The Journal of Frailty & Aging
Volume 10, Number 3, 2021

BRIEF REPORTS

REHABILITATION IN ADULT POST-COVID-19 PATIENTS IN POST-ACUTE CARE WITH THERAPEUTIC EXERCISE

C. UDINA[1], J. ARS[1], A. MORANDI[1], J. VILARÓ[2], C. CÁCERES[1], M. INZITARI[1]

1. REFiT Barcelona research group, Parc Sanitari Pere Virgili and Vall d'Hebron Institut de Recerca (VHIR), Barcelona, Spain; 2. Blanquerna School of Health Sciences, Global Research on Wellbeing (GRoW), Universitat Ramon Llull. Barcelona, Spain.
Corresponding author: Cristina Udina, MD, Parc Sanitari Pere Virgili, C/ Esteve Terradas, 30, 08023 Barcelona, Spain, cudina@perevirgili.cat, ORCID ID: 0000-0002-0140-669X

Abstract: COVID-19 patients may experience disability related to Intensive Care Unit (ICU) admission or due to immobilization. We assessed pre-post impact on physical performance of multi-component therapeutic exercise for post-COVID-19 rehabilitation in a post-acute care facility. A 30-minute daily multicomponent therapeutic exercise intervention combined resistance, endurance and balance training. Outcomes: Short Physical Performance Battery; Barthel Index, ability to walk unassisted and single leg stance. Clinical, functional and cognitive variables were collected. We included 33 patients (66.2±12.8 years). All outcomes improved significantly in the global sample ($p<0.01$). Post-ICU patients, who were younger than No ICU ones, experienced greater improvement in SPPB (4.4±2.1 vs 2.5±1.7, $p<0.01$) and gait speed (0.4±0.2 vs 0.2±0.1 m/sec, $p<0.01$). In conclusion, adults surviving COVID-19 improved their functional status, including those who required ICU stay. Our results emphasize the need to establish innovative rehabilitative strategies to reduce the negative functional outcomes of COVID-19.

Key words: COVID-19, older adults, therapeutic exercise, rehabilitation, post-ICU rehabilitation.

J Frailty Aging 2021;10(3)297-300
Published online February 7, 2021, http://dx.doi.org/10.14283/jfa.2021.1

Introduction

COVID-19's impact increases with age (1). Besides mortality, patients may experience relevant disability, related to serious complications requiring Intensive Care Unit (ICU) admission, which has been linked to physical impairments (2). Less severe cases might experience functional decline due to immobilization due to the disease and isolation measures to prevent transmission. Early and effective rehabilitation interventions are urgent, despite healthcare systems may be overwhelmed and rehabilitation may be disrupted. Therapeutic exercise (TE) is a physical therapy technique used to improve or maintain a person's physical condition through resistance, endurance, flexibility and balance training. The intensity, volume, progression and type of exercise must be individualized based on the physical condition and tolerance during the execution of TE. Previous research shows the benefits of supervised TE in acutely ill patients to improve their physical condition and autonomy through exercise (3). During the early weeks of the pandemic our post-acute care facility had to adapt in order to provide care for COVID-19 patients (4). In addition to maintaining the usual physical therapy interventions for more impaired patients, we created an intensive rehabilitation pathway through TE to facilitate a quick recovery and faster discharge at home. Our aim is to describe the pre-post impact on physical performance of multi-component therapeutic exercise for post-COVID-19 rehabilitation.

Methods

We performed a cohort study of post-acute care patients that overcame COVID-19 and were included in a rehabilitation protocol based on multi-component therapeutic exercise. The inclusion criteria were: 1) ability to walk unassisted pre-COVID-19 (use of cane or walker was allowed); 2) able to stand after the resolution of acute COVID-19; 3) social situation allowed discharge in 10 days. We collected demographics, COVID-19 related variables, comorbidities (sum of hypertension, diabetes, arrhythmia, myocardial infarction, Chronic Obstructive Pulmonary Disease/Asthma, mild cognitive impairment, dementia, other neurodegenerative diseases, stroke, depression, osteoarthritis and low back pain) and prevalence of polypharmacy (5 or more drugs) at admission. Our comprehensive assessment included: pre-COVID functional status with the Barthel Index and Lawton Index and frailty status with the Clinical Frailty Scale (CFS); cognitive function at post-acute admission with the Montreal Cognitive Assessment (MoCA) for global cognition and the Symbol Digit Modalities Test (SDMT) for attention and processing speed. SDMT scores are age-adjusted (5), considering a score of 7 or higher as normal range. The Confusion Assessment Method (CAM) was used to screen for Delirium. These covariates were collected based on clinical and functional aspects that might impact physical function as well as the response to physical exercise. We assessed physical function at day 1 and 10 of the intervention. Those patients who were discharged before day 10 were evaluated at discharge. We performed the Short Physical Performance Battery (SPPB) as a

Received October 24, 2020
Accepted for publication December 28, 2020

Table 1
Baseline characteristics and functional outcomes, in the total sample and stratified by previous ICU admission

Variables	Total (n=33)		ICU (n=20)		Non-ICU (n=13)		p-value
Age, mean (SD)	66.2 (12.8)		58.2 (7.9)		78.4 (8.1)		<0.001
Women, N (%)	19 (57.6)		10 (50)		9 (69.2)		0.3
Comorbidities, mean (SD)	1.5 (1.6)		0.5 (0.8)		2.8 (1.8)		<0.001
Polypharmacy (≥5 drugs), n (%)	24 (72.7)		13 (65)		11 (84.6)		0.26
Pneumonia, n (%)	30 (90.9)		20 (100)		10 (77)		0.052
Pre-COVID-19 functional status							
Barthel Index (0-100), mean (SD)	98.5 (5.8)		100 (0.0)		96.1 (8.9)		0.28
Lawton Index (0-8), mean (SD)	6.7 (2.1)		7.8 (0.5)		4.9 (2.3)		<0.001
Frail (CFS category 4-9), n (%)	4 (12.1)		0 (0)		4 (30.8)		0.02
Cognitive function at study baseline (rehabilitation admission)							
MoCA (0-30), mean (SD)	22.6 (4.8)		22.9 (4.7)		21.6 (5.3)		0.59
SDMT (age-adjusted)	6.5 (2.9)		7 (2.7)		5.7 (3.3)		0.31
Pre-post comparison	**Baseline**	**Change ***	**Baseline**	**Change ***	**Baseline**	**Change ***	**p-value ‡**
Barthel index (0-100), mean (SD)	76.5 (17.4)	18.5 (12.9) †	80.5 (14.7)	18.2 (12.4) †	70.4 (19.9)	18.8 (14.01) †	0.95
SPPB total (0-12), mean (SD)	5.4 (2.7)	3.7 (2.1) †	5.5. (2.8)	4.4 (2.1) †	5.3 (2.6)	2.5 (1.7) †	0.009 †
SPPB balance (0-4), mean (SD)	2.8 (1.3)	0.8 (1.1) †	2.7 (1.3)	1.1 (1.2) †	3.1 (1.2)	0.4 (0.7)	0.068
SPPB gait speed, mean (SD), m/s	0.5 (0.2)	0.3 (0.19) †	0.5 (0.25)	0.4 (0.2) †	0.5 (0.21)	0.2 (0.1) †	0.006†
SPPB chair stand, mean (SD), s	35.4 (21.4)	- 14.1 (16.9) †	33.7 (21.1)	-15.3 (16.9) †	38.1 (22.3)	-12.2 (17.6) †	0.28
Single leg stance test, N (%)	3 (9.1)	10 (30.3) †	1 (5)	9 (45) †	2 (15.4)	1 (7.7)	
Unassisted gait (FAC 4-5), N (%)	19 (57.6)	14 (42.4) †	13 (65)	7 (35) †	6 (46.2)	7 (53,8) †	

Abbreviations: ICU: Intensive Care Unit. MoCA: Montreal Cognitive Assessment. CFS: Clinical Frailty Scale. SDMT: Symbol Digit Modalities Test. SPPB: Short Physical Performance Battery. FAC: Functional Ambulation Category. SDMT normal range ≥ 7. Legend: (*) Pre-post comparison within group with Wilcoxon rank test and McNemar test (significance at a p-level < 0.05 marked with †). (‡) Comparison of the mean change between the ICU and the non-ICU groups with Mann-Whitney U Test (significance at a p-level < 0.05 marked with †).

measure of gait performance (time to walk 4 meters), balance (stand for 10 seconds with feet side-by-side and in semi-tandem and tandem positions) and lower limb strength (time required to stand up and sit down 5 times from a chair without using the arms). Furthermore, we assessed independence for the basic activities of daily living with the Barthel Index, need of assistance to walk with the Functional Ambulation Category (FAC) (6) and the single leg stance test (7). We evaluated exercise capacity with the 6-minute walk test (6MWT) in a sub-sample (for logistical reasons).

The 30-minute 7 days/week multi-component therapeutic exercise intervention (summarized in Figure 1) was led by an expert physical therapist and combined: a) resistance training [1-2 sets with 8-10 repetitions each (intensity between 30-80% of the Repetition Maximum (8))]; b) endurance training (up to 15-minutes aerobic training with a cycle ergometer, steps or walking) and c) balance training (walking with obstacles, changing directions or on unstable surfaces). Additionally, recommendations were provided to decrease daily sedentary behavior. Each session was individualized to each patient's physical condition.

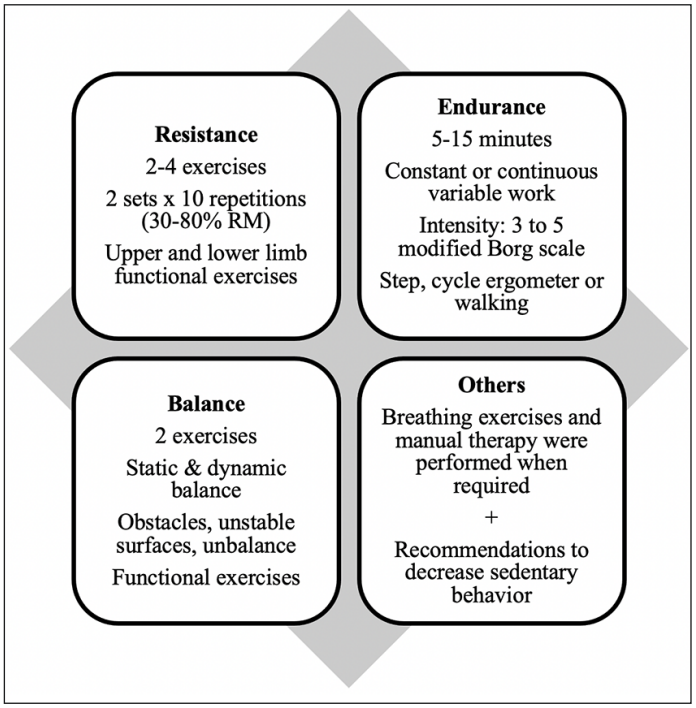
Outcome measures included: SPPB global score, gait speed (m/s), balance score and chair-stand time (seconds), Barthel Index score, ability to walk unassisted (FAC score 4 or higher) and maintain single leg stance for 10 seconds and distance walked during the 6MWT (meters). We used descriptive statistics with mean and Standard Deviation (SD) or frequencies as required. We assessed differences between the initial and final values in the outcome variables with Wilcoxon signed rank test and McNemar test for continuous and categorical variables, respectively. We calculated the mean pre-post change for each continuous outcome variable: Variable POST – VARIABLE PRE. We used Mann-Whitney U test to compare the mean change in the outcomes between patients treated or not in the ICU as well as to compare baseline characteristics in both groups. All statistical analysis was performed with statistical software: IBM SPSS Statistics for Windows, Version 21.0. (Armonk, NY: IBM Corp).

Results

We included 33 patients (66.2±12.8 years, 57.6% women), of whom 90.9% (n=30) presented with pneumonia and 60.6% (n=20) were admitted to the ICU, all (n=20) requiring mechanical ventilation, with a mean ICU stay of 10.3±9.9 days. The sample consisted of pre-COVID-19 well-functioning adults (Barthel Index 98.5±5.8 and Lawton Index 6.7±2.1) with low frailty (CFS score 2.5±1.3) and comorbidity (sum of

comorbidities 1.5±1.6) but high polypharmacy at admission (72.7% (n=24)). Post-ICU patients were younger, with lower comorbidity, better pre-COVID-19 functional status and lower frailty, compared to non-ICU patients (Table 1). Although none of the patients had delirium according to CAM scores at admission, post-COVID-19 cognitive function was mildly impaired in the whole cohort and within both groups. After the intervention (mean duration=8.2±1.7 days), all physical performance measures showed a statistically significant improvement when comparing the initial and final values in the global sample and among post-ICU patients, while non-ICU patients did not improve in balance-related variables. Furthermore, post-ICU patients experienced a greater improvement in SPPB and gait speed mean change compared to non-ICU (4.4±2.1 vs 2.5±1.7, $p<0.01$ and 0.4±0.2 vs 0.2±0.1, $p<0.01$, respectively). None of the patients died during the intervention and all were discharged home. In a subsample of 22 participants (61.9±12.1 years, 63.6% women, 81.8% admitted to the ICU and 95.5% with pneumonia), mean 6MWT walked distance improved from 158.7±154.1 to 346.3±111.5 m ($p<0.001$).

Figure 1
Scheme of the individualized multi-component therapeutic exercise intervention, combining 3 or more modalities daily



Abbreviation: RM: repetition maximum

Discussion

In summary, in our sample of post-COVID-19 adults and older adults, physical function improved after a relatively short therapeutic exercise intervention. This improvement seems clinically meaningful, according to previous studies (9). Compared to the non-ICU group, post-ICU patients showed higher improvements, possibly due to their younger age and better functional, clinical and frailty status pre-COVID-19. Noteworthy, our sample showed mild cognitive impairment post-COVID-19 according to a brief cognitive assessment, which we might speculate as non-preexisting, especially in the ICU group, due to their relatively young age and preserved functional status. This cognitive dysfunction could be related to delirium during COVID-19's acute phase or even be a neurological feature of COVID-19's infection (10). Further research is needed to support these findings and to study long-term effects of COVID-19 on cognition.

Evidence about post-COVID-19 rehabilitation is still scarce, although there is a growing body of literature highlighting the need of rehabilitation strategies. To our knowledge, this is the first study on the effects of intensive rehabilitation through a structured therapeutic exercise intervention of post-COVID-19 patients in post-acute care, a setting able to combine the acute management of these patients with rehabilitative interventions (4). Improving physical function in post-ICU patients is crucial as previous research has shown long-term negative outcomes (11). However, the type of exercise intervention previously reported in post-ICU rehabilitation so far seems not comparable to our intensive and multimodal protocol (12). Previous research shows the efficacy of similar therapeutic exercise strategies tested in acute geriatric units, demonstrating functional benefits of short-term supervised exercise during acute medical illnesses: the reported magnitude of change of 2.4 points in the total SPPB (13) is similar to the change in our non-ICU group, which is indeed older and with a slightly pre-COVID-19 worse clinical and functional profile, compared to the ICU group. According to studies performed with Acute Respiratory Distress Syndrome survivors, the improvement in exercise capacity experienced in the small subsample seems also clinically relevant (14). The cognitive impairment detected among the post-ICU patients is also in line with the findings reported in Acute Respiratory Distress Syndrome survivors (15), however in our opinion the impairment detected in non-ICU patients, deserves further research to shed some light into the potential neurological manifestations of COVID-19.

Main limitations of the study are the small sample size and the absence of a control group to assess the effect of the intervention. Among the strengths, we enrolled adults and older adults post-COVID-19 with different acute care pathways during the acute phase, with a comprehensive assessment of clinical and functional variables.

In conclusion, adults and older adults surviving COVID-19 seem to improve their functional status, despite previous admission to ICU, through a short, individualized, multi-component therapeutic exercise intervention. Further research with controlled, larger samples and longer treatment periods might help elucidate the role of rehabilitation interventions in the reduction of negative functional outcomes of COVID-19,

hence mitigating the potential increase in COVID-19-related disability and health care costs.

Funding: This research did not receive any funding from agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interests: The authors (CU, JA, AM, JV, CC) state that they have no financial nor non-financial conflict of interests. MI received from Nestlé a fee for scientific advice, not related to the work or the topic of the current manuscript.

Ethics approval: The study procedures were approved by the institutional ethics committee. The authors declare that all study's procedures are according to the 1964 Helsinki Declaration and that personal participant's information was treated to ensure complete privacy. Furthermore, all procedures performed during the study were in the context of usual care of patients admitted to post-acute care.

References

1. Borobia A, Carcas A, Arnalich F, et al. A Cohort of Patients with COVID-19 in a Major Teaching Hospital in Europe. J Clin Med. 2020;9(6):1733. doi:10.3390/jcm9061733
2. Ohtake PJ, Lee AC, Scott JC, et al. Physical Impairments Associated With Post–Intensive Care Syndrome: Systematic Review Based on the World Health Organization's International Classification of Functioning, Disability and Health Framework. Phys Ther. 2018;98(8):631-645. doi:10.1093/ptj/pzy059
3. Valenzuela PL, Morales JS, Castillo-García A, et al. Effects of exercise interventions on the functional status of acutely hospitalised older adults: A systematic review and meta-analysis. Ageing Res Rev. 2020;61(xxxx):101076. doi:10.1016/j.arr.2020.101076
4. Inzitari M, Udina C, Len O, et al. How a Barcelona post-acute facility became a referral center for comprehensive management of subacute patients with COVID-19. J Am Med Dir Assoc. June 2020. doi:10.1016/j.jamda.2020.06.015
5. Peña-Casanova J, Quiñones-Úbeda S, Quintana-Aparicio M, et al. Spanish multicenter normative studies (NEURONORMA project): Norms for verbal Span, visuospatial Span, letter and number sequencing, trail making test, and symbol digit modalities test. Arch Clin Neuropsychol. 2009;24(4):321-341. doi:10.1093/arclin/acp038
6. Martin BJ, Cameron M. Evaluation of walking speed and functional ambulation categories in geriatric day hospital patients. Clin Rehabil. 1996;10(1):44-46. doi:10.1177/026921559601000109
7. Bohannon RW, Tudini F. Unipedal balance test for older adults: a systematic review and meta-analysis of studies providing normative data. Physiother (United Kingdom). 2018;104(4):376-382. doi:10.1016/j.physio.2018.04.001
8. Serra-Rexach JA, Bustamante-Ara N, Hierro Villarán M, et al. Short-term, light- to moderate-intensity exercise training improves leg muscle strength in the oldest old: A randomized controlled trial. J Am Geriatr Soc. 2011;59(4):594-602. doi:10.1111/j.1532-5415.2011.03356.x
9. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc. 2006;54(5):743-749. doi:10.1111/j.1532-5415.2006.00701.x
10. Helms J, Kremer S, Merdji H, et al. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med. 2020;382(23):2268-2270. doi:10.1056/nejmc2008597
11. Herridge MS, Tansey CM, Matté A, et al. Functional Disability 5 Years after Acute Respiratory Distress Syndrome. N Engl J Med. 2011;364(14):1293-1304. doi:10.1056/NEJMoa1011802
12. Connolly B, Denehy L, Brett S, Elliott D, Hart N. Exercise rehabilitation following hospital discharge in survivors of critical illness: an integrative review. Crit Care. 2012;16(3):226. doi:10.1186/CC11219
13. Martínez-Velilla N, Casas-Herrero A, Zambom-Ferraresi F, et al. Effect of Exercise Intervention on Functional Decline in Very Elderly Patients During Acute Hospitalization. JAMA Intern Med. 2019;179(1):28. doi:10.1001/jamainternmed.2018.4869
14. Chan KS, Pfoh ER, Denehy L, et al. Construct validity and minimal important diff erence of 6-minute walk distance in survivors of acute respiratory failure. Chest. 2015;147(5):1316-1326. doi:10.1378/chest.14-1808
15. Hopkins RO, Weaver LK, Collingridge D, Parkinson RB, Chan KJ, Orme JF. Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. Am J Respir Crit Care Med. 2005;171(4):340-347. doi:10.1164/rccm.200406-763OC