Long-Term Impact of COVID-19

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Post-COVID-19 patients may experience persistent chest CT abnormalities, decreased lung function, persistent fatigue, and respiratory symptoms, decreased functional capacity, and decreased quality of life up to 6 months after symptom onset or hospital discharge. On average, 8 out of 10 patients had returned to work or reported no work impairment at around 3 months of follow-up.

Keywords: COVID-19 ; persistent symptoms ; long-term effects ; follow-up ; lung function ; respiratory symptoms ; fatigue ; functional capacity ; quality of life

1. Background

The novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has spread rapidly worldwide reaching over 191 million confirmed cases, including 4.1 million deaths as of 21 July 2021 [1]. Although lung abnormalities are found even in asymptomatic patients with COVID-19 [2], most of the cases (81%) have no or mild pneumonia and can be managed at home. Severe (14%) and critical (5%) cases develop severe pneumonia and respiratory failure, which require in-hospital oxygen treatment or mechanical ventilation and are more likely to have long-term effects [3].

Evidence from literature on viral pneumonia indicates that many recovered patients have significant lung changes and are affected by acute respiratory distress syndrome (ARDS), which can negatively impact their lung, physical function and quality of life for months or years [4][5]. Previous studies conducted on patients with severe acute respiratory syndrome (SARS) caused by a SARS coronavirus that was identified in 2003 report long-term decreases in pulmonary function, including reduced lung volume measurement in 7.3% of the patients at 6 months [6]. The most common pulmonary function impairment identified at a 1 year time point was of the forced expiratory volume (FEV1) and diffusing lung capacity for carbon monoxide (DLCO) which were still abnormal in 18.2% and 52.7% of patients, respectively, at 24 months post-SARS [7][8]. Decreases in exercise capacity and health-related quality of life were also found in SARS patients, and only 78% of SARS survivors had returned to work within 24 months [7]. Similarly, signs of severe abnormal pulmonary function were reported in 54.2% of patients with influenza A (H1N1), 1 year post-discharge [9], 59% of the patients reported significant exertion dyspnea, 70% had returned to work, health-related quality of life was poorer than for sex- and age-matched general population groups [10]. Overall, evidence indicates that ARDS patients experience decreases in lung function, exercise endurance, levels of body function (muscle strength, walking capacity, and/or physical activity), and HRQoL, and lower return-to-work rate [11][12][13]. As COVID-19 has recently emerged, the long-term impact of the disease, defined as the signs and symptoms lasting beyond the period of active infection, is just becoming known.

In recent months, the scientific literature has used the term “Long COVID” to describe illness in people who have reported lasting effects of the infection or have had the usual symptoms for far longer than would be expected [14]. Abnormal chest computed tomography (CT) findings and impairment in lung function were found in COVID-19 patients 30 days after hospital discharge [15]. Persistent symptoms such as cough, dyspnea, and fatigue have commonly been reported in post COVID-19 patients between 30 and 56 days after hospital discharge [15][16][17][18][19]. Decreased functional capacity [17] and difficulties with the activities of daily living such as mobility and self-care [17][18][19] were also identified in patients for follow-ups of up to 8 weeks [20]. A study reports that 39% of patients perceived a decrease in their overall health [19] around 6 weeks after symptom onset. 61.5% of patients delayed their return to work at least 5 weeks from symptom onset, the primary reason for which was fatigue and weakness [16], and 38% were absent due to illness [19]. Evidence indicates that COVID-19 can have significant persistent effects on patient outcomes up to 12 weeks after the period of acute infection [21][22][23]. However, the long-term impact of COVID-19 on patient outcomes is still unknown. The aim of this study is to explore persistent effects of COVID-19 beyond 3 months follow-up on patient chest computed tomography (CT), lung function, respiratory symptoms, fatigue, functional capacity, quality of life, and the ability to return to work.

2. Long-Term Impact of COVID-19

Prevalence of chest CT abnormalities and decreased pulmonary function post-COVID-19 aligned with evidence from previous studies, which report abnormal outcomes in patients with viral pneumonias up to 64 months after illness onset [24][25]. Persistent lung abnormalities are significantly associated with disease severity at baseline in various studies [26][27][28][29][30]. However, high prevalence of chest CT abnormalities was not well reflected on PFT and only weak to moderate correlations were found [31][32]. Presence of GGO, commonly identified at follow-up [33][34][26][31][32][27][28][35][36][37][29][38][30], can be a manifestation of a wide variety of clinical features including focal interstitial fibrosis, and inflammation [39]. Residual pulmonary parenchymal abnormalities were correlated with lower DLCO [30], and pulmonary function abnormalities occurred frequently in patients with fibrotic-like changes [33]. Impaired DLCO reported in the PFT [40][33][34][26][31][32][35][36][37][29][30] can be present in interstitial lung diseases or pulmonary fibrosis, which are clinical conditions where the surface area of the alveolar membrane is reduced [41]. DLCO values represent the ability of the lung to transfer gas from the inhaled air into the blood stream and can be used as a marker of the extent of lung damage [42]. Impaired DLCO may be attributed to abnormalities in the distal airways (such as constrictive bronchiolitis with air trapping and secondary reflex vasoconstriction), or to primary vascular disease (that may induce secondary airway disease) [28]. Abnormal DLCO and GGO on chest CT were associated with duration of oxygen supplementation [36].

High prevalence of cough, dyspnea, and fatigue were reported in post COVID-19 patients. Cough and dyspnea can be indicators of impaired lung function [41] and may also affect the execution of an adequate PFT [43]. Dyspnea scores were found to correlate with PFT measurements in COVID-19 patients [31]. Presence of dyspnea is attributed to abnormalities on lung CT scan in 44 of 78 patients (45%), including fibrotic lesions in 18 of 78 cases (23%) and to hyperventilation functional breathing test confirmed dysfunctional breathing in 14 of 78 patients (17%) [35]. Although some evidence supports the theory that breathing problems in COVID-19 patients may be due to fibrotic changes in the lung, it is also suggested that post-viral autonomic dysfunction may contribute to the cause of this and other persistent symptoms [44]. Fatigue, the most prevalent symptom reported by post COVID-19 patients, was identified in one third of the patients and could likely persist for a longer time. A previous study reports that 40% of SARS survivors had chronic fatigue for a mean of 41 months after infection [45]. Post-COVID-19 fatigue is not associated with disease severity in the acute phase or with abnormal chest CT abnormalities [22]. Fatigue was reported together with muscle weakness in one of the studies [46], and with physical decline in another [34]. It is possible that fatigue may have been caused by muscle weakness, respiratory symptoms, and general deconditioning. It has also been suggested that the coronavirus can trigger post-viral fatigue syndromes [47]. More studies will be needed to clarify the cause of fatigue in post-COVID-19 patients and the best way to treat it.

Decreased functional capacity was found in one third of post COVID-19 patients at follow-up. CT abnormalities are not associated with functional performance [29], however, residual signs suggesting pulmonary fibrosis are associated with exercise-induced desaturation [30]. Sixteen percent of patients desaturated upon the 6MWT, desaturators had lower DLCO than non-desaturators [30]. Persistent symptoms, decreased pulmonary function, muscle weakness and physical deconditioning may have contributed to post COVID-19 decreased function and perception of worsened HRQoL. Despite the higher prevalence of multiple post-COVID-19 effects, a large percentage of the patients had returned to work 3 to 4 months after discharge [31][37][48]. Importantly, all studies that reported on this outcome used small sample sizes (ranging from 55 to 76 patients). Furthermore, in the studies that found that all or almost all patients had returned to work, the participants were relatively young (mean age 41.3 SD13.8 and 47.7 SD 15.4 years) and only a small percentage of them had a serious illness that required ICU care [31][37]. Although in Garrigues et al. the group studied was older (mean 63.2 SD 15.7), this outcome was reported only in 46.7% (56/120) of the participants, probably younger patients still active in the workforce. Therefore, a potential explanation for the lower return to work (68%) could be a higher percentage of patients with severe disease at baseline, since 20% of participants were in the ICU [48]. It is also possible that the socio-economic context and available resources may have an impact on the return-to-work process. In general, more studies with larger sample sizes are needed to determine the potential long-term impact of COVID-19 on patients ability to return to work, as well as the possible causes and ways to mitigate them.

Patients with severe COVID-19 disease had higher prevalence of chest CT abnormalities [26][27][28][29][30]. However, inconclusive results were found regarding disease severity and persistent fatigue, respiratory symptoms, pulmonary function, functional capacity, and HRQoL. Evidence suggests that severity of disease during the acute period of infection may have an impact on persistent COVID-19 outcomes. However, only a few studies report the outcomes in relation with disease severity and no direct association between disease severity and post COVID-19 outcomes was observed. Persistent symptoms are also reported in patients with non-severe disease.

3. Conclusions

The results indicate that post-COVID-19 patients may experience persistent respiratory symptoms, fatigue, decreased functional capacity, and decreased quality of life up to 6 months after infection and, on average, around 8 out of 10 of the patients had returned to work at around 3 months follow-up. Outcomes suggest that, in addition to disease severity and lung injury, other potential causes of persistent symptoms, such as post-viral autonomic dysfunction and fatigue syndrome should be assessed and considered when planning post-COVID-19 rehabilitation interventions. Further studies are needed to establish the extent to which post-COVID-19 effects continue beyond 6 months, how they interact with each other, and to clarify their causes and their effective management.

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