Connecting the dots between heart disease, potential for worse COVID-19 outcomes

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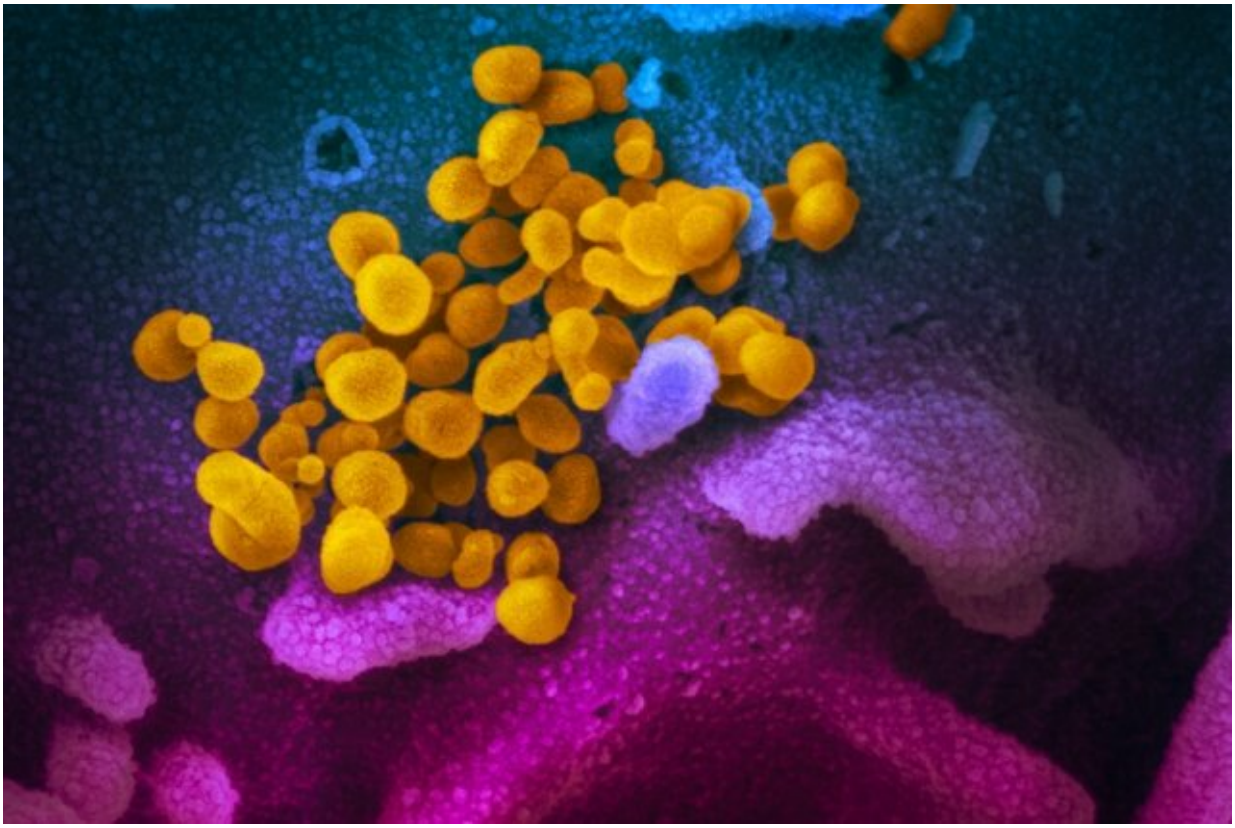

This scanning electron microscope image shows SARS-CoV-2 (yellow)—also known as 2019-nCoV, the virus that causes COVID-19—isolated from a patient, emerging from the surface of cells (blue/pink) cultured in the lab. Credit: NIAID-RML

People with certain heart diseases may be more susceptible to worse

outcomes with COVID-19, but the reason why has remained unknown. New research from Mayo Clinic indicates that in patients with one specific type of heart disease obstructive hypertrophic cardiomyopathy (HCM) the heart increases production of the ACE2 RNA transcript and the translated ACE2 protein.

Normally, this pathological response at the cellular level might be the heart's attempt to compensate for changes caused by disease. Unfortunately, SARS-CoV-2, the virus that causes COVID-19, hijacks these ACE2 receptors on the membrane of cells and uses them to get inside the cells. The virus not only gains entry through ACE2, but also it takes this protein with it, removing a protective signaling pathway that normally counters the negative impact of the hormone angiotensin II. This hormone increases blood pressure and leads to fluid retention.

Over the course of a nearly 20-year study published in *Mayo Clinic Proceedings*, researchers analyzed frozen samples of heart muscle tissue from 106 patients who had surgery for obstructive hypertrophic cardiomyopathy. The control group used heart tissue from 39 healthy donor hearts.

"Of all the RNA transcripts in the entire human genome, our research revealed that the single most upregulated RNA transcript in the heart muscle was ACE2. In fact, we confirmed a fivefold increase in ACE2 protein levels in the heart muscle of these patients with obstructive HCM," says Michael Ackerman, M.D., Ph.D., a genetic cardiologist at Mayo Clinic. "This could connect the dots and potentially explain why patients with certain heart diseases might fare worse with COVID-19."

Dr. Ackerman is director of the Windland Smith Rice Sudden Death Genomics Laboratory at Mayo Clinic and senior author on the study. This study involved national and international investigators.

The next step is to look for other elevated ACE2 levels by analyzing available heart tissue from patients who have died from hypertension and other heart diseases. Lung tissue from COVID-19 victims also could be analyzed to see if ACE2 levels are higher than in normal lung tissue.

"This discovery provides another reason for patients taking angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers to stay on their heart medications, as recommended by all major cardiac societies," says Dr. Ackerman. "Removing these medications in a patient whose heart has elevated protein levels of ACE2 could cause even more tissue damage."

Provided by Mayo Clinic