Identifying patients at risk of post-discharge complications related to COVID-19 infection

Jocelin Hall, Katherine Myall, Jodie L Lam, Thomas Mason, Bhashkar Mukherjee, Alex West, Amy Dewar

Department of Thoracic Medicine, Guy's and St Thomas' NHS Foundation Trust, London, UK

Correspondence to
Dr Jocelin Hall, Department of Thoracic Medicine, Guy's and St Thomas' NHS Foundation Trust, London SE1 7EH, UK; jocelin.hall@gstt.nhs.uk

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ABSTRACT

SARS-CoV-2 infection is a multisystem disease with post-discharge sequelae. We report early follow-up data from one UK hospital of the initial 200 hospital inpatients with slow recovery from the condition. At 4 weeks post-discharge, 321/957 survivors (34%) had persistent symptoms. A structured outpatient clinical assessment protocol was designed, and outcomes from the first 200 patients seen 4–6 weeks post-discharge are presented here. In 80/200 (40%), we identified at follow-up a cardiorespiratory cause of breathlessness, including persistent parenchymal abnormality (64 patients), pulmonary embolism (four patients) and cardiac complications (eight patients). These findings occurred both in patients who had intensive care unit (ICU) admissions and those who had been managed on the ward, although patients requiring ICU admissions were more likely to have a significant cardiorespiratory cause found for their breathlessness, risk ratio 2.8 (95% CI 1.5 to 5.1).

BACKGROUND

On 11 March 2020, WHO declared SARS-CoV-2 or COVID-19 a global pandemic. As of late December 2020, 2 149 551 cases had been recorded in the UK.[1] The long-term outcome for these patients is unknown. However, recent studies indicate potential long-term complications ranging from disturbance of taste/smell,[2] cough,[3] fatigue and dyspnoea[2–5] to more pronounced cardiac,[6] respiratory[3 4 7] and cognitive dysfunction.[3 7]

METHOD

As the early Guy's and St Thomas' Hospital patients diagnosed with COVID-19 were being discharged, a post-COVID clinic was established to address the unmet needs of those with persistent symptoms. All patients attending the Hospital with either a positive PCR for COVID-19 or a negative PCR but a clinical-radiological diagnosis were telephoned 4 weeks after discharge. Those with persistent symptoms and those who had required intensive care unit (ICU) admission were invited for review. Those reporting a return to baseline were offered a chest radiograph at 12 weeks, consistent with national guidance.[8]

Patients attending the clinic were evaluated 4–6 weeks post-discharge by Respiratory or Infectious Disease Specialists. Further details of the follow-up pathway are found in figure 1. History and physical examination were undertaken; data collected on baseline characteristics and function; chest radiograph and blood tests performed; and health status questionnaires completed. Patients completed a 6 min walk test (6MWT) where physically able.

Further assessment was based on physiological impairment and patient-reported symptoms. Available investigations included: dual energy CT or high-resolution CT, ventilation-perfusion scanning, spirometry with gas transfer (limited due to the aerosol-generating nature of the procedure), echocardiography and ECG. Onward referral to other specialist teams for early assessment was effected.

Data collected was analysed using SPSS V.27 (IBM). Variables are expressed as mean±SD for parametrc data or median ±IQR for non-parametric data. ICU versus non-ICU values are compared either by independent samples t-test for parametric variables or by mann-whitney U test for non-parametric variables. Risk ratios are calculated using a X^2 analysis.

RESULTS

By the end of May 2020, 1272 patients had been diagnosed with COVID-19 of whom: 1239 (97%) had PCR-confirmed disease; 241 (19%) patients had died; 74 (6%) remained as inpatients. Of the remaining 957 patients: 122 (13%) were uncontactable, 61 (6%) declined any further follow-up, 139 (15%) were considered unsuitable to attend clinic because they were housebound due to frailty or because they were unwell with unrelated conditions; 314 (33%) had returned to functional baseline. Three hundred and twenty-one (34%) patients reported persistent symptoms and were invited for clinical review. We report data from the first 200 patients with a PCR confirmed diagnosis who were seen due to persistent symptoms.

The mean age was 54.8±15.0, 61.5% were male and the majority were overweight (mean body mass index 28.8±6.1). Further characteristics are described in table 1.

Of the 200 seen, 179 had received inpatient care, the remaining 21 patients been discharged directly from the emergency department. The majority had not been critically unwell and only 55 (27.5%) patients had ever received mechanical ventilation. Other features of their admission are highlighted in table 2.

During evaluation (table 3), patients reported their Medical Research Council (MRC) dyspnoea score (graded 1–5) post-illness and

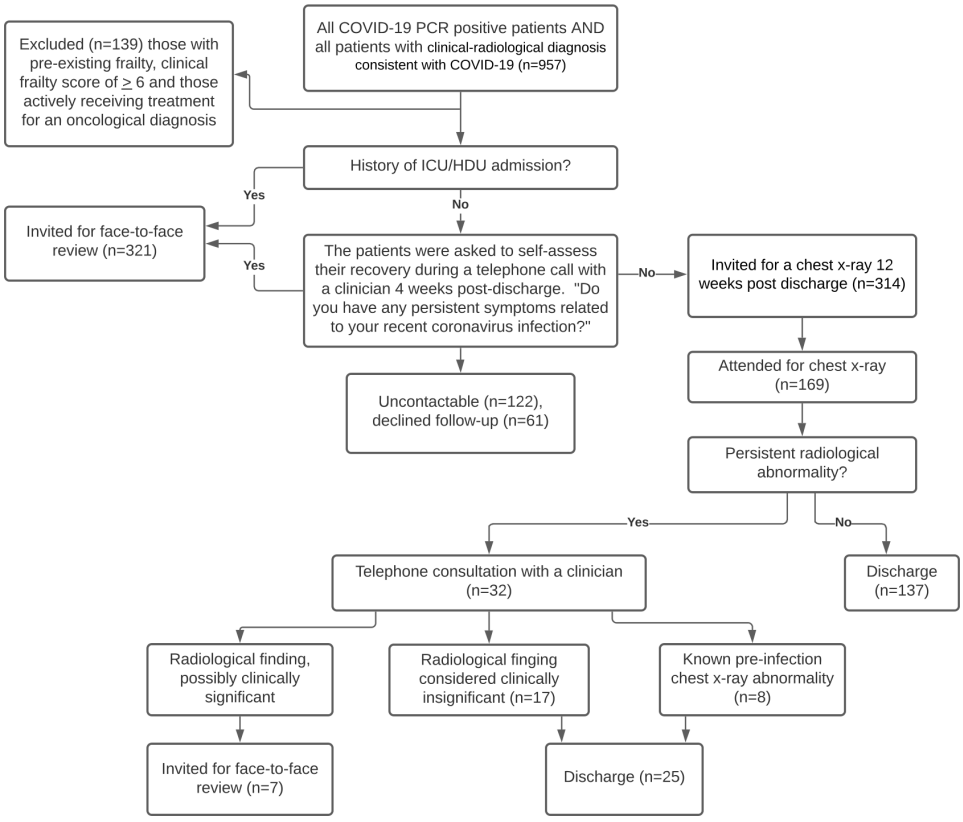

Figure 1 Post-discharge follow-up pathway outcomes. ICU, intensive care unit; HDU, high dependency unit.

retrospectively graded their baseline score pre-illness. A persistent deterioration of two or more MRC points was observed in 36 (18%) patients. Of the 170 patients that underwent 6MWT, 34 (20%) had an oxygen desaturation of 4% or more. Of those that went on to complete lung function tests (n=59), 16 (27%) had a predicted forced vital capacity of 80% or less and 26 (44%) had a transfer factor for carbon monoxide of 70% or less. Screening for anxiety and depression, using standardised tools, identified similar prevalence to that seen in general medical inpatients.[9]

Table 1 Baseline characteristics.

	(n=200)	ICU (n=77)	Non-ICU (n=123)
Age (years) (mean±SD)	54.8±15.0	53.1±14.0	55.7±15.4
Sex (% male)	61.5	66.2	58.5
BMI (kg/m^2) (mean±SD)	28.8±6.1	30.8±14.8	29.1±6.1
Current smokers (%)	30 (15.0)	13 (9.8)	12 (15.7)
Comorbidities (%)			
Obesity	72 (36.0)	37 (48.1)	35 (28.5)
Diabetes	55 (27.5)	21 (27.3)	34 (27.6)
Hypertension	72 (36.0)	32 (41.6)	40 (32.5)
COPD	4 (2.0)	1 (1.3)	3 (2.4)
Cardiovascular risk factors (%) hypertension, diabetes, smoking and obesity			
0	69 (34.5)	17 (22.1)	52 (42.3)
≥1	131 (65.5)	31 (40.3)	32 (26.0)
≥2	68 (34.0)	17 (22.1)	42 (19.5)
≥3	27 (13.5)	11 (14.3)	14 (11.4)
4	2 (1.0)	1 (1.3)	1 (0.8)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.

The dominant finding in those seen was persistent interstitial change in 64 (32%) patients on CT. Other respiratory findings included 4 (2%) patients with a previously unidentified pulmonary embolus, lung infarcts (n=2), *Klebsiella pneumonia* (n=1) and *Pneumocystis jirovecii pneumonia* (n=1). Either a previously undiagnosed or deterioration of existing cardiac cause for ongoing symptoms was found in eight patients (4%): pericarditis, persistent sinus tachycardia, hypertrophic cardiomyopathy and inferior regional wall motion abnormality, an atrial septal defect with new reversal of shunt, pulmonary hypertension, left ventricular hypertrophy and worsening of pre-existing heart failure.

Asymptomatic patients were followed up as per national guidance with chest radiograph at 12 weeks, 169/314 (54%) attended. Of these, 137 (81%) patients had a film reported as normal by a radiologist. The remaining patients were reviewed by telephone, 8 (2.5%) had known preinfection abnormalities to their chest X-ray but 24 (14%) had residual parenchymal change. Seventeen patients (10%) had no symptoms or change in function and so no further follow-up was arranged. For 7/169 (4%) cases, possible persistent issues were identified and these patients were offered face-to-face clinical assessment.

DISCUSSION

With the COVID-19 global pandemic yet to peak, these early results indicate likely long-term morbidity in a significant number of patients. Of those seen, 119/200 (60%) had persistent subjective symptoms despite no radiological or physiological abnormality being identified and these patients with 'post-COVID-19 syndrome' are likely to create a considerable healthcare management dilemma. However, 40% of those seen did have a significant finding. A limitation

Table 2 Admission characteristics

	(n=200)	ICU (n=77)	Non-ICU (n=123)	ICU versus non-ICU
Inpatient (%)	89.5			
Length of stay (days) (median ±IQR)	9±15	20±20	4±7	p<0.001
Oxygen therapy (%)	139 (69.5)	77 (100.0)	62 (50.4)	
Maximum required FiO2 (%)	n (%)			
21	61 (30.5%)	0 (0.0)	61 (49.6)	
24–36	53 (26.5%)	5 (6.5)	48 (39.0)	
40%–60%	35 (17.5%)	21 (27.3)	14 (11.4)	
>60%	51 (25.5%)	51 (66.2)	0 (0.0)	
Invasive mechanical ventilation (%)	55 (27.5)	55 (71.4)	na	
Inpatient systemic steroid treatment, oral or intravenous (%)	29 (14.5)	21 (27.3)	8 (6.5)	
Peak d-dimer (0.00–0.55 mg/L)	3.5±10.6	19.9±25.9	3.1±10.5	p<0.001
Peak ferritin (30–400 µg/L) (median ±IQR)	1360±1450	2492±1518	775±1206	p<0.001
Nadir lymphocyte (1.2–3.5×10^9/L) (median ±IQR)	0.70±0.30	0.6±0.3	0.9±0.5	p<0.001
Peak C reactive protein (0–4 mg/L) (median ±IQR)	241.0±235	304.5±211	102.0±162	p<0.001

FiO2, fractional inspired oxygen; ICU, intensive care unit.

of our work is that only symptomatic patients were physically reviewed, and while only 4% of these patients went on to have significant findings requiring further follow-up, we advise screening for persistent symptoms in all patients in the weeks after discharge to ensure complications are identified. In addition, given these patients were admitted early in the pandemic, our non-ICU cohort had relatively mild disease, with only 50% requiring oxygen therapy. These findings suggest that more thorough follow-up of patients is indicated than is currently recommended under the BTS

Table 3 Structured assessment clinic.

	(n=200)	ICU (n=77)	Non-ICU (n=123)	ICU versus non-ICU
MRC (median ±IQR)	2±1	3±1	2±1	p=0.026
Delta MRC (median ±IQR)	1±1	1±1	1±1	p=0.04
6MWT (n=170)				
Distance (m)	342±169	342±305	429±306	p=0.181
% predicted (median ±IQR)	70.4±42.0	63.9±54.5	70.4±40.8	
Resting SpO2 (%) (median ±IQR)	96.0±2.0	96.0±2.0	96.0±2.3	p=0.996
Nadir SpO2 (%) (median ±IQR)	94±4	94±4	94±4	p=0.858
>4% desaturation	34	12	22	p=0.693
Max HR (median ±IQR)	111±17	108±20	115±16	p=0.310
D-dimer (0.00–0.55 mg/L) (median ±IQR)	0.48±1.00	0.99±1.00	0.46±1.00	p=0.126
Ferritin (30–400 µg/L) (median ±IQR)	164±234	186±234	145±216	p=0.340
Lymphocyte (1.2–3.5×10^9/L) (median ±IQR)	1.9±1.0	2.1±1.0	1.8±0.9	p=0.001
C reactive protein (0–4 mg/L) (median ±IQR)	6.2±2.0	6.5±3.0	2.0±3.0	p=0.597
Questionnaires				
PHQ9 (median ±IQR)	3.0±11.0	7.0±12	8.0±11.3	p=0.621
PHQ9 ≥10 (%)	32 (16%)	11 (14.3)	21 (17.1)	
GAD7 (median ±IQR)	4.0±9.5	8.0±11.0	3.0±6.0	p=0. 168
GAD7 ≥10 (%)	22 (11%)	11 (14.3)	11 (8.9)	
STOPBANG (median ±IQR)	3.0±2.0	3.0±1.0	2.5±1.8	p=0.682
STOPBANG ≥4 (%)	36 (18.0)	12 (15.6)	22 (17.0)	
				RR (95% CI)
Cardiorespiratory cause of breathlessness	81 (40.5)	43 (55.8)	38 (30.9)	2.8 (1.5 to 5.1)
Persistent parenchymal change (%)	64 (32.0)	35 (45.5)	29 (23.6)	2.7 (1.4 to 4.9)
PE (%)	4 (2.0)	1 (1.3)	3 (2.4)	0.5 (0.1 to 5.1)
Other respiratory (%)	5 (2.5)	4 (5.1)	1 (0.8)	6.7 (0.7 to 60.1)
Cardiac (%)	8 (4.0)	2 (2.6)	6 (4.9)	0.7 (0.2 to 2.6)

GAD7, generalised anxiety disorder questionnaire 7; HR, heart rate; ICU, intensive care unit; 6MWT, 6 min walk test; PHQ9, patient health questionnaire 9; RR, risk ratio; SpO2, oxygen saturations; STOPBANG, snoring, tiredness, observed apnoeas, high blood pressure, BMI, age, neck circumference and male gender questionnaire.

guidance,[8] and support the more robust approach advised in by the recently published National Institute for Health and Care Excellence guidelines.[10] The outcome of this cohort of early patients highlights the current limitations of our knowledge of COVID-19 recovery. Planned studies, such as the UK-based post-hospitalisation COVID-19 study (PHOSP-COVID), will further elucidate the clinical trajectory and improve understanding of differences in patient outcomes.

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