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 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.
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 (significance at a p-level < 0.05 marked with †). 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

### 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 (62.9)       | 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 †).
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

| Resistance | Endurance |
|------------|-----------|
| 2-4 exercises | 5-15 minutes |
| 2 sets x 10 repetitions (30-80% RM) | Constant or continuous variable work |
| Upper and lower limb functional exercises | Intensity: 3 to 5 modified Borg scale |
| | Step, cycle ergometer or walking |

| Balance | Others |
|---------|--------|
| 2 exercises | Breathing exercises and manual therapy were performed when required + |
| Static & dynamic balance | Recommendations to decrease sedentary behavior |
| Obstacles, unstable surfaces, unbalance Functional exercises | |

**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.

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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.

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