don't really need to go over. This is a wire-based annuloplasty reduction shown here, and tightening with a core knot after you've established this rail between the pledgets and the two wires that you're using.

The trialign procedure is basically, probably the most quoted procedure or the most common procedure that's been done with this PASTA type of approach. There's a wire placement, a pledget delivery, and then a pication and a lock that basically cinches a portion of the annulus together.

So when the scout trial studying this particular technology in 15 patients, there was a acute procedural success in 100%. You could see that the right coronary artery because of its proximity to tricuspid annular plane may achieve some level of stenosis as a result of this placation.

And so there was an intraprocedural stinting of the right coronary artery in one of the patients in this 15 patient cohort. You can see the 30 day follow up. Some issues with technical success in that there was some single pledget dehiscence because of the friable nature of the tissue these pledgets are going into.

However, no major adverse events. And you can see here that only really great one year survival as far as TR is concerned. Because in natural history, it was 64% survival with severe TR. But here in the 51 patient pooled cohort for scout one and two, there was upwards of 95% freedom of all cause mortality from all cause mortality at 12 months.

Some clinical outcomes shown here. [INAUDIBLE] living with heart failure questionnaire, NYHA classification, 6 minute walk test, or a minute walk test. You can see basically really great outcomes as far as functional status is concerned.

So some annular repair challenges, pacemaker induced leaflet impingement. The TEE quality may be suspect in a lot of these patients. And you may have to rely on some 3D ICE for some aspects of delivering the technology that I've described.

The severity of shelf like annular anatomy can be a factor. The proximity of the right coronary artery can introduce some aspects of interference and morbidity there. A very large annulus can preclude the reduction of TR to less than mild. And there is a learning curve for these technologies. And the procedural times can be very long.

So a little bit more straightforward and maybe a little bit more commonplace in the world today is tricuspid edge-to-edge repair. And so we'll go over the triluminate clinical trials, the six month outcome of those. And then we'll also start talking about the Pascal device, which is another edge-to-edge device that is manufactured by Edwards Lifesciences that's currently in clinical trial with the ACE platform that they now have for a smaller device with. And there's a first commercial multicenter experience that recently got presented that I'll go over as well.

So really we're talking about the mitraclip system. That's basically what I'm showing here. And so the mitraclip system with a cerebral guide catheter, any cerebral sleeve with a clipped delivery system. And this is what triluminate basically is.

And so this study design was used on the third generation mitraclip device. This is not the fourth generation with the variable valve. Sorry, variable clip widths and lengths as we see now. This was basically done on NT as far as the mitraclip is concerned.

And so you could see some of the clinical outcomes that were being studied and who is eligible. You can see the baseline characteristics shown here for these patients and the procedural data. So implant success rate was 100%. They had great acute device success, pretty good acute procedural success.

The device time was acceptable and probably much better than what we've seen with annuloplasty and cinch devices. And the total procedural time and fluoroscopy durations are shown here. The primary safety endpoint of major adverse event was definitely met in this particular cohort. And this has been followed through now in a one year analysis and led to CE mark of the triluminate system. But anyway, point is that it's a very safe system to use.

Additional safety endpoints are shown here. Again, some issues with bleeding and probably more related to the procedure itself and just improper groin closure. You can see here that there are some elevated tricuspid valve mean gradients to be cognizant of and probably less of an issue now that we have different clip sizes for the mitraclip system.

You can see the number of clips that have been inserted greater than-- 79%, 80% of the population had more than one clip implanted. You can see the clipping location here. And most of this was done introspectively. 143 patients out of the pooled subjects basically got clips, or sorry, 143 clips out of 185 clips were placed in the anteroseptal location.

Device effectiveness, you could see from baseline to 30 days to six months. You could see a significant improvement in the severity of tricuspid regurgitation with the TR reduction achieved in 87% of subjects. The proportion of subjects with moderate or less TR increased from 6% at baseline to 57% at 30 days and six months. And six month data here indicates durable repair as they did show out to a year as well. Significant improvements in echo parameters is shown here with regards to the severity of tricuspid regurgitation.

Some dramatic improvements, this is NYHA classification. And you can see a dramatic improvement in NYHA classification out to six months in these patients that we're dealing with debilitating heart failure. Improved clinical outcomes in the Kansas City cardiomyopathy score in a 6 minute walk distance.

So high implant and acute procedural success rates with the triluminates slash mitraclip platform, no major device or procedural related safety concerns, a durable repair, a good improvement in NYHA classification, and early signs of positive [INAUDIBLE] right ventricular reverse modeling, which I didn't show. But basically, it does really maybe strengthens the argument that leaving a little bit of tricuspid regurgitation behind may be a healthy thing to do and not just completely eliminating it because that may actually induce remodeling a little bit more readily than complete reduction or elimination of tricuspid regurgitation.

Moving on to PASCAL, which is the other edge-to-edge repair system. And so this is Edwards Lifesciences. Again, this is a device that had initially been trialed in the mitral space. And this now has CE-mark approval for TR treatment and is being actively studied in a clinical trial in the United States called class TR, which UPMC is involved with. And the new generation of this device Pascal ACE was introduced in October of 2020.

This is just one example of a really successful outcome with a PASCAL device going from a baseline of 5 plus TR to just 1 plus TR. So this was a prospective observational study for German tertiary care centers since the mark until April of 2021. It ends up being 181 patients with a core lab analysis of all echo imaging.

You can see the baseline characteristics shown here. Obviously, patients who have had debilitating heart failure, a pretty even distribution of females and males. And you can see some of the risk data as shown there and comorbidities.

Baseline echocardiographic characteristics are shown there. You could see five grade description of tricuspid regurgitation extending into massive interential. So it's not just severe. But pretty much everyone had severe or more tricuspid regurgitation. So a healthy amount of tricuspid regurgitation.

Functional TR in the vast majority of patients. And you can see some level of right ventricular dysfunction is apparent in most of the patients as well. Procedural and in-hospital outcomes shown here, technical success was excellent. Almost 100% of patients had technical success.

The number of devices that were used or shown there. And then you can see the TR severity grade again as a result of using this device from baseline to discharge. Follow-up outcomes in TR reduction, the TR severity grade goes down significantly. You can see that here.

We have sustained reduction to less than two plus at follow-up. And the TR was reduced by greater than one grade in 92% of patients. Follow-up was available for 77% of patients.

The overall mortality was 11.5%, which is really great for a severe tricuspid regurgitation cohort. Rehospitalization for heart failure less than 20% excellent. And then re-intervention only in 3.6% of patients.

Follow-up outcome with regards to functional status, again, really great improvement in NYHA class and 6-minute walk distance. Follow-up outcome with regards to echocardiographic parameters again. Some reverse remodeling is shown here in our RV end-diastolic diameter and inferior vena cava dimensions. And so signs of remodeling and reduced congestion.

The PASCAL Ace device is the narrower device that can be used. And that may be a little bit better for the tricuspid leaflets, inducing less injury and causing less tension on those leaflets, maybe leading to better outcomes with regards to regurgitation. You can see a technical success when using Ace, the number of devices used, and the reduction to lessen our 2 plus TR is actually comparable, maybe even slightly better with the PASCAL Ace device.

So high technical success, good safety profile with this particular platform, and efficient TR reduction sustained at follow-up. TR is moderate or less than 77%, and reduction greater than 1 grade in 92%. Great functional improvements as measured by those batteries and signs of RV remodeling and reduce congestion as I discussed. Comparable results for PASCAL and the new PASCAL Ace platform.

So then we finally get into replacement. So we've done annuloplasty. We've done edge-to-edge repair. And now we're going to get into replacement.

And so this is one replacement device that is being used in clinical trials now, probably the clinical trial that's farthest along. And that is the EVOQUE tricuspid valve replacement system. Again, manufactured by Edwards.

This has atraumatic anchors that are compatible with pre-existing pacemaker leads and respect the native anatomy. It's got a conforming frame designed to achieve optimal retention force. It's got multiple sizes offered, up to 52 milimeters. As far as the valve size, it's [INAUDIBLE] by a diameter. And it's a 28 [INAUDIBLE] transdermal delivery system. So maybe preclosure would work in something like this. The whole concept here is to basically grab the leaflets from below, secure them, and then deploy the valve. And that's basically as it's been shown in this little movie that I've played for you here.

So moving on to a more real time case with this particular platform, you can see here that this particular patient has pacing leads. And this valve actually works quite well with pacemaker leads because you'll open these anchors. And they've got a nice gap in between them.

You'll secure the leaflets. And then you'll open this valve apparatus basically going from a bottom-up approach. And this will really create a very, I would say, uncomplicated deployment as it would relate to the pacemaker lead. So no lead displacement with this particular deployment.

So the compassionate use experience is shown here. Again, this is actively undergoing study in the [INAUDIBLE] trial, which is the EVOQUE IDE study. And I think the feasibility has recently been completed.

So compassionate use shown from March of 2019 to July of 2027 institutions. 27 consecutive patients with symptomatic severe plus tricuspid regurgitation, high surgical risk. And these are the institutions that enrolled in this particular experience.

Baseline characteristics shown here. STS [INAUDIBLE] risk mortality, upwards of 8 and 1/2 percent. So very high risk surgical cohort greater than-- so 27 patients were inserted into this particular study. Some degree of right ventricular dysfunction, pretty common, mostly functional TR. And pacemaker leads were around in a third of these patients.

And so you could see some of the clinical outcomes shown here. Procedural success was excellent, 93%-- no mortality, no stroke, no intervention, no heart failure, hospitalization. Only one patient needed dialysis afterwards. And only two patients needed a pacemaker afterwards. So really great conduction disturbance rates.

Echocardiographic and clinical outcomes are shown here. TR severity decreases significantly better than with the repair platforms obviously. So by replacing the valve, you can expect TR severity to jump down grades quite easily in patients who actually get a valve deployed. NYHA functional classification shown here. And 68% of the patients ended up having an NYHA class of less than or equal to two out [INAUDIBLE] one year after getting the replacement.

So conclusions, their early experience here demonstrates that the EVOQUE system has had durable efficacy, low rates of mortality and acceptable morbidity in high surgical risk patients at one year. All treated patients achieved significant TR reduction to less than or equal to moderate. 92% achieved trace or mild TR and persistence significant improvement in NYHA functional classification of one year. There are further studies to validate its long term efficacy. The feasibility study, which recently completed and the IDE study, which is currently ongoing for this particular device.

So there are just two take-home slides here. And I've presented them already. Number one, understand the nomenclature.

So by understanding the nomenclature, you can develop a strategy by which to really repair these valves a little bit more effectively. So that means that you have high quality imaging. 3D [INAUDIBLE] echo imaging is crucial, having a good transgastric view where you're able to discern all three leaflets and understanding the anatomy, absolutely critical for designing the mechanism or understanding the mechanism of the tricuspid regurgitation, and designing an appropriate repair approach for a particular anatomy.

And then finally, a lot of technologies out there, a lot of clinical trials ongoing at UPMC. We're very fortunate to have access to many of these technologies. And I'm sure more in the future. This is a very fertile space as far as heart valve therapies are concerned. So I'm looking forward to contributing to UPMC's excellence in really providing progressive care for our patient populations.

So thanks again for your attention today. I really appreciate your time. And if there are any questions about this presentation, feel free to reach out to me directly.