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Released: 03/05/2021
Valid until: 03/05/2022
Time needed to complete: 30 minutes

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New Opportunities to Manage Aortic Stenosis with TAVR

Announcer:
Welcome to CME on ReachMD. This activity, entitled “New Opportunities to Manage Aortic Stenosis with TAVR" is provided by Medtelligence and is supported by an independent educational grant from Medtronic.

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Dr. Giri:
The FDA has approved an expanded indication for several transcatheter heart valves to include patients with severe aortic valve stenosis at low surgical risk. Today, we’ll talk about what that means for your patients.

This is CME on ReachMD and I’m Dr. Jay Giri.

Dr. Jain:
And I’m Dr. Renuka Jain. Thanks so much for having me, Jay.

Dr. Giri:
So let’s dive right in. Dr. Jain, we see a number of patients who meet the standard criteria for severe aortic stenosis, but are convinced that they have no symptoms, at all. So let’s first discuss how we identify severe aortic stenosis in any patient. And then let’s dive in to how we evaluate this “asymptomatic” patient population.

Dr. Jain:
Those are all great questions, Jay. First, I think it’s important to start in the echo lab. Remember that the diagnosis of aortic stenosis is made in the echocardiography laboratory. And it’s really important to do a high-quality echo and identify severe AS. As we can see from our slides, we have a suspicion of severe AS on a short-axis view when we see a very calcified and restricted aortic valve. But the aortic valve area calculation is a combination of 3 values that are done from a standard transthoracic echo. The LVOT VTI, the aortic valve VTI, and then the LVOT diameter. Common sources of error in the diagnosis of severe AS are the LVOT diameter. Remember that that value is squared if it is an error. It’s best made right at the base of the aortic annulus in systole. The LVOT velocity is done by pulse-wave Doppler before the acceleration of the aortic stenosis signal on an apical 3-chamber view. And then finally the aortic valve velocity, which is done by continuous-wave Doppler. It’s really the American Society of Echo standard to obtain the highest velocity of aortic valve velocities using multiple different views.

As you can see in this slide, from the apical 3-view, which is the traditional view that we use, the peak velocity is about almost 4 m/s. From the apex, it’s a little higher at 4 m/s, and when we use the non-imaging or the Pedoff probe at the right sternal border, we actually see an aortic valve velocity of almost 5 m/s on this patient. Really clinching the diagnosis of severe aortic stenosis. Also, important to remember that the dimensional index, the ratio of the LVOT VTI to the aortic valve VTI really helps you to understand the severity of AS. A ratio of 0.25 or less defines severe AS in situations where you can’t see the LVOT very well.

But I think, Jay, it’s also important that there are lots of different subtypes of AS. So not all severe aortic stenosis has a mean gradient of

40, a peak velocity of greater than 4. You can have high-gradient and low-gradient states, normal flows and low-flow states, and these are all really important to understand in the echo lab when you're diagnosing AS. What's very important in these normal flow, low-gradient states where mean gradient is less than 40 but your stroke volume is okay, your EF looks good, that, sort of, paradoxical low-flow, low-gradient AS, is it's always important to make sure that you're not making a measurement error. The low-flow, low-gradient states are the really true low-flow, low-gradient severe ASs and in those cases, low-dose dobutamine can actually be helpful. You normalize the stroke volume and then you also can see if the valve is truly stenotic or if it is just moderately stenotic but appears severe in the setting of low flow. And then, finally, always to remember in low-flow states that there are a lot of factors that contribute to those states in severe AS. You can have restrictive cardiomyopathies, hypertrophic cardiomyopathies, and para-diastolic filling or HFpEF, atrial fibrillation, concomitant mitral stenosis, tricuspid regurgitation, all of these things can lead to reduced stroke volume and can cause errors in your aortic valve diagnosis calculation. And just a quick plug for cardiac CT, which we use a lot here in Wisconsin when we have discrepant aortic valve areas, the valve looks bad, but the gradients of the valve areas don't correlate, we often do a cardiac CT calcium score. Severe AS is likely in a woman when that calcium score is greater than 1,200 and in a man when it's greater than 2,000.

And then, I think, finally, before we move on, we should just comment on your last question about how you differentiate true asymptomatic severe AS from patients who maybe have decreased their activity level because of their severely stenotic valve. And just one last plug for the echo lab. Exercise stress echo can be really, really valuable in diagnosing severe asymptomatic AS as sort of unmasking those symptoms. Remember that when we do these asymptomatic severe AS patients, we really want to make sure that they are truly considered asymptomatic. It is a contraindication by guidelines as well as just by all of us practicing to take a symptomatic severe AS patient and put them on a treadmill. But for the truly asymptomatic severe AS patient, exercise stress testing in a symptom-limited fashion can actually be very, very helpful. As you can see here on this slide, this particular patient's peak velocity started at 4 and went up to 5.5 with exercise. But, Jay, you know, that's not really why we do the exercise stress echo. We don't do it for the gradients to go up because they know that they will with exercise. We do it to take a look at all the other hemodynamics. So poor exercise capacity, a lot of symptoms with exercise in this particular patient post-exercise, LV disfunction and then hypotension ventricular tachycardia, these are all sort of high-risk features that suggest that their AS is not truly asymptomatic.

Hey, Jay, you know, there's been a lot of buzz about approval of TAVR for low-risk patients. I wonder if we might be able to just talk a little bit about low risk and what does low risk really mean?

Dr. Giri:
Well, thanks so much for that question. So, let's get into what these positive low-risk TAVR trials were about; who did they enroll? Well, there were two trials done, one with self-expanding valves and one with balloon-expandable valves. And they both were really positive trials for TAVR. They demonstrated non-inferiority of TAVR against surgical aortic valve replacement in the so-called patient population that is low risk for traditional surgery. The patients enrolled in these trials were age 65 and over, and they universally had trileaflet calcific aortic stenosis. Additionally, these patients had Society of Thoracic Surgeons, or STS, risk scores of less than 4%.

So the expansion of TAVR is quite exciting in the sense of promulgating this innovative new technology into new populations. However, there are certain things that give us pause when we're considering TAVR in the low-risk population, and certainly we can identify many of them on imaging. So, Renuka, when you're considering the preoperative imaging for patients with severe aortic stenosis, what are some characteristics that you look at that may make you think about issues with TAVR versus traditional surgical aortic valve replacement?

Dr. Jain:
Jay, that's an outstanding question, and as you know, when we started TAVR, it was in inoperable patients, high-risk patients, and now in low-risk patients. The guidelines have offered us some guidance as guidelines do, and the guidelines' stance on this is that if you have anatomic features that make you a poor candidate for TAVR, that may be a time where you might consider surgery and also vice versa. And the anatomic considerations we look for are on both echo as well as on CT. As you can see on this slide, LVOT calcification is a really big pause when it comes to TAVR. It can increase the risk of paravalvular leak as well as aortic annulus rupture. As you mentioned earlier, bicuspid aortic valve was excluded from most TAVR trials. There are ongoing TAVR trials of bicuspid aortic valves, but that is also another case where you might pause on TAVR, particularly if they have associated aortopathy which can really be quite a dilated aorta. Porcelain aorta or significant aortic valve calcifications, in my mind, is not a great candidate for surgery and may push you more towards TAVR, although you and I both know that there can be some challenges there with TAVR, as well. Vascular access becomes critical. The people that do best with TAVR are those that are able to get TAVR done, performed with transfemoral access. And then patients that have poor transfemoral access where alternative access sites are proposed, those are people that might lean more towards surgery. Of course, other primary valve disease indications for cardiac surgery would push you more towards surgery. And then low coronary heights become an issue with TAVR. We wouldn't want the TAVR stent to impinge upon the coronaries and cause obstruction. And finally, the annulus size, too big or too small, either way may push you more towards

surgery rather than TAVR.

Jay, though, I'm sure it's the same for you as it is for us. We've certainly done TAVR in all of these anatomic considerations. We've just made a point of letting the patient know ahead of time and having a really shared decision among the surgeons, the interventionalists, us in imaging, as well as the patient.

Dr. Giri:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Jay Giri, and here with me today is Dr. Renuka Jain. We're discussing the new and improved opportunities to manage aortic stenosis with TAVR.

Dr. Jain:
Hey Jay, what do we know about the long-term durability of TAVR?

Dr. Giri:
It's a great question, Renuka, and certainly it's more relevant than ever when we're extending TAVR into low-risk populations. Let's dive into, first, how we define bioprosthetic valve failure. There are actually several mechanisms by which bioprosthetic valves, surgical or transcatheter, fail. Now the first, which we're all familiar with, is endocarditis. I don't need to dive too much into that, you all know to utilize appropriate prophylaxis in patients with valves. Second is an important phenomenon called subacute leaflet thrombosis. Now, this is a phenomenon where, actually, a clot forms on the valves potentially impeding their motion and causing elevated gradients, and in rare cases, sometimes even causing cerebrovascular events. This is actually slightly more common with TAVR than it is with surgical bioprosthesis. The good news is when it's detected, be it after SAVR or TAVR, it often is treatable with a few months of anticoagulation therapy with coumadin.

The next issue that we look at is what we call non-structural valve deterioration. These are issues that don't involve the valve leaflets directly per se, but do involve the bioprosthetic valve failing. This, with TAVR, could, for example, refer to the presence of aortic insufficiency, which causes a patient to do worse over time or become symptomatic over time from that paravalvular aortic insufficiency. This obviously is more common with TAVR than surgical valve replacement.

Another cause of non-structural valve deterioration is patient-prosthesis mismatch. This really just means a valve being placed in a patient that's really too small for their body surface area. This, in fact, is actually a bit more common with surgery than it is with TAVR. In all of these cases, we're not talking about the leaflets falling apart, but we are talking about issues that could lead to valves needing reinterventions or repeat surgeries.

Finally, we get at what everybody is really concerned about, and that's what are the rates of structural valve deterioration [SVD] of the leaflets of a TAVR valve, and what do we know about that? Well, structural valve deterioration or degeneration, in general, is a multifactorial process that unfolds over a course of many years, 8 to 12 years. In bovine valves, it often manifests as calcification or leaflet degradation, leading to valve stenosis. In porcine valves, it can manifest as a leaflet tear that leads to significant aortic insufficiency. There are many risk factors for it, as noted on this slide, but the bottom line is this has been largely studied in surgical valves.

Now how has it been studied and what do we know about it? Well, in this beautiful analysis from *JACC* in 2017, the authors went ahead and looked at all the observational data regarding surgical bioprosthesis durability. And what they found is that there have, in fact, been a number of studies, and many have been large, involving more than a thousand patients. However, they've been notable for almost all being single-arm studies, and they've had highly varied follow-up and highly varied definitions of what structural valve deterioration really means. Oftentimes, it was defined as really the need for reintervention rather than patients who had it picked up by hemodynamic criteria. And for that reason, there's a lot of variability in how this particular issue has been defined in the surgical literature, and there's opportunities to tighten up in future studies how we're looking at it in patients who get surgical aortic valve replacements.

When it comes to TAVR we have actually compared TAVR valves to surgical valves in randomized trials on a population basis. The populations of these trials have been looked at carefully in echocardiograms to see how do the TAVRs square-up against their surgical counterparts? You can see in the left panel of this slide, with the self-expanding randomized trial of intermediate risk patients, SURTAVI intermediate risk, we have data out to 2 years that actually demonstrates larger valve areas and lower mean gradients in those patients treated with TAVR rather than surgery. On the right panel, we have data from a 5-year follow-up of a balloon-expandable randomized trial, once again, of intermediate-risk patients, showing equivalence of mean gradients between surgical valves and transcatheter valves. So when it comes to randomized trial data of these 2 platforms, surgical valve replacement versus transcatheter valve replacements, we're not catching a signal at this intermediate 2- to 5-year time point of transcatheter valves really performing any worse on a population basis from a structural valve deterioration standpoint.

Do we know anything more, and do we know anything specifically about low-risk patients? Well, we do have one randomized trial that was performed in Europe, a little smaller in scope, less than 300 patients, but with excellent methods that did randomize low-risk patients to TAVR versus SAVR and actually has published follow-up to 6 years. This is the NOTION study, demonstrated here in this slide. And you can see that rates of what they call "bioprosthetic valve failure" were equal; 7.5% versus 6.7%, not statistically significantly different between the 2 valve platforms out to 6 years. So, thus far, we are not yet seeing big differences between TAVR valves and surgical valves in terms of durability. However, we need to learn a lot more about both platforms in terms of how they're performing in the long term.

Dr. Jain:
I agree with you, Jay, we have a lot of learning to do about structural valve deterioration. Both echo and CT are helpful in diagnosing and often complimentary, but the early signs, the midterm data of 5 years, is very reassuring for TAVR.

Dr. Giri:
Well, this certainly has been a fascinating conversation, but before we wrap up, Dr. Jain, can you share with our audience your one take-home message?

Dr. Jain:
I'd be happy to. TAVR is a truly transformative technology, and imaging expertise in both echo and cardiac CT are really needed to bring this amazing technology to all patients with risk.

Dr. Giri:
Yeah, and I highly encourage, as I mentioned before, all practitioners out there to find a good valve team in your region that you can partner with to collaborate with the care of these patients so you can tailor the right therapy, transcatheter valve replacement or surgical valve replacement, to the right patient.

Unfortunately, that's all the time we have today. So, I want to thank our audience for listening, and I want to thank you, Renuka, for joining me and for sharing all of your valuable insights. It was great speaking with you, today.

Dr. Jain:
Thanks so much, Jay. It was a great conversation.

Announcer:
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