

Postcoronavirus Disease Chronic Fatigue Is Frequent and Not Only Restricted to Hospitalized Patients

To the Editor:

We read with interest the study of Martillo et al (1) published in the recent issue of *Critical Care Medicine*, who report a high proportion of patients suffering from chronic fatigue 1 month after discharge from hospital for ICU-treated coronavirus disease 2019 (COVID-19). In the last month, physicians became more aware of the post-COVID syndrome, a new syndrome including more than 50 different conditions after a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (2), with fatigue, mental impairment, and dyspnea as the most frequent conditions. The reported frequency of symptoms ranges between 13.3% and 80% (3).

Martillo et al (1) only included patients that were treated on an ICU for at least 7 days in their analyses. However, the vast majority of SARS-CoV-2 patients receive only outpatient treatment. Further, most reports inclusive the study by Martillo et al (1) lack a control group.

Neuropsychiatric disorders are frequently described after other infections as well, for example, for Epstein-Barr virus infections and more broadly for sepsis. Until today, it is unclear whether the reported post-COVID symptoms are more frequent than those described after other infections. Thus, information on post-COVID symptoms in inpatients and outpatients is of special interest.

We reviewed all patients consecutively treated at the post-COVID outpatient clinic of the Jena University Hospital ($n = 108$) and compared them with patients after ICU-treated sepsis or septic shock ($n = 290$), who are a subsample of the "Mid-German Sepsis Cohort" (4).

Between August 2020 and March 2021, 108 patients (59 female, 49 male, median age 50 yr) were included after a median of 6 months after the primary infection with SARS-CoV-2. Forty-five patients (41.7%) had been hospitalized due to SARS-CoV-2 infection, including 19 patients (17.6%) on an ICU, and 63 patients (58.3%) were treated as outpatients, including 11 patients (10.2%) with initially asymptomatic infection.

All patients received a structured screening for neuropsychologic and cognitive disorders. Among them, chronic fatigue and depression occurred frequently in 87.0% and 74.1% of the patients. Interestingly, the severity of the initial infection as defined by the World Health Organization Ordinal Scale was comparable in outpatients (87.3%), inpatients (86.6%), and patients on the ICU (78.9%). Similarly, we observed no evidence for a correlation between the need for oxygen supply the occurrence of chronic fatigue ($p = 0.725$). Interestingly, when comparing the post-COVID patients to patients 6 months after sepsis, post-COVID patients seem to suffer more frequently from chronic fatigue (87.0% vs 35.2%; $p < 0.001$) and depression (74.1% vs 19.7%; $p < 0.001$).

Philipp A. Reuken, MD¹

André Scherag, PhD^{2,3}

Andreas Stallmach, MD^{1,2}

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In sum, our data suggest that neuropsychologic post-COVID symptoms like chronic fatigue and depression seem to be more frequently compared with other infections and are not only restricted to severe cases. Outpatients must be included into post-COVID care programs.

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- 1 *Klinik für Innere Medizin IV (Gastroenterologie, Hepatologie und Infektiologie), Universitätsklinikum Jena, Friedrich-Schiller-Universität Jena, Jena, Germany*
 - 2 *Zentrum für Sepsis und Infektionsforschung (Center for Sepsis Control & Care, CSCC), Universitätsklinikum Jena, Friedrich-Schiller-Universität Jena, Jena, Germany*
 - 3 *Institut für Medizinische Statistik, Informatik und Datenwissenschaften, Universitätsklinikum Jena, Friedrich-Schiller-Universität Jena, Jena, Germany*
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The author replies:

It was interesting to read through the letter by Reuken et al (1). The authors elegantly described their work about the prevalence of neuropsychologic symptoms affecting patients who recovered from mild-to-severe coronavirus disease 2019 (COVID-19). Furthermore, they compared these descriptive findings to patients who recovered from Sepsis enrolled in a German sepsis cohort. Interestingly, the authors found that those patients who suffered COVID-19 had a higher rate of chronic fatigue and depression.

We also appreciate the author's comments about our study (2) published recently in *Critical Care Medicine*. Still, it is essential to highlight that the objective of our report was to describe the frequency of symptoms affecting the core domains of the postintensive care syndrome (PICS) in patients who had critical illness related to severe COVID-19. PICS is now a well-recognized clinical condition, defined as the presence of any impairment affecting the physical, psychiatric, or cognitive domains resulting from critical illness (3). Similar to the report done by Reuken et al (1), we found that patients who suffered COVID-19 had a high rate of psychiatric manifestations; however, we additionally identified an increased frequency of physical impairments (1, 2).

To date, there have been several observational and case series, studies, and multiple reports from patient advocacy groups that have suggested that patients who suffered even a relatively mild COVID-19 infection may experience a wide range of symptoms after recovery from the acute illness (4, 5). This constellation of symptoms which has adopted multiple terms, including "Post-Acute COVID-19," "long COVID," and "post-COVID syndrome," appears to have multisystem involvement and typically includes fatigue, dyspnea, chest pain, and additional psychologic and cognitive symptoms, similar to PICS (3, 5).

Miguel A. Martillo, MD