



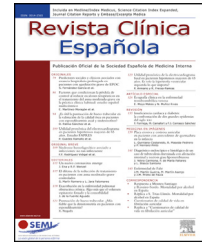
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Revista Clínica Española

www.elsevier.es/rce



CORRESPONDENCE

Another way to approach post-COVID syndrome. From functionality to the symptoms[☆]

Otra forma de abordar el síndrome pos-COVID. De la funcionalidad al síntoma

Dear Director:

Based on its prevalence, impact on quality of life, and use of resources, no one can question the importance of the set of symptoms that a large number of patients report experiencing following acute SARS-CoV-2 infection¹. This importance is accompanied by an outpouring of publications concurring on the lack of agreement regarding very basic aspects such as the definition of a entity which, for the sake of simplicity, we will call post-COVID condition (PCC)²⁻⁵ and which the World Health Organization (WHO) defines as a “set of symptoms that occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually three months from the onset of COVID-19 with symptoms that last for at least two months and cannot be explained by an alternative diagnosis and which generally have an impact on everyday functioning”⁵.

With this as our context, we have read with interest the document titled “Protocol for ongoing care for patients with a COVID-19 diagnosis” (SEMI-SEMERGEN) from our own society, the Spanish Society of Internal Medicine (SEMI), and the Spanish Society of Primary Care Physicians (SEMERGEN)⁶. It is important to highlight the aim of the document, which is to help coordinate between the various levels of care, as this had not yet been previously addressed in such a clear^{7,8} and essential manner, as both patients who required hospitalisation, as well as those who did not, can develop PCC²⁻⁵.

As with acute COVID-19, inter-individual heterogeneity is the general rule of PCC: over 200 manifestations have been

reported with an average of 36 per patient⁹. Some manifestations persist beyond the acute phase, or new onset symptoms may appear, making it a condition that is difficult to categorise. These may also be accompanied by sequelae from the acute phase or those resulting from the actual hospitalisation, such as those of a nutritional¹⁰ and psychological nature. It also features a poorly characterised set of symptoms due to non-specific fatigue, bradyphrenia, pain and an extensive list that mimics fibromyalgia/chronic fatigue syndrome that seems to be rooted in a sustained inflammatory response.

This is usually in addition to the uncertainty created by a discrepancy between the patient’s condition and the typically normal results of additional testing. Regarding the relevance of psychological factors, one study showed for the French population that a large percent of patients attributed their current symptomatology, the basis of their consultation, to a previous case of COVID-19, even in the absence of microbiological evidence of infection¹¹.

A document such as that from the SEMI/SEMERGEN⁶ is a highly necessary tool as both patient and physician are faced with a great deal of uncertainty. However, we would like to offer an assessment as the basis for a proposal that we consider to be different to those available in the literature, including the protocol mentioned here⁶⁻⁸. These publications tend to propose addressing each one of the patient-reported manifestations, thus establishing specific circuits for the evaluation of each symptom. The complexity of this approach is obvious, as it leads to an endless number of appointments and tests as well as pharmacological approaches that rarely end up benefiting the patient¹¹.

Unlike the “symptom by symptom” approach, in our Health Department we have developed a protocol between the Primary Care (PC) and Specialised Care services. We sought to simplify the approach by evaluating impact on function prior to the acute infection rather than assessing manifestations one at a time, with the understanding that those manifestations that had not impacted function/quality of life were not relevant and, therefore, would not benefit from a proactive approach¹².

According to this approach, in a series of 150 patients evaluated between 4 and 12 weeks post-acute COVID-19,

[☆] Please cite this article as: Giner-Galvañ V, Asensio-Tomás ML, Díez-Herrero D, Wikman-Jorgensen P. Otra forma de abordar el síndrome pos-COVID. De la funcionalidad al síntoma. Rev Clin Esp. 2022. <https://doi.org/10.1016/j.rce.2022.03.006>

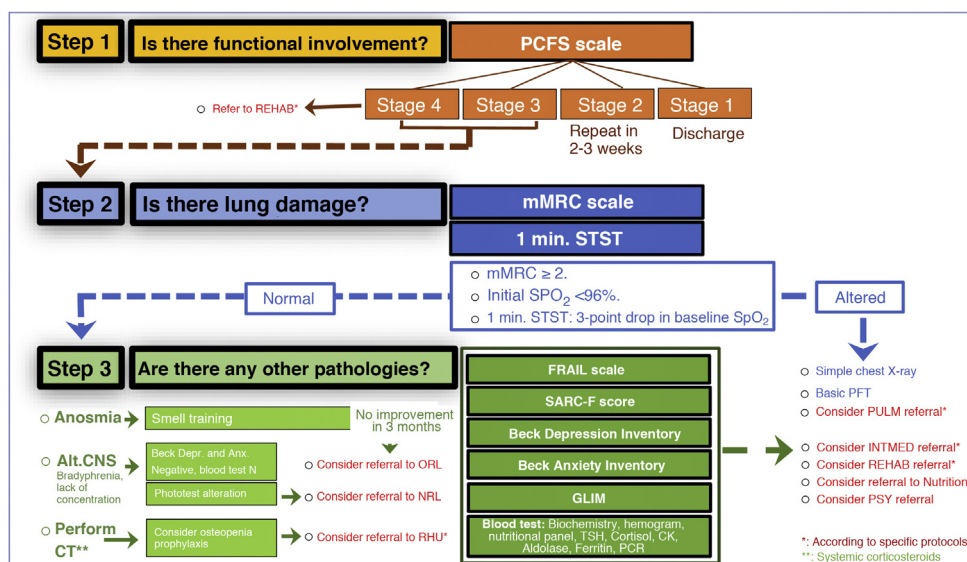


Figure 1 Multidisciplinary follow-up protocol diagram for patients with suspected PCC from the San Juan de Alicante Health Department (Alicante).

1 min STST: 1 min Sit-To-Stand Test; GLIM: Global Leadership Initiative on Malnutrition criteria; mMRC: Modified Medical Research Council Scale; NEUR: neurology; PCC: post-COVID condition; PCFS: Post-COVID-19 Functional Scale; PFT: pulmonary function test; PSY: psychiatry; PULM: pulmonology; REHAB: rehabilitation; RHU: rheumatology; SC: systemic corticosteroids; X-ray: simple radiography.

cardiac sequelae were found in one fourth of the cases, findings that were correlated with worse quality of life and function as measured by the EQ-5D-5L QoL and PCFS scales¹³. For the sake of simplicity, we based the evaluation on validated, self-administered scales conducted during in-person or telephone appointments. The use of validated scales is likely an added value for the more complex, non-validated telephone consult check list from the SEMI/SEMERGEN document which is based on the clinical experience of a single centre.

These scales enable objective progress to be made in the three steps on which the protocol is based, and which consecutively seek to continue responding to the three questions that guide clinicians during evaluation (Fig. 1). Three questions whose aim is to determine: first whether relevant global functional involvement exists, then if there is any pulmonary involvement, and lastly to look for any conditions other than those that are strictly pulmonary. As we can only look at the symptoms, a second contribution to the protocol could be therapeutic action rooted in physiotherapy measures¹⁴ and active clinician follow-up, as creating a reasonable degree of certainty is essential for patients with this condition.

Lastly, bearing in mind the health care burden that monitoring all infected individuals entails, determining which subjects are benefiting from intervention is of utmost

importance¹⁵. Therefore, in line with the SEMI/SEMERGEN proposal, this promotes a model of care that is based on the risk factors with the most evidence of developing PCC, such as: severity of the initial infection, age, and comorbidities. The latter two aspects are summarized in the presented model as classifying patients as complex and chronic. However, in our opinion, these criteria are very general and non-specific and, while it may seem logical to apply said criteria to patients who required hospitalisation, they are likely to be impractical for screening patients seen in a Primary Care setting. Therefore, as a third criteria of severity, we stipulated that at least 6 of the following symptoms had to be present during the first week of acute infection: headache, fever, asthenia, cough, dyspnoea, diarrhoea, rhinorrhoea, ageusia and/or anosmia, myalgia and chest pain.¹⁶ According to this risk classification, we determine whether follow-up should occur via PC or Specialised Care and whether this should be in-person or over the phone (Fig. 2).

We hope that our commentary contributes to the creation of a unified guideline that standardises and ensures ongoing care for patients with PCC and steers away from the complexity of other models that have, on occasion, resulted in the decline of the affected individuals due to exhaustive analysis of symptoms in place of the ultimate functional consequences to the individual.

| A Patient who DID NOT REQUIRE HOSPITALISATION | | | | |
|---|---|------------|--|--|
| X-ray alteration | 6 or more acute* COVID symptoms and/or CC | Risk group | Follow-up | |
| ✗ | ✗ | Low | Patient request: PC Telephone* | |
| ✗ | ✓ | Moderate | 30 days post-discharge PC Telephone* | |
| ✓ | ✗ | | | |
| ✓ | ✗ | | | |
| ✓ | ✗ | | | |

| B Patient who DID REQUIRE HOSPITALISATION | | | | |
|---|-------------------------------|--|------------|---|
| X-ray alteration | 6 or more symptoms* and/or CC | O2 support** | Risk group | Follow-up |
| ✓ | ✗ | ✗ | Moderate | 30 days post-discharge: PC Telephone* |
| ✓ | ✓ | ✗ | | |
| ✓ | ✓ | ✗ | High | 7 days post-discharge: PC Telephone* 30- and 90-days post-discharge: In-person INTMED/PULM |
| ✓ | ✓ | ✓ | | |
| ✓ | ✓ | ✗ | Very high | 7 days post-discharge: PC Telephone* 30- and 90-days post-discharge: In-person PULM |
| | | ICU, HFO and/or NIMV during admission | | |

Figure 2 Follow-up according to the risk of developing PCC whether the patient was hospitalised during the acute phase. CC: chronic complex patient; HFO: high flow oxygen; ICU: intensive care unit; INTMED: internal medicine; NIMV: non-invasive mechanical ventilation; PC: primary care; PCS: post-COVID syndrome; PULM: Pulmonology; X-ray: simple chest radiography. * Headache, fever, asthenia, cough, dyspnoea, diarrhoea, rhinorrhoea, nausea or vomiting, anosmia or ageusia, myalgia, chest pain¹⁵.

** Patient requiring supplementary O₂ during admission for COVID-19 other than high flow oxygen therapy or non-invasive mechanical ventilation.

‡ PCFS scale (post-COVID Functional Scale).

References

- Parums DV. Editorial: long COVID, or post-COVID syndrome, and the global impact on health care. *Med Sci Monit.* 2021;27:e933446, doi:10.12659/MSM.933446.
- Aiyegbusi OL, Hughes SE, Turner G, Rivera SC, McMullan C, Chandan JS, et al. Symptoms, complications and management of long COVID: a review. *J R Soc Med.* 2021;114:428–42, doi:10.1177/01410768211032850.
- Michelen M, Manoharan L, Elkheir N, Cheng V, Dagens A, Hastie C, et al. Characterising long COVID: a living systematic review. *BMJ Glob Health.* 2021;6:e005427, doi:10.1136/bmjgh-2021-005427.
- Anaya JM, Rojas M, Salinas ML, Rodríguez Y, Roa G, Lozano M, et al. Post-COVID syndrome. A case series and comprehensive review. *Autoimmun Rev.* 2021;20:102947, doi:10.1016/j.autrev.2021.102947.
- Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis.* 2021;22:E102–7, doi:10.1016/S1473-3099(21)00703-9.
- Barquillo A, del Corral E, Díaz C, Lumbreras C, Martín V, Morán A, et al. Protocolo para la continuidad asistencial del paciente con diagnóstico de COVID19. [Accessed 20 December 2021]. Available in: <https://www.fesemi.org/sites/default/files/documentos/776.pdf>.

- Sisó-Almirall A, Brito-Zerón P, Conangla Ferrín L, Kostov B, Moragas Moreno A, Mestres J, et al. Long Covid-19: proposed primary care clinical guidelines for diagnosis and disease management. *Int J Environ Res Public Health.* 2021;18:4350, doi:10.3390/ijerph18084350.
- Greenhalgh T, Knight M, A'Court C, Buxton M, Husain L. Management of post-acute covid-19 in primary care. *BMJ.* 2020;370:m3026, doi:10.1136/bmj.m3026.
- Martín-Garrido I, Medrano Ortega FJ. Más allá de la infección aguda por SARS-COV2: un nuevo desafío para la Medicina Interna. *Rev Clin Esp.* 2022;222:176–9, doi:10.1016/j.rce.2021.09.005.
- Gómez-Uranga A, Guzmán-Martínez J, Esteve-Atiéndar PJ, Wikman-Jorgensen P, Núñez-Cruz JM, Espinosa-Del-Barrio L, et al. Nutritional and functional impact of acute SARS-CoV-2 infection in hospitalized patients. *J Clin Med.* 2022;11:2424, doi:10.3390/jcm11092424. PMID: 35566549; PMCID: PMC9103467.
- Matta J, Wiernik E, Robineau O, Carrat F, Touvier M, Severi G, et al. Association of self-reported COVID-19 infection and SARS-CoV-2 serology test results with persistent physical symptoms among French adults during the COVID-19 pandemic. *JAMA Intern Med.* 2022;182:19–25, doi:10.1001/jamainternmed.2021.6454.
- Taboada M, Cariñena A, Moreno E, Rodríguez N, Domínguez MJ, Casal A, et al. Post-COVID-19 functional status six-months after hospitalization. *J Infect.* 2021;82:e31–3, doi:10.1016/j.jinf.2020.12.022.
- Tudoran C, Tudoran M, Pop GN, Giurgi-Onu C, Cut TG, Lazureanu VE, et al. Associations between the severity of the post-acute COVID-19 syndrome and echocardiographic abnormalities in previously healthy outpatients following infection with SARS-CoV-2. *Biology (Basel).* 2021;10:469, doi:10.3390/biology10060469.
- Clemente-Suárez VJ, Beltrán-Velasco AI, Ramos-Campo DJ, Mielgo-Ayuso J, Nikolaidis PA, Belando N, et al. Physical activity and COVID-19. The basis for an efficient intervention in times of COVID-19 pandemic. *Physiol Behav.* 2022;244:113667, doi:10.1016/j.physbeh.2021.113667.
- Jiang DH, McCoy RG. Planning for the post-COVID syndrome: how payers can mitigate long-term complications of the pandemic. *J Gen Intern Med.* 2020;35:3036–9, doi:10.1007/s11606-020-06042-3.
- Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. *Nat Med.* 2021;27:626–31, doi:10.1038/s41591-021-01292-y.

V. Giner-Galvañ^{a,b,c,*}, M.L. Asensio-Tomás^{a,c},
D. Díez-Herrero^{c,d}, P. Wikman-Jorgensen^{a,c}

^a Servicio de Medicina Interna, Hospital Clínico Universitario San Juan, San Juan de Alicante, Alicante, Spain

^b Departamento de Medicina Clínica, Facultad de Medicina, Universidad Miguel Hernández, Elche, Alicante, Spain

^c Fundación para el Fomento de la Investigación Sanitaria y Biomédica (FISABIO), Valencia, Spain

^d Centro de Salud Cabo de las Huertas, Departamento de Salud de San Juan, San Juan de Alicante, Alicante, Spain

* Corresponding author.

E-mail address: giner_vicgal@gva.es (V. Giner-Galvañ).

25 January 2022