



Functioning of post-COVID-19 patients: a cross-sectional study at the outpatient clinic for long-term effects

Sanna Stålnacke, Helena Liira, Velina Vangelova-Korpinen, Hélène Virrantaus, Mari Kanerva, Kirsi Kvarnström, Markku Sainio, Antti Malmivaara, Aki Vuokko, Mikko Varonen, Mikko Venäläinen & Jari Arokoski

To cite this article: Sanna Stålnacke, Helena Liira, Velina Vangelova-Korpinen, Hélène Virrantaus, Mari Kanerva, Kirsi Kvarnström, Markku Sainio, Antti Malmivaara, Aki Vuokko, Mikko Varonen, Mikko Venäläinen & Jari Arokoski (03 Oct 2024): Functioning of post-COVID-19 patients: a cross-sectional study at the outpatient clinic for long-term effects, Scandinavian Journal of Primary Health Care, DOI: [10.1080/02813432.2024.2410986](https://doi.org/10.1080/02813432.2024.2410986)

To link to this article: <https://doi.org/10.1080/02813432.2024.2410986>



© 2024 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group



Published online: 03 Oct 2024.



Submit your article to this journal [↗](#)



Article views: 431




View related articles [↗](#)



View Crossmark data [↗](#)

Functioning of post-COVID-19 patients: a cross-sectional study at the outpatient clinic for long-term effects

Sanna Stålnacke^a, Helena Liira^a, Velina Vangelova-Korpinen^a, Hélène Virrantaus^a, Mari Kanerva^{a,b}, Kirsi Kvarnström^a , Markku Sainio^a, Antti Malmivaara^c, Aki Vuokko^d, Mikko Varonen^a, Mikko Venäläinen^e and Jari Arokoski^f

^aOutpatient Clinic for Persistent Symptom Rehabilitation, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland; ^bTurku University Hospital and University, Turku, Finland; ^cFinnish Institute for Health and Welfare, Orton Orthopaedic Hospital, University of Helsinki, Helsinki, Finland; ^dFinnish Institute of Occupational Health, Helsinki, Finland; ^eDepartment of Medical Physics, University of Turku, Turku, Finland; ^fDepartment of Internal Medicine and Rehabilitation, Division of Rehabilitation, Helsinki University Hospital and Helsinki University, Helsinki, Finland

ABSTRACT

Background: After COVID-19 infection, long-term impacts on functioning may occur. We studied the functioning of patients with post-COVID-19 condition (PCC) and compared them to controls without PCC.

Methods: This cross-sectional study consisted of 442 patients with PCC referred to rehabilitation at the Helsinki University Hospital (HUS) Outpatient Clinic for the Long-Term Effects of COVID-19, and 198 controls without PCC. Functioning was assessed with a questionnaire including WHODAS 2.0. Patients underwent physical testing including a hand grip strength test (HGST) and a 6-minute walking test (6MWT). Lifestyle was assessed by questionnaire and comorbidities were collected as ICD-10 codes from the HUS Data Lake on the HUS Acaademic platform.

Results: The WHODAS 2.0 average total score was 34 (SD 18) (moderate functional limitation) for patients with PCC and 6 (SD 8) (normal or mild limitation) for the controls. The disability was higher in all aspects of WHODAS 2.0 in patients with PCC. Bivariate binomial and multivariable regression analyses showed that the presence of comorbidities, anxiety, depression, and smoking predicted a WHODAS 2.0 score of 24 (moderate functional limitation) or above in the PCC group. The average 6MWT distance was 435m (SD 98m) in patients with PCC and 627m (SD 70m) in controls. HGST measurements showed no significant differences from controls.

Conclusions: In conclusion, patients with PCC had significantly reduced functioning based on WHODAS 2.0 scores and the 6MWT results. Comorbidities, anxiety, depression, and smoking were associated with moderate or severe limitations in functioning. Findings support that PCC is multifactorial and requires a holistic approach to rehabilitation.

KEY POINTS

- The post-COVID-19 condition (PCC) has been shown to negatively impact functioning, quality of life, and mental health, with cognitive and physical impairments being prevalent.
- This study found that patients with PCC had significantly reduced functioning compared to controls.
- Key factors predicting severe disability included comorbidities, smoking, and mental health issues like anxiety and depression.
- The reduced functioning in patients with PCC appears to be multifactorial and not only related to COVID-19 infection.

ARTICLE HISTORY

Received 21 May 2024
Accepted 25 September 2024



KEYWORDS

Post-COVID-19 condition; cross-sectional study; functioning; WHODAS 2.0; 6-minute walk test; hand grip strength

Introduction

Post-COVID-19 condition (PCC) can affect people's functioning in many ways. By WHO, PCC is defined as the continuation or development of new symptoms 3 months after the initial COVID-19 infection, with these symptoms lasting for at least 2 months with no

other explanation [1]. Previous studies of patients with PCC have shown a reduction in functioning and Health-Related Quality of Life (HRQoL) [2–5], and cognitive deficits [6,7]. Depressive symptoms after the initial COVID-19 infection are common [8]. Sleep disorders were common during the pandemic in COVID-19

CONTACT Sanna Stålnacke  sanna.stalnacke@gmail.com  Outpatient Clinic for Persistent Symptom Rehabilitation, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland

© 2024 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

patients, healthcare personnel, and the general population [9]. Returning to previous health may be delayed [10]. The pandemic led to a high mental health burden, especially among healthcare personnel, and higher suicidal ideation and lower well-being in the general population [11]. Also, during the pandemic, the physical activity of many people decreased [12] while the demands of work may have increased [13].

The concept of International Classification of Functioning, Disability and Health (ICF) provides a framework to address physical and psychosocial impairments, limitations to activities, and restrictions to participation [14]. The ICF conceptualizes a person's level of functioning as a dynamic interaction between her or his health conditions, environmental factors, and personal factors. It is a biopsychosocial model of disability, based on an integration of the social and medical models of disability. Overall, the ICF model provides a comprehensive framework that can assist healthcare professionals in understanding and addressing the impacts and different aspects of PCC on an individual's life. WHO Disability Assessment Schedule 2.0 (WHODAS 2.0) is a generic and standardized tool for measuring health and disability at both population and individual levels. It evaluates an individual's functioning in six domains of the ICF including cognition, mobility, self-care, getting along, life activities, and participation [15]. Previous studies using WHODAS 2.0 have shown reduced functioning after COVID-19 based on HRQoL measures [16–19].

There are several possibilities for measuring the effects of physical functioning in patients with PCC. The ability to walk for a distance is a quick and inexpensive measure of physical functioning, and an important component of quality of life since it reflects the capacity to undertake day-to-day activities [20]. The distance of the 6-minute walk test (6MWT) has been lower in the PCC cohorts [21]. Studies have shown the predictive potential of the hand grip strength test (HGST) regarding short and long-term mortality and morbidity [22,23]. Studies concerning HGST measurements in patients with PCC are still scarce [24,25].

So far, descriptions of functioning in COVID-19 have mainly focused on patients after hospitalization or intensive care. The current study aimed to evaluate patients after mild or moderate primary COVID-19 infection referred from primary healthcare to gain a deeper understanding of their needs, and the challenges they face in terms of functioning, and to derive insights that would guide their rehabilitation process. We studied the functioning of PCC patients at Finland's only PCC clinic. Because patients with PCC have

experienced strong subjective symptoms and limitations in their functioning we hypothesized them to exhibit significant reductions in physical functioning and HRQoL compared with subjects without PCC symptoms.

Material and methods

This is a cross-sectional study of patients with PCC referred to rehabilitation at the Outpatient Clinic for Persistent Symptom Rehabilitation, formerly known as the Outpatient Clinic for the Long-Term Effects of COVID-19, at Helsinki University Hospital (HUS), Finland. The recruitment period was 1.6.2021–18.10.2023. The patients admitted to the clinic presented cases of the more severe and prolonged spectrum of persistent symptoms after a mild or moderate home-treated primary COVID-19 infection. Patients were referred mostly from primary health care, and less often from other university hospital clinics. All subjects who agreed to participate and met the inclusion criteria were prospectively recruited. The inclusion and exclusion criteria of the study PCC patients are presented in Table 1. Methods are described in more detail in the protocol paper [26]. A total of 627 individuals were assessed for eligibility to participate in the study. Of these, 185 individuals were excluded for reasons such as declining participation, lack of language skills, or being too unwell to participate. Finally, 442 PCC patients were included in the study.

Control subjects were initially gathered from two separate studies. We first recruited voluntary controls from another clinical study at HUS, which assessed symptoms associated with PCC in individuals who tested either positive or negative for COVID-19 [27]. From this study, we included individuals who tested negative for COVID-19. Secondly, we recruited additional controls through a social media campaign organized by the Finnish Institute of Occupational Health, focusing on an ongoing study about PCC and work capacity in working-age individuals. In this study, participants included were those who had either

Table 1. Inclusion and exclusion criteria of the post-COVID-19 condition patients.

The inclusion criteria	The exclusion criteria
Age ≥ 18 years, referred to the Clinic for Long-Term Effects of COVID-19 either from other hospital units or primary care	Patients not able to fill out the forms in Finnish.
COVID-19 diagnosis ≥ 3 months earlier (confirmed by PCR or antibody testing)	Participation in the study would be unreasonably inconvenient (e.g. patients on bed rest).
Willingness to be enrolled in the study, by signing the informed consent.	

recovered from COVID-19 within three months without prolonged symptoms or had not knowingly had COVID-19 at the time of their recruitment and evaluation. Finally, personal contacts of clinic staff who did not exhibit PCC symptoms were invited to participate in the study. All controls were matched by age, gender, and the timing of infection to reflect the COVID-19 variant that was prevalent at the time.

Registration details Protocol version (1.0) and trial registration data have been registered at www.clinicaltrials.gov (NCT05699512). We followed the STROBE guidelines for cross-sectional studies in the writing process of this article (Table S1).

Questionnaires and register data

Participants were asked to complete a questionnaire detailing their weight (kg), height (cm), employment status (yes/no), tertiary education (yes/no), living alone (yes/no), smoking (yes/no), and weekly rigorous exercise (yes/no) and duration of COVID symptoms (only in PCC patients).

The patient-reported outcome measures (PROMs) were assessed by a questionnaire. The initial survey included the WHODAS 2.0 (WHO Disability Assessment Schedule 2.0), comprising 36 questions across six domains: cognition, mobility, self-care, getting along, life activities, and participation [15]. In WHODAS 2.0, scores ranging from 0 to 4 indicate no limitations in functioning while scores from 5 to 24 reflect mild functional limitation, 25–49 indicates moderate limitation, 50–95 indicates severe limitation, and 96–100 indicates extreme limitation. A person is asked to consider functioning in the period of past 30 days. Furthermore, patients were requested to assess their functional ability on a scale from 0 ('completely non-functional') to 10 ('excellent').

Data on comorbidities and depressive medications (yes/no) and confirmed hospitalization and intensive care during acute COVID-19 (yes/no) were collected electronically from the patients' healthcare data during the previous five years. It covered data from the tertiary care center (Helsinki University Hospital, HUS) and primary care consultations in HUS acute departments. Other primary healthcare data (public or private) or occupational healthcare data was not possible to be included. Data on valid prescriptions was gathered at the time of the visit to the clinic from the HUS Data Lake on the HUS Acamedic platform.

Clinical evaluation

A physician conducted a clinical examination of all patients visiting the outpatient clinic. Recognized

complications associated with acute COVID-19 infections, such as pulmonary fibrosis and intensive care myopathy, were managed in specialized hospital units (pulmonology and internal medicine). Although, they were not typical findings in patients of this study. Before referral to the rehabilitation clinic, other potential or obvious conditions that could explicitly explain the symptoms were systematically ruled out. The clinic's physician (GP or occupational health physician) evaluated, whether symptoms could be explained by the patient's known comorbidities. The physiotherapist measured the blood pressure (mmHg).

Physical function tests

The testing was conducted under the supervision of the Clinic's physiotherapist and encompassed various assessments. These included measuring dominant hand grip strength test (HGST) in kilograms (kg) using a Jamar/Saehan baseline hand dynamometer [28]. The measuring of HGS was performed three times, and the value of the best effort was taken into the statistical analysis. Additionally, a 6-minute walking test (6MWT) in meters (m) was conducted [20].

Ethical approval and consent to participate

The study received approval from the Helsinki University Hospital research ethics committee board under ID HUS/1493/2021 on 06-03-2021. All participants in the study provided written informed consent for their participation.

Data analysis

Survey data was collected in the Helsinki University Hospital Electronic Case Report Form (HUSeCRF), from paper and online surveys. It was merged with registry and clinical measurement data gathered from the HUS Data Lake on the HUS Acamedic platform. In all analyses, the level of significance was set at $p < 0.05$. The statistical analyses were carried out using R statistical computing environment version 4.2.3 (R Core Team, 2016. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>). R packages ggplot2 and kableExtra were used for visualization.

Demographic parameters, along with the total and subdomain scores (mean (SD/%) of WHODAS 2.0, HGST, and 6MWT, were computed and reported. Differences between PCC patients and control subjects

were calculated with the Kruskal-Wallis test for continuous, and the chi-squared test for discrete variables. In all analyses, the level of significance was set at $p < 0.05$.

Bivariate binomial and multivariable regression analyses were conducted to assess personal and environmental factors predicting above or below WHODAS 2.0 score 24 in PCC group. Generally, 24 is considered as the limit of mild and moderate deficit in functioning in WHODAS 2.0 [15]. We also assessed the linear relations between the WHODAS 2.0 score and reference-adjusted functioning measurements (HGST and 6MWT) [20,29].

We used a chi-squared test for each variable analysed in logistic regression with WHODAS to assess whether missingness was associated with WHODAS score above/below 24. No evidence of effects on missingness was found.

Results

The baseline characteristics of study participants are described in Table 2. When comparing the characteristics of individuals with PCC to control subjects, there were no significant differences in terms of age, gender, height, mass, BMI, and systolic blood pressure. Employment rates were lower in the PCC group ($p < 0.001$), and a smaller proportion of this group reported engagement in weekly vigorous exercise ($p < 0.001$). Living alone and smoking habits did not differ significantly between the groups.

The PCC group had a higher mean number of comorbidities ($p < 0.001$) and use of depression medications ($p = 0.001$), and they were more likely to have confirmed hospitalization (8,5%, $p = 0.002$) and intensive care during acute COVID-19 (4,1%, $p = 0.008$). Health conditions such as asthma, anxiety disorder, hypertension, depression, migraine and hypothyroidism were all more prevalent in the PCC group, with statistical significance ranging from $p < 0.001$ for asthma to $p = 0.049$ for migraine.

WHODAS 2.0 scores revealed that the PCC group experienced greater impairments, with higher mean scores indicating worse functionality in all domains ($p < 0.001$) (Table 2 and Figure 1). PCC patients reported moderate or severe limitations in all aspects of functioning, particularly in life activities at home and work, and in participation (Figure 1). The functional ability of patients with PCC was 4.8 on a scale of 0–10, indicating significant functional impairments, while controls rated their functioning at 8.7.

The PCC group exhibited a substantially reduced walking distance in the 6MWT compared to the control group (Table 2). The PCC group and the control group did not show a significant difference in HGST.

In the multinomial regression models, factors predicting moderate or severe disability according to WHODAS 2.0 (score of 24 or more) were one comorbidity (OR 1.9, CI 1.1–3.2), two or more comorbidities (OR 2.6, CI 1.5–4.5), smoking (OR 3.9, CI 1.3–16.5), anxiety disorder (OR 3.4, CI 1.4–10.2) and depression OR 3.4 (CI 1–7.4) (Table 3).

The scatter plots and linear correlations reveal that subjective measures of functional ability, as assessed by WHODAS 2.0 scores, do not effectively predict the results of physical performance tests (HGST and 6MWT) (Figure 2). We also performed adjusted multivariate analyses with age, sex, hospitalization, and treatment in the intensive care unit, but they did not significantly change the results.

Discussion

We found that the functioning of patients with PCC was significantly decreased compared to controls without PCC. Results in WHODAS 2.0 and the 6MWT were weaker in the PCC group than among controls. Key predictors of severe disability included the presence of multiple comorbidities, smoking, and mental health conditions like anxiety and depression in the PCC group.

Patient-reported outcome measures

According to WHODAS 2.0, patients with PCC had difficulties in all dimensions of functioning. Especially the life activities in the household, work, and participation were impaired. Results were similar to those of subjects with mental health problems and physical problems in WHO's WHODAS 2.0 background materials [15]. Our observations, where the average WHODAS scores significantly exceed the 24-point threshold, further emphasize that functional limitations are particularly significant in life activities at home and work, as well as in social participation. This consistency suggests that WHODAS 2.0 is an effective tool for documenting and comparing the extensive impact of functional limitations caused by PCC across various studies. As depicted by WHODAS 2.0, patients with PCC presented similar findings with a scale of 0–10 compared to controls, 4.8 versus 8.7.

Patients with PCC had more comorbid diseases such as asthma, diabetes, migraine, depression, hypertension, and anxiety disorder than controls. Most of them had had at least one chronic comorbidity before their COVID-19 infection. The socioeconomic status and educational level were also lower in the PCC group

Table 2. Characteristics of post-COVID-19 condition (PCC) ($n=442$) and control subjects ($n=198$).

Parameters	Number of subjects (PCC/control)	PCC	Control	P-value [#]
Age (years) Mean (SD)	442/198	44.8 (11.3)	44.9 (10.5)	0.65
Female, N (%)	442/198	312(70.6)	150(75.8)	0.20
Height (cm) Mean (SD)	426/193	170.8 (9.0)	170.8 (9.0)	0.96
Weight (kg) Mean (SD)	406/186	80.3 (19.1)	79.3 (18.7)	0.60
BMI (kg/m ²) Mean (SD)	405/186	27.4 (5.8)	27.0 (5.6)	0.40
HR (bpm) Mean (SD)	224/196	69.3 (10.9)	71.6 (12.4)	0.047
SBP (mmHg) Mean (SD)	222/196	130.6 (16.5)	130.4 (17.5)	0.81
DBP (mmHg) Mean (SD)	222/196	88.7 (10.2)	86.9 (10.0)	0.04
Symptom duration (years) Mean (SD)	248/ NA	0.9 (0.6)	NA	NA
Employed N (%)	428/198	294(68.7)	175(88.4)	< .001
Tertiary education N (%)	420/197	244(58.1)	148(75.1)	0.001
Living alone, N (%)	442/198	117(26.5)	45(22.7)	0.32
Smoking, N (%)	422/194	30(7.1)	13(6.7)	0.87
Weekly rigorous exercise N (%)	85/196	24(28.2)	143(73.0)	< .001
Confirmed hospitalization during acute COVID-19 N (%)	436/148	37(8.5)	1(0.7)	0.002
Confirmed intensive during acute COVID-19 N (%)	436/148	18(4.1)	0(0.0)	0.008
Depression medications N (%)	436/148	50(11.5)	2(1.4)	0.001
Objective physical function tests				
Dominant hand grip strength (kg) Mean (SD)	247/197	35.3 (11.3)	34.0 (9.8)	0.38
6MWT distance (m) Mean (SD)	249/119	435.1 (97.9)	626.8 (69.9)	< .001
The patient-reported outcome measures				
Daily functioning (0-10) Mean (SD)	407/194	4.8 (2.0)	8.7 (1.2)	< .001
WHODAS				
WHODAS2.0 Overall Mean (SD)	423/197	34.4 (17.5)	5.7 (7.9)	< .001
WHODAS2.0 Cognition Mean (SD)	423/197	26.0 (19.6)	4.3 (7.3)	< .001
WHODAS2.0 Mobility Mean (SD)	423/197	26.9 (23.3)	2.4 (7.1)	< .001
WHODAS2.0 Self-care Mean (SD)	423/197	10.8 (14.7)	1.3 (5.7)	< .001
WHODAS2.0 Getting along Mean (SD)	422/197	32.5 (24.9)	8.1 (13.8)	< .001
WHODAS2.0 Life activities in home Mean (SD)	422/196	49.2 (28.1)	11.6 (16.7)	< .001
WHODAS2.0 Life activities in work Mean (SD)	413/196	57.2 (32.2)	8.7 (14.8)	< .001
WHODAS2.0 Participation Mean (SD)	414/196	38.4 (19.6)	5.7 (10.0)	< .001
Comorbidities				
At least one comorbidity N (%)	423/136	228(53.9)	38(27.9)	< .001
Number of comorbidities Mean (SD)	423/136	1.1 (1.4)	0.4 (0.7)	< .001
Various comorbidities				
Asthma N (%)	423/136	67(15.8)	3(2.2)	< .001
Anxiety disorder N (%)	423/136	37(8.7)	3(2.2)	0.01
Back or neck disease N (%)	423/136	36(8.5)	6(4.4)	0.14
Hypertension N (%)	423/136	35(8.3)	2(1.5)	0.004
Sleep apnea N (%)	423/136	33(7.8)	6(4.4)	0.26
Depression N (%)	423/136	28(6.6)	2(1.5)	0.03
Migraine N (%)	423/136	28(6.6)	3(2.2)	0.049
Long-term insomnia N (%)	423/136	16(3.8)	1(0.7)	0.08
Hypothyroidism N (%)	423/136	20(4.7)	1(0.7)	0.04
Cancer N (%)	423/136	10(2.4)	5(3.7)	0.53
Diabetes N (%)	423/136	14(3.3)	0(0.0)	0.05
Cardiac arrhythmia N (%)	423/136	13(3.1)	2(1.5)	0.38
Allergic rhinitis N (%)	423/136	12(2.8)	1(0.7)	0.19
Irritable bowel syndrome N (%)	423/136	10(2.4)	1(0.7)	0.31

N: number of participants, SD: standard deviation, BMI: body mass index, HR: heart rate, bpm: beats per minute, SBP: systolic blood pressure, DBP: diastolic blood pressure, 6MWT: 6-minute walking test, NA: not applicable.

[#]P-values for group differences were obtained using: Kruskal-Wallis and chi-square Test.

compared to controls. In our bivariate binomial regression analysis, we found that factors predicting moderate or severe disability (WHODAS 2.0 score 24 or more) were the presence of comorbidities, smoking, depression, and anxiety disorder.

WHODAS 2.0 has lately been adopted as a national quality indicator in Finland. It gives a comprehensive picture of the patient's ability to function in different areas of life and might reveal areas in which the rehabilitation process in conditions like PCC should focus. However, so far WHODAS 2.0 is still poorly known among GPs and therefore underused in Finnish primary health care. However, it would have the potential

to find rehabilitation targets earlier and with fewer resources, also in patients with PCC. On the other hand, subjective measures of functional ability, as assessed by WHODAS 2.0 scores, do not effectively predict the results of physical performance tests. This suggests that WHODAS 2.0 scores and objective physical performance tests HGST and 6MWT assess different aspects of health and functioning.

Physical function tests

The effects of PCC on physical performance have been examined in various studies using standardized

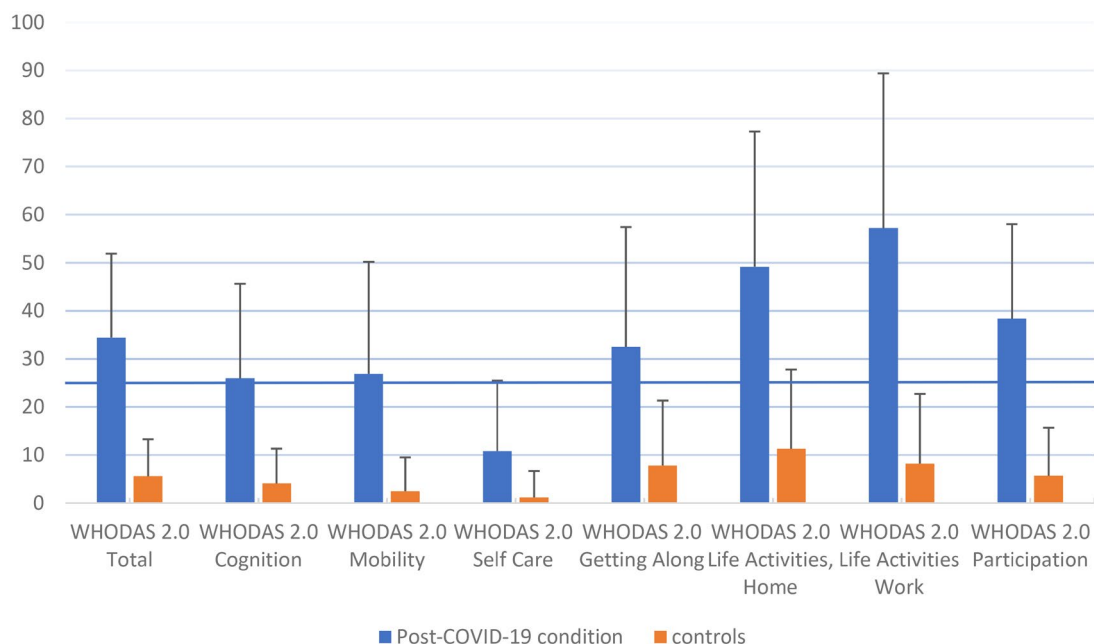


Figure 1. WHODAS 2.0 domain scores (mean, SD): comparative analysis of post-COVID-19 condition patients and controls. Highlighting the 24-point threshold for distinguishing mild to moderate disability.

Table 3. Binomial and multivariable regression analyses predicting WHODAS 2.0 scores above or below 24 adjusted for age and gender in post-Covid-19 condition group.

	Levels	N	OR	95%CI
Number of comorbidities	0	179	Reference group	
	1	109	1.9	1.1-3.2
	1+	130	2.6	1.5-4.5
BMI	Normal	159	Reference group	
	Overweight	138	1.3	0.8-2.2
	Obese	105	1.1	0.7-1.9
Living alone	No	307	Reference group	
	Yes	116	1.2	0.7-1.9
Smoking	No	387	Reference group	
	Yes	30	3.9	1.3-16.5
Depression	No	385	Reference group	
	Yes	33	2.4	1-7.4
Anxiety disorder	No	375	Reference group	
	Yes	43	3.4	1.4-10.2
Confirmed hospitalization during acute COVID-19	No	381	Reference group	
	Yes	37	1.1	0.5-2.5
Confirmed intensive during acute COVID-19	No	400	Reference group	
	Yes	18	0.7	0.3-2.1

BMI: body mass index.

performance tests, such as the 6MWT and HGST [20–24]. In our study, PCC patients walked significantly shorter distances within six minutes compared to healthy controls as also shown previously [30]. This

reflects general physical fatigue and reduced pulmonary and cardiac capacity, which are typical symptoms of PCC. Studies have shown that the results of the 6MWT correlate with the severity of PCC symptoms [31].

The HGST measure is an important indicator of overall muscle strength and functional health [22,23]. The PCC patients have shown reduced HGS, indicating muscle weakness and possible neurological complications that can affect motor control and muscle strength [24]. In our study, there were no differences in HGST results between groups. Differences in study designs and patient cohorts may explain the variations between studies.

A poor WHODAS 2.0 result correlated with a significantly shorter walking distance in the 6MWT test. A weaker correlation was found between WHODAS 2.0 results and hand grip strength. In a recent study, HGST was reduced in patients with ME/CFS only when repeated [25]. The study also included patients with PCC. As for a single squeeze, the result is therefore not necessarily able to reveal muscle fatigue related to PCC.

Strengths and limitations of this study

A strength of this study is that more than 90% of the patients were non-hospitalized in the acute phase of COVID-19 and referred from primary care and making the results more generalizable within the population. Also, hospitalization did not emerge as an independent predictor of functional decline in the



Figure 2. Scatter plots comparing WHODAS 2.0 scores and hand grip strength and 6-minute walking test (6MWT) (adjusted for age, height, and gender) results between post-COVID-19 condition (PCC) patients (red) and control patients (cyan). Linear regression lines illustrate weak correlations within the PCC group, with low R^2 values indicating minimal explanatory power of the linear models.

multivariable model. General practitioners or occupational health physicians at the HUS Post-COVID-19 clinic clinically assessed all patients. All patients were COVID-19 PCR or antigen positive and attended the only post-COVID condition clinic in the country.

A limitation of the study is that the population represents the more severe end of PCC as the rehabilitation clinic is a tertiary care unit that demands a referral from primary health care. Thus, the results cannot be generalized to primary care patients with PCC, who may have better functioning. The controls were also selected and therefore did not necessarily represent average citizens.

A limitation of this study is the potential unequal documentation of comorbidities between controls and patients. There is a concern that controls who utilized primary or occupational health services might have underreported individual diseases. This discrepancy in the recording of diagnostic codes could bias the main findings. Furthermore, the HUS Registry data, which mainly captures specialist care visits, may not fully reflect all conditions documented during outpatient clinic visits.

A further limitation is that questionnaire-based PROM assessments of functioning are subjective. However, the diagnosis of PCC is based on reported subjective symptoms. Consequently, subjective symptoms are the most valid endpoints [32]. Physical tests like a 6MWT and HGST, are semi-objective because they are affected by ill being and require effort. It might also be possible to consider that PCC patients may experience significant variability in their condition

from day to day or over different periods, which could impact their results compared to controls, whose conditions are presumably more stable.

Given that this study is cross-sectional, the observed associations cannot confirm causality or the direction of the relationships between PCC and functional impairments. Future research should include longitudinal studies to track changes over time and better establish causal links between PCC and functional outcomes. Additionally, randomized controlled trials could be useful in assessing the effectiveness of specific rehabilitation interventions for improving functioning in patients with PCC.

Conclusion

In conclusion, the reduced functioning in patients with PCC appears to be multifactorial and not only related to COVID-19 infection. Chronic illnesses, anxiety, and a more vulnerable social status affect the deterioration of functioning in addition to the effects of COVID-19 infection. For GPs, this means that these patients need to be encountered holistically while considering patients' previous health problems, comorbidities, potential anxiety, and socioeconomic circumstances such as work and living conditions.

Implications

Comprehending the functional challenges faced by PCC patients is essential, not only to assist in their return to regular activities but also to navigate the

complexities of their condition in the absence of a known etiology. The goal of functional disabilities characterization was to improve the targeting of aid and support to these patients.

Because of the reduced walking capacity, the patients may be at risk of deconditioning. The 6MWT could be important in monitoring PCC, as it provides objective measures of functional limitations that might go unnoticed with only subjective symptom descriptions. The studies emphasize the need for comprehensive rehabilitation programs that specifically target improving these areas of functionality in PCC patients.

Multisystem symptoms of PCC are strikingly similar to those of functional disorders triggered by acute illnesses [33]. While the hypothesis of PCC corresponding to a functional disorder needs to be tested, its treatment and rehabilitations follows the same lines as for functional disorders [34].

A biopsychosocial approach and multi-professional care, such as help from physiotherapists and psychologists, is often needed to help these patients overcome their problems with functioning. GPs should remember the potential vicious cycle where symptom worry leads to patients' fear of physical activity [34]. This may cause deterioration of overall health and functioning in the long run. Timely support from primary healthcare professionals is needed to overcome these challenges.

Acknowledgments

We thank the study nurses, physical therapists, and colleagues for their attribution. We are grateful to the patients participating in the study. Special thanks go to Susanna McLellan and Jaana Paltamaa for their help with the WHODAS 2.0 questionnaire.

Disclosure statement

The authors declare no conflict of interest relevant to this article.

Funding

This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101057553.

ORCID

Kirsi Kvarnström  <http://orcid.org/0000-0002-3136-5972>

References

- [1] Soriano JB, Murthy S, Marshall JC, et al. A clinical case definition of post-COVID-19 condition by a Delphi

- consensus. *Lancet Infect Dis.* 2022;22(4):e102–e107. doi: [10.1016/S1473-3099\(21\)00703-9](https://doi.org/10.1016/S1473-3099(21)00703-9).
- [2] de Oliveira Almeida K, Nogueira Alves IG, de Queiroz RS, et al. A systematic review on physical function, activities of daily living and health-related quality of life in COVID-19 survivors. *Chronic Illn.* 2023;19(2):279–303. doi: [10.1177/17423953221089309](https://doi.org/10.1177/17423953221089309).
- [3] Havervall S, Rosell A, Phillipson M, et al. Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers. *JAMA.* 2021;325(19):2015–2016. doi: [10.1001/jama.2021.5612](https://doi.org/10.1001/jama.2021.5612).
- [4] Rodríguez-Pérez MP, Sánchez-Herrera-Baeza P, Rodríguez-Ledo P, et al. Headaches and dizziness as disabling, persistent symptoms in patients with long COVID-A national multicentre study. *J Clin Med.* 2022;11(19):5904. doi: [10.3390/jcm11195904](https://doi.org/10.3390/jcm11195904).
- [5] Nielsen TB, Leth S, Pedersen M, et al. Mental fatigue, activities of daily living, sick leave and functional status among patients with Long COVID: a cross-sectional study. *Int J Environ Res Public Health.* 2022;19(22):14739. doi: [10.3390/ijerph192214739](https://doi.org/10.3390/ijerph192214739).
- [6] Crivelli L, Palmer K, Calandri I, et al. Changes in cognitive functioning after COVID-19: a systematic review and meta-analysis. *Alzheimers Dement.* 2022;18(5):1047–1066. doi: [10.1002/alz.12644](https://doi.org/10.1002/alz.12644).
- [7] Ceban F, Ling S, Lui LMW, et al. Fatigue and cognitive impairment in Post-COVID-19 Syndrome: a systematic review and meta-analysis. *Brain Behav Immun.* 2022;101:93–135. doi: [10.1016/j.bbi.2021.12.020](https://doi.org/10.1016/j.bbi.2021.12.020).
- [8] Mazza MG, Palladini M, Poletti S, et al. Post-COVID-19 depressive symptoms: epidemiology, pathophysiology, and pharmacological treatment. *CNS Drugs.* 2022;36(7):681–702. doi: [10.1007/s40263-022-00931-3](https://doi.org/10.1007/s40263-022-00931-3).
- [9] Lin YN, Liu ZR, Li SQ, et al. Burden of sleep disturbance during COVID-19 pandemic: a systematic review. *Nat Sci Sleep.* 2021;13:933–966. doi: [10.2147/NSS.S312037](https://doi.org/10.2147/NSS.S312037).
- [10] Adler L, Gazit S, Pinto Y, et al. Long-COVID in patients with a history of mild or asymptomatic SARS-CoV-2 infection: a Nationwide Cohort Study. *Scand J Prim Health Care.* 2022;40(3):342–349. doi: [10.1080/02813432.2022.2139480](https://doi.org/10.1080/02813432.2022.2139480).
- [11] Phiri P, Ramakrishnan R, Rathod S, et al. An evaluation of the mental health impact of SARS-CoV-2 on patients, general public and healthcare professionals: a systematic review and meta-analysis. *EClinicalMedicine.* 2021;34:100806. doi: [10.1016/j.eclinm.2021.100806](https://doi.org/10.1016/j.eclinm.2021.100806).
- [12] Wunsch K, Kienberger K, Niessner C. Changes in physical activity patterns due to the Covid-19 pandemic: a systematic review and meta-analysis. *Int J Environ Res Public Health.* 2022;19(4):2250. doi: [10.3390/ijerph19042250](https://doi.org/10.3390/ijerph19042250).
- [13] Nyberg A, Rajaleid K, Demmelmaier I. The work environment during coronavirus epidemics and pandemics: a systematic review of studies using quantitative, qualitative, and mixed-methods designs. *Int J Environ Res Public Health.* 2022;19(11):6783. doi: [10.3390/ijerph19116783](https://doi.org/10.3390/ijerph19116783).
- [14] Ustün TB, Chatterji S, Kostansjek N. et al. WHO's ICF and functional status information in health records. *Health Care Financ Rev.* 2003;24(3):77–88.
- [15] Ustün TB, Chatterji S, Kostanjsek N. et al. Developing the world health organization disability assessment

- schedule 2.0. *Bull World Health Organ.* 2010;88(11):815–823. doi: [10.2471/BLT.09.067231](https://doi.org/10.2471/BLT.09.067231).
- [16] Gaur R, Asthana S, Yadav R, et al. Assessment of physical disability after three months in patients recovered from COVID-19: a cross-sectional study. *Cureus.* 2022;14(1):e21618. doi: [10.7759/cureus.21618](https://doi.org/10.7759/cureus.21618).
- [17] Fernandes J, Fontes L, Coimbra I, et al. Health-related quality of life in survivors of severe COVID-19 of a university hospital in northern Portugal. *Acta Med Port.* 2021;34(9):601–607. doi: [10.20344/amp.16277](https://doi.org/10.20344/amp.16277).
- [18] Larsson SB, von Feilitzen GS, Andersson ME, et al. Author Correction: self-reported symptom severity, general health, and impairment in post-acute phases of COVID-19: retrospective cohort study of Swedish public employees. *Sci Rep.* 2023;13(1):313. doi: [10.1038/s41598-022-26999-x](https://doi.org/10.1038/s41598-022-26999-x).
- [19] Hodgson CL, Higgins AM, Bailey MJ, et al. The impact of COVID-19 critical illness on new disability, functional outcomes and return to work at 6 months: a prospective cohort study. *Crit Care.* 2021;25(1):382. doi: [10.1186/s13054-021-03794-0](https://doi.org/10.1186/s13054-021-03794-0).
- [20] Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med.* 1998;158(5 Pt 1):1384–1387. doi: [10.1164/ajrccm.158.5.9710086](https://doi.org/10.1164/ajrccm.158.5.9710086).
- [21] Barker-Davies RM, O’Sullivan O, Holdsworth DA, et al. How long is Long-COVID? Symptomatic improvement between 12 and 18 months in a prospective cohort study. *BMJ Mil Health.* 2023;3:e002500. doi: [10.1136/military-2023-002500](https://doi.org/10.1136/military-2023-002500).
- [22] Norman K, Stobäus N, Gonzalez MC, et al. Hand grip strength: outcome predictor and marker of nutritional status. *Clin Nutr.* 2011;30(2):135–142. doi: [10.1016/j.clnu.2010.09.010](https://doi.org/10.1016/j.clnu.2010.09.010).
- [23] Rantanen T, Guralnik JM, Foley D, et al. Midlife hand grip strength as a predictor of old age disability. *JAMA.* 1999;281(6):558–560. doi: [10.1001/jama.281.6.558](https://doi.org/10.1001/jama.281.6.558).
- [24] do Amaral C, da Luz Goulart C, da Silva BM, et al. Low handgrip strength is associated with worse functional outcomes in long COVID. *Sci Rep.* 2024;14(1):2049. doi: [10.1038/s41598-024-52401-z](https://doi.org/10.1038/s41598-024-52401-z).
- [25] Walitt B, Singh K, LaMunion SR, et al. Deep phenotyping of post-infectious myalgic encephalomyelitis/chronic fatigue syndrome. *Nat Commun.* 2024;15(1):907. doi: [10.1038/s41467-024-45107-3](https://doi.org/10.1038/s41467-024-45107-3).
- [26] Virrantaus H, Liira H, Posharina T, et al. Prognosis of patients with long COVID symptoms: a protocol for a longitudinal cohort study at a primary care referred outpatient clinic in Helsinki, Finland. *BMJ Open.* 2023;13(10):e072935. doi: [10.1136/bmjopen-2023-072935](https://doi.org/10.1136/bmjopen-2023-072935).
- [27] Kantele A, Paajanen J, Pietilä JP, et al. Long COVID-associated symptoms prevalent in both SARS-CoV-2 positive and negative individuals: A prospective follow-up study. *New Microbes New Infect.* 2023;56:101209. doi: [10.1016/j.nmni.2023.101209](https://doi.org/10.1016/j.nmni.2023.101209).
- [28] Peters MJ, van Nes SI, Vanhoutte EK, PeriNomS Study group, et al. Revised normative values for grip strength with the Jamar dynamometer. *J Peripher Nerv Syst.* 2011;16(1):47–50. doi: [10.1111/j.1529-8027.2011.00318.x](https://doi.org/10.1111/j.1529-8027.2011.00318.x).
- [29] FinHealth 2017 Study–Methods. In: K. K. Borodulin Sääksjärvi, editors. Finnish institute for health and welfare. Helsinki; 2019. p. 132.
- [30] Sirayder U, Inal-Ince D, Kepenek-Varol B, et al. Long-term characteristics of severe COVID-19: respiratory function, functional capacity, and quality of life. *Int J Environ Res Public Health.* 2022;19(10):6304. doi: [10.3390/ijerph19106304](https://doi.org/10.3390/ijerph19106304).
- [31] Kersten J, Wolf A, Hoyo L, et al. Symptom burden correlates to impairment of diffusion capacity and exercise intolerance in long COVID patients. *Sci Rep.* 2022;12(1):8801. doi: [10.1038/s41598-022-12839-5](https://doi.org/10.1038/s41598-022-12839-5).
- [32] Flottorp SA, Brurberg KG, Fink P, et al. New NICE guideline on chronic fatigue syndrome: more ideology than science? *Lancet.* 2022;399(10325):611–613. doi: [10.1016/S0140-6736\(22\)00183-0](https://doi.org/10.1016/S0140-6736(22)00183-0).
- [33] Teodoro T, Chen J, Gelauff J, et al. Functional neurological disorder in people with long COVID: A systematic review. *Eur J Neurol.* 2023;30(5):1505–1514. doi: [10.1111/ene.15721](https://doi.org/10.1111/ene.15721).
- [34] Alme TN, Andreasson A, Asprusten TT, et al. Chronic fatigue syndromes: real illnesses that people can recover from. *Scand J Prim Health Care.* 2023;41(4):372–376. doi: [10.1080/02813432.2023.2235609](https://doi.org/10.1080/02813432.2023.2235609).