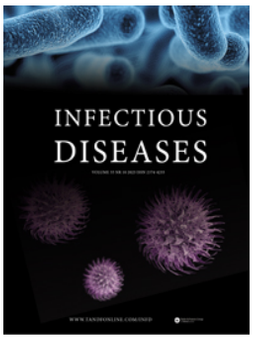

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RESEARCH ARTICLE

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Persisting symptoms common but inability to work rare: a one-year follow-up study of Finnish hospitalised COVID-19 patients

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ABSTRACT

Background: Difficulties in recovery persisting for months have been reported in patients with severe COVID-19. Our aim was to investigate respiratory and overall recovery one year after hospital discharge.

Methods: Finnish patients hospitalised due to COVID-19 during the first wave of the pandemic were recruited to a survey of symptoms, quality of life (RAND-36), work status, and health care use one year after hospital discharge. Patients with lung function test and chest x-ray results available from 3-6 months after hospital discharge underwent spirometry and a chest x-ray at one year.

Results: Ninety-six patients responded to the one-year survey, 32 underwent spirometry and 32 a chest x-ray. Of those working full-time before COVID-19, median duration of sick leave was 40 days and 10% had not returned to work at one year. Health-care service use related to COVID-19 after discharge was reported by 79%, 50% using primary care, 34% occupational health care and 32% specialist care, respectively. Tiredness, fatigue, and physical difficulties increased in follow-up ($p = 0.022$–0.033). Quality of life did not change. Chest x-ray abnormalities decreased in follow-up, with an abnormal chest x-ray in 58% at 3–6 months and 25% at one year. A restrictive spirometry pattern was more common at one year (16 vs. 34%, $p = 0.014$).

Conclusions: Prolonged symptoms are common, some patients have decreased lung function, and a small minority of patients still have not returned to work one year after severe COVID-19. This calls for further research into the underlying causes and risk factors for prolonged recovery.

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Introduction

COVID-19 was declared a pandemic by the World Health Organisation in March 2020 [1]. While most COVID-19 cases are mild, some patients fall severely ill: during the first wave of the pandemic, it was estimated that up to 14% of COVID-19 patients needed hospitalisation, of which a fifth required intensive care [2–5]. In later waves of the pandemic, the risk of severe illness has decreased due to vaccinations and the surfacing of the omicron variants, which less often lead to severe disease [6,7].

Follow-up studies of COVID-19 patients have shown persisting symptoms, decreased lung function, and radiological abnormalities months after acute infection, especially in patients with severe COVID-19 [8–11]. Although the incidence of severe and critical COVID-19 has decreased, the long-term symptoms could still be widely experienced, as they appear to be even more common in outpatients [12,13]. Persisting symptoms have been described up to two years after hospitalisation [14]. Moreover, long durations of sick leave in COVID-19 patients have been described, but studies on hospitalised patients are scarce [15,16].

In the FINCOVID-19 study, we have studied the recovery of Finnish adult patients hospitalised due to COVID-19 during the first wave of the pandemic in 2020 [17]. In the previously published 6-month follow-up study, most patients reported some symptoms and 11% had not returned to work full-time. In the present study, our aim was to investigate persisting symptoms, recovery of lung function and presence of radiological abnormalities one year after severe COVID-19. Moreover, we aimed to assess the length of sick leave and the need to use health care services after hospital discharge.

Materials and methods

Patient selection and study design

This study is part of the FINCOVID-19 study, which was approved by the Research Ethics Committee of Helsinki University Hospital (§148 HUS/1922/2020). Inclusion criteria to the FINCOVID-19 study were hospitalisation due to laboratory-confirmed SARS-CoV-2 infection (International Classification of Diseases code U07.1) between March and June 2020 in Helsinki University Hospital cohort wards, age over 18 years, and sufficient language skills in Finnish, Swedish, or English [17]. The first survey was conducted six months after hospital discharge. Patients who responded to the first survey, were recruited to the second survey one year after hospital discharge.

Additionally, a subset of patients underwent spirometry and a chest x-ray one year after hospital discharge. At the Helsinki University Hospital, patients hospitalised due to COVID-19 were routinely referred to the COVID-19 follow-up clinic if they had been admitted to the intensive care unit or if the ward clinician classified their disease as severe. These follow-up visits 3–6 months after hospital discharge included lung function tests and a chest x-ray. The 6-month FINCOVID-19 survey respondents were screened for those with results available from the 3–6-month follow-up visits and were recruited to spirometry and a chest x-ray one year after hospital discharge.

The flowchart of patient selection is illustrated in Figure 1. Altogether, 103 patients were included in the present study. Ninety-six patients responded to the survey (response rate 72%). Fifty-eight patients were recruited to one-year spirometry and chest x-ray, of which thirty-three patients were included in the spirometry/chest x-ray group (participation rate 57%): 31 underwent both spirometry and a chest x-ray, one patient underwent only chest x-ray and one only spirometry. Written informed consent was obtained from all participants.

Methods

Participants undertook a survey six months and one year after hospital discharge. The 6-month follow-up protocol has been previously described [17]. The one-year survey consisted of a 12-item symptom questionnaire, the modified Medical Research Council (mMRC) dyspnoea scale, RAND-36 quality of life questionnaire,

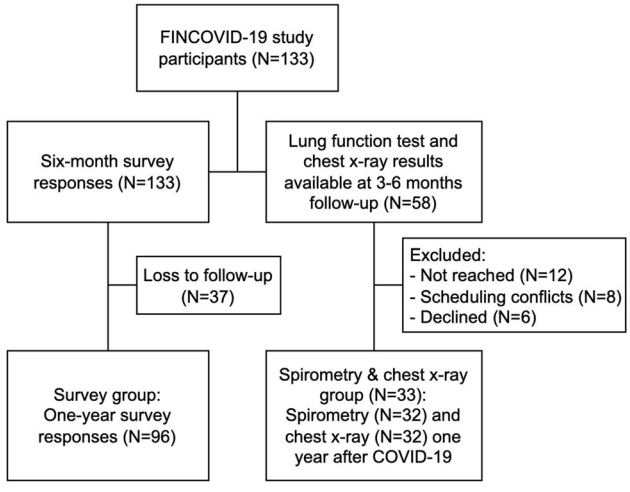

Figure 1. Flowchart of patient selection.

and questions about duration of sick leave and use of health care services due to COVID-19 related problems after hospital discharge. Both questionnaires were available in Finnish, Swedish, and English.

The symptoms in the 6-month questionnaire were cough, dyspnoea, tiredness, fatigue, dizziness, gastrointestinal symptoms, difficulties while moving, loss of taste or smell, sleeping problems, and mood problems. Two additional symptoms, joint pain and memory problems/brain fog, were added to the one-year symptom questionnaire, as new knowledge of these being common symptoms of COVID-19 had emerged after the first follow-up study. Symptoms were reported on a scale of 0, "not at all" to 10", all the time". Symptoms were considered severe, if the answer was 6-10 on the 0-10 scale. In the 6 months questionnaire, patients were asked to additionally report experienced symptoms retrospectively one month before COVID-19.

One-year spirometry and chest x-rays were performed in the Aava Medical Centre and results were compared with the measurements performed 3-6 months after hospital discharge in the Helsinki University Hospital. Spirometry variables evaluated were forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and forced expiratory ratio (FEV1/FVC). A significant bronchodilator response was defined as an increase of 12% and >200 ml in FVC or FEV1. Obstruction was defined as FEV1/FVC <0.70 and restriction as FVC z-score < −1.65. Finnish reference values were applied [18]. Chest x-rays were evaluated by radiologists of the Aava Medical Centre according to the clinic's routine protocol.

Clinical data were extracted from electronic medical records. Data collected were comorbidities, duration of admissions, and supplementary oxygen therapy.

Statistical analysis was performed using SPSS version 27 (IBM SPSS Statistics for Windows and Macintosh, IBM Corp, NY, USA). Between-group differences were analysed using the Chi-square or Mann–Whitney *U* test where appropriate and repeated-measure data were analysed with the McNemar or Wilcoxon signed ranks test where appropriate. *p* Value less than 0.05 was considered statistically significant.

We created two multivariate models to assess chest x-ray changes and restrictive spirometry pattern over time. To correct the possible selection bias and modelling the principal outcome variables with the most clinically relevant predictors, we used the probit Heckman regression model. Age, sex, BMI, and asthma were considered as candidate variables, and the variables to the final model were selected by Akaike information criterion (AIC). The models were fitted by Stata 18.0.

Results

Study population

The patients' background and clinical characteristics are presented in Table 1. The patients completed the 6-month survey 186 days (median; IQR 162–203 days) and the one-year survey 397 days (median; IQR 375–411 days) after hospital discharge, respectively. Spirometry and chest x-ray were performed 383 days (median; IQR 372–403) after hospital discharge.

Working status and the use of health care services

Of the 58 patients working full-time before COVID-19, 46 (79%) had returned to work full-time and four (7%) part-time at six months follow-up. Seven patients (12%) had not returned to work, and one did not answer. At one-year follow-up, 46 (79%) patients reported working full-time and six (10%) part-time. Six patients (10% of the previously full-time working patients) had not returned to work, and of those, the median age was 59 years (IQR 56–60 years). The patients who had returned to work full-time reported a median sick-leave duration of 40 days (IQR 30–60 days). No statistically significant association was found between not returning to work at one year and age ($p = 0.669$), sex ($p = 1.000$), BMI ($p = 0.179$), comorbidities ($p = 0.159$–1.000), smoking ($p = 0.179$), hospital length of stay ($p = 0.274$), ICU length of stay ($p = 0.581$), or duration of invasive mechanical ventilation ($p = 0.070$).

Sixty-nine patients (72%) reported using health care services due to COVID-related issues at least once during the one-year follow-up. Forty-eight patients (50%) reported using primary health care, 33 (34%) occupational health care and 31 (32%) specialty care, respectively. The frequencies of health care service use are illustrated in Figure 2. Age, sex, BMI, comorbidities or length of hospital stay were not associated with the use of health care services related to COVID-19 in univariate analysis.

Symptoms and quality of life

At one year's timepoint, the most commonly reported symptoms were tiredness (88% of respondents), fatigue (79%), and sleeping problems (70%), the distributions of which are illustrated in Figure 3. The means of reported

Table 1. Background characteristics of the study population.

	Survey respondents $N = 96$	Spirometry & chest X-ray group $N = 33$
Age (years)	60 (55–68)	62 (55–68)
BMI (kg/m^2)	28.1 (23.9–31.7)	29.0 (26.7–32.3)
Comorbidities		
None	33 (34%)	11 (33%)
Hypertension	43 (45%)	14 (42%)
Diabetes type 2	13 (14%)	6 (18%)
Asthma	19 (20%)	5 (15%)
Sleep apnoea	7 (7%)	5 (15%)
Coronary artery disease	8 (8%)	4 (12%)
Hyperlipidaemia	21 (22%)	4 (12%)
Hypothyroidism	7 (7%)	2 (6%)
Neurological disease	–	3 (9%)
Nicotine product use		
Current smoker	3 (3%)	–
Former smoker	43 (45%)	15 (45%)
Pack-years*	8 (3–25)	12.5 (3–36)
Work status before COVID-19		1 Missing
Full-time	58 (60%)	17 (52%)
Part-time	4 (4%)	3 (9%)
Retired or unemployed	34 (35%)	12 (36%)
Length of hospital stay (days)	10 (6–18)	18 (12–30)
Admitted to intensive care unit	28 (29%)	22 (69%)
ICU length of stay (days)	12 (7–20)	10 (3–17)
Mechanical ventilation	20 (21%)	14 (44%)
Duration of mechanical ventilation (days)	14 (9–22)	13 (8–16)
Supplementary oxygen therapy, peak flow of O2 (l/min) (if not intubated)	4 (1–10)	10 (4–15)

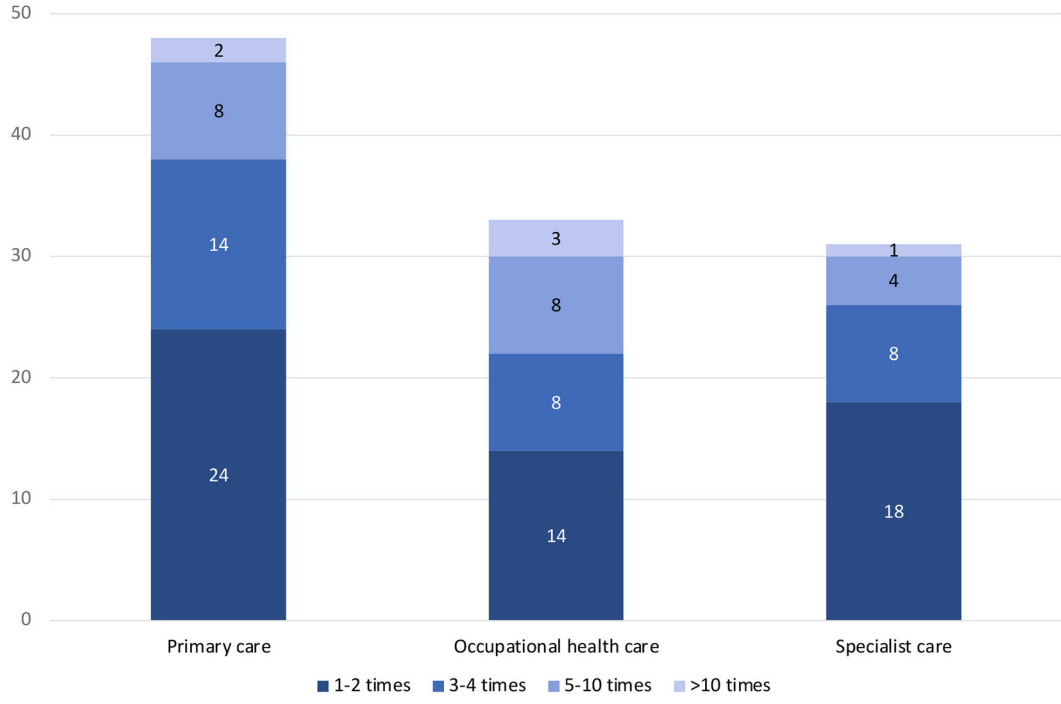

Figure 2. Reported health care service use in 96 Finnish patients during one year after hospital discharge.

symptoms at one month before, six months after and one year after COVID-19 are illustrated in Figure 4. Tiredness was the most common symptom at all timepoints, with a mean of 2.07, 3.86, and 4.54, respectively, on a scale of 0–10 (median 1.0, 4.0, 4.0; IQR 0–3, 2–6, 2–7). Tiredness, fatigue, and difficulty moving increased from 6 months to one year (Supplementary Table 1). There were no statistically significant changes in other symptoms. Five patients were symptom-free at 6 months and four patients at one year. At six months and one year, women reported more sleeping problems ($p = 0.026$ and $p = 0.023$, respectively) and mood problems ($p = 0.015$ and $p = 0.005$, respectively). There were no significant between-gender differences in other symptoms.

Experiencing one or more severe symptoms was more common at one year, with 60 patients (65% of responses) reporting one or more severe symptoms (6–10 on the scale of 0–10) at one year and 36

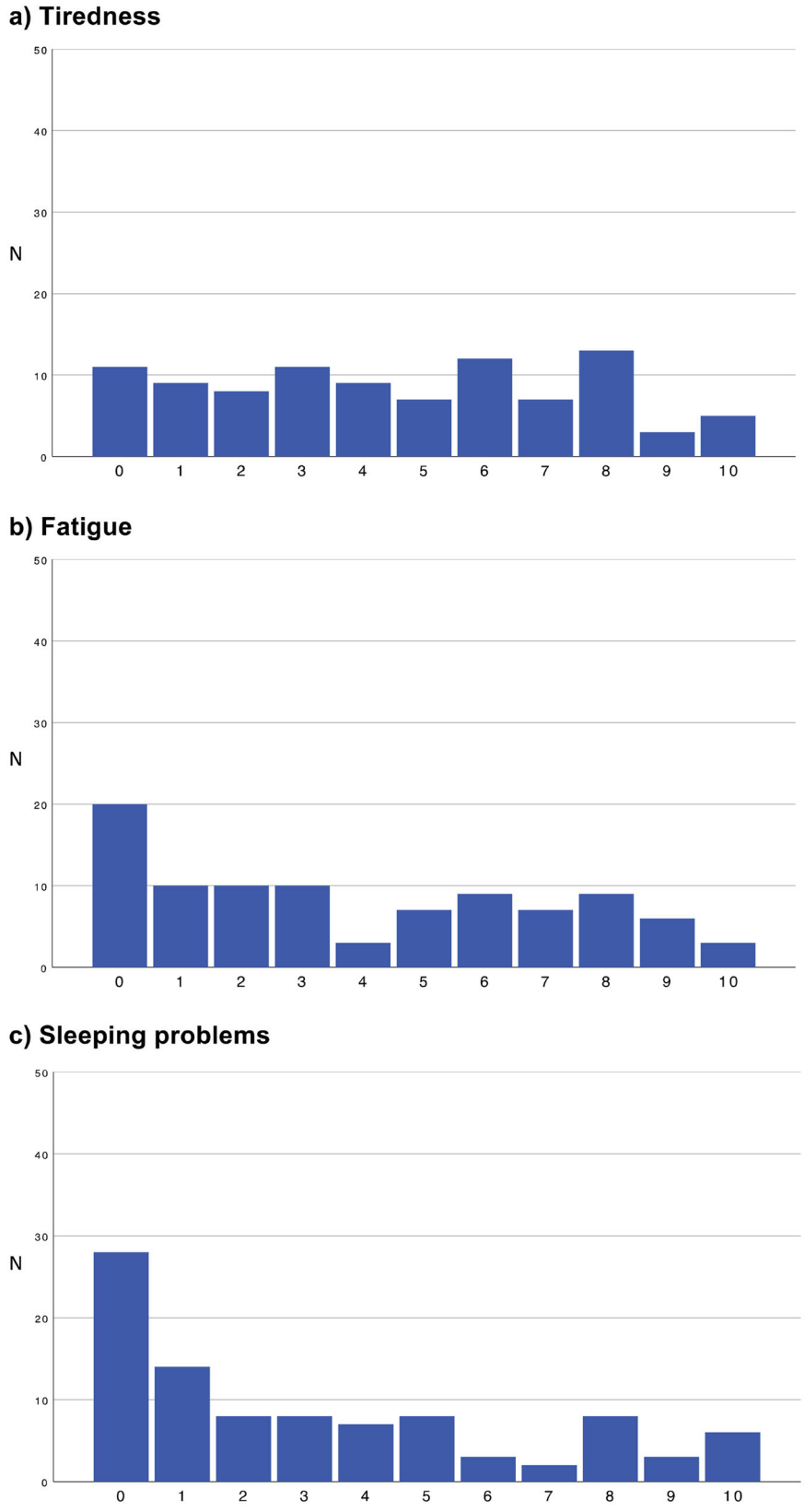

Figure 3. Distribution of the three most common symptoms on a scale of 0-10 one year after COVID-19.

patients (43% of responses) at six months ($p < 0.001$), respectively. Experiencing one or more severe symptoms at one year's timepoint was not associated with age ($p = 0.280$), sex ($p = 0.283$), BMI ($p = 0.115$), comorbidities ($p = 0.167–1.000$), length of hospital stay ($p = 0.791$), length of ICU stay ($p = 0.938$), or duration of mechanical ventilation ($p = 0.109$) in univariate analyses.

Dyspnoea as assessed by the mMRC dyspnoea scale is illustrated in Figure 5. There was no statistically significant change from six months to one year ($p = 0.710$). At one year, 15/94 patients (16%) reported mMRC ≥ 2.

Quality of life did not change statistically significantly from six months to one year in any of the eight RAND-36 dimensions. At six months, women had lower quality of life in six of eight dimensions: physical functioning ($p = 0.009$), emotional role functioning ($p < 0.001$), energy/fatigue ($p < 0.001$), emotional well-being ($p < 0.001$), social functioning (0.003), and general health perceptions ($p = 0.002$). At one year, a statistically significant difference between genders remained only in two dimensions: energy/fatigue ($p = 0.032$) and emotional well-being ($p = 0.037$).

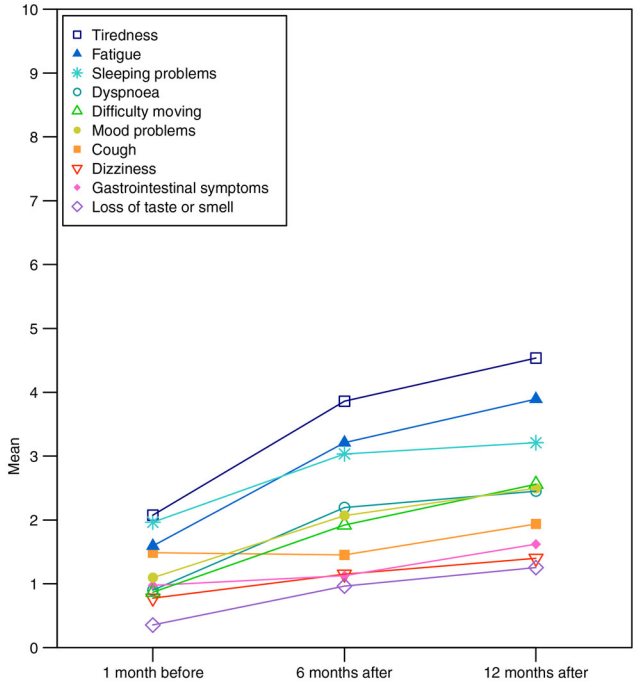

Figure 4. The means of reported symptoms one month before, six months and one year after COVID-19.

Spirometry and chest x-rays

The spirometry and chest x-ray findings are summarised in Figure 6. A restrictive spirometry pattern was found in 16% and in 34% at 3-6 months and one year, respectively, increasing statistically significantly in follow-up ($p = 0.031$). In univariate analysis, restriction in spirometry at one year was not associated with an abnormal chest x-ray at one year or reported dyspnoea. Two patients had a diagnostic bronchodilator response at one year, one of which had no previous history of asthma or COPD. Chest x-ray was normal in 24/32 (75%) patients at one year. Eight patients (25%) had minor residual infiltrates, two patients (6%) had minor blunting of the costophrenic angle, and one patient had pleural thickening which was present in the patient's chest x-rays before COVID-19.

In multivariate analysis, chest x-rays improved from 3-6 months to 12 months (Supplementary Table 2). A restrictive spirometry pattern slightly increased from 3–6 to 12 months and a higher BMI was associated with a

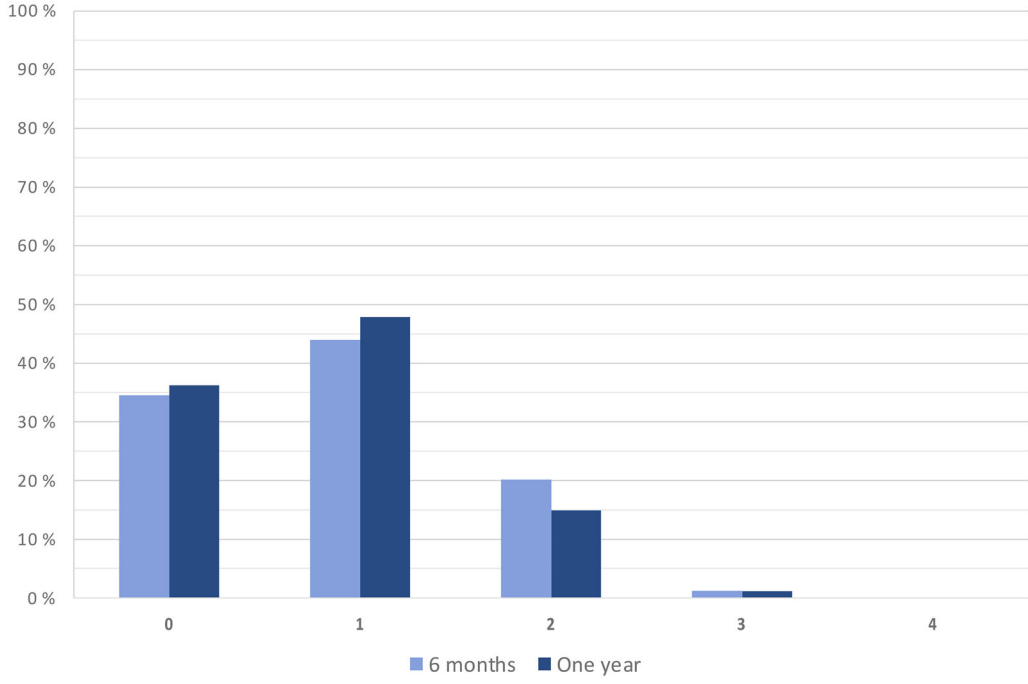

Figure 5. The mMRC Dyspnoea Scale six months and one year after COVID-19.

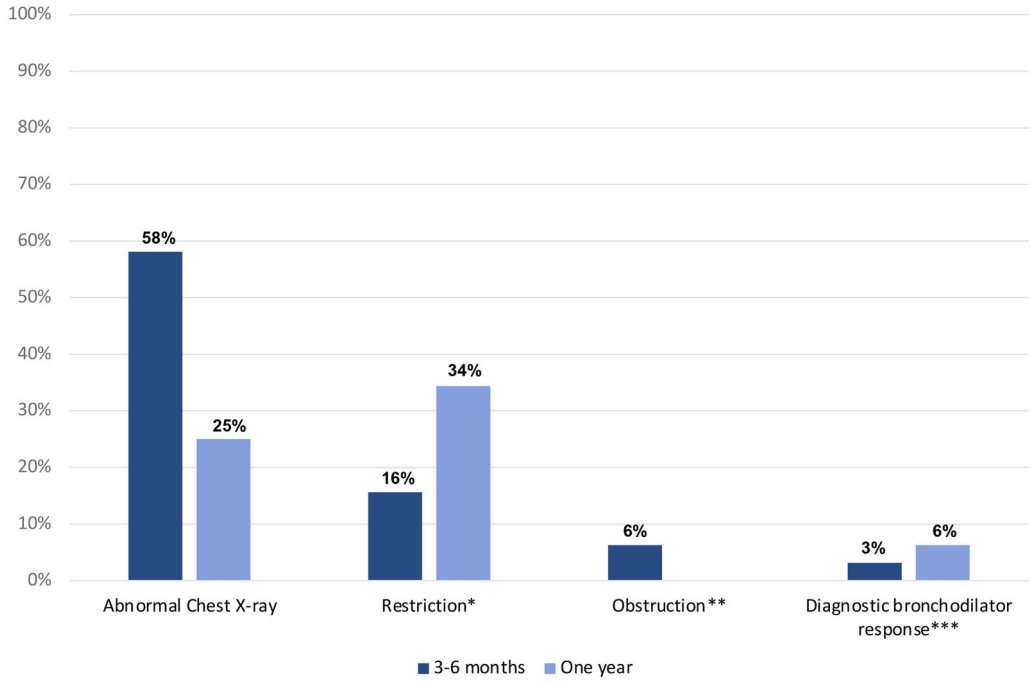

Figure 6. Summary of lung function and chest X-ray findings at 3–6 months and one year after COVID-19. *FVC z-score < -1.65; **FEV1/FVC <0.70; ***increase of 12% and >200 ml in FVC or FEV1.

restrictive pattern at 12 months (Supplementary Table 3). In selection bias analysis, female sex decreased the likelihood to participate ($p = 0.005$ for chest x-rays; $p < 0.001$ for spirometry). Age had a J-curve-like effect on the likelihood to participate in spirometry, as it first decreased but then increased with older age. BMI did not increase in follow-up from 3-6 months to one year in patients with a new restrictive pattern at one year (median 30.3 vs. 29.4, $p = 0.528$).

Discussion

Our main findings were that symptoms were frequently reported in our study population still one year after COVID-19 but severe burden, as assessed by frequent use of health care services or long-term inability to work, focused on a small group of patients.

While most patients returned to work within two months of severe COVID-19, 10% of the patients working full-time before COVID-19 had not returned to work after one year. A similar percentage has been reported in a previously published one-year follow-up study of COVID-19 patients [19]. In our study, not returning to work was not explained by age, sex, BMI, or comorbidities. Furthermore, disease severity, as assessed by hospital or ICU length of stay or duration of intubation, was not associated with the work status of the patients who had previously worked full-time. Median duration of sick leave was 40 days in our population, which is somewhat longer than in a recent Swedish study, where the median duration of sick leave due to COVID-19 was 35 days [16]. However, the Swedish study included non-hospitalised patients. Hospitalised patients have been described to have longer durations of sick leave than non-hospitalised patients in a recent Norwegian study [15].

Use of health care services due to COVID-19 related issues was common during the one-year follow-up. However, most patients reported using health care services only a few times, while a small portion of patients reported using health care services more than 10 times. In a Norwegian study of non-hospitalised patients with COVID-19, an increased use of primary health care services was observed up to 2–3 months after initial infection [20]. In another study, both primary care and specialty care visits increased after COVID-19 compared to the situation prior the infection [21].

Reported tiredness, fatigue, and difficulties while moving increased in follow-up and severe symptoms were more common. Fatigue increasing from six to 12 months after COVID-19 has been reported in a recent Chinese study [19]. Dyspnoea as assessed by the mMRC did not change significantly in follow-up, with 16% reporting mMRC ≥ 2 at one year, corresponding to the findings of Eberst et al. [22].

The increase in symptoms could have several underlying causes. First, selection bias could lead to overestimating the prevalence of symptoms, as symptomatic

patients could be more prone to taking surveys. However, the response rate in the present study was high, as only patients who had responded to the previous survey were included in the one year survey. Second, as our study did not have a control group, we do not know whether the experienced symptoms are related to COVID-19 itself or other factors. Mental health problems have increased globally during the pandemic not just in patients with COVID-19, but also in healthcare professionals, quarantined individuals, and the chronically ill [23]. Thus, the increase of symptoms might not be related to COVID-19 but other factors influencing the current society and environment. Additionally, although the six-month survey included the patients' restrospective evaluation of symptoms one month before COVID-19 to adjust for the effect of comorbidities on symptom burden, temporary changes in health were not controlled and could affect the responses.

Quality of life neither improved nor decreased from six months to one year. However, the sex differences reduced in follow-up and remained only in two dimensions of the RAND-36 quality of life after one year, compared to six of the eight dimensions at six months. In addition, sleeping problems and mood problems were more common in women both at six months and at one year. In Hong Kong, a general decrease in women's quality of life during the COVID-19 pandemic has been observed [24].

Chest x-rays improved in follow-up but radiological abnormalities persisted in some patients, which is in line with previously published studies [10]. Interestingly, the number of patients with restrictive spirometry pattern increased in one year's timepoint. This finding is contrary to previously published studies, where ventilatory function has improved in one year's follow-up [19,23]. Post-COVID-19 pulmonary fibrosis (PCPF) has been described in the literature, but is still somewhat debated, as the reversibility of radiological abnormalities after COVID-19 is still unclear [25]. However, PCPF seems unlikely to explain our spirometry finding in our study population, as none of the patients had clear signs of fibrosis in chest x-rays, and in addition, the chest x-rays improved over time. CT scans could give further information but were not included in our study protocol. Although many follow-up studies have utilised CT scans, chest x-rays have also been used widely in both the acute phase and the follow-up of COVID-19 patients [26,27].

In the multivariate model, only higher BMI was associated with restriction at one year, although the p-value remained slightly above the pre-determined level of statistical significance of 0.05. Obesity can lead to restriction in spirometry. We hypothesised that an increase in BMI during the pandemic could explain the increase in restriction. However, when separately investigating the subset of patients with new-onset restriction at one year, their BMI did not significantly change between the time points.

The selection analysis of the chest x-ray and spirometry subgroup suggested that older and male patients could be overrepresented in our sample, and was corrected for in the final statistical model. It should be noted that the spirometry and chest x-ray subgroup already represents patients with a more severe disease, as predominantly those with the most severe initial disease were referred to the 3-6 month follow-up visits. Therefore, the results should not be generalised to all COVID-19 patients or patients with milder disease.

The strengths of our study include a comprehensive evaluation of the patients in functional testing and imaging as well as self-reported symptoms and quality of life. During the first wave of the pandemic, Finnish COVID-19 cases centred heavily in the Helsinki University Hospital, and the study population represents a significant portion of all patients hospitalised in Helsinki University Hospital due to COVID-19 during the study period (March to June 2020). Loss to follow-up was relatively small (28%) between six months and one year. The patients in our study were recruited before the surfacing of the newer omicron variant that causes a clinically milder disease [13]. As a result, our sample is clinically and temporally homogenous.

The main limitation of our study is the lack of a control group, as especially experienced symptoms and quality of life are subject to many possible confounders. The prevalence of the surveyed symptoms in healthy adults is not known, and our symptom questionnaire has not been validated, although a similar symptom survey with a 0-10 scale has been used in a British follow-up study of COVID-19 patients [28]. Furthermore, prolonged symptoms and decreased quality of life have been described after other severe pulmonary infections and acute respiratory distress syndrome (ARDS), suggesting the prolonged recovery might not be specific to COVID-19 [29,30]. ARDS patients have been found to have lower quality of life than patients recovering from other critical illnesses [31]. Interestingly, a recent Spanish study observed better quality of life in COVID-19-related ARDS than non-COVID-19 ARDS [32]. However, only a fifth of our survey respondents needed mechanical

ventilation due to COVID-19, with the majority of respondents recovering from a less severe disease, although all patients were hospitalised. The underlying causes of the persisting symptoms still need further investigation.

Conclusions

Prolonged symptoms were experienced widely in our study population but few patients had not returned to work. According to the self-reported symptoms one month before COVID-19, although retrospectively reported, it seems that patients still feel worse after one year compared to the situation prior to COVID-19. Our findings emphasise the need to identify patients who are at risk for prolonged recovery in order to prevent prolonged absence from work, and the amount of costs to society and individual well-being.

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Author contributions

AL collected, analysed, and interpreted the data and wrote the original draft of the manuscript. All authors revised the manuscript critically for important intellectual content and read and approved the final manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data are available from the corresponding author AL on reasonable request.

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