The infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can lead to a new disease called long-COVID-19 or post-acute COVID-19 syndrome. Although over 200 symptoms have been reported, the most common are breathlessness, fatigue, and cognitive impairments. The authors from the United Kingdom and Germany conducted this pilot prospective study to evaluate hyperpolarized (HP) xenon 129 (129Xe) magnetic resonance imaging (MRI) measurements of the pulmonary red blood cell (RBC)-to-alveolar tissue barrier ratio, as a surrogate of abnormal gas exchange, in patients diagnosed with post-COVID syndrome.

Most patients with long COVID syndrome typically have normal pulmonary function test results, and some have a normal or mildly abnormal diffusing lung capacity for carbon monoxide (DLCO). In some patients with post-COVID syndrome, chest computed tomography (CT) scans revealed fibrotic lung abnormalities that may be partially responsible for their respiratory symptoms. Certain studies that used cardiac magnetic resonance imaging (MRI) to investigate the prevalence and extent of cardiac abnormalities in patients diagnosed with post-COVID syndrome have found that 8% of patients with normal cardiac results had pulmonary abnormalities (fibrosis/atelectasis).
https://discovermednews.com/non-ischemic-myocardial-fibrosis-in-long-covid-patients/

Hyperpolarized 129Xe MRI pulmonary measurements are driven by the unique properties of inhaled 129Xe gas, which in the healthy human lungs instantaneously fills the terminal bronchi and lung parenchyma, participates in transmembrane diffusion through the alveolar-capillary membrane, and binds to red blood cells (RBCs) in the pulmonary capillaries. This pulmonary functional imaging method provides a noninvasive way to simultaneously capture a subvoxel snapshot during inhaled gas delivery, flow, diffusion, and RBC binding throughout the entire lungs.

It should be noted that the HP129Xe MRI scan provides regional information on pulmonary vasculature integrity and enables the assessment of ventilation and gas transfer across the alveolar epithelium into RBCs even when CT scans and lung function test results are normal or nearly normal.

***About the Study and Results***

The authors investigated HP 129Xe MRI measurements of the pulmonary RBC-to–alveolar tissue barrier ratio, as a surrogate of abnormal gas exchange, in small groups of nonhospitalized and posthospitalized patients diagnosed with long COVID syndrome. The participants also had chest CT scans, spirometry, a 1-minute sit-to-stand test, and measurements of hemoglobin level and Dyspnea-12 score.

36 participants were enrolled, 11 diagnosed with post-COVID syndrome who had never been hospitalized for acute COVID-19, 12 with post-COVID syndrome who had been hospitalized for acute infection, and 13 healthy volunteers who had not been infected with SARS-CoV-2. The SARS-CoV-2 infection was confirmed by reverse transcription–polymerase chain reaction or positive anti-SARS-CoV-2 antibodies. Hospitalized post-COVID Patients had no history of intubation. None of the nonhospitalized post-COVID patients had evidence of previous pneumonia, but the authors mentioned the possibility that all were not imaged during their acute infection. Participants with long COVID syndrome had no evidence of interstitial lung or airway disease or a history of smoking more than ten packs a year.

The mean time from infection with SARS-CoV-2 was 287 days ± 79 days for nonhospitalized participants and 143 days ± 72 days for posthospitalized participants.

Both groups of long COVID patients, nonhospitalized and posthospitalized, had breathlessness, with mean Dyspnea-12 scores of 9 ± 5 and 10 ± 5, respectively. The mean hemoglobin level for nonhospitalized and posthospitalized participants was 144 g/L ± 15

and 145 g/L ± 14, respectively. There was no evidence that oxygen saturation changed before or after the mBORG sit-to-stand test.

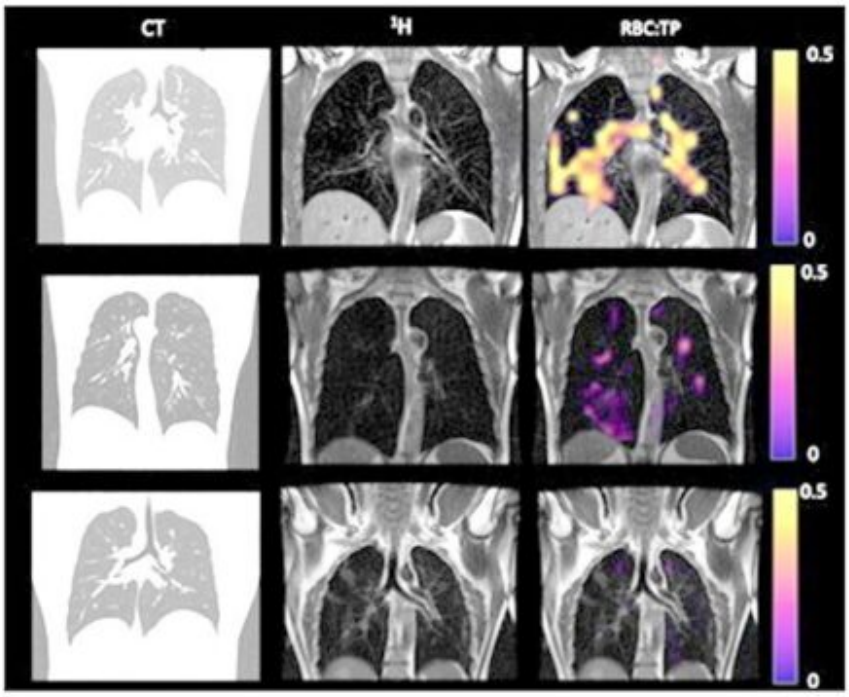
CT findings were normal or nearly normal. The spirometry measurements did not differ between the two subgroups.

*HP 129Xe MRI measurements of the pulmonary RBC-to–alveolar tissue barrier ratio*

Both groups, nonhospitalized and posthospitalized patients had significantly lower 129Xe MRI RBC-to-alveolar tissue barrier ratio than healthy volunteers, which indicates abnormal gas exchange. The HP129Xe MRI scan abnormalities were only marginally greater in the posthospitalized participants than in the nonhospitalized participants, but there was no significant difference between the two subgroups.

The non-hospitalized group had a lower DLCO, which measures pulmonary vascular integrity, than the posthospitalized group, and its values correlated with the RBC-to–alveolar tissue barrier ratio. The authors stated that the nature of this abnormality needs further investigation.

According to the authors, pathophysiological mechanisms that underlie the changes in HP129Xe MRI after COVID-19 remain unresolved. A lower 129Xe MRI RBC-to-barrier ratio in long COVID patients suggests that SARS-CoV-2 infection may have caused some microstructural abnormality to one or two volumes, such as pulmonary embolism, pulmonary blood flow alterations, or alveolar membrane thickening, which leads to decreased blood volume. It is expected that these factors decrease diffusing capacity.




CT, proton ($^1$H), and proton and RBC:TP imaging from post-hospitalized COVID patients. There is minimal damage on CT, and yet highly heterogeneous and low RBC:TP in the lungs of post-hospitalized COVID-19 patients.

*Picture from the original article of Grist et al.*

*Conclusion*

Hyperpolarized pulmonary xenon 129 MRI measurements of the pulmonary red blood cell-to-alveolar tissue barrier ratio showed abnormal gas exchange in patients diagnosed with long COVID syndrome. A lower 129Xe MRI RBC-to-alveolar tissue barrier ratio was detected in both, posthospitalized and nonhospitalized participants, suggesting abnormal oxygen and carbon dioxide gas exchange.

The authors concluded that underlying pathophysiological mechanisms behind post-COVID

symptoms remain poorly understood, making treatment decisions hard, if not impossible.

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### *Journal Reference*

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