Innovations

Functional Capacity and Health-Related Quality of Life in Long Haulers of Covid-19

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Abstract

Background: *'Long-COVID-19' or 'COVID-19 long-haulers' are patients who experience symptoms for >28 days after diagnosis of COVID-19, whether laboratory-confirmed or clinical. Some symptoms such as fatigue may be continuous, while others are intermittent. These continuous symptoms affect functional capacity as well as quality of life. Thus, it becomes important to focus on both the dimensions following discharge of COVID-19 patients. This study aims to assess the functional capacity and health-related quality of life in long haulers of COVID.* ***Methodology:*** *An observational study was carried out which included 124 participants with a history of COVID-19. They were given an EQ-5D-5L questionnaire for the assessment of Health-related quality of life. Then, patients were asked to perform 6MWT and findings were recorded.* ***Result:*** *The study showed significant adverse effects on functional capacity in long haulers of COVID-19. A significant negative correlation was also found between the total distance walked in 6MWT and quality of life as assessed by EQ-5D-5L. ($p< 0.05$).* ***Conclusion:*** *Long haulers of COVID-19 have declining effects on functional capacity and health-related quality of life.*

Keywords: *Long haulers of COVID-19, Functional capacity, 6MWT, Quality of life, EQ-5D-5L.*

Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) is a novel species that causes the respiratory condition known as COVID-19. It is a major pandemic resulting in substantial mortality and morbidity worldwide. (1) Those infected with SARS-CoV-2 commonly develop symptoms 4-5 days after the exposure. According to WHO, globally, as of 6thApril 2023, there have been 762,201,169 confirmed cases, including 6,893,190 deaths.

SARS-CoV-2 infection has a wide range of clinical presentations, with the majority of patients having a mild disease with a favourable prognosis. However, for a significant proportion of hospitalized patients (20%-67%), SARS-CoV-2 may cause severe illness with rapid disease progression resulting in acute respiratory distress syndrome (ARDS).(2)

Emerging research shows a burden of chronic symptoms and reduced quality of life in COVID-19 survivors. (3)COVID-19 can present with a wide range of symptoms. While a significant number of infected patients remain asymptomatic, most develop flu-like symptoms such as fever, rhinorrhoea, dyspnoea, or cough. Acute COVID-19 symptoms include throat pain, muscle or body aches, loss of taste or smell, and diarrhoea. Patients with COVID-19 most often are symptomized with acute symptoms even though patients may have been accompaniedby asymptomatic, mild, moderate, or severe disease. (4)

The primary reason for hospitalization due to COVID-19 is pulmonary involvement which can advance to SARS.In addition, cardiac affection is seen in around 30% of hospitalized patients, with an enlarged risk of acute myocarditis, myocardial injury, and heart failure, which may alter functional capacity in the long term. Thromboembolic complications have also been outlined in some patients with COVID-19 and are linked with a poor prognosis. Musculoskeletal complications may result from long periods of hospitalization and immobility and can include fatigue, muscle weakness, and polyneuropathy. (5)

While the majority of COVID-19 patients recover within a few weeks, some people continue to have signs months after their first infection.Perego coined the terms "long haulers" and "long hauler of COVID-19" to describe the persistence of symptoms weeks or months after the original infection.(6,7)There can be the persistence of one or more symptoms of acute COVID-19, or the appearance of new symptoms. 'Long-COVID-19' or 'COVID-19 long-haulers' generally describe those persons with COVID-19 who experience symptoms for >28 days after diagnosis, whether laboratory-confirmed or clinical. (8)In other words, post-COVID-19 syndrome is the time lag between microbiological recovery and clinical recovery. (9)Some individuals with COVID-19 endure ongoing, waxing and waning symptoms that prevent them from fully recovering.

Patients with long COVID-19 can experience multiple symptoms that involve the lungs and other parts of the body. These symptoms include weakness, exhaustion, muscle discomfort, low-grade fever, coughing, chest pain (also known as "lung burn"), headaches, cognitive blunting (often known as "brain fog"), pins and needles, rashes, mental health issues such as mood swings, and thromboembolic illness. (8)Other reported symptoms include gastrointestinal upset, rashes, metabolic disruption (such as poor control of diabetes), depression, and other mental health conditions. Skin rashes can take many forms including vesicular, maculopapular, urticarial, or chilblain-like lesions on the extremities (so-called COVID-19 toe). (10) Some symptoms such as fatigue may be continuous, while others are intermittent. (8)

According to an Italian study, 87% of the discharged patients still had at least one symptom 60 days later. 55% of these experienced three or more symptoms, compared to 32% who had one or two. These patients showed no signs of fever or acute sickness. Fatigue (53.1%), reduced quality of life (44.1%), dyspnoea (43.4%), joint discomfort (27.3%), and chest pain (21.7%) were the most frequently mentioned issues. Other symptoms included cough, skin rash, palpitations, headache, diarrhoea, and a "pins and needles" sensation. In addition to experiencing mental health conditions such as anxiety, sadness, and post-traumatic stress disorder, patients also reported being unable to do basic daily tasks. (11)

The exact factors behind the persistence of symptoms are yet to be identified. The duration of chronic inflammation (convalescent phase) or immune response/autoantibody generation, rare virus persistence in the body, non-specific hospitalization effects, sequelae of critical illness, post-intensive care syndrome, complications related to corona infection, or complicating factors can all contribute to the persistence of symptoms. (12)

A few factors that are frequently linked to the development of prolonged COVID-19 have been identified via the follow-up of patients who have recovered from COVID-19. Women have a twice as high risk of long COVID-19 compared with males. Aging, the presence of co-morbidities, and more than five symptoms seen during the acute stage of the illness are linked to a higher likelihood of long-term COVID-19 development. (13)

The ability to carry out daily tasks which require sustained aerobic metabolism is referred to as functional capacity. The respiratory, cardiovascular, and skeletal muscle systems work together to determine an individual's functional capacity. For assessing functional capacity, a cardiopulmonary exercise test is commonly used to measure maximal oxygen consumption directly. The 6MWT evaluates the functional exercise capacity. The 6MWT measures a patient's functional status about their everyday activities if they have a cardiopulmonary condition. Gender, age, and height are all closely related to the walking distance. (14)

Health-related quality of life (HRQoL)is a multi-dimensional ideaconsisting of domains that include physical, mental, emotional, and social functioning. Instruments used for the evaluation of

patients' HRQoL can be categorized as "generic" or "disease-specific," which have their inherent limitations and strengths. (15)EuroQOL-5 Dimensions-5 Levels (EQ-5D-5L) is a popular instrument used for the assessment of generic HRQoL, cost-utility of healthcare interventions, and computation of quality-adjusted life years for patients.

Limited evidence isavailable regarding the functional capacity and health-related quality of life of long haulers of COVID-19. So, more research study needs to be done to assess the functional capacity and health-related quality of life in long haulers of COVID-19.

Material and Methods

This is an observational study done on 124 Long haulers of COVID-19 subjects in the Vadodara district of Gujarat state, India over a period of 12 months. Convenient sampling was used to select the sample from the city. Inclusion criteria were; confirmed COVID-19 infection by SARS-CoV-2 real-timePCR (RT-PCR) using nasopharyngeal swaps, availability of past medical records, at least one persistent symptom for at least 60 days after the diagnosis or 30 days after recovery, and subjects who experienced symptoms for >28 days after the diagnosis. Whereas subjects with a history of pre-existing lungdisease before getting COVID-19, mental disability, and history of musculoskeletal/neurological conditions affecting the performance of 6MWT were excluded from the study.

The study was registered with the Institutional Ethics Committee and also with the Clinical Trial Registry-India (CTRI/2022/11/047249). The recruited participants were asked to fill out a consent form and made aware of the 6 MWT and EQ-5D-5L questionnaire under the direct supervision of the study investigator. After the detailed explanation, participants were made to sit on comfortable chairs and EQ-5D-5L questionnaires were given to participants for their responses.Then subjects were explained in detail about the procedure of 6MWT and then they were asked to perform the test according to the standard American Thoracic Society (ATS) guidelines.A pulse oximeter, sphygmomanometer, cones, stopwatch, and Borg's scale were used to conduct the 6MWT.

Results

In this study, a total of 130 participants who had a history of COVID-19 were recruited from Vadodara city. Out of which, 6 participants were excluded who were not meeting the inclusion criteria. Here, 1 participant was excluded due to Asthma, 2 were excluded due to inability to comprehend English, and 3 were excluded due to unavailability of RT-PCR report.The remaining 124 participants were assessed for functional capacity using the 6-Minute Walk Test (6MWT) and quality of life using the EQ-5D-5L questionnaire.

Table I: Baseline data of participants

Characteristic	**Mean ± S.D.**
No. Of subjects	124
Age (years)	35.98 ± 15.83
VAS score (EQ-5D-5L)	78.9 ± 10.18
Gender	Female: 61
	Male: 63

As shown in Table II, differencesinPre-Vitals, ImmediateVitals, and Post 3-minute Vitals were taken and a comparison of the same shows a statistically significant difference ($P<0.001$) i.e. there is a significant effect of COVID-19 on functional capacity in long haulers of COVID-19. The mean 6MWT distance in this study is 451.04 meters.

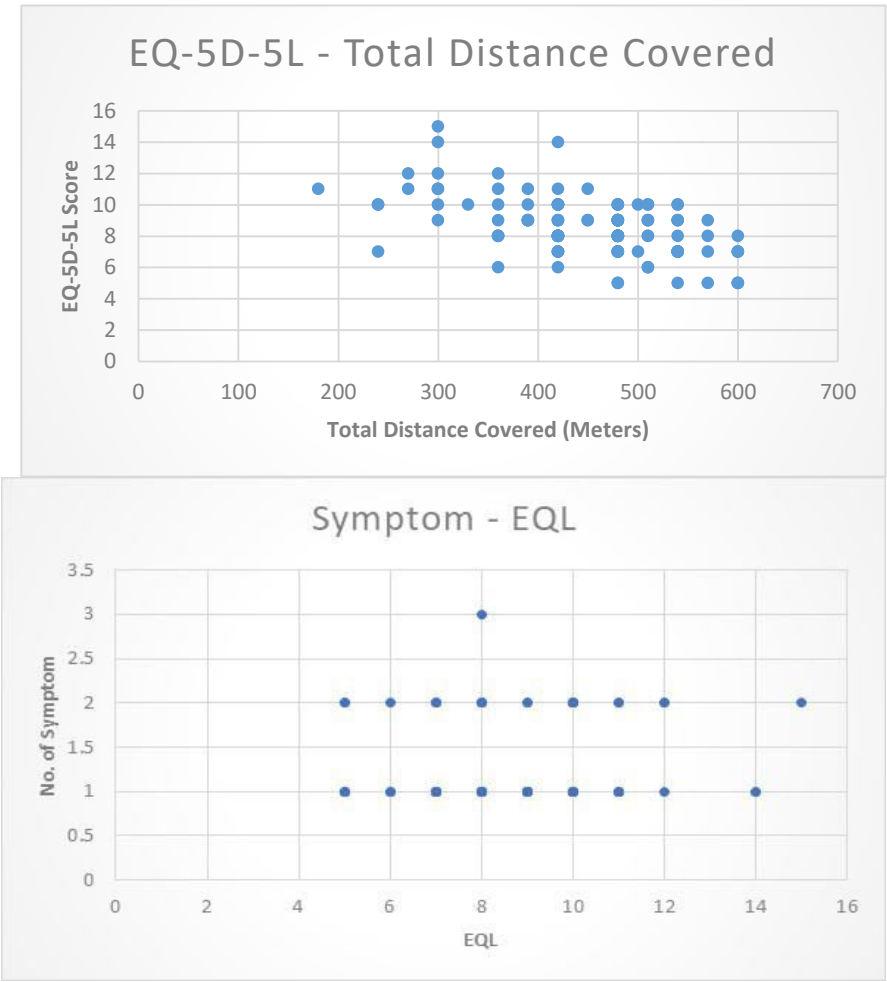
Table II: Various parameters of 6MWT

6-Minute Walk Test Significance						
Outcome Measures	**Pre - Vitals (Mean ± SD)**	**Immediate Vitals (Mean ± SD)**	**Post 3 Min. Vitals (Mean ± SD)**	**H statistic**	**P Value**	**Remark**
PR	74.54 ± 7.1	84.84 ± 9.21	78.3 ± 7.56	90.08	<0.001	Significant
RR	15.21 ± 1.66	21.47 ± 4.18	18.59 ± 7.18	165.18	<0.001	Significant
BP (Systolic)	121.61 ± 9.27	131.17 ± 7.7	125.44 ± 8.58	72.07	<0.001	Significant
BP (Diastolic)	82.05 ± 6.46	89.31 ± 5.64	83.74 ± 5.95	85.96	<0.001	Significant
RPE	6.15 ± 0.47	10.86 ± 1.27	7.24 ± 1.29	259.80	<0.001	Significant

PR is Pulse rate in rate per minute, RR is Respiratory rate in Rate per minute, BP is Blood pressure in mm/hg and RPE is Rate of perceived exertion.

Figure I: Correlation between EQ-5D-5L and total distance covered

Figure II: Correlation between the number of symptoms and EQ-5D-5L



A significant negative correlation existed between the EQ-5D-5L scoring and total distance covered in 6MWT ($p < 0.05$) (Table III & Image I) which means as the EQ-5D-5L score increases (reduced health-related quality of life), distance covered in 6MWT decreases.

In this study, 96 participants had one symptom, 27 participants had two symptoms and 1 participant had three symptoms of COVID-19. As seen in Table III and Figure II, there is no significant correlation between thenumber of symptoms and HRQoL ($P = 0.269$). Thus, it states that the number of symptoms does not have any effect on the quality of life of long haulers of COVID-19.

Table III: Various correlations by Pearson's correlation coefficient

Test Variable	Pearson's r	P Value	Conclusion
Total Distance – EQ-5D-5L	-0.54	<0.01	Significant Negative Correlation
No. of Symptom – EQ-5D-5L	0.10	0.269	No Significant Correlation
No. of Symptom - Total Distance	-0.18	0.17	No Significant Correlation

Figure III: Correlation between the number of symptoms and total distance covered

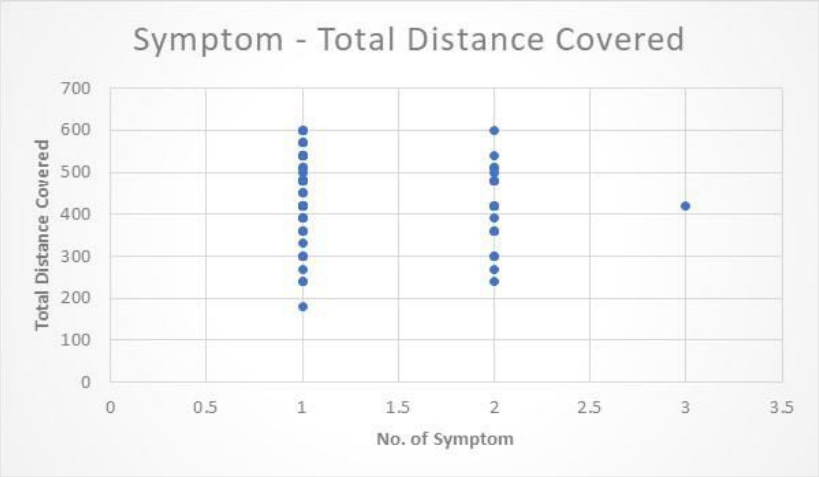


Table III and Figure III also show that there is no significant correlation between the total number of symptoms in long haulers of COVID-19 and the total distance covered in 6MWT (P = 0.17). Hence, it is proved that the total number of symptoms does not have any effect onthe total distance walked in 6 MWT, eventually proving that it is not associated with a reduction in functional capacity.

Discussion

The majority of literature on COVID-19 has focused on the potential pathophysiology of the illness and the treatment of acute scenarios during hospitalization days, however, there is limited information available on post-COVID-19 sequelae and "long-haulers". (16)

In this study, the correlation between the COVID-19 long hauler symptoms and quality of life was found to be non-significant, which could be because this study was conducted a long time after the COVID-19 pandemic was over, so it is possible that participants might not have the same effect of long haulers symptoms on quality of life as it might have been when the pandemic was at its peak. This correlation is not consistent with a systematic review and meta-analysis done by Lopez-Leonwhich showed that 80%of individuals with a confirmed COVID-19 diagnosis continue to have at least one symptom beyond 2 weeks of acute infection which will eventually lead to a decrease in quality of life. (17)

This study noted that fatigue was one of the most recurring symptoms among study participants.One systemic review showed that Dyspnoea and cough were found in 24% and 19% of patients, respectively. (17)Radiographic abnormalities persisted in over two-thirds of patients in a follow-up study in China among non-critical COVID-19 hospitalized patients 90 days after discharge but exact radiographic findings were not assessed in this study. (18) A report published by the CDC mentioned symptoms like sudden loss of body weight, ear pain, eye problems, sneezing, cold nose, burning feeling in the trachea, dizziness, heart palpitations, pain/burning feeling in the lungs, sicca syndrome, vertigo, a feeling of pain between the shoulder blades, and confusion which were not studiedby any other research publications. (19)

The mean age group in this study was 35.98 ± 15.83 years and gender distribution alsoshowed a greater number of females which suggests that Long COVID-19 can be present in mostly middle age groups and commonly in females. These findingscorrelate with the study by Sudre C. et al which also showed affection in similar age groups(45.97 ±15.8)and gender distribution (57% female). (20) Contrarily to this, one systemic research found COVID-19 prevalence in children and adolescents at 25.24%. (21)

Our findings also show that the long hauler of COVID-19 hasa direct effect on reduced functional capacity in individuals which is supported by a study done by Barrato C. et al who stated that functional limitations appear to be primarily caused due to impaired peripheral oxygen extraction following COVID-19 and decreased oxygen content leading to anaemia which eventually leads to fatigue. (22)In this study, the number of females is more which states that they have more impairment in functional capacity which is consistent with findings of another systemic review where they stated that lower 6MWT distance was also substantially correlated with female sex and pre-existing comorbidities.Female sex, pre-existing comorbidity, and ARDS (vs non-ARDS) were associated with lower 6MWT results.In our population, the average 6 min walk test distance was 451.04 meters. Patients in recovery from serious illnesses usually do significantly worse, with an average 6-minute walk of 361 meters.In the same cohort of patients with severe ARDS, results were even worse (281 [55-454] meters). This may be because of extended periods of mechanical ventilation (21 days) and intensive care unit (ICU) stay, which led to more severe muscle wasting and weakness. (23)In one study,the patients had a considerable probability of experiencing fatigue symptoms together with significant movement restrictions, which were confirmed by a shorter 6MWT distance. (24).In a 6-month follow-up study from China, patients who received invasive or non-invasive respiratory assistance (including high-flow oxygen) walked similar distances to our study, with a median distance of 479 meters. (6)

In this study, a negative correlation was found between the total distance walked in 6MWT and health-related quality of life which was assessed by the EQ-5D-5L questionnaire (P <0.01). This negative correlation suggests that participants with poor health-related quality of life havea lower total distance covered in 6MWT. On the other hand, there was no correlation between the number of symptoms and health-related quality of life (P = 0.269) which suggests that the number of symptoms had no direct effect on the total distance walked in 6MWT. The mean VAS score which is one of the components of the EQ-5D-5L questionnaire is 78.9 ± 10.18. Here, 100 indicates the best quality of life and 0 indicates the worst quality of life. The VAS score of this study is supported by another study done in Italy and their mean VAS score was 78.22 following 6 months of COVID-19. (21)Daher et al. in their cohort study discovered reduced EQ-VAS ratings (i.e., a median value of 63 [53-80]) after 2 months following hospital discharge in a group of 33 non-intubated COVID-19 patients. (24)The lengthy hospital stay, pre-existing diseases, and post-viral exhaustion, a symptom that survivors of severe COVID-19 frequently experience, are all likely contributing factors to the overall decline in quality of life. (12)

In the present study, we also found that there was a significant correlation between Pre vitals (P<0.001) and post-immediate vitals (P<0.001) and Post 3 min vitals (P<0.001) in 6MWT which suggests that long haulers of COVID-19 do not have any effect on vitals' recovery after 6MWT. (Table 2) The vitals included pulse rate, respiratory rate, blood pressure, and rate of perceived exertion.

So, according to the results of the present study, we concludethat functional capacity and health-related quality of life are impaired in long haulers of COVID-19. Thus, this eventually opens the scope for physical therapy in patients with long haulers of COVID-19 as it involves multiple systems of the body and so a holistic approach of treatment is required.

Conclusion

This study concludes that long haulers of COVID-19 have declining effects on functional capacity and health-related quality of life.

Limitations

- There can be other long haulers of COVID-19 symptoms which are rarely seen but they were not assessed in this study.
- This study was done a long time after the COVID-19 pandemic was over, so it was difficult for investigators to collect samples.

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