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Symptomatic, biochemical and radiographic recovery in patients with COVID-19

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ABSTRACT

Background The symptoms, radiography, biochemistry and healthcare utilisation of patients with COVID-19 following discharge from hospital have not been well described.

Methods Retrospective analysis of 401 adult patients attending a clinic following an index hospital admission or emergency department attendance with COVID-19. Regression models were used to assess the association between characteristics and persistent abnormal chest radiographs or breathlessness.

Results 75.1% of patients were symptomatic at a median of 53 days post discharge and 72 days after symptom onset and chest radiographs were abnormal in 47.4%. Symptoms and radiographic abnormalities were similar in PCR-positive and PCR-negative patients. Severity of COVID-19 was significantly associated with persistent radiographic abnormalities and breathlessness. 18.5% of patients had unscheduled healthcare visits in the 30 days post discharge.

Conclusions Patients with COVID-19 experience persistent symptoms and abnormal blood biomarkers with a gradual resolution of radiological abnormalities over time. These findings can inform patients and clinicians about expected recovery times and plan services for follow-up of patients with COVID-19.

Key messages

► How quickly do the symptoms, radiography and biochemistry of patients with COVID-19 who had been admitted to hospital or attended the emergency department take to resolve, and how frequently do they access healthcare?

► The majority of patients with COVID-19 are still symptomatic at a median of 53 days post discharge and 72 days after symptom onset and 18.5% of patients had unscheduled healthcare visits in the 30 days post discharge.

► These data provide a further description of the recovery period following COVID-19 infection.

The symptomatic and radiographic recovery times, risk of short-term complications, optimal timing of follow-up and prevalence of long-term sequelae are still uncertain. The studies of recovered patients that are available have described a prolonged burden of symptoms following hospital discharge.[3–9] However, some features of recovery which are less well characterised include the rate of recovery of symptoms, recovery in non-hospitalised patients and patients without a positive PCR swab, biochemical and haematological recovery and healthcare utilisation.

We collected symptomatic, radiographic, biochemical and healthcare utilisation data from patients with COVID-19 who attended a follow-up clinic after discharge from hospital. We describe the recovery times for these parameters, examined the factors associated with symptomatic and radiographic recovery and recorded unscheduled healthcare use in these patients.

INTRODUCTION

Since initial detection of SARS-CoV-2 almost 110 million cases of COVID-19 have been confirmed worldwide, with an estimated global death toll of almost 2.4 million.[1] Patients with more severe disease require hospitalisation and large numbers of patients have survived and been discharged from hospital. The clinical features of hospitalised patients with COVID-19 have been well described[2]; however, less data are available on the recovery period of patients after discharge.

METHODS

Study design and participants

This retrospective cohort study collected data from adult patients who attended a COVID-19 follow-up clinic between 1 May 2020 and 21 July 2020. Patients who had either been admitted to, or attended the emergency departments (ED) of the three acute hospitals of Imperial College Healthcare NHS Trust (ICHNT) between 21 March 2020 and 13 June 2020 were identified. ICHNT is one of the largest NHS Trusts in London that provides care for an urban population in North West London. Patients were identified either on the basis of a positive SARS-CoV-2 PCR test, or a clinical diagnosis of COVID-19 with a negative PCR (or no swab taken) if they had typical clinical, radiological and biochemical features consistent with COVID-19 as assessed by a consultant physician and had been treated as COVID-19. Patients were invited to attend the clinic but patients who were judged to be too frail to attend or who lived outside the area were excluded. Five patients acquired coronavirus infection while in hospital and were not included in the illness duration and length of stay (LOS) analyses. The project was registered with the audit team under the Directorate of Acute and Specialist Medicine ICHNT (registration number 488).

Patient and public involvement

Patients and the public were not involved in the design and conduct of this project.

Identification of patient variables

Relevant data were extracted from patient hospital records. Data collected from the first patient encounter included information on: demographics, comorbidities, frailty score[10] and The National Early Warning Score 2 (NEWS2).[11] Admission chest radiographs were reported by FRCR certified Trust radiologists using the British Society of Thoracic Imaging (BSTI)/NHS England (NHSE) endorsed validated reporting template (normal, classic/probable COVID-19, indeterminate and non-COVID-19) and the severity score recorded (mild, moderate and severe).[12 13] Blood test results were recorded, including C reactive protein (CRP, normal value <5 mg/L), ferritin (normal value <300 mg/L), D-dimer (normal value <500 mg/L), troponin (normal value <5 mg/L) and blood lymphocyte count (normal value >1×10^9/L).

For hospitalised patients, details were collected on LOS, maximal inspired fraction of oxygen (FiO_2) required (room air, ≤0.4, >0.4), history of intubation and inpatient investigations for venous thromboembolism (VTE). Where chest radiographs and blood tests were repeated, the most abnormal result was recorded.

A standard proforma was used to record symptoms (cough, breathlessness, chest pain and fatigue) and unscheduled healthcare visits in the 30 days post discharge. Patients were asked to estimate their exercise tolerance prior to hospital admission and currently, using the Medical Research Council (MRC) questionnaire,[14] and the presence of ongoing psychological trauma assessed using a standardised tool.[15] A sit-to-stand test was carried out to detect exercise-induced desaturation (a fall in oxygen saturation of ≥4%)[16] and chest radiographs and blood tests carried out. Chest radiographs were reported by FRCR certified Trust radiologists and were defined as resolved (if normal or had returned to baseline), significantly improved, not significantly improved or worse using BSTI radiographic follow-up of COVID-19 reporting templates.[17] BSTI reporting templates with codes were embedded into the radiology information system to facilitate consistency of reporting and allow categorisation of radiographic appearances. Reporting template training for radiologists was performed by subspeciality thoracic radiologists.

Statistical analysis

Continuous and categorical variables were presented as median (IQR) and number (%), respectively. Patients were classified according to the level of care received: 'ED only' patients attended the ED but were not admitted to hospital; 'Level I' patients were admitted and required ward-based level of care; 'Level II/III' patients were admitted and required either invasive or non-invasive ventilatory support. To analyse the relationships between time between hospital discharge and clinic review, Level I patients were divided into patient seen <42 days (Early), between 42 and 56 days (Intermediate) and >56 days post discharge (Late).

Logistic regression models were conducted, using complete case analysis, to measure any association between a patient's clinical characteristics during admission and any (1) persistent radiological abnormalities, or (2) breathlessness, at follow-up. Model covariates included clinically relevant explanatory variables identified a priori: age, gender, socioeconomic status, NEWS2, CRP, lymphocyte count, admission radiograph severity, maximal oxygen requirement, intubation and time from discharge to follow-up. Analyses were performed using R V.3.4.

RESULTS

Patient demographics

Four hundred one patients attended the clinic and were included in the final analysis (table 1). Median age was 59 years, 76.3% had a positive SARS-CoV-2 PCR test, 59.6% of patients were male, median Rockwood frailty score was 1 (IQR 1–3), 15.5% worked in the health or social care sectors, 81% had a body mass index ≥25% and 61.8% were of black, Asian and minority ethnic origin. Most patients (315, 78.5%) were in the Level I group; 38 (9.5%) were Level II/III (32 intubated) and 48 (12%) patients were in the ED-only group. Patients with a positive PCR had higher oxygen requirements compared with PCR-negative patients, but otherwise there were no differences in their demographics or disease severity markers.

Table 1 Patient demographics at index admission or presentation

	All (n=401)	ED only (n=48)	Level I (n=315)	Level II/III (n=38)
M:F	239:162 59.6%/40.4%	23:25 47.9%/52.1%	190:125 60.3%/39.7%	26:12 68.4%/31.6%
Age (median and range)	59.0 (21–95)	54.0 (23–84)	61.0 (21–95)	52.5 (30–80)
BMI (n=381)				
<18	4 (1%)	1 (2.2%)	3 (1%)	0 (0%)
18.5–24.9	69 (18%)	9 (19.6%)	55 (18.5%)	5 (14%)
25–29.9	149 (39%)	16 (34.8%)	119 (40%)	14 (39%)
30–39.9	136 (36%)	14 (30.4%)	105 (35%)	16 (44.4%)
>40	23 (6%)	6 (13%)	16 (5.5%)	1 (2.6%)
Comorbidities				
Any	324 (81%)	35 (73%)	266 (84.4%)	23 (60.5%)
Diabetes mellitus	112 (27.9%)	6 (12.5)	99 (31.4%)	7 (18.4%)
Hypertension	168 (42%)	15 (31.25%)	142 (45%)	11 (29%)
CVS	74 (18.5%)	8 (16.7%)	62 (19.7%)	4 (10.5%)
Cancer	31 (7.7%)	3 (6.35%)	25 (7.9%)	1 (2.6%)
Asthma	61 (15.2%)	10 (20.8%)	48 (15.2%)	3 (8%)
COPD	20 (5%)	2 (4.2%)	17 (5.4%)	1 (2.6%)
BAME background (n=372)	227/372 (61%)	29/43 (67.4%)	172/292 (58.9%)	27/38 (71.1%)
Smoking (n=360) Current/ex/never	10/91/263	3/7/31	7/75/219	2000/9/24

BAME, black, Asian and minority ethnic; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVS, cardiovascular disease.

Hospital admission/ED attendance characteristics

The characteristics of the index hospital admission or ED attendance are shown in table 2. The median duration of symptoms prior to admission was 8 days and the median LOS was 5 days. Three hundred one (75.5%) patients had mild–moderate disease based on assessment of chest radiograph and 310 (77.3%) required a maximum FiO_2 ≤0.4. Forty-nine (12.2%) patients were investigated for VTE in hospital of which 13 (3.3%) were positive.

Clinic data

The median time from discharge until clinic appointment was 53 days (IQR 36–67) and the median time from symptom onset was 72 days (IQR 55.75–89) (table 3). Seventy-five per cent of patients were still experiencing symptoms at follow-up: 46.4% reported breathlessness, 45.1% fatigue, 30.5% cough and 23.8% chest pain. Among symptomatic patients, 63.1% experienced at least two symptoms. Level II patients were most likely to be symptomatic (89.5%) and those in the ED only group were least likely to be symptomatic (70.8%). 40.8% of patients reported not returning to their preillness exercise tolerance level, and MRC score was significantly higher than preadmission scores (baseline median MRC=1, clinic median MRC=2, p<0.0001). 13.1% of patients desaturated on the sit-to-stand test and 15% of

patients scored positive for psychological distress related to their hospital admission. 47.4% (126/309) of patients had an abnormal chest radiograph. Twenty-one per cent had a high CRP, 16.7% had a high ferritin and 34.8% had a high D-dimer level. There were no differences between patients with a positive PCR and those with a clinical diagnosis, other than a higher prevalence of elevated D-dimer in PCR-positive patients (table 4).

Healthcare utilisation post discharge

Seventy-four patients (18.5%) had COVID-19 related unscheduled healthcare visits (to primary or secondary care). These visits resulted in 12 CT pulmonary angiograms (CTPAs) (including two diagnoses of pulmonary embolism (PE)), 2 thoracic CT scans and 8 chest radiographs. A further 18 patients had investigations for VTE from the clinic with 1 CTPA positive for a previously undiagnosed chronic PE.

Relationships between time from discharge and recovery

Among the Level II patients, 109 (35.0%) were seen <42 days from discharge, 79 (25.3%) at 42–56 days and 124 (39.7%) at >56 days post discharge (table 5). There was no difference in the proportion of patients reporting symptoms between the different time points (p=0.38).

Table 2 Clinical data during index admission or emergency department attendance

Admission data by level of care and PCR status during index presentation

	All (n=401)	Level I (n=315)	Level II/III (n=38)	ED only (n=48)	PCR +ve (n=307)	PCR –ve (n=94)
Symptom duration prior to admission, Median (IQR)	8 (5–12.5)	8 (5–13)	7 (6–12)	8.5 (6–11.75)	8 (5–12)	9 (5–14)
Length of stay, Median (IQR)	5 (3–9)	5 (3–8)	24.5 (14–47.75)	N/A	6 (3–10.5)	3 (0–6)
Chest radiograph						
Normal	9 (2.2%)	7 (2.2%)	0	2 (4.2%)	7 (2.3%)	2 (2.1%)
Mild	144 (36%)	110 (34.9%)	0	34 (70.8%)	105 (34.1%)	39 (41.5%)
Mild–moderate	35 (8.7%)	27 (8.6%)	0	8 (16.8%)	25 (8.1%)	10 (10.6%)
Moderate	113 (28.1%)	103 (32.7%)	6 (15.7%)	4 (8.4%)	92 (29.9%)	21 (22.3%)
Moderate–severe	42 (10.5%)	36 (11.4%)	6 (15.7%)	0	34 (11%)	9 (9.6%)
Severe	58 (14.5%)	32 (10.2%)	26 (68.4)	0	45 (14.6%)	13 (13.8%)
NEWS2, Median (IQR)	5 (3–6)	5 (3–6)	7 (5–8)	2.5 (1–3)	5 (3–7)	4 (3–6)
Oxygen requirements						
No oxygen	85 (21.2%)	43 (13.7%)	0	42 (87.5%)	48 (15.6%)	37 (39.4%)
≤FiO_2 0.4	225 (56.1%)	219 (69.5%)	0	6 (12.5%)	186 (60.6%)	39 (41.5%)
>FiO_2 0.4	53 (13.2%)	53 (16.8%)	0	0	43 (14%)	10 (10.6%)
CPAP/Intubation	38 (9.5%)	0	38	0	30 (9.8%)	8 (8.5%)
C reactive protein						
>ULN	381/390 (97.7%)	309/315 (98%)	38/38 (100%)	34/37 (92%)	6/307 (2.0%)	3/83 (3.6%)
Median (IQR)	137.4 (0–546.2)	135.7 (0–430.5)	313.9 (111.5–546.2)	37 (0.9–250.2)	139.5 (80.5–218.7)	121 (45.5–182.6)
Ferritin						
>ULN	285/331 (86.1%)	238/274 (86.9%)	36/38 (94.70%)	11/19 (58%)	233/265 (87.9%)	52/66 (78.80%)
Median (IQR)	1029 (34–24973)	924 (50–24973)	2605 (238–8288)	386 (34–2368)	1056 (511–2275.5)	894 (414–2323)
D-dimer						
>ULN	297/322 (92.2%)	245/265 (92.5%)	38/38 (100%)	14/19 (73.70%)	231/251 (92%)	66/71 (93%)
Median (IQR)	1461 (270–20 000)	1411 (270–20 000)	9786 (1081–20 000)	847 (270–3959)	1514 (899–3572)	1403 (786–3699)
Lymphocyte count						
<LLN	279/401 (69.6%)	231/315 (73.3%)	32/38 (84.20%)	17/48 (35.40%)	218/307 (71%)	61/96 (63.50%)
Median (IQR)	0.8 (0.1–5.8)	0.8 (0.1–5.8)	0.6 (0.2–2.9)	1.25 (0.2–4.4)	0.8 (0.5–1.1)	0.9 (0.7–1.3)

CPAP, Continuous Positive Airways Pressure; LLN, Lower Limit of Normal; NEWS2, National Early Warning Score 2; ULN, Upper Limit of Normal.

Table 3 Clinical parameters at clinic attendance by level of care during admission

	All (n=401)	ED only (n=48)	Level I (n=315)	Level II/III (n=38)
Time to clinic from discharge (days) Median (IQR)	53 (36–67)	82.5 (65.25–93.5)	50.5 (35–61)	43 (32–51.25)
Time to clinic from illness onset (days) Median (IQR)	72 (55.75–89)	91 (74.75–102.5)	66 (52–82)	84 (69–84.5)
Abnormal chest radiograph	176/390 (45.0%)	8/46 (17.4%)	145/306 (47.4%)	25/38 (65.8%)
Symptoms	301/401 (75.1%)	34/48 (70.8%)	232/315 (73.7%)	34/38 (89.5%)
C reactive protein Patients>ULN	84/399 (21.0%)	7/47 (14.9%)	68/314 (21.7%)	9/38 (23.7%)
Ferritin Patients>ULN	66/396 (16.7%)	5/47 (10.6%)	59/311 (19.0%)	2/38 (5.3%)
D-dimer Patients>ULN	137/394 (34.8%)	10/46 (21.7%)	117/310 (37.7%)	10/38 (26.3%)

Significantly more patients in the Early group had cough compared with the Late group (Early 48.8%, Late 32.7%; p=0.02), breathlessness was most common in the Intermediate group (Early 44.1%, Intermediate 71.9%, Late 53%; p=0.0047), and fatigue was more common in the Late group (Early 48.8%, Intermediate 59.7%, Late 73.3%, p=0.004). The prevalence of abnormal chest radiographs fell significantly with increased length of time from hospital discharge (Early 66.4%, Intermediate 48%, Late 29.5%; p<0.0001; table 5). There was no difference in the prevalence of high CRP between the time points but elevated ferritin and D-dimers were less prevalent in the Late group compared with the Early group.

Factors associated with breathlessness and abnormal chest radiograph at follow-up

Longer time to clinic was associated with significantly lower odds of an abnormal chest radiograph: Intermediate and Late groups had 0.37 (95% CI 0.20 to 0.68) and 0.17 (95% CI 0.09 to 0.30) fold lower odds of abnormalities, compared with the Early group. Controlling for other parameters, patients aged above 60 years and above 80 years had 8.4 (95% CI 2.71 to 28.6) and 4.6 (95% CI 1.17 to 19.0) fold higher odds of abnormal chest radiograph compared with those aged 20–40 years, respectively. Patients with greater severity of illness (CRP, NEWS2, lymphocyte count, chest radiograph severity, oxygen requirement, intubation) during admission were more likely to have an abnormal chest radiograph on follow-up. Controlling for other parameters, patients with moderate or severe chest radiograph score during hospital admission had 2.13 (1.19–3.85) and 3.28 (1.59–6.90) fold higher odds of abnormal chest radiograph at follow-up, compared with those with mild chest radiograph score. Similarly, patients who had maximal FiO_2 >0.4 during admission had 3.36 (1.17–9.94) times higher odds of an abnormal chest radiograph compared with those requiring room air only. Intubation was not independently associated with resolution of chest radiograph changes (adjusted OR=0.745; 95% CI 0.24 to 2.34).

Table 4 Clinical parameters at clinic attendance by PCR status

	PCR +ve (n=307)	PCR –ve (n=94)	P value
Time to clinic from discharge (days) Median (IQR)	52 (35–61)	56 (40–83)	0.0011
Time to clinic from illness onset (days) Median (IQR)	71 (54–85)	76 (56.75–94.25)	0.0083
Abnormal chest radiograph	137/306 (44.8%)	39/93 (41.9%)	NS
Symptoms	236/307 (76.9%)	67/94 (71.3%)	NS
CRP Patients>ULN	68/305 (22.3%)	12/94 (12.8%)	NS
Ferritin Patients>ULN	50/303 (16.5%)	15/93 (16.1%)	NS
D-dimer Patients>ULN	113/302 (37.4%)	23/92 (25%)	0.03
Healthcare utilisation	59/307 (19.2%)	23/94 (24.5%)	NS

Table 5 Clinic parameters by time to clinic

	Early (n=109)	Intermediate (n=79)	Late (n=124)
Time to clinic from illness onset (days) Median (IQR)	48 (35–82)	64 (50–99)	85 (61–133)
Symptomatic patients	86 (78.9%)	58 (73.4%)	89 (71.8%)
Patients with number of symptoms (%) 1/2/3/4	34.5/35.7/23.8/6.0	35.1/33.3/22.8/8.8	38.9/34.4/20.0/6.7
Individual symptoms			
Cough	42 (48.8%)	19 (33.3%)	28 (32.0%)
Breathlessness	38 (44.2%)	48 (71.9%)	47 (53.3%)
Chest pain	27 (31.4%)	22 (38.6%)	29 (32.2%)
Fatigue	42 (48.8%)	35 (59.7%)	65 (73.3%)
Abnormal chest radiograph	71/107 (66.4%)	36/75 (48.0%)	37/121 (29.5%)
CRP	17/108	18/78	20/122
Patients>ULN	−15.70%	−23.20%	−16.40%
Ferritin	28/107	16/78	16/123
Patients>ULN	−25%	−20.50%	−13%
D-dimer	48/107	22/76	47/122
Patients>ULN	(45%.0)	−29.00%	−38.50%

Early follow-up (<42 days); Intermediate follow-up (42–56 days) and Late follow-up (>56 days).
CRP, C reactive protein.

DISCUSSION

We report a prolonged burden of symptoms, persistent radiological and biochemical abnormalities and frequent unscheduled healthcare visits in patients with COVID-19 following hospital admission or ED attendance. More severe acute illness and increased age were associated with persistent chest radiographic abnormality.

The clinical illness caused by the novel coronavirus SARS-CoV-2 has been well characterised[2]; however, the recovery period is not as well described. Recovery time from pneumonia is influenced by many factors including illness severity, age and comorbidities[18] but most patients with non-COVID pneumonia recover by 10–21 days[18–20] and only 35% have unresolved symptoms at 28 days.[21] A COVID-19 WHO document states that 'typically people recover from COVID-19 after 2 to 6 weeks'.[22]

Studies of recovery time have had varying results with some reporting that most patients recover by 4 weeks[5] whereas others report most patients are still symptomatic at 6[3] and 8[6 7] weeks post discharge. Limitations of published studies have included small cohorts,[5 23] patients seen at early postdischarge time points[5 8] and lack of data on non-hospitalised patients[7 8 23] and patients with a clinical COVID-19 diagnosis.[6 8 23]

Our study provides additional data to the published studies as we examined outcomes at different time points and recorded time from illness onset; we included patients not admitted to hospital and patients with a clinical diagnosis of COVID-19 and we examined factors that predict recovery and recorded data on healthcare utilisation. In keeping with other studies, we report a high prevalence of symptoms in patients following hospital admission or ED attendance with COVID-19. There was no significant difference in the percentage of patients reporting symptoms between those seen up to 6 weeks and those seen at 8 weeks and beyond. The latter group were seen at a median of 85 days from illness onset and still 71.8% were symptomatic. Even among patients who were not admitted to hospital seen at a median of 82.5 days from ED attendance and 91 days from illness onset, 70.8% were still symptomatic. There was no difference in reported symptom between PCR-positive and PCR-negative patients. Therefore, our study adds to the literature describing prolonged symptoms following acute COVID-19 infection and extends these observations to non-hospitalised patients and those with a clinical diagnosis of COVID-19.

The most common residual symptoms were fatigue, breathlessness and cough. In non-COVID CAP, breathlessness and fatigue resolve on average 25 days and cough 13.6 days from symptom onset,[15] so recovery from COVID-19 appears to be significantly prolonged. The prevalence of individual symptoms varied, with cough more common earlier in the recovery period while fatigue was more prominent later. It is possible that variation may relate to underlying pathophysiology, but symptoms may be influenced by when patients recommence normal levels of activity after discharge, patient expectations and ability to exercise during the pandemic-related lockdown. The subjective nature of symptoms such as breathlessness and complex influences on patient experiences of this may explain the poor association between disease

severity markers and residual breathlessness in our study, in comparison to the stronger correlations with objective chest radiographic abnormality. Further studies are needed to understand how and why symptoms change during the recovery period. Forty per cent of patients had not returned to their baseline exercise capacity after discharge. Impaired exercise capacity may in part be a result of patients self-isolating and the limitations imposed on exercising outside. It remains unclear what proportion of patients will experience impaired exercise capacity in the longer term, but these patients may place a significant burden on rehabilitation services in the future. Fifteen per cent of patients had anxiety symptoms and the provision of counselling and psychology services may need to be expanded to provide for patients with COVID-19.

Almost a quarter of patients in our study reported chest pain, despite the WHO not currently listing this as a COVID-19 symptom. 68.6% of patients hospitalised with non-COVID CAP experience chest pain,[24] with a median time to resolution of 7–9 days.[18] The aetiology of the chest pain is unclear as investigations such as CTPA and cardiac enzymes were negative. There has been considerable concern about the occurrence of VTE in COVID-19,[25] but only one chronic PE was identified that likely occurred during the acute phase of COVID-19. Therefore, these data provide some reassurance that VTE risk is not elevated in the postdischarge period despite suggestive symptoms and biomarkers, although CTPAs can potentially miss subsegmental pulmonary emboli and a recent report highlighted the possibility of potential undiagnosed myocardial injury in patients with COVID-19.[26] The threshold at which investigations are requested in these patients may need to be raised and further studies are needed to understand the pathophysiology of persistent symptoms.

There are conflicting data regarding radiographic resolution following COVID-19. A Chinese study reported complete radiological resolution on CT scan in 53% of 149 hospitalised patients at 3 weeks postdischarge,[27] whereas another Chinese study reported 52% of patients had pulmonary fibrosis at 58 days post discharge.[28] In non-COVID CAP, 53%–68% of chest radiographs are normal at 4 weeks post discharge.[29 30] In our cohort, 45% of chest radiographs were abnormal at follow-up, similar to the 38% reported by Mandal et al,[6] but higher than the 23% reported by Sykes et al.[23] There was a clear trend towards radiographic resolution with longer time from discharge but even in patients seen at >56 days, 29.5% of chest radiographs were abnormal, as were 17.4% in patients who were not hospitalised. There was a similar prevalence of abnormal chest radiographs in PCR-positive and PCR-negative patients. Patients with more severe acute illness and older patients were more likely to have radiographic abnormalities, so radiographic resolution will vary across different patient subgroups. Our findings of a halving of abnormal chest radiographs between the Early and Late time points support the British Thoracic Society recommendation that patients with COVID-19 should have a follow-up chest radiograph at 12 weeks post discharge, rather than the standard 6 weeks.[31] The prevalence of long-term radiological abnormalities following COVID-19 remains unknown.

18.5% of patients accessed unscheduled healthcare for COVID-related issues after discharge. AUK study reported that 40% of COVID-related calls to a specialist advice telephone service for primary care physicians related to persistent symptoms.[31] (This is linked to the correct reference but it should be 31 not 30) Our data should provide reassurance to patients experiencing persistent symptoms that the recovery period following COVID-19 infection is prolonged and persistent symptoms are common. This knowledge should help reduce unnecessary investigation; however, more data in larger cohorts are needed and symptomatic patients will still require careful assessment by clinicians.

Our study has several limitations. We were only able to include a select cohort of patients as extremely frail patients were not seen, while others declined the invitation to attend. This cohort was from a single centre split across three geographical locations but, due to their inner city locations, the three hospitals serve a diverse population. Symptoms were recorded by asking patients if they were present or not, we did not use standardised tools to assess symptom severity or quality of life. Chest radiographs were only classified as resolved or not resolved and the degree of improvement was not recorded.

In conclusion symptomatic, radiographic and biochemical recovery times following COVID-19 infection are prolonged with older age and more severe acute illness associated with non-recovery. Healthcare utilisation during the recovery period is common. Follow-up of patients with COVID-19 has imposed considerable strain on healthcare resources that will be further intensified following subsequent waves of infection. These results should lead to revised advice as to the expected recovery time from COVID-19, reduce unscheduled healthcare use and investigations, ensure that PCR-negative patients and non-hospitalised patients are also followed up and aid with planning the appropriate timing of follow-up and targeting of high risk patients.

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REFERENCES

1 WHO coronavirus (COVID-19) Dashboard. Available: https://covid19.who.int/ [Accessed 18 Feb 2021].
2 Zhou F, Yu T, Du R, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054–62.
3 Carfì A, Bernabei R, Landi F, *et al*. Persistent symptoms in patients after acute COVID-19. *JAMA* 2020;324:603–5.
4 Halpin SJ, McIvor C, Whyatt G, *et al*. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *J Med Virol* 2021;93:1013–22.
5 Wang X, Xu H, Jiang H, *et al*. Clinical features and outcomes of discharged coronavirus disease 2019 patients: a prospective cohort study. *QJM* 2020;113:657–65.
6 Mandal S, Barnett J, Brill SE, *et al*. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. *Thorax* 2020. doi:10.1136/thoraxjnl-2020-215818. [Epub ahead of print: 10 Nov 2020].
7 Arnold DT, Hamilton FW, Milne A, *et al*. Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: results from a prospective UK cohort. *Thorax* 2020. doi:10.1136/thoraxjnl-2020-216086. [Epub ahead of print: 03 Dec 2020].
8 Hall J, Myall K, Lam JL, *et al*. Identifying patients at risk of post-discharge complications related to COVID-19 infection. *Thorax* 2021;76:408–11.
9 Sykes DL, Holdsworth L, Jawad N, *et al*. Post-COVID-19 symptom burden: what is Long-COVID and how should we manage it? *Lung* 2021;11:1–7.
10 Royal College of Physicians. *National early warning score (NEWS) 2: standardising the assessment of acute-illness severity in the NHS. Updated report of a working Party*. London: Royal College of Physicians, 2017.
11 Hare SS, Rodrigues JCL, Nair A, *et al*. The continuing evolution of COVID-19 imaging pathways in the UK: a British Society of thoracic imaging expert reference group update. *Clin Radiol* 2020;75:399–404.
12 Hare SS, Tavare AN, Dattani V, *et al*. Validation of the British Society of thoracic imaging guidelines for COVID-19 chest radiograph reporting. *Clin Radiol* 2020;75:710.e9–4.
13 Fletcher C. Standardized Questionaries on respiratory symptoms. *Br Med J* 1960;2:1665.
14 Lang AJ, Stein MB. An abbreviated PTSD checklist for use as a screening instrument in primary care. *Behav Res Ther* 2005;43:585–94.
15 Crook S, Büsching G, Schultz K, *et al*. A multicentre validation of the 1-min sit-to-stand test in patients with COPD. *Eur Respir J* 2017;49:1601871.
16 COVID-19 BSTI Reporting templates. The British Society of thoracic imaging. Available: https://www.bsti.org.uk>covid-19-resources [Accessed 17 Sep 2020].
17 Wyrwich KW, Yu H, Sato R, *et al*. Observational longitudinal study of symptom burden and time for recovery from community-acquired pneumonia reported by older adults surveyed nationwide using the cap burden of illness questionnaire. *Patient Relat Outcome Meas* 2015;6:215–23.
18 Wootton DG, Dickinson L, Pertinez H, *et al*. A longitudinal modelling study estimates acute symptoms of community acquired pneumonia recover to baseline by 10 days. *Eur Respir J* 2017;49:1602170.
19 El Moussaoui R, Opmeer BC, de Borgie CAJM, *et al*. Long-term symptom recovery and health-related quality of life in patients with mild-to-moderate-severe community-acquired pneumonia. *Chest* 2006;130:1165–72.
20 Metlay JP, Atlas SJ, Borowsky LH, *et al*. Time course of symptom resolution in patients with community-acquired pneumonia. *Respir Med* 1998;92:1137–42.
21 World Health Organization. What we know about. Long-term effects of COVID-19. Available: https://www.who.int/docs/default-source/coronaviruse/risk-comms-updates/update-36-long-term-symptoms.pdf?sfvrsn=5d3789a6_2 [Accessed 17 Feb 2021].
22 Wyrwich KW, Yu H, Sato R, *et al*. Community-Acquired pneumonia: symptoms and burden of illness at diagnosis among US adults aged 50 years and older. *Patient* 2013;6:125–34.
23 Rockwood K, Song X, MacKnight C, *et al*. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;173:489–95.
24 Middeldorp S, Coppens M, van Haaps TF, *et al*. Incidence of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost* 2020;18:1995–2002.
25 Huang L, Zhao P, Tang D, *et al*. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. *JACC Cardiovasc Imaging* 2020;13:2330–9.
26 Liu D, Zhang W, Pan F, *et al*. The pulmonary sequalae in discharged patients with COVID-19: a short-term observational study. *Respir Res* 2020;21:125.
27 Huang W, Wu Q, Chen Z, *et al*. The potential indicators for pulmonary fibrosis in survivors of severe COVID-19. *J Infect* 2021;82:e5–7.
28 Bruns AHW, Oosterheert JJ, El Moussaoui R, *et al*. Pneumonia recovery: discrepancies in perspectives of the radiologist, physician and patient. *J Gen Intern Med* 2010;25:203–6.
29 Bruns AHW, Oosterheert JJ, Prokop M, *et al*. Patterns of resolution of chest radiograph abnormalities in adults hospitalized with severe community-acquired pneumonia. *Clin Infect Dis* 2007;45:983–91.
30 George PM, Barratt SL, Condliffe R, *et al*. Respiratory follow-up of patients with COVID-19 pneumonia. *Thorax* 2020;75:1009–16.
31 Kumar K, Mak V, Groom K, *et al*. Respiratory specialists working in different ways: development of a GP Hotline and respiratory support service during the COVID-19 pandemic. *Future Healthc J* 2020;7:e88–92.