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LETTER TO EDITOR

Definition of Cut-Off Score between COVID-19 Acute Phase and Post-COVID-19 Syndrome: Indispensable Element to Consider in the Use of Instrumental and Clinical Tests

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The COVID-19 pandemic has probably been the worst public health calamity of the 21st century [1]. At the first peak of infection during the early to mid-2020s, much was unknown about the pathophysiology, COVID-19 phenotypes, pharmacologic and supportive management, rehabilitation, and outcomes [2-4]. With precision and celerity, several safe and effective vaccine prototypes were developed to achieve the desired herd immunity and reduce intensive care unit admission and death [5]. Scales have also been designed to measure the impact of COVID-19 on people's quality of life, the performance of normal activities and some others specific to certain conditions [6]. However, there is also talk of post-COVID-19 syndrome and the impact it has on the global burden disease and human quality of life [4,7]. This constitutes a risk period for the development of complications or diseases that did not exist before the acute phase of COVID-19 [4,7]. So, is there really a cut-off score that differentiates the acute phase of COVID-19 from the post-COVID-19 syndrome, which allows to increase the specificity of clinical and diagnostic tools?

Some authors such as Rodríguez-Hernández YA [8] state that the post-COVID-19 phase is divided into 3 phases: Immediate (3 weeks - 4 weeks), sub-chronic (4 weeks - 12 weeks) and chronic (after 12 weeks) [8]. However, this definition is arbitrary. Particularly, it has been seen that a considerable volume of those who develop complications during the acute phase of COVID-19 partially recover and die during the post-COVID-19 phase from target organ injury. This gives rise to the various phenotypes described, such as post-COVID-19 neurological syndrome, post-COVID 19 tachycardic syndrome, among others. But in reality, it is not known with certainty the relapse caused by SARS-CoV-2 in certain tissues, which is almost always manifested by the same symptoms (fatigue, asthenia, tiredness, neuropsychiatric symptoms, dyspnea, among others) [8].

Currently, when conducting studies and case series/case reports, patients are indiscriminately included and measured in a similar manner, even though the pathophysiologies of the acute phase of COVID-19 and post-COVID-19 syndrome are different. For example, a prospective study in India included patients who

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tested positive for COVID-19 two weeks earlier. 1234 patients were enrolled and followed for up to 3 months, with evidence that 40% persisted with symptoms [9]. However, they found that 18% resolved symptoms at 4 weeks, 12% up to 12 weeks and 10% after 12 weeks. In other words, these authors used as a cut-off score for the onset of the post-COVID phase, from 2 weeks after the onset of symptoms [9]. On the other hand, Crispo, et al. [10] state that The UK's National Institute for Health and Care Excellence defined post-COVID syndrome or Long Covid, as the persistence of symptoms after 12 weeks; and based on this cut-off score, they propose some follow-up strategies [10]. But if one thing is certain, it is that much of the morbidity and mortality occurs long before the age of 3 months.

The above forces us to consider the need to quickly define a cut-off point for the start of the post-COVID-19 syndrome phase, taking into account that many interventions depend on being executed within the appropriate time frame. Tabacof, et al. [11] conducted a cross-sectional study evaluating the impact of post-COVID 19 syndrome on physical function, cognitive function and quality of life [11]. Of 156 participants studied, the median time since the acute phase of COVID-19 was found to be 351 days (range 82 to 457). Of these, 82% reported fatigue, 60% headache and 67% some type of difficulty in performing cognitive processes [11]. Physical exercise, distress and dehydration were the main agents that exacerbate the symptoms. Finally, it was concluded that post-COVID-19 syndrome substantially affects the quality of life of COVID-19 patients [11]. Unfortunately, the fact of taking a population with such a long observation period without strict follow-up allows the presence of a large number of biases; however, it is clear the existence of the post-COVID-19 syndrome and its relevance in the medical field.

It is necessary to carry out well-designed prospective multicenter studies to better understand this phenomenon and to propose effective programs to control morbidity and mortality in this risk period. In the meantime, strict follow-up of those with COVID-19 and comorbidities that increase the risk of decompensation should be reinforced. Finally, as long as there are no solid programs of short- and long-term follow-up and rehabilitation of post-COVID-19 syndrome by different specialties at a global level, it is not possible to say with certainty what will be the evolution of the patient and the state of his functional capacity, since the permanent affectation of an organ or system can compromise the total systemic functioning of the individual [12]. For the most part, the current evidence comes from samples of high-income countries, therefore, it is heterogeneous and results cannot always be extrapolated to other population groups with different sociodemographic characteristics. This suggests that much research remains to be done before a cut-off score can be defined, which would allow a robust evidence-based definition to be proposed.

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