Post-acute COVID-19 condition or syndrome (PACS), defined as persistent symptoms that persist for more than 12 weeks following the initial infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can affect individuals of all ages. Children and adolescents commonly have less severe variants, but persistent cardiopulmonary symptoms, such as chronic fatigue, dyspnea, headache, and cardiac palpitations, are reported in these age groups. In this study, German authors utilized phase-resolved functional lung (PREFUL) magnetic resonance imaging (MRI) to investigate pulmonary dysfunction in pediatric post-COVID syndrome. The authors stated that the lung function in children and adolescents with PACS differs from that of healthy children and that characteristics of the PREFUL MRI scan are correlated with the clinical manifestations of post-COVID syndrome.

Previous pulmonary imaging studies that utilized dynamic contrast-enhanced MRI or computerized tomography (CT) in adults with PACS identified various alterations of perfusion. Because of radiation exposure and the necessity for an intravenous contrast agent, CT is not used as a standard diagnostic tool in children suspected of having PACS. Therefore, objective measures for assessing pulmonary alterations in cases of pediatric PACS are limited. Phase-resolved functional lung (PREFUL) MRI is a contrast agent-free and radiation-free imaging modality performed during free breathing, which allows quantification of static and dynamic regional ventilation and perfusion parameters in chronic pulmonary diseases.

A prior study that utilized an alternative MRI method, inhaled hyperpolarized xenon 129 (^{129}Xe) MRI, to investigate gas exchange in adult patients diagnosed with PACS, revealed a lower pulmonary red blood cell-to-alveolar tissue barrier ratio in both groups of participants, those hospitalized and non-hospitalized during acute COVID-19, suggesting abnormal oxygen and carbon dioxide gas exchange. The complementarity of these imaging modalities suggests that a multimodal approach may provide further pathophysiologic insights.
https://discovermednews.com/long-covid-patients-have-abnormal-gas-exchange-measured-by-129xe-mri-red-blood-cells-to-alveolar-tissue-barrier-ratio/

About the study

The study was conducted in children and adolescents with PACS and age and sex-matched healthy control participants with similar infection history and vaccination status. Inclusion criteria for the consecutively enrolled group with PACS were: age less than 18 years, confirmed SARS-CoV-2 infection, symptoms persisting for at least 12 weeks following

COVID-19, and normal electrocardiographic results. Inclusion criteria for the healthy control group were normal electrocardiographic and clinical examinations and spirometry findings. Exclusion criteria were: acute SARS-CoV-2 infection, pregnancy, smoking history, cardiopulmonary or other critical diseases, the use of lung medication, and contraindications to MRI.

All participants underwent phase-resolved functional lung (PREFUL) MRI, pulmonary function testing, physical examination, and symptom assessment through anamnesis interviews on the same day of the MRI scan. Pulmonary function was tested by measuring the predicted values for forced expiratory volume in 1 second and forced vital capacity according to the recommendations of the American Thoracic Society. The Bell score was used to assess symptom severity and functional disability.

PREFUL MRI parameters, such as regional ventilation, flow-volume loop correlation metric, quantified perfusion, ventilation and perfusion defect percentages, and ventilation-perfusion ratios, were compared between participants with PACS and healthy controls.

Results

The study included 54 participants with a median age of 15 years (11–17 years) (27 participants with PACS and 27 matched healthy controls). In both groups, 48% (13 of 27) were boys. The groups did not differ in height, weight, body surface area, or body mass index. In the group with PACS, the median time between a confirmed COVID-19 diagnosis and the first visit to the post-COVID pediatric outpatient clinic was 30 weeks. None of the participants required hospitalization.

SARS-CoV-2 infection was confirmed in 24 participants with PACS with the reverse transcriptase-polymerase chain reaction test, in two participants with professional antigen tests, and in one participant with a self-administered antigen test.

84% of participants with PACS (23 of 27) and 89% (24 of 27) of healthy controls were vaccinated.

In the pediatric patients with PACS, 18 different clinical symptoms were identified, with an average of 5.3 symptoms per participant (5.9 for males and 4.7 for females). All pediatric patients with PACS reported fatigue, followed by reduced physical capacity (96%), shortness of breath (64%), difficulties with concentration (56%), dyspnea (44%), insomnia (37%), muscle pain (33%), dizziness (33%), headaches (39%), chest pain (26%), abdominal pain

(26%), and joint pain (22%).

The triad of symptoms, fatigue, reduced physical capacity, and shortness of breath emerged as the most prevalent (59%) in all participants with PACS. Interestingly, fatigue, decreased physical capacity, and sleep disorders or concentration difficulties were the most common symptoms (reported by 53%) among female participants with PACS.

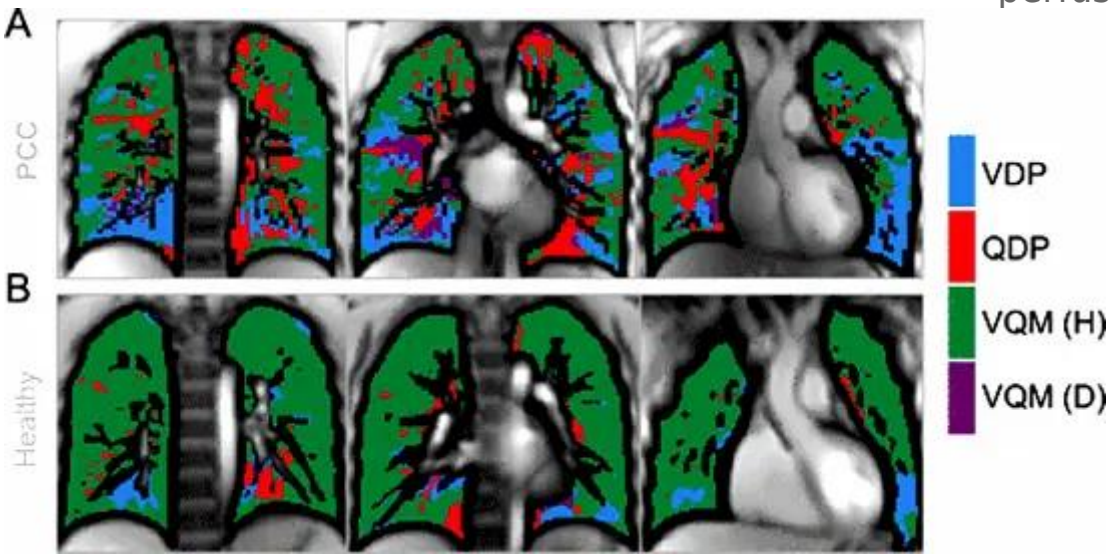
A subgroup of 21 patients with PACS (14 males and 7 females) presented with cardiopulmonary symptoms, such as reduced physical capacity, and at least one lung symptom, such as shortness of breath, dyspnea, or bronchial hypersensitivity.

Pulmonary function testing results were normal in all participants.

Results of PREFUL MRI Scan

PREFUL MRI demonstrated reduced regional ventilation and perfusion in children and adolescents with PACS compared to healthy controls. There was no evidence of differences between groups for other ventilation parameters. The subgroup with cardiopulmonary symptoms of PACS exhibited increased defects in dynamic ventilation and perfusion compared with control participants.

Analysis of the potential correlation between PREFUL MRI parameters, pulmonary function testing, fatigue severity, and cardiopulmonary measures revealed that ventilation or perfusion PREFUL MRI parameters did not correlate with pulmonary function tests in children and adolescents with PACS. However, there was a correlation between a higher ventilation-perfusion mismatch (exclusive perfusion defect) and increased heart rate.



Images show coronal sections of phase-resolved functional lung MRI defect maps in ***(A)*** *a 17-year-old male participant with post-COVID-19 condition and cardiopulmonary symptoms with a ventilation defect percentage of 17%, a perfusion defect percentage of 16%, a ventilation/perfusion (V/Q) match healthy percentage of 64%, and a V/Q mismatch defect of 3%.* ***(B)*** *a healthy control participant, with a ventilation defect percentage of 9%, a perfusion defect percentage of 5%, a V/Q match healthy percentage of 86%, and no V/Q mismatch defect.*

Conclusion

The authors emphasized that, to their knowledge, this is the first comprehensive assessment of functional lung parameters using an advanced MRI technique in an extensive, well-characterized sample of children and adolescents with post-COVID syndrome. Although global lung function tests showed no significant differences between the groups, PREFUL MRI parameters revealed subtle pulmonary changes in children and adolescents with PACS, such as reduced regional ventilation and perfusion.

The subgroup with cardiopulmonary symptoms of PACS exhibited increased defects in dynamic ventilation and perfusion compared with control participants. According to the authors, increased dynamic ventilation defects may indicate underlying structural abnormalities, such as potential remnants of atelectasis or early fibrotic changes. Higher perfusion defects observed in the subgroup of PACS with cardiopulmonary symptoms may indicate incomplete recovery due to microthrombotic remnants, immune cell accumulation, endotheliitis, and platelet adhesion within a thrombogenic microenvironment. Alternatively, subtle right cardiac abnormalities may contribute to changes in pulmonary circulation.

Conventional tests of pulmonary function may underestimate the extent of respiratory involvement in pediatric patients with PACS. This study improved the understanding of post-COVID pathophysiology and provided a basis for future research. The authors concluded that further research should prioritize multicenter longitudinal studies with larger cohorts to evaluate lung abnormalities at different stages following COVID-19, and the findings of this study

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