

# Letters

## RESEARCH LETTER

### Persistent Symptoms in Patients After Acute COVID-19

In Italy, a large proportion of patients with coronavirus disease 2019 (COVID-19) presented with symptoms (71.4% of 31 845 confirmed cases as of June 3, 2020).<sup>1</sup> Common symptoms include cough, fever, dyspnea, musculoskeletal symptoms (myalgia, joint pain, fatigue), gastrointestinal symptoms, and anosmia/dysgeusia.<sup>2-4</sup> However, information is lacking on symptoms that persist after recovery. We assessed persistent symptoms in patients who were discharged from the hospital after recovery from COVID-19.

**Methods** | In the waning phase of the pandemic, beginning on April 21, 2020, the Fondazione Policlinico Universitario Agostino Gemelli IRCCS in Rome, Italy, established a post-acute outpatient service for individuals discharged from the hospital after recovery from COVID-19. All patients who met World Health Organization criteria for discontinuation of quarantine (no fever for 3 consecutive days, improvement in other symptoms, and 2 negative test results for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] 24 hours apart) were followed up. At enrollment in the study, real-time reverse transcriptase-polymerase chain reaction for SARS-CoV-2 was performed and patients with a negative test result were included.

Patients were offered a comprehensive medical assessment with detailed history and physical examination. Data on all clinical characteristics, including clinical and pharmacological history, lifestyle factors, vaccination status, and body measurements, were collected in a structured electronic data collection system. The COVID-19 postacute outpatient service is currently active, and further details about the patient evaluation protocol are described elsewhere.<sup>5</sup>

In particular, data on specific symptoms potentially correlated with COVID-19 were obtained using a standardized questionnaire administered at enrollment. Patients were asked to retrospectively recount the presence or absence of symptoms during the acute phase of COVID-19 and whether each symptom persisted at the time of the visit. More than 1 symptom could be reported. The EuroQol visual analog scale was used to ask patients to score their quality of life from 0 (worst imaginable health) to 100 (best imaginable health) before COVID-19 and at the time of the visit. A difference of 10 points defined worsened quality of life. All analyses were performed using R version 3.6.3 (R Foundation).

This study was approved by the Università Cattolica and Fondazione Policlinico Gemelli IRCCS Institutional Ethics Committee. Written informed consent was obtained from all participants.

**Table. Demographic and Clinical Characteristics of the Study Sample (N = 143)**

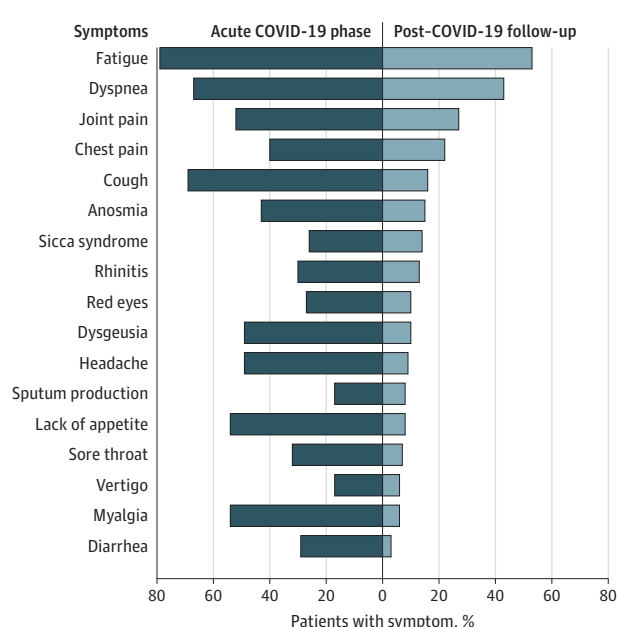
| Characteristics                                  | Value       |
|--|-------------|
| Age, mean (SD), y                                | 56.5 (14.6) |
| Female sex, No. (%)                              | 53 (37.1)   |
| Body mass index, mean (SD) <sup>a</sup>          | 26.3 (4.4)  |
| Vaccination, No. (%)                             |             |
| Seasonal influenza                               | 32 (22.4)   |
| Pneumococcus                                     | 13 (9.1)    |
| Diagnoses, No. (%)                               |             |
| Chronic heart disease                            | 7 (4.9)     |
| Atrial fibrillation                              | 4 (2.8)     |
| Heart failure                                    | 4 (2.8)     |
| Stroke   | 2 (1.4)     |
| Hypertension                                     | 50 (35)     |
| Diabetes   | 10 (7)      |
| Kidney failure                                   | 3 (2.1)     |
| Thyroid disease                                  | 26 (18.2)   |
| Chronic obstructive pulmonary disease            | 13 (9.1)    |
| Active cancer                                    | 5 (3.5)     |
| Immune disorders                                 | 16 (11.2)   |
| Regular physical activity, No. (%)               | 90 (62.9)   |
| Smoking status, No. (%)                          |             |
| None   | 63 (44.1)   |
| Active   | 15 (10.5)   |
| Former   | 65 (45.4)   |
| Acute COVID-19 characteristics, No. (%)          |             |
| Pneumonia diagnosed                              | 104 (72.7)  |
| Intensive care unit admission                    | 18 (12.6)   |
| Oxygen supplementation                           |             |
| Oxygen therapy                                   | 77 (53.8)   |
| Ventilation                                      |             |
| Noninvasive                                      | 21 (14.7)   |
| Mechanical                                       | 7 (4.9)     |
| Pharmacological treatments during acute COVID-19 |             |
| Antiretroviral                                   | 102 (71.3)  |
| Hydroxychloroquine                               | 104 (72.7)  |
| Azithromycin                                     | 59 (41.3)   |
| Anti-IL-6 drugs (tocilizumab)                    | 44 (30.8)   |
| Length of hospital stay, mean (SD), d            | 13.5 (9.7)  |
| Post-acute COVID-19 follow-up characteristics    |             |
| Days since symptoms onset, mean (SD)             | 60.3 (13.6) |
| Days since discharge, mean (SD)                  | 36.1 (12.9) |
| Persistent symptoms, No. (%)                     |             |
| None   | 18 (12.6)   |
| 1 or 2   | 46 (32.2)   |
| ≥3   | 79 (55.2)   |
| Worsened quality of life, No. (%) <sup>b</sup>   | 63 (44.1)   |

Abbreviation: COVID-19, coronavirus disease 2019.

<sup>a</sup> Calculated as weight in kilograms divided by height in meters squared.

<sup>b</sup> Quality of life was assessed using the EuroQol visual analog scale, ranging from 0 (worst imaginable health) to 100 (best imaginable health). Worsened quality of life was defined by a 10-point difference in health status before COVID-19 vs at the time of the visit.

Figure. COVID-19–Related Symptoms



The figure shows percentages of patients presenting with specific coronavirus disease 2019 (COVID-19)–related symptoms during the acute phase of the disease (left) and at the time of the follow-up visit (right).

**Results** | From April 21 to May 29, 2020, 179 patients were potentially eligible for the follow-up post-acute care assessment; 14 individuals (8%) refused to participate and 22 had a positive test result. Thus, 143 patients were included. The mean age was 56.5 (SD, 14.6) years (range, 19–84 years), and 53 (37%) were women. During hospitalization, 72.7% of participants had evidence of interstitial pneumonia. The mean length of hospital stay was 13.5 (SD, 9.7) days; 21 patients (15%) received non-invasive ventilation and 7 patients (5%) received invasive ventilation. The characteristics of the study population are summarized in the **Table**.

Patients were assessed a mean of 60.3 (SD, 13.6) days after onset of the first COVID-19 symptom; at the time of the evaluation, only 18 (12.6%) were completely free of any COVID-19–related symptom, while 32% had 1 or 2 symptoms and 55% had 3 or more. None of the patients had fever or any signs or symptoms of acute illness. Worsened quality of life was observed among 44.1% of patients. The **Figure** shows that a high proportion of individuals still reported fatigue (53.1%), dyspnea (43.4%), joint pain, (27.3%) and chest pain (21.7%).

**Discussion** | This study found that in patients who had recovered from COVID-19, 87.4% reported persistence of at least 1 symptom, particularly fatigue and dyspnea. Limitations of the study include the lack of information on symptom history be-

fore acute COVID-19 illness and the lack of details on symptom severity. Furthermore, this is a single-center study with a relatively small number of patients and without a control group of patients discharged for other reasons. Patients with community-acquired pneumonia can also have persistent symptoms, suggesting that these findings may not be exclusive to COVID-19.<sup>6</sup>

Clinicians and researchers have focused on the acute phase of COVID-19, but continued monitoring after discharge for long-lasting effects is needed.

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**Concept and design:** All authors.

**Drafting of the manuscript:** Carfi, Landi.

**Critical revision of the manuscript for important intellectual content:** Bernabei, Landi.

**Statistical analysis:** Carfi.

**Supervision:** Bernabei, Landi.

**Conflict of Interest Disclosures:** None reported.

**Additional Information:** The members of the Gemelli Against COVID-19 Post-Acute Care Study Group are listed in reference 5.

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