

## Transcript Myocarditis What's new for 2025

Dr. Kyle Klarich: Hi, this is Kyle Klarich coming to you from Rochester, Minnesota. With our interview with the expert session. Today we are going to be speaking about myocarditis, what's new in 2025. I'm very pleased to be joined by a world's expert on this topic, Dr. Leslie Cooper, who is Elizabeth C. Lane, PhD and M. Nadine Zimmerman, PhD, professor of Internal Medicine at Mayo Clinic College of Medicine and consultant in the Department of Cardiovascular Medicine, Mayo Clinic, Florida. His career is actually focused really on cardiomyopathies and especially the autoimmune variants of myocarditis. He has coordinated the 1995-97 International Giant Cell Myocarditis Registry, the giant Myocardio, Myocarditis Treatment Trial, and led the international teams on the role of Endo myocardial biopsy disease in the AHA/ACC/ESC for the Global Burden of Myocarditis for the WHO Gates Foundation. He has authored over 300 peer reviewed journal articles and book chapters. He has also co-founded the Myocarditis Foundation and in cooperation to detect and support affected families education and research around myocarditis. So as you can tell, he has more than enough expertise in this area to really help us with this interview with the experts on myocarditis what's new in 2025. Les, thanks for being here,

Dr. Leslie Cooper: Kyle. Thank you so much. It's really great to be with you today and to share some of the innovations from 2024, in particular the American College of Cardiology Expert Consensus Decision Pathway on the Management of Myocarditis. There are a number of new findings and new recommendations in this EDCP, which I think will be of interest to your readership and your listeners.

Dr. Kyle Klarich: I couldn't agree more. I think maybe we'll start just with the basics. Like when should a clinician even start to think about myocarditis in the clinical setting, either in the hospital or in the outpatient setting?

Dr. Leslie Cooper: For sure. Kyle, Myocarditis is a great mimicker. It can present like an acute myocardial infarction with chest pain or pericarditis. It can present with heart failure with shortness of breath and symptoms of fluid congestion or sometimes as a serious arrhythmia such as ventricular tachycardia or heart block, the most common presentation is chest pain. So it's important when more common reasons such as ischemic heart disease are excluded to think about an inflammatory and, and possibly viral cause for heart disease.

Dr. Kyle Klarich: Well, that's great advice. I think, you know, we see so many patients coming in through the emergency department that we have to rule out ischemic causes, but many times we get a little bit confused when things don't line up. So what tests should we be relying on to help us with the diagnosis of myocarditis?

Dr. Leslie Cooper: For sure, Kyle, in the, in the first presentation, the standard and and somewhat non-specific tests such as a troponin and NT-proBNP or BNP and an echocardiogram with an EKG are the basic triage tests that everyone should get. If there's an indication for myocarditis such as a basal septal aneurysm in the setting of sarcoid, for example, or other unexplained cardiomyopathy or arrhythmias, you would go on to a pivotal test. The two pivotal tests are cardiac MRI and in select cases, a PET scan.

Dr. Kyle Klarich: That's great. Yeah, I think those are gonna be used echoes, you know, as near and dear to my heart as a noninvasive cardiologist. But I think oftentimes when I'm in the hospital setting, I see patients come in and you get the echo findings of, you know, an aneurysm or you might find sort of generalized hypokinesis, doesn't really follow the usual wall motion pattern that we'd expect with ischemia. Is that, is that correct? Is that's how I would escalate to MRI or PET scan the ECHO findings. Non-specific sometimes, as you pointed out.

Dr. Leslie Cooper: That's right, Kyle. There are certain patterns like you might think of the basal septal aneurysm for sarcoid or perhaps other non-ischemic location aneurysms for chagas disease or other systemic inflammatory disorders like lupus. All of these are clues, but none of them are specific for any one entity. So when you get an echo or an EKG, for example, that shows unexplained high degree heart block, think about specific forms and sometimes inflammatory causes of heart disease.

Dr. Kyle Klarich: Very interesting. And that's great advice. I know that the new consensus statement has discovered or at least defined four stages of myocarditis. Could you explain those?

Dr. Leslie Cooper: For sure. This is one of the innovations in the new 2024 EDCP statement and stage A as in heart failure or ischemic heart disease are people at risk. For example, if you had a patient who was receiving an immune checkpoint inhibitor for cancer therapy, they would have perhaps a one in 300 to one in 100 risk, depending on, on whether they were receiving more than one inhibitor or the development of myocarditis. Similarly, if you had a patient who had a known DESSA plaque mutation, they would have a small risk of recurrent myocarditis. You would think about those people as stage A. Stage B would be people who have been screened. For example, somebody with pulmonary sarcoid who had a positive cardiac MRI on screening would stage B asymptomatic. But with evidence of structural heart disease, once symptoms develop, that would be our classic stage C patients presenting with chest pain or shortness of breath or an arrhythmia. And finally stage D, which would be end stage cardiomyopathy, requiring ventricular assist device to support, support or inotropic support. Those are all patients who you would want to be managed with a multidisciplinary care, usually at a tertiary care center with expertise in myocarditis

Dr. Kyle Klarich: Also, that really is very consistent with what we've come to understand about heart failure, valvular heart disease, and now myocarditis basically the same format. So that's very helpful. You know, one of the other things that has been recently talked about in the literature and in conferences and pretty new to me in fact, is the genetics that are involved with myocarditis. I know that you've been very passionate about this and I wonder if you could explain to our audience when genetic testing should be considered in those patients with myocarditis.

Dr. Leslie Cooper: That's right, Kyle. As, as you know, when we went through medical school, when we were in residency and fellowship, myocarditis like peripartum cardiomyopathy was thought to be environmental. Perhaps it was a virus, perhaps it was another injury, but it was not a genetic disease like we think of hypertrophic cardiomyopathy. However, we've discovered in the last decade that in patients with severe forms of myocarditis, for example, significant ventricular arrhythmias or patients with severely reduced ejection fraction, that the rate of a positive cardiomyopathy gene pathogenic or likely pathogenic mutation is approximately 20%. And those are in adults in children, it's even higher in some reports. And so based upon those reports that have accumulated over the past 10 years from Europe and Asia and North America, the current EDCP recommends genetic testing for cardiomyopathy genes be offered to patients with new onset suspected or definite myocarditis. I would personally add, in addition to the EDCP guidelines, that those patients with a family history of positive of myocarditis or those patients who've had multiple recurrent episodes should especially be considered for testing.

Dr. Kyle Klarich: Well, basically anyone you could offer to almost anyone who has had, but primarily you definitely wanna offer it to those that have had a family history of myocarditis, those that have had a recurrent episodes of myocarditis in their own personal history. Is that correct?

Dr. Leslie Cooper: That's right. Especially the ones with more severe disease myocarditis accompanied by sustained or symptomatic ventricular arrhythmias or myocarditis associated with a left ventricular ejection fraction of less than 40%.

Dr. Kyle Klarich: Right. So severe disease, recurrent episodes, family history of myocarditis.

Dr. Leslie Cooper: Exactly.

Dr. Kyle Klarich: Great. And then, you know, one thing I always struggle with in the hospital is what to tell a patient after they've had myocarditis about activity and follow up.

Dr. Leslie Cooper: Great questions, Kyle. When you make the diagnosis, say by MRI in a young man with chest pain or by a PET scan, it doesn't end there. In even the simple myocarditis where they respond to colchicine say and a low dose of nonsteroidals and the chest pain goes away, you should still get, according to the EDCP, an echocardiogram at two to four weeks, at least for LV function because a small percentage of people will continue to deteriorate after the initial presentation. With respect to return to play, we do recommend in the EDCP three month window where you are active performing activities of daily living and perhaps even a recreational level sports, but not NCAA level one athletics, for example. That could be competitive single tennis or similar high level sustained activity because at least in our multiple studies in animal models and in epidemiologic studies, you can get a worse cardiomyopathy or even ventricular arrhythmias if you have sustained high level activity in the setting of active inflammation.

Dr. Kyle Klarich: So you wanna wait to, so for the, the run of the mill, you'd start out with colchicine and nonsteroidals, is that correct? To whether treatment? Correct.

Dr. Leslie Cooper: So there, there are case control studies published some very recently this year suggesting that there's about a 50% decrease in the rate of recurrent myopericarditis in those patients treated with Colchicine over a two year window. There is an ongoing clinical trial in France called the Argo trial, which is addressing specifically the question of the benefit of Colchicine for myopericarditis. So we do avoid non-steroidal anti-inflammatory agents in patients with low ejection fraction because of the risk of worsening heart failure

Dr. Kyle Klarich: And then after that the follow up would be 2-4 weeks or an echocardiogram and clinical assessment for return to sport. You have a three month window between three and six months where you start low level activity but not NCAA level activity?

Dr. Leslie Cooper: That's correct, and there may be some exceptions. For example, in we learned from the covid experience that there could be young athletes who had covid with MRI evidence of inflammation, but minimal symptoms who might be able to return sooner than three months. But for a typical viral myocarditis requiring hospital level care, I would say three months would be the the data or what we have data for. But although there are, it's all done with shared decision making, recognizing that there are not a lot of prospective data to guide that decision.

Dr. Kyle Klarich: Well that's great. Well, there's a lot of detail there and we would encourage everyone to have a chance to look at the a CC expert care decision pathway, which has been recently proposed, and I think that would be very helpful. Is there any other teaching points you'd like to make prior to us leaving this wonderful conversation?

Dr. Leslie Cooper: No, Kyle, I, I, I just add that heart biopsy is reserved for patients who are particularly severe. Those who have unexplained cardiogenic shock, those who have myocarditis associated with sustained or symptomatic ventricular arrhythmias of a few weeks duration where you might think of a giant cell myocarditis or other serious autoimmune condition. Most of the patients who present with a normal ejection fraction and chest pain can do well with just an MRI and don't require a biopsy.

Dr. Kyle Klarich: Well, that's awesome. Well, thank you for those points. A lot of information packed in this conversation. We appreciate all your insights and expertise. Thank you very much, Dr. Cooper.

Dr. Leslie Cooper: You're well. Thank you so much, Kyle. Great to be with you.