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Patient-related outcomes in patients referred to a respiratory clinic with persisting symptoms following non-hospitalised COVID-19

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Abstract

Survivors of COVID-19 can present with varied and persisting symptoms, regardless of hospitalisation. We describe the ongoing symptoms, quality of life and return to work status in a cohort of non-hospitalised COVID-19 survivors with persisting respiratory symptoms presenting to clinic, who consented and completed patient-reported outcome measures. We identified fatigue, reduced quality of life and dysregulated breathing alongside the breathlessness. Those with co-existent fatigue had worse mood and quality of life and were less likely to have returned to normal working arrangements compared to those without fatigue. For non-hospitalised people with persisting symptoms following COVID-19 referred to a respiratory assessment clinic, there was a need for a wider holistic assessment, including return to work strategies.

Keywords

COVID-19, recovery, long-standing impacts, PROMs, respiratory, breathlessness

Introduction

A large proportion of patients surviving COVID-19 acute infection, whether or not they required hospital admission, have persisting and varied symptoms including exercise intolerance, breathlessness, fatigue, pain, anxiety and depression.[1,2] The Office of National Statistics[2] recently reported that an estimated one million people in the United Kingdom self-reported experiencing 'long' COVID symptoms >4 weeks after suspected infection. This demonstrates a wider physical and psychosocial impact beyond the acute illness phase.[1] Recent studies of hospitalised and non-hospitalised cohorts[1,3] identified a number of symptoms and post-COVID phenotypes spanning mental and physical health.

For those with persisting respiratory symptoms, there is a diagnostic need, one met in Nottingham through a focused diagnostic assessment respiratory clinic. In order to further understand the wider symptom burden and impact, a research arm (Nottingham Recovery from COVID Research Platform) with patient-related outcome measures (PROMs) was integrated for consenting patients.

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Here, we characterise these PROMs in an initial group of patients following COVID-19 illness not requiring hospitalisation with persisting respiratory symptoms.

Methods

Design

A single-centre prospective observational cohort study (NCT04710836) commenced in December 2020 following ethical approval. Data presented includes 42 patients recruited up until 16 April 2021.

Participants

Patients were referred from primary care with persisting (>3 months) respiratory symptoms requiring diagnostic assessment following COVID-19 but who did not require initial hospital admission. The initial COVID-19 diagnosis was ascertained where there was a robust clinical history and confirmed where available, with a positive PCR test. Where COVID-19 was not a likely initial illness, the patient was not invited to participate in this study. An invitation to consider research was made during their first consultation, via telephone or clinic attendance. Written informed consent was provided.

Questionnaires were completed by post for all patients with demographic and COVID-19 data extracted from medical records. The Medical Research Council (MRC) dyspnoea score and Nijmegen scores were only obtained in patients attending a face-to-face appointment.[4,5] All outcomes were collected within a 4-week window of the consultation.

Outcomes

Demographic data included age, gender, body mass index (BMI)s and occupation. Measures undertaken for clinical purposes such as the MRC dyspnoea score[4] and Nijmegen Questionnaire (NQ) were included, with a diagnostic threshold of 23 or more applied to the NQ to delineate for breathing dysregulation.[5] The following research measures were collected: cough (Leicester Cough Questionnaire), fatigue (Chalder's Fatigue Scale (CFS)), health-related quality of life (HRQoL (EQ-5D-5L)), sleep (Pittsburgh Sleep Quality Index (PSQI)), psychological stress (HADS) and return-to-work questionnaire. Patients were categorised into fatigued and non-fatigued groups according to the CFS diagnostic threshold of ≥29.[6]

Analysis

Statistical analyses were performed using SPSS (v26; SPSS Inc., Chicago, IL, USA). Data are presented as mean ± SD or median [IQR]. Parametric t-tests, or non-parametric equivalents, and chi-squared analyses were performed to compare differences between groups. A correlation matrix was designed using Spearman's rank correlation coefficients. $p < 0.05$ was considered statistically significant.

Results

The 42 participants were predominantly from a white European ethnic background ($n = 38$) with a mean age of 49 ± 10 years, BMI 28.7 ± 8.5 kg/m^2 and a MRC of 2.0 [1.0]. 67% were female. The mean time from COVID-19 diagnosis to clinical consultation attendance was 44 ± 11 weeks; 11 patients had a confirmatory positive PCR test. A large number of patients had an elevated NQ score (65%). Fatigue was identified in 15 patients. Table 1 presents data relating to other PROMs in the whole group and according to fatigued and non-fatigued status. More people in the fatigued group had a HADS depression score >11 ($p = 0.002$) and a worse EQ-5D-5L index score ($p = 0.002$). The PSQI was worse in the fatigued group ($p = 0.013$), with greater sleep disturbance ($p = 0.020$), daytime dysfunction ($p = 0.018$) and worse sleep efficiency (69% vs 80%, $p = 0.025$) identified in the subdomains. There was a lower proportion of persisting fatigue patients returning back to their previous working hours than in the non-fatigue group. Associations between PROMs are reported in Figure 1. Of those working prior to COVID-19 illness ($n = 38$), a large number were key workers: $n = 25$.

Discussion

This study presents commonly reported PROMs for 42 patients diagnosed with COVID-19 experiencing persistent respiratory symptoms requiring a diagnostics assessment and who did not require initial hospital admission. The cohort consisted predominantly of female patients, of working age and there was reduced HRQoL. There was a high prevalence of dysregulated breathing and fatigue.

Although referred into the diagnostics assessment clinic with breathlessness (and at consultation the breathlessness was troublesome), on the MRC score, these did not register with classical severity. This was mainly as most were previously fit and healthy and kept very active prior to COVID-19. One third of patients classified as fatigued, as has been recognised in the post-hospital population.[7] Reported fatigue has ranged markedly in the studies to date, with a higher proportion fatigued in the non-hospitalised population than those hospitalised.[3] Mandal et al.[8] noted fatigue in 69% of patients at 378 days, and Huang et al.[9] identified 63% with self-reported fatigue or muscle weakness at 153 days post-discharge; however, our data, in a non-hospitalised population, is lower than this. In a non-hospitalised population, Petersen et al.[10] reported a similar incidence to the current study (<30%) 4 months following acute illness. In a slightly

Table 1. PROM scores in all subjects and according to fatigued and non-fatigued status.

	n	All	*n*	Fatigue	*n*	Non-fatigued	*p*-value
Age (years)	42	49 ± 10	15	49 ± 7	27	50 ± 12	-
Gender	42	14M/28F	15	4M/11F	27	10M/17F	-
Chalder's fatigue score (0–33)	42	26 ± 6	15	32 ± 1	27	22 ± 5	<0.001
Leicester cough score (3–21)	41	17 ± 3.3	14	16 ± 4	27	17 ± 3	0.406
EQ-5D-5L							
Today's health status (VAS 0–100)	42	52 ± 20	15	46 ± 20	27	55 ± 19	0.172
Index score (−0.329,1)	42	0.55 ± 0.23	15	0.42 ± 0.2	27	0.62 ± 0.2	0.002
HADS							
Anxiety score (0–21)	42	10.1 ± 5.1	15	11.8 ± 5.8	27	9.2 ± 4.6	0.121
Proportion ≥11	42	17 (40%)	15	8 (53%)	27	9 (33%)	0.211
Depression score (0–21)	42	9.7 ± 4.5	15	12.5 ± 4.1	27	8.1 ± 4	0.002
Proportion ≥11	42	19 (45%)	15	11 (73%)	27	8 (30%)	0.007
PSQI (0–27)	42	9.7 ± 3.8	15	11.6 ± 3.5	27	8.7 ± 3.5	0.013
NQ (0–64)	31	28 ± 12	13	27 ± 12	18	28 ± 11	0.852
Elevated NQ (≥23)	31	20 (65%)	13	9 (69%)	18	11 (61%)	0.329
Back to previous work hours – yes	38*	18 (47%)	13	3 (23%)	25	15 (60%)	-

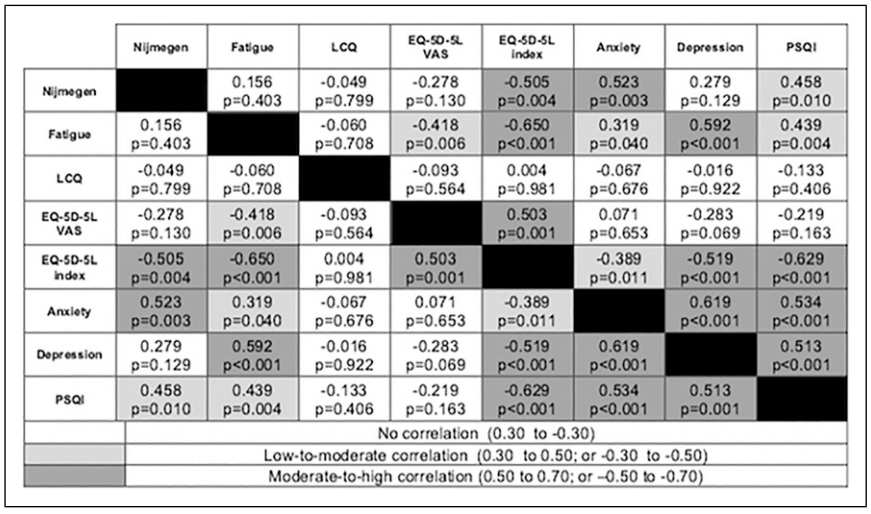

Figure 1. Correlation matrix showing strength of relationships between patient outcomes.

younger cohort (44 years), Augustin et al.[11] only identified 9.7% at 4 month follow-up, which may be explained by the use of a self-reported approach to capture fatigue.

When comparing PROMs between fatigued and non-fatigued patients, other PROMs were more evident in those with fatigue including worse HRQoL, depression and sleep quality. This is similar to other studies which report worse HRQoL in symptomatic patients.[1] Mental health burden has also been described as a significant factor following hospitalisation by Naidu et al.,[12] particularly for those with pre-existing anxiety and depression. One area to highlight is the likely impact on return to work, particularly noticeable given the working age, raising important questions of support required to facilitate return to work.

An unavoidable limitation of this data relates to the lack of confirmatory PCR testing of the initial COVID-19 and therefore a reliance on a strong clinical diagnosis by a respiratory specialist,[13] given the vast majority of patients were from the first wave of the pandemic. The duration from initial COVID-19 illness to clinic review seems in part due to prolonged initial presentation to primary care, a period of monitoring in primary care and then a wait after referral, given a steady but limited respiratory clinic availability (as this coincided with the second wave of the pandemic).

These early findings highlight the importance of approaching patients with persisting breathlessness through a multidisciplinary assessment inclusive of the diagnostics.

Whilst this is a relatively small sized study, there are signals in the wider PROMs worthy of further consideration and incorporation into a holistic assessment in order to optimise recovery and improve return to work and activities of daily living.

Conclusions

The present study characterises the extent and nature of PROMs in a population of patients following COVID-19 illness not requiring initial hospitalisation but referred in for diagnostic assessment with persisting breathlessness. Patients had poor quality of life and dysregulated breathing and a significant number were fatigued. The impact of the wider persisting symptoms in this group who were defined by their persisting breathlessness requires a multidisciplinary assessment and the development of return to work interventions.

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Author contributions

The initial research plan and design were conceived by IPH and CEB, who were awarded the funding. THD and AJ contributed equally as first authors in collecting data, drafting the manuscript and analysing data. AG, IPH and CEB contributed to the critique and writing of the manuscript. CEB is guarantor.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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