OBSERVATIONS: CASE REPORTS

Symptoms After COVID-19 Vaccination in Patients With Persistent Symptoms After Acute Infection: A Case Series

Background: Some patients develop prolonged symptoms after acute SARS-CoV-2 infection (1). Because the immunologic basis for this is unknown, uncertainty exists about whether vaccination against SARS-CoV-2 might worsen the associated symptoms (2). Anecdotal reports have suggested both a potential benefit and worsening of symptoms after vaccination, with the uncertainty leading to vaccine hesitancy among some affected persons (2).

Objective: To describe quality of life and symptoms after SARS-CoV-2 vaccination in a series of patients with persistent symptoms 8 months after hospitalization with COVID-19.

Case Series: The cases described here were identified from among 163 patients admitted to a single U.K. hospital with COVID-19 and prospectively recruited to an observational study with clinical follow-up at 8 months after admission (December 2020 to January 2021) (3). Every 12 weeks, we administered the Short Form-36 Health Survey (SF-36) and the Warwick–Edinburgh Mental Wellbeing Scale (WEMWBS) and performed a standardized review of ongoing symptoms. Participants who were symptomatic at 8 months and who subsequently received the Pfizer-BioNTech (BNT162b2) or Oxford-AstraZeneca (ChAdOx1nCoV-19) vaccine between January and February 2021 were identified.

All participants were reassessed at approximately 1 month after vaccination, and quality-of-life questionnaires and review of symptoms were repeated, with specific questions on whether symptoms had improved, stayed the same, or worsened. Participants were only asked to confirm vaccination status after symptom assessment to minimize bias due to a perceived association between the assessment and vaccination. They were subsequently asked about adverse effects temporally related to the vaccine.

Of the 78 participants who attended the 8-month follow-up, 2 could not be contacted and 32 had not yet received a vaccine. Among the remaining 44 participants who had received 1 dose of vaccine, 36 (82%) reported at least 1 persistent symptom and are described here. The **Table** summarizes patient characteristics.

Participants had a high burden of persistent symptoms at 8 months, with a median of 4 symptoms per patient (interquartile range [IQR], 2 to 5) and a total of 159 symptoms overall. A wide variety of symptoms were reported across multiple organ systems, with fatigue (75%), breathlessness (61%), and insomnia (53%) predominating (**Figure**). At this prevaccination time point, quality of life was markedly reduced from population norms (4), with a median Mental Component Summary score of 40 (IQR, 29 to 51) and a median Physical Component Summary score of 35 (IQR, 25 to 40).

Participants were telephoned a median of 30 days after vaccination (IQR, 26 to 36 days) to investigate changes in symptoms and quality of life. Among the 159 symptoms reported before vaccination, 37 (23.2%) had improved, 9 (5.6%) had worsened, and 113 (71.1%) were unchanged (**Figure**). There was no significant worsening in quality-of-life metrics before versus after vaccination (*t* test $P > 0.1$ for all SF-36 comparisons). Mental well-being (as measured by the WEMWBS) was stable in vaccinated participants before and after vaccination (median, 49 [IQR, 42 to 54] vs. 50 [IQR, 40 to 59], respectively). A large proportion (26 of 36 [72%]) reported transient (<72 hours' duration) systemic effects after vaccination, including fever (44%), myalgia (22%), and headache (19%). This is consistent with other observational studies of vaccine adverse effects in persons with previous SARS-CoV-2 infection (5). No difference in any outcome measure was identified between the Pfizer-BioNTech ($n = 18$) and Oxford-AstraZeneca ($n = 18$) vaccines (*t* test $P > 0.1$ for all comparisons).

Discussion: This report presents a series of patients with robust measures of quality of life and symptoms both before and after vaccination. Limitations include the small sample size and the inability to blind participants to their vaccination status. Also, because the U.K. national policy prioritized vaccination for older age groups and adopted a delayed second-dose approach, it was not possible to suitably match vaccinated and unvaccinated persons, and we can only provide data for participants after their first vaccine dose. However, these observations may provide reassurance to the increasing number of persons experiencing long-term symptoms after acute SARS-CoV-2 infection that receipt of a messenger RNA or adenoviral vector vaccine is not associated with a decrease in quality of life or worsening of symptoms. Further work that includes appropriate unvaccinated controls is needed to confirm the trajectory of persistent symptoms after COVID-19 vaccination.

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Table. Participant Characteristics

Characteristic	Participants ($n = 36$)
Median age (IQR), *y*	64 (53–73)
Male, *n (%)*	21 (58)
Female, *n (%)*	15 (42)
White, *n (%)*	29 (86)
Black, Asian, or ethnic minority, *n (%)*	5 (14)
Mean body mass index (SD), kg/m^2	31.8 (8.0)
Comorbidities, *n (%)*	
Type 1 diabetes	0 (0)
Type 2 diabetes	4 (11)
Heart disease	10 (28)
Chronic lung disease	13 (36)
Details of COVID-19 hospitalization, *n (%)*	
Intensive care and/or noninvasive ventilation required	11 (31)
Oxygen supplementation required	26 (72)
PCR positive for SARS-CoV-2 during hospitalization	30 (83)
SARS-CoV-2 antibody positivity at 3 mo	32 (89)
8-mo follow-up (prevaccination)	
Median SF-36 MCS score (IQR)	40 (29–51)
Median SF-36 PCS score (IQR)	35 (25–40)
Median WEMWBS score (IQR)	49 (42–54)
Median number of persistent symptoms reported (IQR)	4 (2–5)
Vaccine received, *n (%)*	
Pfizer-BioNTech BNT162b2	18 (50)
Oxford-AstraZeneca ChAdOx1nCoV-19	18 (50)

IQR = interquartile range; MCS = Mental Component Summary; PCR = polymerase chain reaction; PCS = Physical Component Summary; SF-36 = Short Form-36 Health Survey; WEMWBS = Warwick-Edinburgh Mental Wellbeing Scale.

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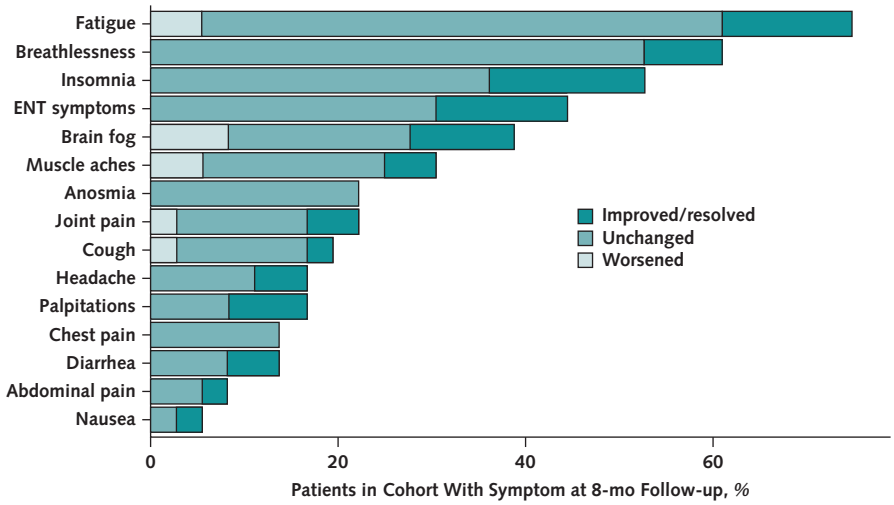
Figure. Changes in symptoms 1 month after SARS-CoV-2 vaccination among patients with symptoms at 8-month follow-up.



ENT = ear, nose, and throat.

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