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Original Research

Follow-up of functional exercise capacity in patients with COVID-19: It is improved by telerehabilitation

Ines Martin [a,b,c], Fred Braem [c], Lia Baudet [c], William Poncin [a,b,c], Stéphane Fizaine [c], Frank Aboubakar [a,b,d], Antoine Froidure [a,b,d], Charles Pilette [a,b,d], Giuseppe Liistro [a,b,d], Julien De Greef [d], Halil Yildiz [d], Lucie Pothen [d], Jean-Cyr Yombi [b,d], Leïla Belkhir [b,d], Gregory Reychler [a,b,c,*]

[a] Service de Pneumologie, Cliniques Universitaires Saint-Luc, Brussels, Belgium
[b] Institut de Recherche Expérimentale et Clinique (IREC), Pôle de Pneumologie, ORL & Dermatologie, Université Catholique de Louvain, Brussels, Belgium
[c] Secteur de Kinésithérapie et Ergothérapie, Cliniques Universitaires Saint-Luc, Brussels, Belgium
[d] Department of Internal Medicine and Infectious Diseases, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium

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ABSTRACT

Background: The impact of the COVID-19 pandemic on functional exercise capacity seemed quickly clinically evident. The objective of this study was to assess the functional exercise capacity of patients with severe COVID-19 and to evaluate the effect of a telerehabilitation program in the specific context of the COVID-19 pandemic.
Method: Patients hospitalized for severe or critical COVID-19 were recruited. The functional exercise capacity (1-min sit-to-stand test (STST)) was prospectively quantified at discharge. A telerehabilitation program was then proposed. A control group was composed with the patients refusing the program.
Results: At discharge, none of the 48 recruited patients had a STST higher than the 50th percentile and 77% of them were below the 2.5th percentile. SpO2 was 92.6 ± 3.0% after STST and 15 patients had oxygen desaturation. After 3-months of follow-up, the number of repetitions during STST significantly increased either in telerehabilitation ($n = 14$) ($p < 0.001$) or in control groups ($n = 13$) ($p = 0.002$) but only one patient had a result higher than the 50th percentile (in Telerehabilitation group) and 37% of them were still under the 2.5th percentile for this result. The improvement was significantly and clinically greater after the telerehabilitation program ($p = 0.005$). No adverse events were reported by the patients during the program.
Conclusions: Patients hospitalized for COVID-19 have a low functional exercise capacity at discharge and the recovery after three months is poor. The feasibility and the effect of a simple telerehabilitation program were verified, this program being able to substantially improve the functional recovery after three months.

1. Introduction

The coronavirus disease 2019 (COVID-19) emerged as a pandemic associated to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since the onset of the pandemic in Wuhan, China, COVID-19 has caused more than 84 million cases and 1.85 million deaths worldwide, as of December 31, 2020. The clinical presentation is mild in about 80% of cases, moderate to severe in 15% of cases and critical in 5% of cases [1]. Those with severe or critical form required to be admitted to the hospitals for treatment. In Belgium, April 2020 showed the peak incidence of the first wave, reaching around 600 hospitalized patients on a daily basis. Out of those 20% were in Intensive care unit (ICU) (www.sciensano.be).

It became rapidly obvious to the clinicians that the impact of the COVID-19 pandemic on functional exercise capacity would be important. Indeed, many hospitalized patients also developed multi-organ diseases influencing this capacity and reducing the quality of life. While data about the long-term follow-up of these patients with COVID-19 [2]have only been emerging recently, the musculoskeletal dysfunctions and muscle weakness are already observed during the hospitalizations. The viral infection is directly responsible for the fundamental cellular and tissue-level dysfunctions [3]. In addition, COVID-19

* Corresponding author. Pulmonology unit, Cliniques Universitaires St-Luc (UCL), Avenue Hippocrate 10, 1200, Brussels, Belgium.
E-mail address: gregory.reychler@uclouvain.be (G. Reychler).

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musculoskeletal disorders are also indirectly associated to the systemic inflammation and its treatment, which is also being reinforced probably by the required isolation of the patient in the room to avoid spreading of the virus. Finally, critically ill patients who required prolonged mechanical ventilation support also suffered from severe acquired muscle weakness due to inflammation, corticosteroids use, and prolonged immobilization, ultimately generating muscle and skeletal frailty.

In Belgium, containment rules during the first wave involved a national lockdown and thus closure of all sport or leisure activities, restricting the patient's ability to recover on their own with standard services promoting physical activities.

We hypothesised that the functional exercise capacity and the muscular strength can be unrecovered at discharge and that the full lockdown imposed in Belgium at that time could significantly hamper recovery.

The aim of this study was [1] to assess the functional exercise capacity of patients with COVID-19 at hospital discharge, and [2] to evaluate the feasibility, the safety, and the effect on recovery of a telerehabilitation program initiated after discharge within the specific context of COVID-19 pandemic.

2. Method

2.1. Design of the study and settings

This single-center prospective observational study was conducted in the COVID-19 wards of Cliniques universitaires Saint-Luc (Brussels). It was based on the Statement for STrengthening the Reporting of OBServational studies in Epidemiology (STROBE). The study was conducted in two phases. The first part assessed the functional exercise capacity of patients hospitalized with COVID-19 between April and May 2020. The second phase investigated the feasibility, safety and effects of a telerehabilitation program in these patients. The study was approved by the local ethics committee (2020/06AVR/200, 2020/06AVR/201).

2.2. Patients

All hospitalized patients with laboratory-confirmed COVID-19 were prospectively assessed for eligibility and the functional exercise capacity was quantified at discharge (Part 1). A telerehabilitation program was then proposed to all the patients included in Part 1 (Part 2). To be included, COVID-19 pneumonia has to be confirmed by positive RT-PCR on a nasopharyngeal swab, and lung infiltrates on a lung HRCT or chest X-ray. To be eligible, the patients had to spend more than 48 h in the hospital for severe or critical COVID-19, based on the NIH definition and had to be discharged during April or May. Individuals who had SpO2 <94% at ambient air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, respiratory frequency >30 breaths/min, or lung infiltrates >50% were categorized as severe. Critical Illness was defined by respiratory failure, septic shock, and/or multiple organ dysfunction syndrome. The patients were only included on a voluntary basis in the telerehabilitation program (Part 2). The patients were excluded from Part 1 if they previously had a diagnosed chronic respiratory disease and from Part 2 if their pulsed oxygen saturation (SpO2) decreased more than 4% during STST at discharge.

2.3. Interventions

2.3.1. Part 1

Each subject performed a 1-min sit-to-stand test (STST) at discharge to assess their functional exercise capacity.

2.3.2. Part 2

Patients who had agreed to participate in the telerehabilitation program entered this phase. The other patients were automatically included in the control group. The telerehabilitation program was synchronous, which refers to real-time clinician-patient interactions. It involved a videoconferencing platform (Teams, Microsoft, Redmond, WA, USA), laptop, phone or tablet and a web camera. An experienced physiotherapist involved in the pulmonary rehabilitation program supervised the remote telerehabilitation. Patients performed home based exercises twice a week for 6 weeks. The first two sessions were individually performed to assess the physical condition of the patient and to check the proper execution of the exercises. From the second week onwards, the sessions were performed in groups of 4 patients at a time. Each session was composed of 50 min including 30 min of endurance exercises followed by upper and lower body muscular strengthening. The intensity of the endurance training was fixed based on a 6-point score on the Borg scale. The upper and lower body muscles training was performed with materials available in the home environment of the participants (bottles of water and a chair). The participants were instructed to do 2–3 series of 8–12 repetitions for each exercise. After each session, patients received a file summarizing all the executed exercises. They were encouraged to perform unsupervised exercises 3 times a week, using the provided templates.

2.3.2.1. One-minute sit-to-stand test (STST). The 1-min STST was performed based on the protocol previously described by Ozalevli [4]. With the hands on their hips to avoid use of arm as support, the subjects were asked to stand up and sit down completely from a chair and as many times as possible (height = 46 cm) during 1 min. A demonstration test was previously performed and standardized instructions were given to the subjects before the test by an experienced physiotherapist.

No encouragements were provided during the test. If necessary, resting periods were tolerated during the test but the countdown timer continued.

2.3.2.2. Outcomes. Anthropometric parameters were noted. The number of completed sit-to-stand repetitions during each 1-min STST was recorded at discharge and 3 months later in both groups. These results were expressed in absolute values and in percentiles based on the population-based reference values from Strassmann [5].

The heart rate (HR) and pulsed oxygen saturation (SpO2) were quantified by a finger pulse oximeter (Onyx, Nonin, USA) and perception of dyspnea was assessed by the visual analog scale (from zero "no shortness of breath at all" to 10 "maximum shortness of breath"). These outcomes were recorded at the beginning and at the end of each STST and after a 1-min recovery time. First two outcomes were expressed in absolute and relative values.

The local standard of care for all discharged patients involved several lung function tests and high resolution computed tomography (HRCT) performed 3-month later. Spirometry and lung diffusing capacity for carbon monoxide (DLCO) measurements were performed according to ATS/ERS guidelines. Results were expressed in percentages of the predicted values (Global Lung Function Initiative (GLI) reference values). The high resolution computed tomography (HRCT) was performed and a percentage opacity score was obtained (CT Pneumonia Analysis software, Siemens Healthineers, Forchheim, Germany). It is defined as the percentage of lung abnormalities volume compared to the total lung volume without distinction between ground glass, consolidations, or reticulations. *Statistical analyses.*

Data was analysed using SPSS 27.0 (IBM software, Armonk, NY, USA) for Windows. Descriptive analysis was performed. Cardio-respiratory parameters were expressed by the difference between initial and final values and expressed as a percentage of the initial value (for cardio-respiratory parameters) whereas dyspnea changes were expressed in absolute value. The data was presented as mean and standard deviation or median with range after verifying the normality of the distribution by Kolmogorov-Smirnov test.

Similarly, the comparisons of similar data between discharge and follow-up were performed by the paired Student T-test or the Wilcoxon Test. The relationship between the number of repetitions and other parameters was verified by the Spearman coefficient of correlation (rho). The changes in STST, dyspnea, SpO2 and HR were greater compared with the non-telerehabilitation group. Chi-square was used to compare the proportion (gender, ICU, oxygen). A p-value lower than 0.05 was considered as significant.

3. Results

3.1. Part 1

A total of 103 patients with COVID-19 were eligible. The functional exercise capacity was assessed in 48 severe (n = 35) or critical (n = 13) COVID-19 hospitalized patients at discharge. Three patients who had previously been diagnosed with a chronic respiratory disease (idiopathic pulmonary fibrosis [1] and COPD [2]) were excluded. The demographic characteristics of the patients are highlighted in Table 1.

At discharge, the SpO_2 at rest was higher than 90% for all patients (95.3 ± 2.0%). The median dyspnea score at rest was 1 (0–7). The mean number of repetitions during STST was 16 ± 8 [14; 19]. None of the patients had a result in STST higher than the 50th percentile and 77% of them were below the 2.5th percentile. One patient was unable to stand up from the chair. At the end of the STST, the SpO_2 was 92.6 ± 3.0% [91.7; 93.6]. It was lower than 90% (minimum: 87%) for only 4 patients but 15 patients had oxygen desaturation (>4% decrease). The mean differences in HR and dyspnea score between the start and end of the STST were 21.6 ± 19.4% [15.6; 27.7] and 5 [1–10], respectively.

The data of the follow-up regarding the lung function are displayed in Table 2. No particular impairment was observed with the parameters in the normal range based on the predicted values. When considering all HRCT lesions in these patients, the median opacity score was 1.24% at three months.

An inverse significant correlation was only found between the number of repetitions at discharge and the length of stay in the intensive care unit (rho = −0.657; p = 0.011). Neither dyspnea, nor pulsed oxygen saturation (at rest or at effort) were correlated with the number of repetitions.

3.2. Part 2

Fifteen patients accepted to participate in the telerehabilitation program but one of them chose to abandon after the first session for privacy reasons and was therefore not included in the final evaluation. No adverse events were reported by the patients during the program. The baseline characteristics of the patients are highlighted in Table 1. No difference in the demographic characteristics or in the severity ratio was observed between the two groups at baseline (Table 1). The severity of the COVID-19 that was determined by the need of oxygen supply, the length of hospital stay and a stay in intensive care unit, was similar in the two groups. The results are detailed in Table 3. The SpO_2 at rest was higher than 90% for all patients (96.7 ± 1.5% [96.0; 97.4]). At baseline, the cardio-respiratory parameters were similar between the two groups and in a normal range, either before or after STST. SpO2 was higher than 90% for all the patients and only one patient had oxygen desaturation.

Even if the number of repetitions during STST was dramatically small, it was similar in the two groups. After 3-months of follow-up, the number of repetitions during STST significantly increased either in telerehabilitation (p < 0.001) or in control groups (p = 0.002) but only one patient had a result higher than the 50th percentile (in the telerehabilitation group) and 37% of them were still under the 2.5th percentile. The improvement was significantly and clinically greater after the telerehabilitation program (p = 0.005). The increase in HR after STST was also higher in this group. The change in dyspnea after STST was similar in both groups. No patient reported to participate in an official healthcare intervention such as physiotherapy or complementary therapies.

Table 2
Lung function parameters of the patients at 3 months of follow up.

	Total n = 27
DLCO (% pred)	79.2 ± 18.2
FEV1/FVC (% pred)	102.5 ± 12.6
FEV1 (% pred)	90.6 ± 25.2
FVC (% pred)	90.0 ± 19.8
IC (% pred)	99.2 ± 23.0

Data are presented as mean ± standard deviation.
DLCO: lung diffusing capacity for carbon monoxide; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; IC: inspiratory capacity.

4. Discussion

This study was performed with severe or critical patients hospitalized for COIVD-19 and it included two parts. The first part was aimed at

Table 1
Demographic characteristics of the patients in the different groups.

	Total n = 48 (baseline)	Telerehabilitation n = 14	Control n = 13	p value (tele vs control)
Age (years)	61.5 ± 10.5 [58.5; 64.6]	60.8 ± 10.4 [55.6; 65.9]	61.9 ± 10.7 [57.9; 66.0]	0.990
Gender (M/F)	28/20	11/3	6/7	0.082
Weight (kg)	88.6 ± 21.7 [81.1; 96.0]	95.3 ± 27.6 [80.0; 110.5]	83.6 ± 14.8 [76.6; 90.5]	0.191
Height (cm)	167.6 ± 18.8 [161.8; 173.4]	168.6 ± 29.6 [152.8; 184.3]	167.0 ± 8.1 [163.8; 170.2]	0.786
BMI (kg/cm2)	29.0 ± 4.7 [27.4; 30.6]	29.7 ± 5.2 [27.3; 32.2]	28.1 ± 3.9 [26.0; 30.3]	0.324
ICU (y/n)	13/35	4/10	2/11	0.410
Length of stay (d)	16.1 ± 9.1 [5.0; 16.5]	16.3 ± 9.6 [11.6; 21.1]	16.1 ± 9.1 [12.7; 19.5]	0.317
Oxygen (y/n)	44/4	12/2	12/1	0.586

Data are presented as mean ± standard deviation [CI95%] or proportions.
*: significant difference between groups.
M: male; F: female; ICU: intensive care unit; y/n: yes/no; d: day.

Table 3
Comparison of the results from the telerehabilitation and control groups.

	Telerehabilitation (n = 14)	Control (n = 13)	p value
At discharge			
SpO2i (%)	95.1 ± 1.9 [94.2; 96.1]	94.8 ± 1.9 [93.8; 95.8]	0.655
HRi (bpm)	90.5 ± 17.3 [81.5; 99.6]	86.2 ± 15.3 [77.9; 94.5]	0.547
Dyspneai	0 (0–3)	2 (0–5)	0.836
STST (n)	17.6 ± 4.7 [15.1; 20.0]	13.6 ± 7.6 [9.5; 17.8]	0.123
SpO2f (%)	91.8 ± 3.3 [90.0; 93.5]	92.5 ± 1.7 [91.6; 93.4]	0.568
HRf (bpm)	110.5 ± 18.5 [100.8; 120.2]	102.0 ± 15.4 [93.6; 110.4]	0.260
Dyspneaf	5 (3–8)	5 (1–10)	0.966
Change between discharge and 3-month follow-up			
Delta HR (bpm)	42.6 ± 25.2 [29.4; 55.8]	23.1 ± 12.1 [16.5; 29.7]	0.036
STST change (n)	10 (5–19)	5 (-4–11)	0.004
Dyspnea change	2.5 (-2–7)	2 (0–6)	0.560

Data are presented as mean ± standard deviation or median (range).
SpO2: pulsed oxygen saturation, HR: heart rate; i: initial; f: final; STST: sit-to-stand test; bpm: beat by minute.

the assessment of the functional exercise capacity in these patients at discharge and after three months. The second part evaluated the feasibility, safety, and efficacy of a telerehabilitation program when immediately initiated at discharge in the particular conditions of a complete lockdown. We highlighted that the functional exercise capacity assessed by the STST was dramatically reduced at discharge. Moreover, its recovery was uncompleted after three months for all the patients. However, the patients who participated in the telerehabilitation program showed a better recovery.

This study highlights three key points of this new disease and the daily life conditions. First, the patients with severe COVID-19 presented a low functional exercise capacity at discharge, an observation in striking contrast with their almost complete recovery in terms of lung function or HCRT lesions based on expected normal values before the COVID-19. This recovery was similar to the data from the respiratory follow-up of a larger cohort of patients with severe COVID-19 [6]. This discrepancy between the functional exercise capacity limitation and the lung function or HRCT impairments was previously described. The functional exercise limitation was dramatically prevalent in all the patients as illustrated by several repetitions below the 50th percentile of predicted values. As it could be expected, the only observed predictor of this limitation at discharge was the length of stay in an intensive care unit as previously observed in other medical conditions [7]. Moreover, the length of stay reflects the severity of the disease for patients with COVID-19. However, such a reduced functional exercise capacity could be expected based on the knowledge from the others Coronavirus epidemies [8]. This functional limitation should be considered as severe regarding our results. Moreover, the number of repetitions during STST in our patients with COVID-19 was similar (n = 19) to a large cohort of patients with COPD (n = 374), which were noticeably slightly older (67 y.o.) [9]. That illustrates the immediate and important physical consequences of severe COVID-19. Even if we do not have access to the data regarding the physical level of the patients before the hospitalization, it can be expected to be within a normal range and cannot explain the measured functional limitation. We hypothesised that this physical limitation could contribute to the fatigue and dyspnea associated with the long-term follow-up of patients with COVID-19 [10,11].

Secondly, this functional exercise limitation persisted even if the cardio-respiratory recovery was achieved based on parameters after three months. Indeed, the SpO_2, dyspnea and lung function cannot predict this limitation because these parameters were normal or close to the normality at the time of the follow-up. Moreover, no correlation was observed with these outcomes. While the number of repetitions during STST at discharge increased after three months, it remains dramatically low with around 40% of the patients being under the 2.5th-percentile value. The exact mechanisms underlying this low functional exercise capacity should be specifically investigated in dedicated studies. Other concomitant recent studies found similar limitations and the "long COVID-19" term even appeared, partly due to this condition, fatigue and dyspnea. This term describes patients that report lasting effects of the infection or usual symptoms for far longer than which would be expected [12].

Thirdly, this study highlighted the feasibility, safety, and efficacy of a telerehabilitation program in the particular context of a complete lockdown. We expect that the pandemic of COVID-19 and the changes implied by the risk of spreading the virus and the lockdown will considerably modify the care system in the future. Indeed, although pulmonary rehabilitation is a evidenced-based treatment for many chronic respiratory diseases, it has been associated with barriers notably related to travel, transport and disability [13]. Moreover, at the time of the study, these programs were not accessible for the patients at discharge from hospital due to the sanitary restrictions. The telerehabilitation was previously investigated in COPD and other chronic infection such as HIV patients [14] and achieved similar clinical benefits than programs performed in hospital settings [15]. However, it remained unfrequently used before the pandemic. Quickly after the pandemic has been proclaimed, various online programs of physical activities have been developed for the entire population to fight against the sedentary lifestyle associated with the imposed restriction of movement. Telerehabilitation followed this movement. This study highlighted the feasibility of an adapted telerehabilitation even if the included patients presented very low functional exercise capacity and did not have specific equipment at home. No adverse events were reported, and all the participating patients attended and completed the program. Moreover, the effectiveness of such a program is suggested by our results. Indeed, the patients who followed this short and incomplete program of pulmonary rehabilitation at home recovered a better functional exercise capacity after three months than the other ones.

Some limitations related to this study have to be acknowledged. This study was performed at the peak of the first COVID-19 wave in Belgium. This context was unprecedented and explains the great number of unassessed patients caused by the exceptional pressure to discharge patients and thus to maximise free beds in hospital. For the same reason, it can hardly be transposed to previous or future situations. The almost complete lockdown associated with the period of inclusion and the risk perception of these patients have probably contributed to the lack of recovery as illustrated by the results of some studies about the lower physical activity level of some populations [16]. The influence of the lockdown on the functional exercise capacity should have to be considered as a factor related to extrinsic motivation but these conditions were similar for all the patients. This is even a strength of the study. Despite the lockdown, the population was encouraged to exercise non-intensively in outdoor public spaces in Belgium and a national survey including 15,737 people demonstrated that the level of physical activity was non-uniformly modified either by increasing or by decreasing the physical activity level [16]. Moreover, the intrinsic motivation certainly played a role in the recovery of the functional exercise capacity. As the patients participated on a voluntary basis to the telerehabilitation program, they could also be involved in other activities or healthy interventions that contributed to the better recovery. Even if the control group reported no participation to such official activities, personal participation to online activities cannot be verified. Similarly, COVID-19 has been also associated with psychosocial consequences that could be reduce in the patients who participated to the telerehabilitation program, and with comorbidities (many patients were overweighed) that can also have affected this recovery. This last point is strongly suggested by the high recovery of lung function and HRCT abnormalities. Moreover, the sample of patients did not include the most critical patients hospitalized during the first wave because these patients required a longer hospital stay in the intensive care unit. Indeed, these patients were still not discharged. It is because the period of recruitment soon after the beginning of the pandemic that was chosen to reduce the influence of the end of the lockdown restrictions. We are however unable to determine the influence of this parameter in our results.

Even if the conditions were unusual, we hypothesised that such telerehabilitation programs will be used more widely soon. They should be adapted to fit more closely with the international pulmonary rehabilitation guidelines [17] to further enhance our demonstrated benefits. Finally, some medical treatments could have influenced the functional exercise capacity, such as corticosteroids (concerning 36% of the patients from this cohort) which have a well-known detrimental effect on muscle function and homeostasis.

In conclusion, severe or critical patients hospitalized for COVID-19 have a low functional exercise capacity at discharge and the recovery after three months is poor, irrespectively of the results of lung function tests. More important, the feasibility and safety of a simple telerehabilitation program was verified in these patients when immediately initiated at discharge. This program was able to substantially improve the functional recovery after three months.

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CRediT authorship contribution statement

Ines Martin: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Visualization. **Fred Braem:** Investigation, Writing – review & editing. **Lia Baudet:** Investigation, Writing – review & editing. **William Poncin:** Methodology, Formal analysis, Investigation, Writing – review & editing. **Stéphane Fizaine:** Investigation, Writing – review & editing. **Frank Aboubakar:** Resources, Writing – review & editing. **Antoine Froidure:** Resources, Writing – review & editing. **Charles Pilette:** Resources, Writing – review & editing. **Giuseppe Liistro:** Resources, Writing – review & editing. **Julien De Greef:** Resources, Writing – review & editing. **Halil Yildiz:** Resources, Writing – review & editing. **Lucie Pothen:** Resources, Writing – review & editing. **Jean-Cyr Yombi:** Resources, Writing – review & editing. **Leïla Belkhir:** Resources, Writing – review & editing. **Gregory Reychler:** Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Visualization, Supervision.

Declaration of competing interest

None.

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