Transcript Details
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How Does COVID-19 Affect the Heart?

Dr. Brown:
It has become clear throughout the COVID-19 pandemic that the lungs are far from the only organ ravaged by this disease. The heart, like many others, is deeply affected by the virus, and now that a series of autopsies have pinpointed the cardiac changes that occur, today we're going to be exploring those changes, and how they're different from what anyone might have expected.
For ReachMD, this is Heart Matters, and I'm Dr. Alan Brown. Joining me today is Dr. Richard Vander Heide, Professor and Director of Pathology Research at LSU Health, New Orleans School of Medicine, who led a team of pathologists that performed autopsies on COVID-19 patients. Dr. Vander Heide, thank you so much for joining the program today.

Dr. Vander Heide:
Thank you for having me, it's a pleasure.

Dr. Brown:
So, I'm fascinated by your research, so we might as well jump right into the discussion. Can you share with us what you expected when you first set out to do autopsies on your first COVID-19 patients?

Dr. Vander Heide:
Sure, that's actually a great question, because that's how I really got interested in this in the first place, because when the pandemic first hit, people were wondering exactly what was gonna happen in terms of which organs are gonna be affected. So I did a little bit of reading, and turned out that some of the earlier studies that came from China had indicated that there was fulminant myocarditis present in 7% of the patients that they had seen in China. So, knowing that, I thought, well certainly myocarditis is as a big concern for patients in the U.S. as well, so when we started these autopsies, we were very interested, and expected actually, to see at least some degree of what we call myocarditis.

Dr. Brown:
So, we heard that same discussion, that there was a lot of myocarditis going on. So what did you actually see that led you to conduct this study?

Dr. Vander Heide:
Well, it's interesting. We were fortunate, because here in New Orleans, we have a brand new hospital. So we jumped in right away, knowing that we had the facilities that were able to do it, and so, when we first started these autopsies, we noticed, the lung changes, which we published earlier. But in that same study that we published in Lancet, we also included ten hearts that we had also seen with some of those early patients, and what we documented in that particular early publication was that we did not see what was typically associated with myocarditis. And so, of course we've done several more autopsies and now we're up to almost 40 autopsies in our series here. And again, we were extending our study, looking again for the presence of myocarditis as is typically defined. And we have not been able to find anything in an adult patient to date that looks like myocarditis as defined by the old Dallas criteria which everybody's familiar with.

Dr. Brown:
So, can I ask you a little bit about how you designed the study? Were there clinical cues that suggested myocarditis to the clinician, or were these autopsies on patients with COVID in general?

Dr. Vander Heide:
Yeah, that's a great question. So this is a sequential autopsy study, so we took the first 22 cases that we were able to obtain family

permission for the autopsy, and again it's important to note that these are all patients who died of COVID-19 disease.

Dr. Brown:
Yeah, so necessarily having clinical suggestion of myocarditis.

Dr. Vander Heide:
Not necessarily, but in some patients, there was certainly concern, because a lot of these patients had small bumps in cardiac enzymes the more sensitive ones were the troponin enzymes, and so there was concern amongst the clinicians whether there was cardiac damage. And of course, they had read the same studies we did, so there was a lot of concern early on with the ICU teams and the pulmonary critical care teams, as well as the cardiologists, whether there was actual cardiac manifestations that were accelerating or contributing to these patients' demise.

Dr. Brown:
For those just tuning in, this is Heart Matters on ReachMD. I'm Dr. Alan Brown, and today I'm speaking with Dr. Richard Vander Heide about his study that found surprising cardiac changes in COVID-19 patients. So, Dr. Vander Heide, then let's jump right over to the results of your study, a little bit about what it was designed, and then, what the overall findings were.

Dr. Vander Heide:
Yeah, so we took a sequential series of 22 autopsies, and what we did is we dissected the heart and submitted routine sections to look at the heart microscopically. But we also went back and looked at all the clinical values that these patients had when they were in the ICU and when they were in the hospital. So we were trying to correlate together some of the laboratory findings with what we were finding with the microscopic findings . And so, what we had found, interestingly, the hearts ranged in size from 340 grams to over a kilogram, so they were some people with significant hypertension, and of course, they had the same comorbidities that everybody reads about. But what was interesting in light of what the concern was with the clinicians regarding presence of cardiac injury and perhaps significant injury was that we didn't really find any significant atherosclerosis, which we defined as a narrowing of greater than 50% in any vessel. That was only present in about five of our 22 patients. And more importantly, we didn't identify any acute coronary thrombi whatsoever. One thing we did find that was interesting was that in several patients, there was a severe right ventricular dilatation, which we defined as the ratio between the right and left ventricle cavity of greater than 1:1. And that was present in nine cases, and that seemed to be associated with a large increase in brain natriuretic peptide, or BNP. So what we hypothesized was that a lot of the cardiac injury that people were probably seeing with the small elevations in troponin was actually related primarily to the pulmonary disease. And so what we think happened was the severe stress on the pulmonary circuit from the underlying pulmonary disease in some patients, as well as obviously the severe diffuse alveolar damage that these patients were suffering, put a lot of stress on the heart, and that stress resulted in dilatation of the right ventricle, as well as, accounted for the small bumps in cardiac enzymes that were seen in these patients.

Dr. Brown:
Yeah, that's fascinating. Well obviously, there's a big focus on the thrombotic characteristics of the disorder now, and the incidence of pulmonary emboli in these patients. I'm sure it goes without saying that you looked for that in the lungs of the patients who had the RV dilation, and I'm assuming that they had RV dilation independent of pulmonary emboli.

Dr. Vander Heide:
Yes, exactly. They had that independently of the pulmonary emboli, but as you indicate virtually all of these patients had some degree of microvessel thrombotic presence in the lungs. A couple of patients had a large pulmonary embolus, which was the cause of death in that patient, but interestingly, he also had a D-dimer of 45,000, which is extremely elevated. So, we're correlating along with all the other things that we're monitoring currently as our study continues. We're looking at the coagulation parameters from a clinical standpoint, and trying to better correlate with patient outcome as well as what we're seeing in the lungs as well as the heart.

Dr. Brown:
Yeah, that's fascinating. So putting together what you found and a lack of finding myocarditis, which certainly all of us have expected was common, what should we take away from the work that you've done, and how do you think we ought to use that information to better treat our patients?

Dr. Vander Heide:
Well I think in a more basic level I've developed a hypothesis related to what we saw in the hearts. More importantly than that, the lack of myocarditis led me to think about different potential basic cellular mechanisms for these cells to die, because the stress on the right side indicated the left side was suffering increased stress as well. But that really, in the absence of significant coronary disease, doesn't usually generally cause a significant myocyte necrosis. So, I've looked a little deeper into the literature, and there were some early studies that came out from China that the virus itself actually has a significant propensity to invade endothelial and parasites. So

endothelial cells and parasites, which are the cells that are wrapped around endothelial cells, although only 16% of the cells in the heart, seem to be carrying about 70% of the viral load. So reading that, I really started to think about this being primarily a vascular disease, and so what I think is going on is that the virus enters through the ACE2 receptors, and they're present in the heart as well as the endothelium. And so I think what's going on is the virus is disseminating through vascular channels, and what that is causing is reaction in endothelial cells, which at the very small vessel level, can lead to increased clotting, which we are seeing in all the other organs. So I think the endothelial involvement leads to some small vessel thrombosis in the heart, probably through platelet thrombosis, which can lead to these small amounts of myocyte necrosis in the associated small increase in cardiac enzymes.

Dr. Brown:
So, I assume that high pulmonary pressures might be part of the reason for the right heart failure as well as the cardiac involvement.

Dr. Vander Heide:
So basically, what happens is the infection goes to the endothelium and the parasites. And of course, in addition to that, there is also cytokine generation through the infections. So, I'm not sure whether there is direct injury from the cytokines which is causing endothelial dysfunction, thrombosis, or whether it's the infection of the virus itself into the endothelium, but whatever it is, I think the combination of the diffuse alveolar damage which is causing an increase in hypoxia and workload on the right side, coupled with this endothelial dysfunction/thrombosis, is really what's leading to these small individual myocyte necroses that we're seeing. Although there's lots of studies that suggest that the troponin levels correlate with outcome, I think that in adult patients, at least, the small enzyme releases that people are seeing in these patients are related primarily to stress induced by the pulmonary effects on the right side circulation, crossing over and causing these stresses on the left side, which in the face of this endothelial infection, and/or cytokine generation, leads to the necrosis.

Dr. Brown:
Have you looked at patients who present with what looks like an acute coronary syndrome by ECG and enzymes? There have been some publications suggesting that probably the virus leads to plaque rupture and may promote an acute coronary syndrome by that mechanism. So I'm wondering have you, or are you interested in looking at patients who present with ST elevation who have COVID, that end up expiring?

Dr. Vander Heide:
Yeah absolutely we are. And that's what we're always looking for, and in fact, the case we did yesterday was exactly the situation. There was a patient who had been diagnosed with COVID in June, had apparently recovered, and then presented with an acute coronary-type presentation. So we're very anxious to find out what we're gonna see in his heart. But, in addition to that, we've also had a case recently which we published in Annals of Internal Medicine. It was a 31-year-old African American woman, who had also had COVID, recovered, and then presented with an acute cardiac arrest and died. She's 31, you wouldn't expect to have a lot of coronary disease. But we didn't see any kind of an acute arterial thrombosis in her either, even though she presented with what looked to be like an acute coronary event like anybody else would. But what we did see was, again, some of these same vascular changes that we saw with the other patients, but they seem to be more severe. And so we thought that actually may have been a manifestation of the multi-inflammatory system disorder that has been described more recently in children, rather than adults. But I think that was a secondary post-inflammatory response. But I think the heart, it still can be a primary target of that secondary infection, which is why I think we are seeing all these cardiac findings in kids, is that their primary infections might be very minimal or mild, but when they get another exposure, I think the secondary response seems to be centered on the heart, and it's not so much a coronary thrombosis as it is a vascular swelling and occlusion through that mechanism. We don't have a lot of direct data to support that yet, but we're still working on gathering more to support that hypothesis.

Dr. Brown:
I hope we have a chance to speak to you again, as those theories continue to be investigated in more detail. So, thank you Dr. Vander Heide, for joining me to talk about these fascinating results. It was great having you on the program.

Dr. Vander Heide:
Thank you, Dr. Brown

Dr. Brown:
For ReachMD, I'm Dr. Alan Brown. To access this episode, and others from Heart Matters, visit www.reachmd.com/heartmatters where you can Be Part of the Knowledge. Thanks for listening.