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## Looking into Long-Term Cardiovascular Impacts of COVID-19

### Dr. Sorrentino:

You're listening to *Heart Matters* on ReachMD. I'm Dr. Matthew Sorrentino. And joining me today to discuss the long-term cardiovascular impact of COVID-19 is Dr. William Li. Dr. Li had spoken to us earlier in the pandemic about COVID-19 complications, but now we're going to explore so-called "long COVID" and its effect on the heart.

Dr. Li, welcome, and great to have you back.

### Dr. Li:

Well thank you, Dr. Sorrentino. It's great to be back.

### Dr. Sorrentino:

We are still living in COVID. I can't believe it's two years later or more and we're still in our COVID pandemic. And I know in my practice in cardiology we're seeing more and more patients who had COVID a year ago, two years ago, and still having symptoms. Can you explain to us some of these long-term cardiovascular effects that you're seeing in patients who have recovered from COVID-19?

### Dr. Li:

COVID is a new human disease, and as we have studied it and started to understand what we're up against, we're seeing that it's a condition that actually has two parts. There's acute disease, which has a great deal of variety in its presentation and its severity, everything from asymptomatic to critically ill to a lethal illness. And the classical thinking is that you have it for ten days, and then you're safe to go back, and you're mostly recovered, and that, I think, has held true for the majority of people. However, in about a third of the people, we actually know that there are long-term sequelae. We call this the post-acute sequelae of COVID, or PASC, more commonly known as long COVID, and this also involves the heart.

We have lots of other symptomatology—brain fog, fatigue—but the heart is one of the ones that I think patients notice immediately because they can have racing heart; they can have chest pain. These are sort of symptoms that often will bring people right to medical attention because they're worried that it may actually be another manifestation of serious underlying heart disease, like coronary disease.

### Dr. Sorrentino:

So acutely, we are seeing patients who clearly have cardiovascular risk of COVID. We certainly have seen patients with myocarditis. Is there any evidence that patients who have had more of a severe infection in the hospital, myocarditis—are they more susceptible to long COVID? Or even if you had mild symptoms not requiring hospitalization, can you still have some of these manifestations a year later?

### Dr. Li:

Yes, you can. And we're just now starting to peel apart, really observationally, what some much these longstanding effects can be.

So myocarditis can be one of the significant symptoms of long-term cardiovascular complications of COVID. But this study from the VA I thought was really interesting. It involved 11.5 million people over the course of 12 months and looked at people a year later and compared them to contemporary and historical controls to see what cardiovascular complications would be above and beyond what the baseline would be. And so myocarditis and pericarditis were found to be 85% or higher elevated in terms of risk for people who actually had recovered from COVID, and the risk of these cardiovascular complications increased based on the severity of their illness, meaning that if they weren't hospitalized, they had some risk; if they were hospitalized, they had greater risk; and then if they were in the ICU, it was even a higher risk for cardiovascular complications, including myocarditis.

**Dr. Sorrentino:**

I would say that one of the most common complaints I see in patients following COVID is palpitations. This POTS, postural orthostatic tachycardia syndrome, which seems to be a common sequelae that we are seeing in many of these patients. How do these patients present? And what are the classic symptoms that would make you think about POTS in a patient?

**Dr. Li:**

Right. Well, sudden onset of palpitations, tachycardia classically, is one of the manifestations of POTS, and it's called POTS because it's often postural, so changing position from sitting to standing or even walking upstairs and changing your position can often trigger this. Now the actual etiology of POTS is not quite fully worked out. Some people believe that there's a vagal component to it as well, so a disinhibition from the vagus nerve may also be one of the components. The pathophysiology is something that I'm really digging deep into to try to understand what is causing this panoply of cardiovascular symptoms. For POTS, these can be young people, they could be very physically fit, some of them can be athletes, and they can go from having fatigue and then sort of recovering to suddenly realizing that they get lightheaded and they start feeling palpitations when they change their position.

**Dr. Sorrentino:**

It has been frustrating in the past to treat patients with POTS. I'm sure this is true also with the post-viral form of POTS. Is there any recommendations that you can give to some of these patients on how they can relieve some of these symptoms?

**Dr. Li:**

I'm going to kind of put on my researcher's hat and try to give you kind of a deep dive because POTS in long COVID clinics, which are now getting to be established around the country, there are different techniques that people are using to kind of address POTS. What I'm interested in is really understanding the pathophysiology. And something that my group was involved with in the very early part of the pandemic, in May 2020, we actually took a look at autopsy tissues of people who had died of COVID. So these were often people in the ICU. And we looked not only in the lung, but we looked in all the organs, including the heart. And one of the common denominator features that we saw under the electron microscope was the actual coronavirus, the SARS-CoV-2 virus, binding to and entering the vascular endothelial cell. This was happening in the lung. It was happening in the heart. It was actually happening in the testes. It was happening in the liver. We saw this all throughout the body in autopsy studies. And what we began to theorize that has now turned out to be, I think fairly well-accepted is that there is a clear microvascular pathology, a microangiopathy that occurs in COVID.

And so one of the big questions, including in the myocarditis, in the dysrhythmias, even in the ischemic heart syndromes, in the thromboembolic syndromes, is whether or not there's endothelial damage. Now endothelial damage is not only in the in the larger vessels, but can also happen in a vasa vasorum, and in the vasa nervorum, or the microcirculation supplying nerves as well. So that's another interesting part of this pathology is, are we actually having viral pathology along the vessels that are feeding the nerves, and does that contribute to the dysrhythmia?

**Dr. Sorrentino:**

For those just joining us, you're listening to *Heart Matters* on ReachMD. I'm Dr. Matthew Sorrentino, and I'm speaking with Dr. William Li about the long-term cardiovascular complications caused by COVID-19.

Will, you mentioned these vascular effects of the virus. I assume that that also may increase the risk for thrombotic events. Are we seeing long-term thrombotic events with long COVID patients as well?

**Dr. Li:**

Yes, absolutely. The VA study I was referencing that looked at 11.5 million patients and compared, the incidence of long-term, meaning 1 year out, thromboembolic events did indeed find that there was an elevated risk of pulmonary embolism by 2-fold compared to case controls, DVTs, deep vein thrombosis, also by 2-fold, and even superficial vein thromboses. So you would not normally expect this after a typical viral infection, an influenza or some other type of upper respiratory infection to manifest itself a year out. And we really do believe that the microthrombosis that we've clearly documented in acute disease may wind up also happening in long-term disease for similarly this, continued microvascular damage.

Now the question that comes up is, Why isn't the endothelial repaired? Why is there continued injury? Endothelial cells will repair themselves. We've got progenitor cells that come from the bone marrow that are stimulated as a matter of physiological repair. And so one of the other questions that arises in people with long COVID is whether or not there are hidden reservoirs of the SARS-CoV-2 that are maintained in the body as long as a year or even more.

**Dr. Sorrentino:**

Do you have any sense about how long it takes for patients to get better, or is this going to be even longer term for many of these patients?

**Dr. Li:**

So here we are with 1 pandemic that seems to be abating from the initial serious surges, and so people are starting to relax, but the fact that if there are these long-term sequelae, especially cardiovascular sequelae, coming out a year later—you're talking about a second pandemic to emerge from the first. And when it comes to cardiovascular disease, you're talking about another situation that can not only compromise the quality of life, and literally, you know, the VA study showed that there was increased cardiogenic shock, increased MI, increased stroke; these are lethal complications—this also potentially threatens to once again overburden the healthcare system. I think we need to realize that we're still very much, in the medical community, at the beginning of understanding a new human disease. The acute disease we're starting to get a better handle on, but I think that there are some real mysteries about these long-term conditions that we all need to be not only intellectually engaged in as physicians and healthcare providers, but I think we need to be concerned about from a public health perspective as well.

**Dr. Sorrentino:**

So I guess we're going to be talking about this for a long time to come. So, Will, thanks so much for joining us today. It was great speaking with you.

**Dr. Li:**

A real pleasure, Matt. Thank you for having me on.

**Dr. Sorrentino:**

For ReachMD, I'm Dr. Matthew Sorrentino. To access this and other episodes in our series, visit [ReachMD.com/HeartMatters](https://ReachMD.com/HeartMatters), where you can Be Part of the Knowledge. Thanks for listening.