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Editorial
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Unmasking the Silent Struggle: Championing Post-COVID Sequelae Detection

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Editorial

Following the worldwide COVID-19 outbreak, a new challenge arises that, although frequently overlooked, has a major impact on the lives of many survivors. For those who have battled COVID-19, the long-term effects, also referred to as Post-COVID Sequelae (PCS) or "long COVID," have become a concerning reality. The identification and treatment of these post-COVID syndromes are not only medically urgent, but also socially responsible, requiring greater attention to detail and comprehensive approaches [1].

Beyond bringing PCS into the public eye, the primary obstacle to its successful therapy is the fact that a great number of people—including some healthcare professionals—may not be completely aware of the wide spectrum of symptoms that can linger long after the original infection. A wide range of issues, including mental health issues, respiratory issues, cognitive impairment, and debilitating weariness, can be caused by PCS. By shedding light on these sequelae, we empower both the public and medical community to recognize and respond to the lasting impact of the SARS-CoV-2 [2].

Comprehending the underlying mechanisms of PCS and its diagnostic tools is essential. The complex nature of PCS demands a multifaceted approach, combining clinical assessments, advanced imaging, and laboratory tests. For instance, multimodality data are currently being explored for multiple COVID-19 clinical activities, such as diagnosis and detection, prognosis assessment, disease severity characterization, and monitoring and prediction of interventional effects. While they work well in confirmed COVID-19 cases, the slow progression of the disease and the subtle symptoms of PCS often make it hard to diagnose the condition and even harder to distinguish its symptoms from those of other illnesses in PCS patients. The availability of multimodal data, including physiological parameters, pathological findings, symptomatic findings/clinical data, imaging data, and data from genomics, transcriptomics, proteomics, immunomics, epigenomics, metabolomics, and interactomics, along with high-throughput genome sequencing and the promising developments in clinical Machine Learning (ML) and Artificial Intelligence (AI), could enable a comprehensive understanding of PCS and potentially inform better patient care than could be possible with a single modality [3].

Accumulating data appears to suggest that specific brain dysfunction, also known as brain fog, is a reliable and early potential visible indicator of the majority of PCS symptoms, despite the fact that PCS syndrome is a multisystem disorder that commonly affects the respiratory, cardiovascular, hematopoietic and endocrine systems, as well as the central nervous system. This supports a multimodal detection approach using ML that encompasses brain imaging such as MRI (Magnetic Resonance Imaging), FDG-PET (Fluorodeoxyglucose (FDG)-Positron Emission Tomography (PET)) along with data from individual modality targeting brain. Applying ML algorithms to multimodal data allows for pattern recognition and prediction of potential sequelae based on complex interdependencies among different data types. Integration of these diverse data sources enables a holistic understanding of PCS, aiding in early detection, personalized treatment plans, and long-term monitoring of patients' health. As part of the US National Institutes of Health's RECOVER (Researching COVID to Enhance Recovery) initiative, Wang et al., for example, have identified four sub phenotypes of long COVID using EHRs (Electronic Heath Records) and a ML approach. These findings suggest that stratified patient care pathways could be used to manage long COVID clinically [4-8].

ML has also shown to be a potent technique for determining individualized risk profiles by

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determining whether a patient with COVID-19 is more likely to have PCS. It's expected that the multimodal ML approach would be able to accurately forecast and evaluate the vaccination's long-term effectiveness while also enhancing PCS patients' crisis management. Notably, PCS has proven challenging to design clinical trials since it is still a syndrome as opposed to a disease with a wide range of symptoms that vary among patients and within the same patient. A multimodal ML analysis could be useful in accurately enrolling real PCS patients in a clinical trial that looks at a certain possible intervention [9].

Additionally, the good thing is that ML can continuously learn and adapt as new data becomes available. This adaptability is crucial in a rapidly evolving field like COVID-19 research, where understanding of the virus and its long-term effects is still unfolding. This is particularly important because, in the face of environmental threats like the COVID-19 pandemic, generalized data collected during the pandemic may help to clarify the structure and evolution of new research fields like PCS, as well as their research behavior during a crisis. This information could then be used to inform policymakers' decisions and support scientific and technological advancement in human society. Especially, multimodal data on PCS from post-COVID-19 research would enable these generalized, crisis-driven data to be honed and scrutinized from new perspectives. This calls for a substantial increase in post-pandemic research, particularly in the diagnostic domain where collaboration between data scientists and healthcare professionals is becoming increasingly critical to utilizing ML to its fullest potential for the benefits of individuals impacted by PCS [10].

Together, there is a longer war being waged against COVID-19, and one crucial front in this war is our dedication to supporting the diagnosis of PCS after infection. While significant progress has been made, challenges persist in diagnosing and managing PCS. The evolving nature of the syndrome requires continuous adaptation of diagnostic criteria and approaches. Additionally, addressing the long-term consequences of the syndrome necessitates ongoing research to refine existing methods and develop new strategies. Lastly, through education, research, holistic healthcare, dedicated clinics, and supportive legislation, we can dispel the uncertainty around PCS and provide a path forward for those who are silently battling with its aftereffects. Championing research initiatives focused on understanding the underlying mechanisms of long COVID will not only enhance our diagnostic capabilities but also pave the way for targeted interventions and treatments.

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