

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).¹ Common symptoms include cough, fever, dyspnea, musculoskeletal symptoms (myalgia, joint pain, fatigue), gastrointestinal symptoms, and anosmia/dysgeusia.²⁻⁴ 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.⁵

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)

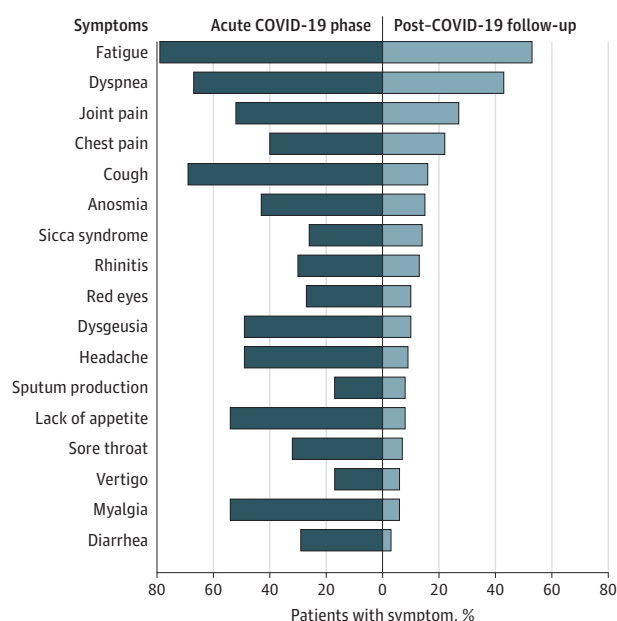
Characteristics	Value
Age, mean (SD), y	56.5 (14.6)
Female sex, No. (%)	53 (37.1)
Body mass index, mean (SD) ^a	26.3 (4.4)
Vaccination, No. (%)	
Seasonal influenza	32 (22.4)
Pneumococcus	13 (9.1)
Diagnoses, No. (%)	
Chronic heart disease	7 (4.9)
Atrial fibrillation	4 (2.8)
Heart failure	4 (2.8)
Stroke	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. (%) ^b	63 (44.1)

Abbreviation: COVID-19, coronavirus disease 2019.

^a Calculated as weight in kilograms divided by height in meters squared.

^b 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-19.⁶

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.

1. Istituto Superiore Sanità. *Sorveglianza Integrata COVID-19 in Italia*. Published 2020. Accessed June 8, 2020. https://www.epicentro.iss.it/coronavirus/bollettino/Infografica_3giugno%20ITA.pdf

2. Docherty AB, Harrison EM, Green CA, et al; ISARIC4C Investigators. Features of 20 133 UK patients in hospital with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ*. 2020; 369:m1985. doi:10.1136/bmj.m1985

3. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA*. 2020;323(13):1239–1242. doi:10.1001/jama.2020.1585

4. Landi F, Barillaro C, Bellieni A, et al. The new challenge of geriatrics: saving frail older people from the SARS-CoV-2 pandemic infection. *J Nutr Health Aging*. 2020;24(5):466–470. doi:10.1007/s12603-020-1356-x

5. Gemelli Against COVID-19 Post-Acute Care Study Group. Post-COVID-19 global health strategies: the need for an interdisciplinary approach. *Aging Clin Exp Res*. Published online June 11, 2020. doi:10.1007/s40520-020-01616-x

6. Metlay JP, Fine MJ, Schulz R, et al. Measuring symptomatic and functional recovery in patients with community-acquired pneumonia. *J Gen Intern Med*. 1997;12(7):423–430. doi:10.1046/j.1525-1497.1997.00074.x