Long COVID-19 exercise capacity linked to abnormal blood clotting markers

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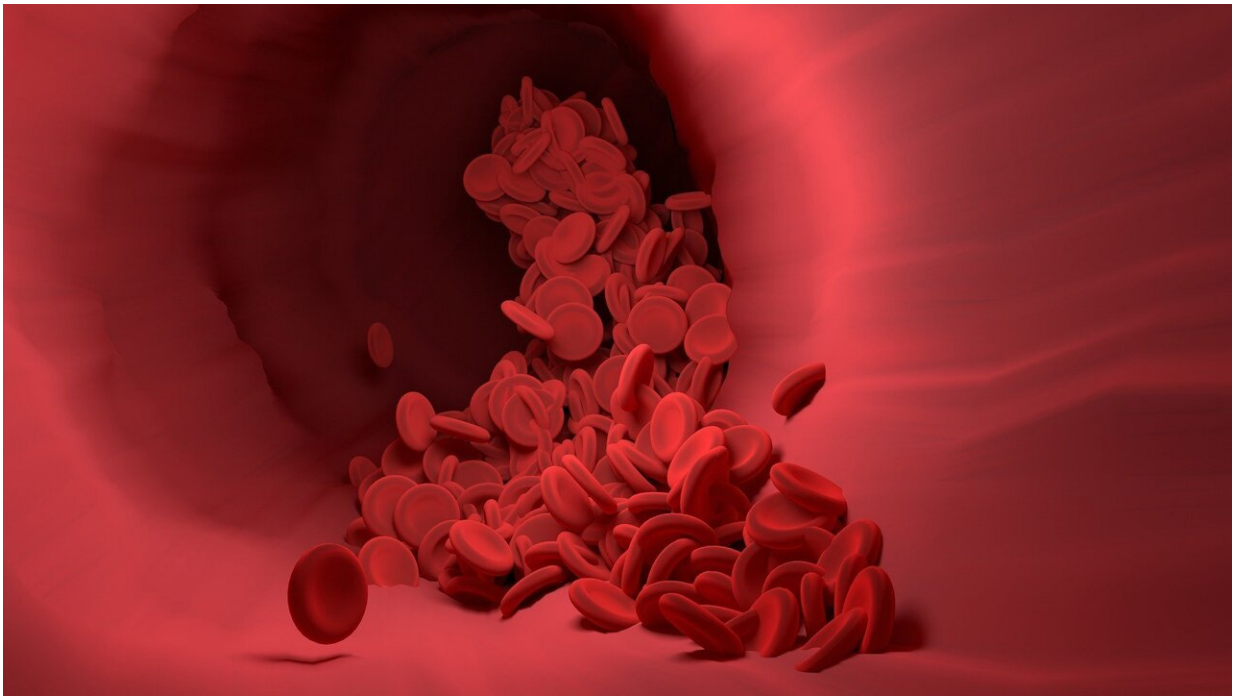

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According to a study published today in *Blood Advances*, people suffering from long COVID may face an increased risk of abnormal blood clotting. Investigators also found that this blood abnormality was four times more likely in those experiencing difficulties with basic exercise more than 12 weeks after their COVID-19 infection. The study, the first to report an association between abnormal blood clotting tests

and reduced exercise capacity in people with long COVID, offers important new insight into the potential mechanisms behind the longer-term effects of COVID-19 infection.

Long COVID (also known as Post-COVID Syndrome), a condition that occurs in people previously infected with COVID-19, results in symptoms that persist months after the initial onset of infection. Common symptoms include fatigue, chest pain, shortness of breath, and brain fog, and one study published in *JAMA Network Open* estimates that up to half of all people who recover from infection continue to experience lingering symptoms. Since long COVID is an emerging condition, its biological basis is not fully understood. This research provides insight into the underlying medical mechanisms, such as damage to cells that line blood vessels, of the disease.

"By definition, this syndrome occurs when one experiences COVID-related symptoms long after the onset of infection that we can't attribute to any other cause or diagnosis," explained study author Nithya Prasannan, of the Department of Haematology at the University College London Hospital. "This study offers us laboratory and clinical evidence to begin to understand why some people experience long COVID symptoms."

To conduct this study, a team led by Dr. Melissa Heightman assessed people in an outpatient Post-COVID clinic between July 2020 and May 2021. Participants were said to have long COVID if they experienced symptoms three months after the onset of their original COVID-19 infection and if those symptoms persisted for at least two additional months—in the absence of other contributing diagnoses.

Researchers measured abnormal blood clotting markers by assessing the relative levels of two proteins in the body. They analyzed the ratio of Von Willebrand factor (VWF), a protein important in blood clotting, to

ADAMTS13, a protein that cuts or splices VWF to prevent it from clogging blood vessels. If this ratio was raised, meaning that there was significantly more VWF than ADAMTS13 in the bloodstream, scientists characterized patients as being in a pro-thrombotic state, meaning that they could face a greater risk of developing blood clots.

Participants also completed exercise tests, performing timed activities such as walking on a flat surface and/or repeatedly going from sitting to standing position from a chair while wearing oxygen monitors. Researchers measured oxygen levels and tested participants' blood before and after exercise to measure their lactate levels, which helped describe participant response to exertion. During exercise, the body converts glucose (sugar) into energy using oxygen. However, when oxygen levels are depleted, the body starts producing lactate instead, which can be turned into energy without oxygen. In the study, patients who exhibited a significant decrease in oxygen levels (measured by a sensor on the patient's finger) while exercising and/or a rise in lactate afterward were said to demonstrate an impaired exercise capacity. Notably, patients with raised levels of blood clotting markers were also four times more likely to have an impaired exercise capacity.

In the future, Dr. Prasannan and her colleagues aim to assess patient bloodwork using different research platforms over the course of their long COVID illness to assess how their risk of thrombosis might change with the progression of their symptoms. She suggested that this additional monitoring could not only help confirm possible mechanisms underlying long COVID, but also offer insight into the effects of potential treatment options for the condition.

"I hope that people will view this research as a step forward in understanding what causes long COVID, which will hopefully help us guide future treatment options," explained Dr. Prasannan. "I encourage people experiencing long COVID to participate in clinical trials when

available because the more data we have, the better we can understand this condition."

More information: Nithya Prasannan et al, Impaired exercise capacity in post-COVID syndrome: the role of VWF-ADAMTS13 axis, *Blood Advances* (2022). DOI: 10.1182/bloodadvances.2021006944

Destin Groff et al, Short-term and Long-term Rates of Postacute Sequelae of SARS-CoV-2 Infection, *JAMA Network Open* (2021). DOI: 10.1001/jamanetworkopen.2021.28568

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