

## Tricuspid Regurgitation– Causes and Management

**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** - Hi, my name is Paul Friedman. I'm chair of the Department of Cardiovascular Medicine at Mayo Clinic in Rochester, Minnesota, and I'm delighted to have with me my colleague Dr. Mackram Eleid, professor of Medicine, and also the director of our structural interventional clinic. Mac, thanks for joining me.

**Dr. Eleid** - Thanks for having me, Paul. It's great to be here.

**Dr. Friedman** - And today I'd like to talk about tricuspid regurgitation because that field and the options have been changing so dramatically, especially over the past couple years and you've been spearheading that change for us. The first question is maybe just a little background for our listeners. How do people who have tricuspid regurgitation typically present and how are they diagnosed?

**Dr. Eleid** - That's a great question, Paul. It's often a very subtle onset with tricuspid regurgitation, and often times it happens in patients who are elderly and may have been slowly decreasing their activity levels. And so it may not be a very obvious abrupt onset of symptoms, but typically patients will notice fatigue as one of the earlier signs or symptoms. They'll also have dyspnea with activity as another common symptom. And it's not until much later in the process that we'll see the right heart failure signs that that we think of with more advanced right heart failure like edema, abdominal distension, and increasing need for diuretics.

**Dr. Friedman** - In the past, it was a valve that was not commonly intervened, not at least not in isolation, but that's rapidly changing. Why is that?

**Dr. Eleid** - Historically, it's the significance of the tricuspid valve was not fully understood. We've had a lot of studies now that have shown us that the more severe the TR is, the worse the prognosis is, and it is an independent predictor of mortality based on the quantitation of the tricuspid regurgitation based on echocardiography. That's been one advance. The other problem is just the comorbidities of the population and often times patient have, patients have advanced kidney disease, they may have had a prior cardiac surgery and there are just comorbidities and advanced age that make them not ideal candidates for surgery.

**Dr. Friedman** - So you have a patient in your clinic, you've made the diagnosis of tricuspid regurgitation. They've got the typical murmur made worse with inspiration. The question arises what are the common mechanisms and how does the, the cause of tricuspid regurgitation impact potential treatment options?

**Dr. Eleid** - That's something that we continue to learn about and I, we don't have a a consensus about that, but we do have several observations. One is that the earlier we treat the tricuspid regurgitation, the better the technical result we can get with a transcatheter therapy like edge to edge repair or annuloplasty. So one of the themes that we're seeing now is earlier treatment will yield better results similar to what we're seeing on the mitral valve. So the functional mechanisms of TR or the most common ones that we see, We have atrial functional, which is due to annular dilatation in the setting of longstanding atrial fibrillation. And then we have ventricular functional TR, which is associated with pulmonary hypertension and left heart disease. Then we also have device lead related TR, which is a little bit less common and that can be managed in different ways as well. And then of course primary TR, which is due to either leaflet, prolapse or other abnormalities of the leaflets.

**Dr. Friedman** - Does the cause impact the potential treatment option?

**Dr. Eleid** - In some ways it does. When we're looking at the transcatheter therapies, edge to edge repair can be applied to a lot of the different mechanisms. But if it is a more dramatic case of lead related TR where the leaflet is impinged or there's a major leaflet motion abnormality by a a device lead or a even perforation, then edge to edge repair may not be the best option and we may look for a replacement. And those themes are also similar for surgery I think as well.

**Dr. Friedman** - So what are some of the interventional treatment strategies that have been deployed to treat tricuspid regurgitation?

**Dr. Eleid** - Well, the most common one, as I had mentioned in previous topics here, edge to edge repair is the one that's been done the most worldwide and it's actually approved in several countries, in Canada, and also in Europe. It's, it's approved for treatment of the tricuspid valve. In the US it's in clinical trials still. We've had one randomized trial that has already been published on edge to edge repair. We also have replacement valves that are in the clinical trial phase as well that are showing a lot of promise. And then finally also there's been some experience with Annuloplasty as well as a treatment that can be done percutaneously.

**Dr. Friedman** - Does the one you select depend on anatomic features or mechanism, or is it too early to say because they're all still investigational?

**Dr. Eleid** - There definitely are some anatomic features that we look at. For instance, for edge to edge repair, we try to avoid patients with very severe tethering of the leaflets or a very large coaptation gap of 10 millimeters or more because we tend to have a lot more residual TR with patients that are treated with that modality. We look at the annulus size, which is often highly, that's a major factor for a replacement valve because the valve has to be matched to the size of the annulus and right heart. So different replacement valves will have different range of sizes that they can treat. So that's another important variable.

**Dr. Friedman** - What are the the potential benefits of correcting tricuspid regurgitation with a transcatheter repair?

**Dr. Eleid** - And we're still learning about that and what we've seen so far is improvements in quality of life. In, in the Triluminate randomized trial that was published earlier this year, there was a significant improvement in the Kansas City cardiomyopathy questionnaire score in patients who had edge to edge repair compared to guideline directed therapy, which is essentially diuretics. And now we're also starting to use SGLT2 inhibitors in patients. So for sure we're seeing quality of life improvements at at least so far in this one trial. We have two other randomized trials that will be coming out in the next couple of years that'll also shed further light on what the benefits are. We expect maybe heart failure hospitalizations might be less and other other outcomes, I think, we'll, we'll just have to see what the studies show.

**Dr. Friedman** - As you know, the patients that I've referred have often been related to device TR that is, you know, they've, they've gotten great clinical benefit from a pacemaker and then 5 or 10 years later they develop severe TR but they've been dramatic, it's like a Lazarus effect where they're hospitalized and lose 20, 25 pounds of fluid weight, recurrent hospitalizations. And then after the procedure's done, they're telling me they're walking miles and it's a dramatic thing. Have you noticed a difference in the response based on the mechanism or cause am I seeing a bias population because the leads are causing it or do you think it's generalizable or do I just have a skewed observation in a positive direction?

**Dr. Eleid** - I share the same observations as you. I've seen a lot of pretty dramatic effects in many patients even without the device lead related. I think you and I have even shared a patient that we treated with edge to edge repaired with just isolated TR from a related to AFib, and that patient also had a dramatic improvement. So I think the mechanism, I've seen similar improvements regardless of the mechanism. So I'm expecting at least the studies that we've been involved in to see maybe more dramatic benefits in the randomized trials than what we've seen so far. But, but I know, you know, those, I think we're always slightly biased. So, and, and so that's why we need these, these randomized trials to see exactly what those benefits are.

**Dr. Friedman** - And, and tell us a little bit more about the patient experience. That is, how long are they typically hospitalized for? How long until they experience benefit? Do you have a sense of whether the dosage of diuretics is, is modified over time or is this augmenting the benefit of, of, you know, a stable diuretic dose recognizing a lot of the publications are, we're waiting on them, but what, what's your sense to date of what a patient might expect?

**Dr. Eleid** - I think that's, it's highly dependent on the chronicity of their right heart dysfunction and their kidney disease. If a patient is on very low dose diuretics and they have only mild RV dysfunction, those patients typically only stay one night in the hospital. And we often will continue a diuretic regimen and when we see them back in 30 days, at that point we'll usually think about weaning down the diuretic or in some cases even completely stopping it if they were already on a low dose. But I think the patients who already have significant RV enlargement and RV dysfunction, I expect that they'll always need some diuretic. But we will try to lower those, the frequency or the magnitude of those doses as we see them in follow up. But I don't usually do that right away. But the patients with more advanced volume overload and edema, we, we definitely take time to optimize them before and after the intervention. So those, those can be several days in in the hospital.

**Dr. Friedman** - Now I suspect that many of the people watching or listening to this like me will be more involved in caring for patients before and after the procedure as opposed to doing the procedure. So what are some of the potential risks that we should be aware of and what are the things we should look for when we see patients in follow-up after this procedure? When do you want us to call you right away and say that this is something that needs attention versus adjust medications and, and continue to see them ourselves?

**Dr. Eleid** - Luckily we've seen that the interventions have a pretty good safety record thus far as in terms of complications, it is general anesthesia procedure and we do transesophageal guidance. So patients will often have some mild throat discomfort after the procedure. There is some bleeding risk because a lot of the patients are on anticoagulation, so we watch for that in the, in the first several days and week after the procedure in terms of their access site. But the risk there is relatively low device detachment with a edge to edge repair device from the leaflet is also very uncommon. It's in the few percent range, less than 5%. We would usually detect that on transthoracic echo. So not always something really that would be detected just at a standard visit. So I think the biggest thing is just related to bridging and patients being off of their anticoagulation and coming back on and making sure they're getting therapeutic and they're not off of anticoagulation for too long if they have atrial fibrillation.

**Dr. Friedman** - And in terms of anticoagulation choice, you know, we're often reluctant in surgical valves to use the DOACs, certainly for mechanical valves. That's not so true for bioprosthetic valves. Tell me a little bit about what agents have been used in the, in these studies, in patients getting tricuspid valves and then the follow-up question will be something that you and I have encountered. A patient has atrial

fibrillation and then they're interested maybe in left atrial appendage occlusion to eliminate the need for anticoagulation. Will their valve negate that, will it require chronic anticoagulation?

**Dr. Eleid** - I think for replacement valves, there's concern about leaflet thrombosis. We see that in surgical bioprosthetic tricuspid valves as well. And we don't have enough data in the transcatheter replacement valves to know exactly what that incidence is with and without anticoagulation. What we're doing now for self-expanding aortic valve for instance, is at least six months of anticoagulation. It can be either with a vitamin K antagonist or a direct oral anticoagulant. And so we do allow either one with surgical valves. I've observed that there, that there, the warfarin is probably the, the lowest risk of thrombosis there in that position for edge S surgery repair, it's a little more flexible. There's a lower risk of thrombosis, so, so it's basically we continue what the patient was already on, but 90% of these patients have AFib. So unless they've had left atrial appendage like closure with a device or surgically, then we would generally resume anticoagulation. But I think it's a great question that you raise. As you know, I, I don't think we have any data that the benefit of left atrial appendage closures is negated if you get a replacement valve on the tricuspid side. And, and if those do fail, we can treat them with valve and valve too. So I think patients who are high bleeding risk, it's, it's an important therapy to have for them. So we just need more time, I think.

**Dr. Friedman** - Yeah, sure. And then before we conclude, I'm gonna ask you to speculate a little bit, and that is, what about patients with significant multi valvular disease? Do you think we're getting to a day where there can be percutaneous multi valve interventions to treat multiple lesions? Or do you think that when you get to that point, at least in the next five years, surgical approaches are preferred?

**Dr. Eleid** - We've definitely made a lot of progress and even, even now when we have patients present with aortic stenosis and mitral regurgitation and they're not low risk candidates for surgery, then we are often treating them with stage transcatheter interventions. And I think we're doing the same for patients who have combined with tricuspid regurgitation too. So, so I, I think we're already at that point, but we haven't though, got to the point of concomitant transcatheter valve repairs as much. Although we have done several patients with edge ed repair on both the mitral and the tricuspid valve with good results. I think there's logistical challenges more than anything to doing that. And so that, that needs to be explored further. I think

**Dr. Friedman** - Well certainly a fascinating topic where the landscape is dramatically changing for the better as we really now have options for patients that were even hard to imagine not that many years ago. So Mac, thank you for joining me and enlightening all of us on, on these new treatment options and for spearheading so many of these trials here for us so that we have these options for our patients.

**Dr. Eleid** - Thanks. Thank you, Paul. Thanks for the great discussion.

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