

## **Aortic Regurgitation**

Announcer: Welcome to the Mayo Clinic cardiovascular continuing medical education podcast. Join us each week to discuss the most pressing topics in cardiology and gain valuable insights that can be directly applied to your practice.

Dr. Friedman: Hello. My name is Paul Friedman. I'm Chair of the Department of Cardiovascular Medicine at Mayo Clinic. and I'm delighted to have with me today, Dr. Vidhu Anand, who is a specialist in echocardiography, valvular heart disease, among other conditions. Dr. Anand, thank you for joining me.

Dr. Anand: Thank you for having me.

Dr. Friedman: Today, I wanna talk about aortic regurgitation. Sort of from bedside, to imaging, to intervention, and what type of intervention. Maybe we can start with a few basics. What is aortic regurgitation?

Dr. Anand: Aortic regurgitation is leaky aortic valve. It can be caused by a number of different reasons. Abnormality in the valve leaflets or cusps itself, or dilatation of the aortic root. It's estimated prevalence is about 0.5 to 2.2% for moderate or greater severity.

Dr. Friedman: How do you diagnose it? We'll start with physical examination and then we'll move on to imaging studies.

Dr. Anand: Typically, the patients present with dyspnea on exertion. They may have heart failure symptoms on presentation. The first test that is usually ordered and helps with the diagnosis is echocardiography. Of course, the bedside examination is very important and critical, as for all different cardiac conditions. On physical examination, some of the key features, associated with aortic regurgitation include wide pulse pressure, low diastolic pressure. And in fact, a diastolic blood pressure lower than 60 millimeter mercury is associated with high mortality. So it's very important to pay attention to physical examination. Tachycardia is also associated with poor prognosis. Other than a wide pulse pressure, patients will have bounding pulses everywhere and there's usually a holo diastolic decrescendo murmur of aortic regurgitation auscultated at upper sternal border. And the severity typically suggests the degree of regurgitation or severity of regurgitation. However in patients with acute regurgitation, the murmur may not be as loud as one would expect. Then there are other signs of left heart failure that may be present as well.

Dr. Friedman: You have someone in front of you and you think there may be aortic regurgitation, what's the next step?

Dr. Anand: So after a suspicion of aortic regurgitation from history and physical examination, sometimes even ECG and chest x-ray can be rarely helpful. Could show cardiomegaly or left ventricular hypertrophy on ECG And then the next test that's ordered, and usually helps with the diagnosis is echocardiography. Echocardiography plays a key role in both diagnosis, asserting the mechanism, etiology of aortic regurgitation, as well as to determine if patient may have certain markers or indicators to determine the timing for surgery. So using echocardiography, we

can determine the severity. It's very important in aortic regurgitation that a comprehensive assessment of valve morphology, etiology and mechanism of aortic regurgitation is performed. And a very detailed evaluation of degree of regurgitation through quantification is very important because the jet can be eccentric and visual estimation using color, Doppler may not be adequate, and is usually not adequate to evaluate the severity. So every attempt should be performed to quantify the degree of regurgitation, quantify by either PISA estimation to determine the regurgitated volume or by some other measures, such as vena contracta, the width of the jet, and looking at the abdominal aorta for the hollow diastolic reversals, which indicate several are. Once the severity is determined, it's also very important to look at both etiology and mechanism. And it's important to keep in mind that those two things are separate. There are three different mechanism types. Type one is associated with normal cusp motion. So it's either caused by leaflet perforation or dilated ascending aorta. Type two is associated with excess cusp motion, as seen in bicuspid aortic valve. Type three is associated with restricted cusp motion, which is seen in inflammatory valve disease, such as syphilis, lupus, and sometimes bulky infective endocarditis vegetations can also restrict the leaflet motion. Now, this is mechanism and it's different from etiology. And I'll give you an example. So a patient with infective endocarditis can either have type one mechanism because of leaflet perforation or type three because of restricted leaflet motion. Similarly, ascending aortic aneurysm can have a type one mechanism because of normal leaflet motion and just incomplete coarctation or type three, because of a dissection flap prolapsing through the cusp. Or even type two, if there is bicuspid aortic valve and associated with cusp prolapse. It's important to differentiate between the two because it can affect the surgical plan again and management for the patient.

Dr. Friedman: Got it. So mechanism and etiology obviously are different. When you're first seeing the patient, 'cause in a minute we'll talk about timing of interventions and types of interventions because there's a lot of new findings coming out in that space. But again, just to make sure we cover our table with the basics before we move on. So when you see a patient with aortic regurgitation, you're already thinking of a broad differential. Maybe you can lay that out a little bit more, and what kind of testing do you do to make sure you're not gonna miss something in that differential.

Dr. Anand: That's a great question. So typically echocardiography is the first test that would help you diagnose the condition and the severity. But sometimes transthoracic echocardiogram is not enough because the jet may be very eccentric and may even be difficult to quantify. So it's important to use other modalities such as transesophageal echocardiogram or cardiac MRI, when the diagnosis is questionable or the mechanism and etiology are unclear. Then the next step is, like you mentioned, timing for surgery. And also there is role of different modalities. Besides echocardiography and using other modalities such as TEE, transesophageal echocardiography or cardiac MRI, which has role in determining timing for surgery. There is also a role of cardiac biomarkers that is being explored to identify the optimal timing for surgery.

Dr. Friedman: Review, maybe a little bit. When is the optimal timing? How do you relate to imaging, findings and of those, you and others have been making some recent observations about volumes versus linear measurements, tell us about the impact of those and what exactly does that mean?

Dr. Anand: That's a great question. Before we dive into it, I wanna just spend a few moments to talk about the natural history of aortic regurgitation. It was studied from 1970s to '80s and '90s by Dr. Bonow and his group. Aortic regurgitation, as we know, causes both pressure and volume overload to the left ventricle, which leads to eccentric hypertrophy and left ventricle dilatation. This left ventricle dilatation is well tolerated for years, sometimes decades, before there is onset of irreversible myocardial injury that is followed by systolic dysfunction or drop in ejection fraction, followed by symptoms, and then death. So now knowing this natural history of the disease, the aortic valve surgery per guidelines is recommended for symptoms, irrespective of ejection fraction. And in asymptomatic patients, if there is drop in ejection fraction, less than 55%, or there is significant left ventricular enlargement, left ventricular and systolic dimension more than 50 millimeter or index and systolic dimension, more than 25 millimeter per square. Now these cutoffs come from old studies from 1980s and '90s and estimated using linear dimensions and EMO echocardiography which has its inherent limitations. And at that time, there was high surgical mortality of up to 10 to 20% of aortic valve surgery. Since then there has been advancement in surgical techniques and we have newer generation prosthetic valve. So it's time to re-look at the optimal timing for surgery. So our group here at Mayo Clinic did a study evaluating the role of left ventricular volumes in determining the optimal timing for surgery. Left ventricular remodeling or size is better evaluated through volumetric assessment which is now recommended by American Society of Echocardiography Chamber Quantification Guidelines. Left ventricular remodeling may not be symmetric, and the linear dimensions may not be able to capture the true enlargement. And our group found that volumes were better and more strongly associated with outcomes such as mortality, as well as symptoms. And they were independent and more strongly associated with these outcomes. An interesting finding was that nearly 30% patients in our cohort had LV dimensions that were below the cutoff for intervention per guidelines but had enlarged volume, more than 45 ml per meter square, which is the cutoff determined through spine curve analysis. So 30% patients had already significant left ventricular remodeling and enlargement which is not captured by linear dimension. And this study kind of suggested that the left ventricular remodeling and aortic regurgitation may be like a football, rather than a soccer ball, and more oblong, and more pronounced from base to apex, and not captured adequately by the linear dimensions. So there is a role of left ventricular volumes. It does need to be assessed further in prospective studies and multicenter studies before it can be incorporated into the guidelines. But at this point, I do think, in patients who are low surgical risk younger patient and have a large volume, it should be considered in the shared decision making while determining the timing for surgery.

Dr. Friedman: So clearly as we have more sophisticated measurements we can see subtleties in the patterns that that one summary measurement obviously is gonna miss. And I think we'll be learning more. And so today in your practice, then you're taking this into account and discussing it with the patient. If the volume is increased, even if the linear dimension is still within what would've been considered a watch and weight number?

Dr. Anand: Exactly. Yes. So our center is a center of excellence and we have very low operative risks. So in patients who are young, and are overall low risk for operation, I do consider this in shared decision making. Besides this, there are number of other novel markers that are being evaluated and have been studied, such as global longitudinal strain assessment through echocardiography. So if it is less negative than 19 1/2%. If there is presence of fibrosis as

assessed by late gadolinium enhancement in cardiac MRI suggesting subclinical myocardial dysfunction, or if there is serial drop in injection fraction but hasn't yet met the cutoff of less than 55% or serial echoes showing increase in LV size then those are other things that we consider. There's also role of biomarkers such NT-proBNP that is being evaluated. So a lot of things being evaluated to determine the optimal timing of surgery, which is certainly needed in low risk patients to have the best patient outcomes particularly in centers of excellence.

Dr. Friedman: Yeah, now really remarkable how we're understanding the disease better and therefore able to diagnose its trajectory and determine when to intervene. Which then brings up the next point, you decide that an intervention is warranted, either because of volumes, because of standard dimensions, because of symptoms, what treatment options now are there to choose from? Cause that's evolving as well. It's no longer simply aortic valve replacement. And so tell us about those and how you decide.

Dr. Anand: Yes, so if we determine that patient needs surgery and it is the right time then the options are aortic valve replacement either mechanical or bioprosthetic valve. And to decide between the two, we take into account number of different things but the most important is age of the patient. So in younger patients, we typically prefer mechanical valves which have longer life. Although the downside is patients need lifelong anticoagulation with warfarin but there is a role of aortic valve repair particularly in younger patients who are active in lifestyle and want to avoid anticoagulation. At this time the role is maybe a little bit limited but as the surgery is perfected to achieve durability and long term success, and made widely available, I think, it is going to be expanded in terms of its yields. And here at Mayo clinic, certainly, we have surgeons who can perform aortic valve repair with good success and very low risk of complication. And it is a really attractive option, particularly, as I mentioned for younger patients with bicuspid aortic valve.

Dr. Friedman: So as you look into your crystal ball into the future, what do you think will be the big impacting new developments affecting aortic regurgitation into the next two to five years or a little beyond?

Dr. Anand: I see that we will be offering surgery to patients earlier than the cutoff in guidelines and those cutoffs are likely to change and they will include volumetric assessment and some of the novel markers, such as, later gadolinium assessment by MRI, and maybe left ventricular global longitudinal strain. And there would be emphasis on indexed dimensions and indexed volumes which are very important for women. Because women can have a significant LV enlargement before they reach the cutoff of 50 millimeter. So it's very important to have index numbers. And so I see that being highlighted in the guidelines and I see that there may be even more role of aortic valve repair and expansion of the centers of expertise.

Dr. Friedman: So one size does not fit all. As we learn more centers of excellence will really be leading the charge in these newer diagnoses and treatments. And then I'm gonna ask you to speculate, because speculation is the only thing any of us can do in this next question, but that is, we've seen more and more valve procedures become, either percutaneous or minimally invasive, as opposed to open surgeries. Aortic regurgitation has been a little recalcitrant to that approach thus far, do you see that changing in the future? Just comment on that, if you would.

Dr. Anand: I think that is again a great question. And as the centers of experience and excellence expand and the valve repair and robotic are minimally invasive surgeries are perfected to achieve both long-term success and durability, because those are somewhat of concerns at this point, I see that in future, their utilization will expand, and there're certainly more attractive options for younger patients in particular

Dr. Friedman: Dr. Vidhu Anand, thank you for joining me. Really an interesting topic that's seen a lot of evolution and a lot of exciting things to come. Thank you for a very informative discussion.

Dr. Anand: Thank you so much for having me.

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