



Correspondence

Post-COVID 19 neurological syndrome: The need to define a cut-off score between the acute and post-COVID 19 phases

Dear Editor,

The COVID-19 pandemic is increasingly raising questions about the prognosis of underlying disease and the sequelae of COVID-19 disease, which depend on the phenotype developed by this condition. Post-COVID-19 syndrome has been defined as the persistence or de novo appearance of signs and/or symptoms which may or may not have been present during the acute phase of COVID-19, which are associated with target organ damage and affect the performance of activities of daily living [1–8]. So far, there is scarce and low-level (IV–V) evidence [1–8], which has discussed this concept and which highlights the importance of investigating the burden of disease it may cause, although there are studies that have shown that mortality and the risk of dying from multi-organ involvement after the acute phase of COVID-19, in the range of 30–90 days, is high [5–9].

The cut-off scores currently defined are arbitrary and have not been drawn from primary studies with specific research questions, but are drawn from some peer-reviewed reviews and quick guides, based on the time to resolution of the acute phase of COVID-19 [10]. Ståhlberg et al. [4] defined as a cut-off score in their review on post-COVID-19 tachycardia syndrome, the persistence of symptoms 4–12 weeks or more than 12 weeks after the onset of COVID-19 symptomatology [4]. However, they did not take into account those cases where the acute phase is prolonged, finding positivity in nucleic acid amplification or polymerase chain reaction tests even 20–25 days after the onset of infection, which still constitutes the acute phase of infection [9,10]. Studies have found that the tropism of SARS-Cov-2 in different organs and the susceptibility of some individuals to overactive inflammatory responses can cause the virus to persist in the tissue for a prolonged period of time, triggering minor or major pathological events in response to a stressor [11]. This is the main immunobiological argument to explain the causal relationship between the appearance of complications in the first 45–60 days, even in young people without specific risk factors [1]. Therefore, this syndrome not only constitutes a phase where symptoms such as fatigue, dyspnea or tiredness remain [4–6], but also represents a high-risk period, since it is not known in cases where there is silent target organ damage or undiagnosed personal history [7]. One of the most important phenotypes to define and investigate is the post-COVID-19 neurological syndrome, taking into account that the neurological involvement substantially compromises the functional capacity of the individual [1–3].

It has been shown that in patients with or without neurological manifestations during the acute phase of COVID-19, the cytological and biochemical study of cerebrospinal fluid, as well as neuroimaging, reveal significant alterations that represent inflammatory activity [12]. Those cases with intense neuroimmunologic reactivity may trigger clinical pictures consisting in acute myelitis, acute disseminated encephalomyelitis, acute hemorrhagic necrotizing encephalitis or acute

hemorrhagic leukoencephalitis, ischemic stroke, cytotoxic lesion of the corpus callosum or mild encephalopathy reversible splenium lesion, Guillain-Barré syndrome and seizures, which can substantially reduce the functional capacity of the person affected by irreversible neurological injury, and be very evident during the post-COVID-19 phase [1, 9–13]. However, at present, where there is wide coverage of mass vaccination plans, how is post-COVID-19 syndrome defined? viral load control and lack of symptoms or under-diagnosis with other types of seasonal respiratory infections is an aspect that will hinder the accurate diagnosis of COVID-19 and post-COVID-19 syndrome in those with silent target organ damage.

It is uncertain whether there is greater activation of immune complexes and neurological inflammatory activity during the acute or post-COVID-19 phase [14], whether the negativity of molecular tests or simply the persistence or de novo appearance of symptoms long after the onset of the first symptoms, are sufficient to define a cut-off score. The importance of establishing a cut-off score will allow the design of strategies aimed at initiating neurorehabilitation at the right time, to objectively define the affectation of the quality of life and the natural history of neuroinflammation, to avoid underdiagnosis and wrong therapies. We believe that this should be promoted more strongly in countries where there is a high prevalence of neurological disorders, such as neurovascular disorders or Alzheimer's disease or other dementias, considering the risk of complication, decompensation, disability and death. It is necessary to carry out prospective multicenter studies that massively evaluate the recording of neurological signs and/or symptoms according to the time of evolution, and obtain results that generate evidence of the highest quality.

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Author contribution

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