

Katherine E. Di Palo ([00:17](#)):

Welcome to the American Heart Association's pericardial disease podcast series. This is episode four, Beyond Acute Recurrent Pericarditis. I'm Dr. Katherine Di Palo, clinical program manager of the hospital readmissions reduction program at Montefiore Medical Center and assistant professor of medicine at Albert Einstein College of medicine in the Bronx, New York.

Katherine E. Di Palo ([00:41](#)):

Joining me today are two esteemed guests with the expertise in the field of Pericarditis. First we have Dr. David Lin, senior consulting Cardiologist at Minneapolis Heart Institute at Abbot Northwestern Hospital in Minneapolis, Minnesota. We've also got Dr Farshad Forouzandeh, Interventional Cardiologist at the Cardiovascular Interventional Center, Harrington Heart and Vascular Institute, University Hospitals and associate professor of medicine and cardiology at Case Western Reserve University School of Medicine in Cleveland, Ohio.

Katherine E. Di Palo ([01:24](#)):

Our first three episodes have focused on Acute Pericarditis. We're going to shift gears into Recurrent Pericarditis. Over the next 30 minutes we'll cover prevalence, diagnostic criteria, initial pharmacotherapy and provide insight on care delivery strategies to decrease the economic burden of Recurrent Pericarditis and improve patient outcomes. Future episodes will cover pathophysiology, chronic pericarditis and long term complications. As a disclaimer, we will be discussing off-label indications for certain drugs. Dr. Forouzandeh, can you describe the timing and the diagnostic criteria?

Farshad Forouzandeh ([02:08](#)):

Thank you so much Katherine, for the introduction and I appreciate the opportunity from American Heart Association to be on this podcast, and also bringing up this important entity of pericarditis to everybody's attention, that can affect numerous patients, at least 5% of the acute chest pain presenting patients, to the emergency rooms. In the previous podcast there was the discussions about what is Acute Pericarditis. Today, as you mentioned, the focus is recurrent but I want to remind everybody on how we diagnose the Acute Pericarditis. So, there are four major criteria that we use. One is the chest pain, which is a sharp chest pain, usually is better when the patient is sitting up and leaning forward. Next is the precordial friction rub, which is also better auscultated when the patient is leaning forward. And then EKG changes, which typically [inaudible 00:03:01] elevation diffusely, and PR segment depression diffusely.

Farshad Forouzandeh ([03:05](#)):

But what I would like to emphasize is that the EKG changes, especially when we are talking about Recurrent Pericarditis, can be not present. So the EKG can be absolutely actually silent in the setting of Recurrent Pericarditis, because the diffuse elevation in ST and depression in PR segments, can completely normalize. The patient may go in and have diffused deep T inversions, but that also can normalize after a while. Therefore, the EKG changes are not as useful when we are talking about a Recurrent Pericarditis. They may or may not be present.

Farshad Forouzandeh ([03:40](#)):

The next also is precordial effusion, the findings based on the echocardiogram and other imaging modalities that can help. But what really distinguishes an acute episode of Pericarditis versus Recurrent Pericarditis is the time interval between the two, meaning that there should be at least four to six weeks

of symptom free interval, from the time that the patient had that first episode of Acute Pericarditis. And if they have any more symptoms after this four to six weeks symptom free interval, we would call it a Recurrent Pericarditis. The reason for this four to six weeks is the usual time that we have to basically spend to treat the patient, including the tapering of the medications that we use for Acute Pericarditis.

Farshad Forouzandeh ([04:28](#)):

So, let's say the patient comes back, they have two weeks of symptom free interval and they have another episode. That is not considered to be a Recurrent Pericarditis, but rather it is called Incessant Pericarditis. And also, if the patient continues to have symptoms for more than three months, that is when we are talking about Chronic Pericarditis. So really, the timeline changes the definition of which kind of pericarditis we are talking about. And the importance of actually knowing these categories is really when to go to the next line of the therapies, when to add other medications and think about what do next to treat these patients appropriately.

Farshad Forouzandeh ([05:10](#)):

And as a matter of fact, cases of Acute Pericarditis, the importance of full treatment, I would say, meaning that to include the medications that we have to do and to do the tapering correctly, is to avoid the Recurrent, actually, Pericarditis. Because many patients with Acute Pericarditis, if you do not treat them, they may actually get better, but the problem is many of them may come back with recurrent episodes. So that's really the goal of treating Acute Pericarditis, is to prevent, or at least decrease the chance of recurrent episodes of pericarditis. The other thing I would like to highlight here, is to look for inflammatory markers when we are talking about Recurrent Pericarditis, again, because some of the other changes like the EKG changes may not be as much present, is to look for fever, to look for leukocytosis, elevated ESR, elevated CRP, other inflammatory markers, to see if there's any episode of Recurrent Pericarditis going on or not.

Farshad Forouzandeh ([06:07](#)):

So that's how actually we defined really these two together, but also, clinically, I would like to highlight that there are some other features that we may see in Acute Pericarditis, such as the precordial effusion or even cardiac tamponade. These are less actually common in the setting of Recurrent Pericarditis. So that's also something to keep in mind about Recurrent versus an Acute episode of Pericarditis.

Katherine E. Di Palo ([06:34](#)):

I think that's a great overview, and really just understanding that timeline, the intervals, the presentation, it may not be the same as the initial, the EKG changes may or may not be there, but how common is this, Dr. Lin? How common is Recurrent Pericarditis, and are there any risk factors or predictors for recurrence?

David Lin ([07:00](#)):

Well, thank you for having me today. Pericarditis is the most common disease of the pericardium and viruses are the most prevalent ideology in the developed world. So up to about 30% of the patients with an Acute Pericarditis episode will experience a recurrence after the initial symptom free period of four to six weeks, and colchicine may have that risk. Patient with a history of Recurrent Pericarditis, however, are more likely to suffer from recurrent events. So about 50% will have additional attacks when treated with traditional NSAIDs alone.

David Lin ([07:37](#)):

The ideology of Recurrent Pericarditis remains unclear. It's likely related to some type of immunogenic response that perpetuates the underlying disease, instead of recurrent viral infections. Incomplete treatment certainly can contribute as well. Other factors, that will increase a recurrence, include a history of multiple prior recurrence. So perhaps recurrence begets recurrence, corticosteroids and female gender, these are all factors that leads to increased recurrences.

Katherine E. Di Palo ([08:09](#)):

I think it's really remarkable that colchicine can have a 50% reduction in recurrence. Dr. Forouzandeh, what is the role of colchicine now in Recurrent Pericarditis? Can you walk us through the literature or evidence that can give us direction on colchicine's role?

Farshad Forouzandeh ([08:29](#)):

Sure. Very actually important point, as you mentioned. In the setting of Acute Pericarditis, along with the aspirin or NSAID that we use to treat patients, we should use colchicine. And that is the 0.5 or 0.6 milligram twice daily, for basically to be followed for three months, in the setting of Acute Pericarditis. And in the setting of Recurrent Pericarditis, is to be followed at least for six months when we are dealing with Recurrent Pericarditis. And that's so important, and there are multiple actually trials that they actually showed the effect of colchicine to reduce the episode of further recurrence, if you will. One is the core trial, which was colchicine for Recurrent Pericarditis, and this was an 84 consecutive patients that were enrolled in this trial when they had their first episode of Recurrent Pericarditis, not the acute, but the Recurrent Pericarditis.

Farshad Forouzandeh ([09:27](#)):

And they were assigned to receive either aspirin alone or combination of aspirin with colchicine, and the dose there was one to two milligram on the first day, followed by 0.5 milligram once or twice daily, for six months. Again, the six months duration is the duration for colchicine use in the setting of Recurrent Pericarditis. And in this study, it was shown that the patient who received colchicine, the rate of further episode of recurrence was down to about 24 versus 51% at 18 months follow up. So, that was a remarkable actually decrease in the rate of further recurrent episodes. Again, another trial called Corp Trial, and this was colchicine for Recurrent Pericarditis trial. Again, they had 120 consecutive patients with their first episode of Recurrent Pericarditis that were randomized to a more broad anti-inflammatory therapy, including aspirin or ibuprofen or prednisone, in combination with colchicine in one group and in the other group with no colchicine with the same dosing, as we mentioned for the core trial.

Farshad Forouzandeh ([10:37](#)):

And also the similar findings, meaning that at 18 months follow up, the group that they had received colchicine, along with any of those three antiinflammatory agent, they had 24% versus 55% risk of actually further episode of Recurrent Pericarditis.

Farshad Forouzandeh ([10:56](#)):

Again, Corp Two Trial, this was a bigger study, 240 patients. They had two or more episode of Recurrent Pericarditis. So these are the patients that were even actually having more episode, more resistant to the initial treatment. And they were randomized again to placebo or colchicine for six months. These actually patients also had about 22% versus 51% in the control group for the risk of having further

episodes of pericarditis. So definitely there's a lot of studies, this three where some of them that I mentioned, but there are more actually randomized clinical trial. There are meta analysis actually showing the same thing and definitely, there's a huge role for this medication, the setting of Recurrent Pericarditis. However, there is also side effect profile that we need to be aware of as clinician prescribing this medication. The one that we are all familiar with is the GI, gastrointestinal side effect and intolerance, that can affect five to 10% of the individuals.

Farshad Forouzandeh ([12:00](#)):

And most of the time by lowering the dose and try to basically use a smaller dose, we can avoid that, or at least to some extent attenuate that. But the more serious side effects are very, very rare, meaning that it happened in less than one person or patient, that's for bone marrow suppression, [inaudible 00:12:18] toxicity, muscle toxicity. But again, those are very, very rare actually side effects and most people, even for other purposes, not for pericarditis, when they use this medication for decades in their life, they did fairly well. So again, I think this is a great medication to be used for this specific-

Katherine E. Di Palo ([12:37](#)):

And Dr. Lin, I want to get your perspective on colchicine because we heard in previous podcasts that the evidence is there, this is something we should be prescribing for the initial Acute Pericarditis, yet it's not always done in practice. We also know that yes, there are serious side effects, but patients often avoid taking medications because it's the common ones. They don't like the GI upset. And from your perspective, from your experience in practice, how often are you seeing non-adherence, whether it be from the provider or from the patient, that leads to a Recurrent Pericarditis?

David Lin ([13:15](#)):

Yeah, I think the difficulty with adherence to the medication it's in part due to cost, although colchicine has been around for decades and decades, at times, it can be relatively expensive, especially when you're talking about six months or longer in patients who have pericarditis. And often, we try to start [inaudible 00:13:39] in the United States at 0.6 milligrams daily, as opposed to twice a day, because it's easier for patient to take the medication, as opposed to having side effect and have to reintroduce the medication again. So I think these are risk factors, and with pericarditis although the mortality is extremely low, the morbidity is high, it can really affect the patient's quality of life. And when that happens, then people's behavior change and their compliance with medication change when they just don't feel well.

Katherine E. Di Palo ([14:14](#)):

Absolutely. And I think when it turns into a chronic therapy, the cost can add up, when you can know it can lead to polypharmacy, and these are all things that can impact adherence. While we're talking about medications, let's bring up corticosteroids. So in episode three, there was a great line from Professor Pircato, and he likened corticosteroids in pericarditis to selling your soul to the devil. Dr. Lynn, how should we approach corticosteroids in Recurrent Pericarditis?

David Lin ([14:52](#)):

Maybe not to the devil, maybe just the boogiemán. I don't know. Kidding aside, I mean, corticosteroids are actually extremely effective in alleviating pericarditis symptoms and suppressing the inflammation. However, they're numerous side effects, the need for prolonged use, the difficulty with tapering and the risk of a dependence, complicates their role. So I think the most important factor, and this has been

mentioned before, is that patient needs to be treated properly with the traditional insets and colchicine, at a correct dose, and then for the appropriate duration, because one risk factor is insufficient treatment.

David Lin ([15:33](#)):

So when we talk about adequate treatment, we talked about use ibuprofen 800 milligrams, three times a day, aspirin, a thousand milligrams, four times a day, indomethacin 50 milligram, every eight hours, and this is with colchicine. Now corticosteroids can be used and especially in patient who have refractory symptoms, despite high doses of insets and colchicine or low patient who has contraindications to insets and colchicine, but it really should be a third line therapy.

David Lin ([16:04](#)):

The other thing is, is that it's critical when we're using steroids to administer the lowest dose that's needed to achieve symptom resolution. And often, that's like 0.2 to 0.5 milligram per kilogram per day. And the lower dose has been associated with less treatment failure, less recurrence, less hospitalization and less adverse effect, than the conventional dose, which you see as a milligram per kilogram. Another high cause of recurrence is that we taper the steroids too quickly. The dose decrease really should only start when the patient is completely asymptomatic and their CRP has normalized. So typically, that doesn't happen for at least a couple weeks. And the tapering should be very slow, and we're talking about over months and not days, or weeks. And all efforts should be made to circumvent monotherapy with steroids. If a recurrence happen during tapering, avoid escalating the dose instead intensify insets, or introduce an analgesic.

David Lin ([17:08](#)):

And now there's robust data about using an interleukin one blocker in Recurrent Pericarditis, and it might become part of the treatment paradigm before we reach out for steroids. And as pericarditis symptoms can have a dramatic negative effect on the patient's quality of life, I think educating your patient about treatment course, the risk of recurrence, the extremely low mortality, will probably go a long way to provide some predictability and some reassurance about this very, very difficult condition.

Katherine E. Di Palo ([17:39](#)):

So to our listeners, we're going to be shifting gears a little bit, but really just in summary, the suboptimal management of the Acute Pericarditis really can lead to these recurrences. So it's so, so important the first time around, right drug, right dose, right duration. Now, optimal management, are there some best practices that health systems can utilize to improve outcomes? And are there opportunities for standardization? So I'm going to ask a couple different areas to Dr. Forouzandeh and Dr. Lin, how do you approach Recurrent Pericarditis and even the Acute Pericarditis, in terms of a standard practice, whether it's on the inpatient side or the outpatient of side, and often in transitions of care, as we know, this can be challenging from both patient provider and system perspective?

Farshad Forouzandeh ([18:35](#)):

That's actually a very good question, Katherine. Like anything else in medicine, if you are not thinking of a diagnosis, you actually are not going to diagnose that patient with that condition. So, so many of us dealing with patients coming to the emergency room with chest pain or coming to the office with chest pain, we are so focused on coronary artery disease, which of course is more prevalent. But at the same

time, there are patients that they have symptoms and sign suggestive for pericarditis that they can be overlooked.

Farshad Forouzandeh ([19:03](#)):

So it's so important upfront to have this differential diagnosis and think about it, get the appropriate testing going, diagnose the patient as [inaudible 00:19:14] to put the patients on right treatment from the beginning, something we have been emphasizing on these podcasts. For our actually system, we don't have as of now a protocol in place in terms of order set, let's say, but definitely one thing we are doing with our trainees, is to make the awareness, meaning that, keep the education going on. Any opportunity we have to interact with the Ed physicians, that they see these patients upfront to think about pericarditis under differential diagnosis.

Farshad Forouzandeh ([19:43](#)):

For our residents when they're seeing these patients, when they're reading the EKGs, to think about these things. As I mentioned, the EKGs are not a hundred percent. That's again, very important thing to consider because many times I see a trainee coming in and say, "Oh, this is not my pericarditis because the EKG is normal." So that's something that we should be careful about, to look at the whole actually patient as a system and not just one factor to rule in or rule out the diagnosis, such as pericarditis that sometimes can mimic many other conditions. So definitely I think there's more opportunity for education and definitely podcast series such as these are going to be helpful for our clinician, I would say also for trainees and for patients to know this entities exists. Because again, if we don't think of it, we are a not going to find it.

Farshad Forouzandeh ([20:32](#)):

We're not going to treat it appropriately. As mentioned by Dr. Lin, this is an entity that people may benefit a lot from reassurance, meaning that this is a condition we can take care of. It's going to be time consuming. It's going to be sometimes chronic. They have to come in and get the appropriate treatment to tolerate their actual medications. We may need to add proton pump inhibitors or whatnot, to be able to tolerate the NSAIDs, for example. So just give them the awareness, give them the expectations and then more education, more education and more education, to really get this awareness going on. So I think that will help a lot. Definitely having protocol in place and orders said if needed, but the condition is not as common.

Farshad Forouzandeh ([21:15](#)):

I would say again, just looking from a more practical aspect, because we all deal with electronic medical records systems and how complicated it can be to keep developing more orders, set more orders set for each condition, I think that can make things a little bit convoluted sometimes. So, but again, having the awareness, going for the right diagnosis and right treatment from the get go, I think that's the key to diagnosis this condition and treat it appropriately.

Katherine E. Di Palo ([21:44](#)):

And Dr. Lin, how about your practice? Any best practices or tips that you can share with our listeners when it comes to a standardized approach?

David Lin ([21:55](#)):

Yeah, no, I completely agree with the previous comments. Currently we don't have an order set ready, but it's a work in progress for us, but I think a order set is an excellent idea, and it will likely reduce the variability in patient treatment and also ensure that complete therapy with NSAIDs and colchicine,, while minimizing the use of corticosteroids. And if a steroid is used, we'll make sure that high dose and rapid tapering is avoided with a very detailed order set and a care path pathway. And not only that, if there's any concern about the treatment, we try to incorporate events imaging such as cardiac MR, to help with the diagnosis. So far, for our group, including our ER physicians, we rely on more educational programs such as again, journal clubs, grand rounds, and conferences to update our or physicians.

Katherine E. Di Palo ([22:51](#)):

The economic burden of Recurrent Pericarditis is significant, and that's from two perspectives, healthcare resource utilization and work loss. Dr. Lin, can you describe some of the drivers of these costs?

David Lin ([23:06](#)):

So patients with Recurrent Pericarditis can experience really debilitating symptoms, and the treatment are often prolonged with associated side effects. So when we look at records from insurance database, it shows about 15% of the patients with idiopathic pericarditis, experience at least one recurrence, and of those, about 40% go on to have multiple recurrences. And these recurrences has a medium duration, about three years. So this is a prolonged condition.

David Lin ([23:36](#)):

And the observed rates of hospitalization, outpatient visits, ER visits, are all significantly higher among patient who have multiple recurrence, than those without. So hospitalization is the main driver of increased healthcare costs between the multiple recurrence cohort versus the no recurrence cohort. And specifically, it's about threefold difference that was observed. In addition, then you have medical absenteeism, you have disability costs, and those are all significantly higher among patients who have multiple recurrences. The observed protracted disease course and the high cost associated with multiple recurrence, I think that emphasizes the need for targeted therapy, in addition to the conventional treatment that we have.

Katherine E. Di Palo ([24:24](#)):

In terms of the patient perspective, now they've been given a diagnosis and as you mentioned, mean duration of three years, this can really significantly impact health related quality of life, as well as that work impairment and these activity restrictions, they can be very frustrating. Dr. Forouzandeh, how do you approach the discussions on longitudinal management and the disease course when it can be years to resolution?

Farshad Forouzandeh ([24:57](#)):

Like almost any chronic condition, I think a very important thing is for the patient and the physician to develop that trust and relationship, and understanding that what the nature of this disease is. I think thee more relevant and pertinent information we can tell the patient about this condition, is going to help them to understand their expectations.

Farshad Forouzandeh ([25:20](#)):

In terms of the physical activity as I think it was mentioned in previous podcasts, there are very limited data available. It's not that we have a robust data on how much activity they can do. But just anecdotally, the very intense activity can actually, either because of more friction, more physical contact of the pericardium or some of the inflammatory pathways may get activated. So it is best to avoid those very intense activities, again, when the patient is having an active episode. And then other than that, moderate activity, healthy amount of activity and exercise is actually reasonable for these patients to continue.

Farshad Forouzandeh ([25:59](#)):

Again, we are talking about a condition which has chronicity as part of the nature of it. So you cannot have the patient for years, not to be a active and deal with other actually risk factors and so on and so forth going on. So having the connection with the patient, reassuring them about the nature of this disease and have the expectations, I think is so important. And many times, what other important factor is, these patients, they get this episode of chest pain and every time they have any sort of chest pain, they think they're having another episode. So they come to ED, they seek medical care, which is understandable. But again, if you tell them what they have to look for also beside the pain itself, that will help them to understand, is this going to be another episode that they should be worried about or not, or maybe seeing them sooner in the outpatient setting so that you can evaluate them appropriately.

Farshad Forouzandeh ([26:52](#)):

Many times, if somebody has put the patient on long term steroid, one thing that can help is to see if you can taper and maybe even stop the steroid for five to seven days, especially if the patient chest pain does not appear to be another episode. Just have them about a few days of not having a steroid and treat their pain with some analgesic and see how they do, and then re-exam the patient. Get the EKG, get the inflammatory markers if needed, do more imaging testing, chest extra echocardiography, again, as much as it's needed, to see if there's really an evidence for another episode of pericarditis or not.

Farshad Forouzandeh ([27:28](#)):

And it is surprising to see many of these patients, they may have chest pain for other reasons. They think it's pericarditis, but it is not. So you can avoid for them to come to the ED to be on more treatment for a longer period of time.

Farshad Forouzandeh ([27:43](#)):

And again, as this connection and trust develops, I think the patient would have a great relationship with you. And I remember one of my own patient, actually, he was out of town and he was doing a virtual visit few months ago, had a chest pain episode after about a year being completely symptom free. And he was worried, he was in another estate across the country. He asked for a virtual visit, we just did a visit with him. And from what he told me and I did some labs distance, and everything came out okay. And in about a week, I followed up with him, no more pain, nothing.

Farshad Forouzandeh ([28:14](#)):

But he was so worried that he didn't know what to do. He was in another estate. There would be insurance implications and the costs and not being in your hometown. So all pf those things, I think these are the patients we should be very attentive to. Again, dealing with chronic disease condition, you

have to have that kind of mentality when you are dealing with these patients, hopefully that will help them. And you can get them through this episode and this condition, hopefully successfully

Katherine E. Di Palo ([28:39](#)):

Dr. Lin, what's your approach when it comes to both shared decision making and education? Do you utilize multidisciplinary team, because it's a lot for patients? And I think that point that Dr. Forouzandeh brought up, which is understanding what's normal in terms of the chronic disease versus what is not, to avoid that unnecessary ED utilization, especially when it's ED utilization and the patient isn't known, so they may undergo a complete workup again for chest pain. So what are some best practices from your perspective, for longitudinal management?

David Lin ([29:21](#)):

I think the most important thing moving forward once the patient has been diagnosed with Recurrent Pericarditis, is that availability of the physicians to the patients and also to have frequent follow ups. And Olo's approach will minimize the risk of patient going to the emergency department, which itself is a big cause for the healthcare system, and also for the patient. We also educate our nurses as well, because they're usually the frontline when the patient call, and show a lot of empathy when they go through with the patient as to what is going on and what their symptoms are.

David Lin ([30:00](#)):

And often, as we walk through the symptoms with the patients, sometimes with additional diagnostic testing, whether it is inflammatory markers or echocardiography or cardiac MRI, doing those things can usually help the patient manage their disease, without being admitted to the hospital or without going to the emergency department.

Katherine E. Di Palo ([30:24](#)):

Well, this has been a really great discussion. And the first as we switched from Acute Pericarditis to Chronic and Recurrent Pericarditis. So thank you to Dr. Lin and Dr. Forouzandeh for joining me. Thank you to our listeners for joining and participating in this episode, Beyond Acute Recurrent Pericarditis. This podcast series on pericardial disease is supported by an education grant from Kiniksa Pharmaceuticals. For more education opportunities, please visit the AHAs website [@learn.heart.org](#), and be sure to tune in for our next episode, The Pathophysiology of Recurrent Pericarditis. Thanks again.