Balance performance in patients with post-acute COVID-19 compared to patients with an acute exacerbation of chronic obstructive pulmonary disease and healthy subjects

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COVID-19 leaves important sequelae in patients, not only in those who had the experience of a critical illness but also in patients with severe form. Understanding the impairments allows us to target rehabilitation to patients' real needs; balance impairments are an assumed sequela of COVID-19, but no study has specifically evaluated balance performance in these patients. Their performance was compared to that of patients with a pulmonary disease that leads to systemic diseases, such as patients with an acute exacerbation of chronic obstructive pulmonary disease (PwAECOPD), and of healthy subjects. A total of 75 subjects were assessed: 25 patients with COVID-19 (PwCOVID) with a severe form in the acute phase, 25 PwAECOPD and 25 healthy subjects sex- and age-matched. A stabilometric platform was used to evaluate static balance, both with eyes open and closed, while the dynamic balance was assessed with the Mini-BESTest and the Timed Up and Go test. When compared to healthy subjects, results showed that PwCOVID had worse performance in both static ($P<0.005$) and dynamic ($P<0.0001$) balance, with a large effect size in all measures (>0.8). Moreover, PwCOVID showed similar results to those of PwAECOPD. In conclusion, PwCOVID showed a balance deficit in both dynamic and static conditions. Therefore, as for PwAECOPD, they should require not only respiratory rehabilitation but also balance and mobility physiotherapy to prevent today's PwCOVID from becoming tomorrow's fallers. *International Journal of Rehabilitation Research* 45: 47–52 Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

On 11 March 2020 the WHO declared severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) a pandemic disease, named COVID-19 [1]. It has put enormous pressure on healthcare systems worldwide with an unprecedented demand on rehabilitation care for postinfection recovery [2]. Even if the majority (80%) of people infected with COVID-19 presents mild-to-moderate disease characterized by fever, persistent cough and dyspnea as most commonly reported symptoms [3,4], a considerable number of subjects, generally older than 65 years and with comorbidities require hospitalization and have very serious sequelae (about 20%) [5]. Rehabilitation providers are an important link in the continuum of care, facilitating the early well-tolerated discharge to home. In the post-acute phase, it is recommended a rehabilitation program which addresses not only the respiratory dysfunctions but also the motor impairments [2]. In fact, Belli *et al*. [6] reported low physical functioning and impaired performance in activities daily living (ADL) in patients with COVID-19 (PwCOVID), similar to the level found in patients with acute exacerbations of chronic obstructive pulmonary disease (PwAECOPD) who are weakened, have low physical functioning, reduced lower-limb muscle strength, gait deficits and balance impairments [7]. Though there are no specific studies assessing balance impairments in PwCOVID, several authors have supposed postural instability in these patients, therefore suggesting the need for balance rehabilitation [8].

In this study, we assessed balance impairments in PwCOVID discharged from inpatient rehabilitation and compared findings with data from PwAECOPD and healthy subjects, to better understand the issues to be addressed in the rehabilitation process and the consequences for patients with the post-COVID syndrome.

Methods

Design and participants

All patients admitted to the COVID-19 Rehabilitation Unit of Istituti Clinici Scientifici Maugeri (Gattico-Veruno, Piedmont, Italy) between November and December 2020 with a diagnosis of severe COVID-19 in the acute phase [1] were screened for inclusion. Indeed, during the pandemic, the institute was reorganized to host PwCOVID with confirmed infection; in the COVID-19

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Rehabilitation Unit patients underwent specific rehabilitation and were discharged home upon obtaining two consecutive negative swabs.

Inclusion criteria at baseline were: (1) a confirmed infection of SARS-CoV-2 and a diagnosis of severe COVID-19 in the acute phase, (2) age >18 years, (3) capacity to understand simple verbal commands, (4) ability to walk independently, (5) in stable clinical conditions, (6) signature on a general consent form. We excluded patients with other neurologic or respiratory diseases in addition to COVID-19 and not in stable clinical conditions. Moreover, patients who needed, for reasons of clinical complications, a long stay (i.e. more than 30 days, as per Piedmont regulations), were considered particularly frail and not recruited for these assessments.

From the 62 patients screened for eligibility, we recruited 25 PwCOVID (40%); 21% of screened patients were excluded because of assistance needed in walking, 14% for clinical instability, 13% for other neurological or respiratory diseases, 7% for failure to understand the tests and 5% for orthopedic problems that affect gait.

We recorded the clinical characteristics of PwCOVID, as shown in Table 1. Moreover, a physician administered the Cumulative Illness Rating Scale (CIRS: 0, none; 4, extremely severe; total score range 0–56) as an indicator of health status; higher total scores reflect greater disease burden [9]. The recruited patients were assessed ~1 day before discharge from rehabilitation by a physiotherapist with several years of experience in balance and gait assessments.

To compare balance performance, we extracted preexisting data of 25 age- and sex-matched PwAECOPD and 25 healthy subjects from the database of the Posture and Movement Laboratory. PwAECOPD had been hospitalized in the previous 2 years for about 1 month for acute exacerbation of COPD and were assessed ~1 day before discharge from rehabilitation. To complete the tests, inclusion criteria were similar: (1) age >18 years, (2) capacity to understand simple commands, (3) ability to walk independently, (4) signature on a general consent form. In the same way, patients with other neurological or respiratory disease in addition to AECOPD and a nonstable clinical condition were excluded from the assessment. Orthopedic problems that affect gait were also considered as an exclusion criterion. PwAECOPD were graded by Global Initiative for Chronic Obstructive Lung Disease: $n=3$ were at stage A, $n=8$ were at stage B, $n=6$ were at stage C and $n=8$ were at stage D. Nine PwAECOPD were on long-term oxygen therapy: 1 l/min ($n=2$), 1.5 l/min ($n=1$), 3 l/min ($n=4$) and 4 l/min ($n=2$). As with PwCOVID, assessors had recorded the clinical characteristics and CIRS of PwAECOPD. To match the two patient groups, the CIRS total score was used to extract PwAECOPD from the laboratory's database.

Finally, the third group was represented by the healthy subjects. Over the years, they have been generally recruited from among patients' relatives to create an internal database with nonpathologic data. For inclusion and exclusion criteria, see the aforementioned for PwAECOPD population.

Table 1 presents the characteristics of the overall sample. Participants signed a general consent allowing future use of their records for medical research and all evaluations were approved by the Institutional Review Board (approval number #p128).

Assessments

We assessed static balance on a stabilometric platform, with eyes open and eyes closed. Body sway was recorded by means of a 3-strain gauge force platform (QFP, Medicapteurs, France). Patients stood barefoot with eyes open facing a target placed at 50 cm distance, and with eyes closed. The feet were placed at an angle of ±15° from the sagittal plane and the distance between the heels was 2 cm. Two trials for each visual condition were performed, each lasting 51 s. The forces acting on the platform were sampled at 5 Hz [10]. A software program (WinPosture 2000) calculated the sway area as the 95% confidence ellipse of the dispersion of center of pressure (CoP) positions (mm^2), and the sway path as the distance covered by the moving instantaneous CoP (mm) [7]. For each subject, the values of these variables were obtained by averaging the data of the two trials performed for each visual condition. A previous study found reliability, expressed by interclass correlation coefficient (ICC), of

Table 1 Comparison between groups' characteristics

	PwCOVID (n=25)	PwAECOPD (n=25)	Healthy subjects (n=25)	P value
	mean (SD)	mean (SD)	mean (SD)	
Sex, female (%)	7 (28%)	8 (32%)	11 (44%)	0.47
Age (years)	68.3 (9.4)	70.4 (8.3)	70.0 (5.8)	0.63
Body weight (kg)	75.4 (10.8)	67.2 (13.7)	70.3 (14.9)	0.09
Height (m)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	0.08
BMI (kg/m^2)	25.8 (3.2)	24.2 (5.1)	26.3 (4.5)	0.18
MMSE score	27.3 (1.8)	27.4 (1.5)	28.1 (1.4)	0.62
CIRS total score	22.8 (3.3)	22.2 (3.5)		0.53
Oxygen therapy (n)	7	9		0.54

BMI, body mass index; CIRS, cumulative illness rating scale; MMSE, Mini-Mental State Examination; PwAECOPD, patients with acute exacerbation of chronic obstructive pulmonary disease; PwCOVID, patients with COVID-19.

CoP-based variables acquired with QFP ranging from 0.76 to 0.94 in the eyes open condition and from 0.92 to 0.97 in eyes closed condition [11].

An expert physiotherapist of the Laboratory of Posture and Movement of the Istituti Clinici Scientifici Maugeri, who had previously assessed the healthy subjects and the PwAECOPD sample, carried out all the evaluations.

We administered the Mini Balance Evaluation Systems Test (Mini-BESTest): each item is scored from 0 (unable to perform) to 2 (normal performance) with a total score range 0–28. It is a scale assessing dynamic balance, presenting face validity [12] and is used also in patients with COPD [13].

Moreover, subjects performed the Timed Up and Go (TUG) test, that is the shortest, simplest clinical balance test with demonstrated reliability for predicting risk of falls in PwAECOPD [14]. Subjects performed one practice trial to familiarize themselves with the procedure and then three test trials. We recorded with a stopwatch the time interval (s) to perform each trial and averaged the values of the three trials performed. All subjects performed the test without the use of walking aids.

Statistical analysis

Results are reported in the text and tables as mean ± SD and in figures as mean ± standard error (SE). A test for normality (Shapiro–Wilk) was performed in all variables. To detect differences between clinical characteristics of the three groups, χ^2 test was performed for the percentage of females (contingency table 3 × 2) and the number of subjects in oxygen therapy (contingency table 2 × 2); one-way analysis of variance (ANOVA) for age, height, body weight and BMI, and Mann–Whitney U-test for Mini-Mental State Examination and CIRS total score.

In the case of stabilometric variables (sway area and sway path), a two-way ANOVA between groups (PwCOVID, PwAECOPD and healthy subjects) as independent factors and within repeated measures (eyes open and eyes closed) was conducted. When ANOVA gave a significant result ($P < 0.05$), the post-hoc Tukey test was conducted and the Bonferroni correction was applied.

In the case of ordinal variables (Mini-BESTest and TUG test), the Kruskal–Wallis test was conducted to compare scores across groups (PwCOVID, PwAECOPD and healthy subjects). When the test was significant, the post-hoc Mann–Whitney test with the Bonferroni correction was applied.

To investigate the clinical meaning of differences between patients' groups and healthy subjects, Cohen's 'd' effect size was calculated: values >0.2 represent a small effect size, around 0.5 a moderate and ≥0.8 a large effect size [15]. All statistical analysis was performed using Statistica (StatSoft Inc., Tulsa, OK, USA).

Power analysis

In our study, a large difference between healthy subjects and patients (PwCOVID and PwAECOPD) was found in dynamic balance performance (TUG test and Mini-BESTest) and in stabilometric variables (sway area and sway path) during eyes open condition. Hence, a retrospective power calculation was conducted, which showed that a minimum sample of 18 subjects per group would have 80% power to detect a large difference (effect size 'd' larger than 0.4) between patients and healthy subjects with an alpha set at 0.05 in dynamic balance performance (TUG test and Mini-BESTest). For stabilometric variables in eyes open condition, a sample of 25 subjects per group would have 80% power to detect a difference of 0.37 of effect size 'd' between patients and healthy subjects with an alpha set at 0.05. On the contrary, with respect to the previous measures, the stabilometric variables (sway area and sway path) in eyes closed condition showed only a moderate to small effect size in the comparison of healthy subjects with PwAECOPD. Therefore, for future studies assessing differences between patients and healthy subjects in the stabilometric variables in eyes closed condition, more than 90 subjects per group should be collected.

Results

The 25 PwCOVID, with real-time reverse transcription PCR-confirmed SARS-CoV-2 infection, had a length of stay of 12.5 (8.1) days in the acute care; 5 had unilateral lung pneumonia, 20 bilateral lung involvement. Continuous Positive Airway Pressure was required in 9 PwCOVID out of 25, while 4 required a Venturi Mask and 5 a nasal cannula. Patients were home-discharged after obtaining two consecutive negative swabs, with a mean stay in the rehabilitation of 29.9 (9.3) days.

The mean Mini-BESTest score was significantly different between groups (Kruskal–Wallis ANOVA ($P < 0.0001$)); at post-hoc analysis, healthy subjects scored higher than PwCOVID ($P < 0.0001$) and PwAECOPD ($P = 0.011$). As reported in Table 2, the difference in score of the Mini-BESTest between patients and healthy subjects was large, with an effect size exceeding 0.8 for both groups of patients.

Kruskal–Wallis ANOVA showed a significant difference in the time taken to perform the TUG test between groups ($P < 0.0001$); at post-hoc, PwCOVID and PwAECOPD did not differ significantly ($P = 0.274$), while healthy subjects performed better than both PwCOVID ($P < 0.0001$) and PwAECOPD ($P = 0.008$). As for the Mini-BESTest, also in the TUG test the effect size of the differences between patients and healthy subjects was larger than 0.8 (Table 2).

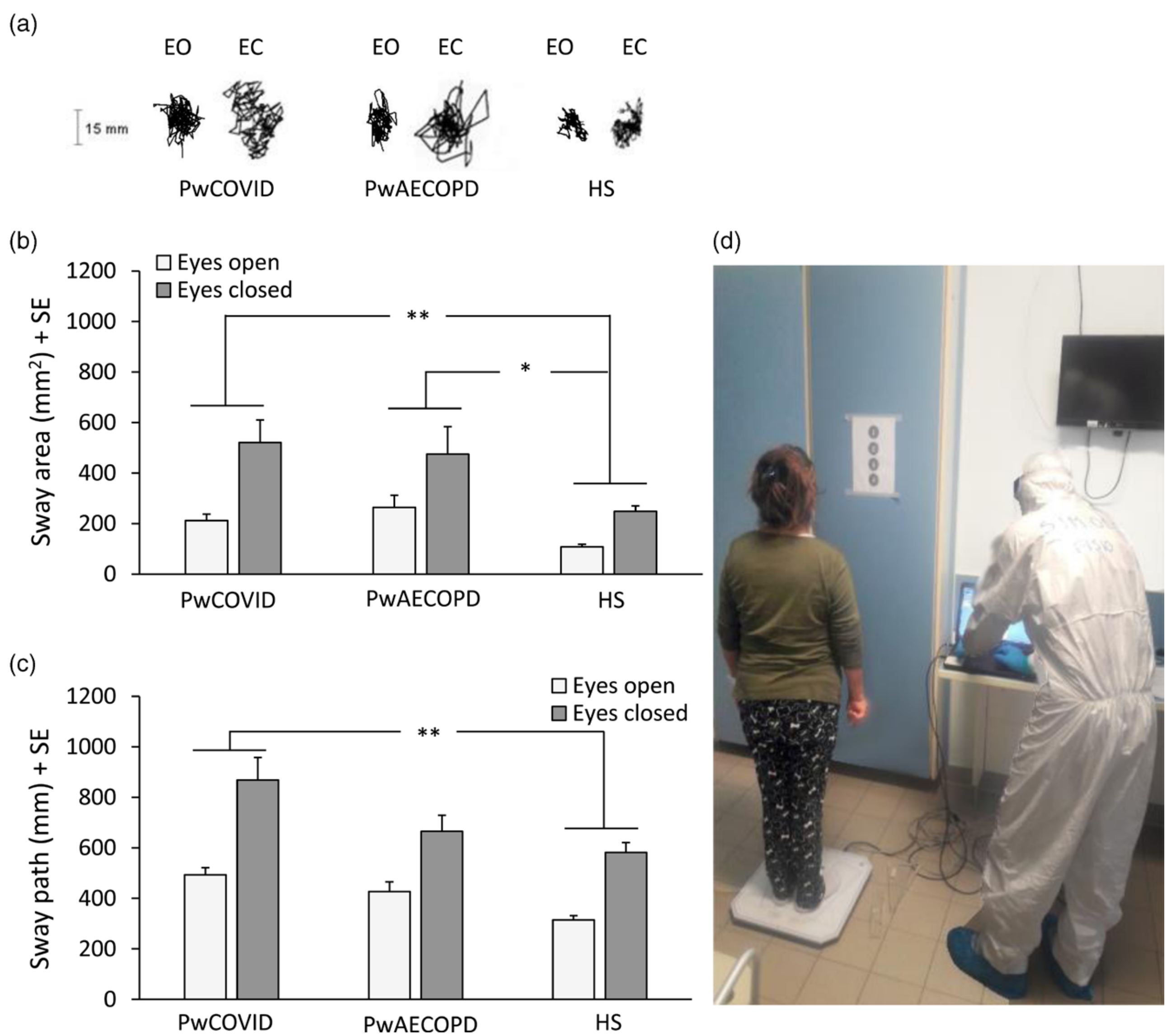
In static balance (Fig. 1), sway area was much larger in PwCOVID and PwAECOPD than in healthy subjects ($P = 0.003$ and $P = 0.009$, respectively). ANOVA showed

Table 2 **Comparison between groups' balance assessments**

	PwCOVID (*n*=25)	PwAECOPD (*n*=25)	Healthy subjects (*n*=25)	PwCOVID vs healthy subjects		PwAECOPD vs healthy subjects		PwCOVID vs PwAECOPD	
	mean (SD)	mean (SD)	mean (SD)	Effect size	*P* value	Effect size	*P* value	Effect size	*P* value
Mini-BESTest (tot. score)	20.3 (5.5)	22.2 (4.4)	25.3 (2.2)	1.18	<0.0001	0.87	0.001	0.37	0.198
TUG test (s)	10.3 (2.4)	9.3 (2.2)	7.8 (1.0)	1.35	<0.0001	0.90	0.003	0.44	0.136
Sway area eyes open (mm^2)	211.7 (128.1)	264.6 (230.3)	107.6 (53.3)	1.06	<0.0001	0.95	<0.0001	0.23	0.363
Sway path eyes open (mm)	493.5 (140.7)	427.5 (188.0)	314.6 (83.3)	1.55	<0.0001	0.77	0.009	0.40	0.237
Sway area eyes closed (mm^2)	521.4 (442.1)	474.5 (546.1)	248.1 (113.1)	0.85	<0.0001	0.57	0.003	0.09	0.761
Sway path eyes closed (mm)	868.4 (445.9)	665.2 (318.8)	581.9 (198.4)	0.83	0.001	0.31	0.295	0.52	0.071

PwAECOPD, patients with acute exacerbation of chronic obstructive pulmonary disease; PwCOVID, patients with COVID-19; TUG test, Timed Up and Go test.

Fig. 1



(a) Inset at the top shows an example of a stabilometry recording of center of foot pressure in a representative PwCOVID, PwAECOPD and HS, during quiet stance with EO and EC. (b) The histogram show the sway area of the center of pressure for PwCOVID, PwAECOPD and HS, during quiet stance with EO and EC. (c) The histograms show the sway path of the center of pressure for PwCOVID, PwAECOPD and HS, during quiet stance with EO and EC. (d) Stabilometric assessment was performed by a physiotherapist with a stabilometric platform (Medicapteurs, France), in a room of the COVID-19 Rehabilitation Unit specifically equipped as a Posture Laboratory. Error bars represent the respective standard error, SE. EO, eyes open; EC, eyes closed; HS, healthy subjects; PwAECOPD, patients with acute exacerbation of chronic obstructive pulmonary disease; PwCOVID, patients with COVID-19. *, $P<0.05$; **, $P<0.005$.

an effect of group ($F=5.30$; df = 1.72; $P=0.005$) and vision ($F=40.20$; df = 1.72; $P<0.0001$). No interaction was found between the group and vision. Sway path was larger in PwCOVID than healthy subjects ($P=0.001$). ANOVA showed an effect of group ($F=6.87$; df = 1.72; $P=0.002$) and vision ($F=93.14$; df = 1,72; $P<0.0001$), but there was no interaction. PwCOVID showed a large effect size compared to healthy subjects in all stabilometric measures considered, with values of effect size ranging from 0.83 to 1.55, as detailed in Table 2. Conversely, PwAECOPD showed a large effect size compared to healthy subjects only in sway area in the eyes open condition. The effect size of all other three stabilometric measures ranged from small to moderate.

Discussion

COVID-19 has a strong impact on patients' health. The number of post-COVID-19 patients requiring rehabilitation is likely to outnumber the regular capacity of specialized pulmonary rehabilitation clinics [6]. It is therefore clear that a broad-spectrum rehabilitation program is needed, equipped for patients returning home after hospitalization.

Several studies underline the importance of a global rehabilitation program in PwCOVID. In fact, despite the low average age and the disappearance of respiratory symptoms, discharged patients show significant deficits in ADLs [6]. Patients with the critical disease have major long-term sequelae labeled 'post-ICU syndrome', resulting in numerous physical impairments, for example balance problems and muscular weakness [16]. PwCOVID recruited in this study did not have a post-ICU syndrome, having a severe disease in the acute phase and not a critical disease (i.e. acute respiratory distress syndrome, sepsis and multi-organ failure) requiring intubation. Nevertheless, our patients, who were community dwelling before COVID-19 without severe comorbidities and who received ~1 month of specialized rehabilitation, showed an impaired balance performance more than 40 days after COVID-19 onset.

Compared with healthy subjects, PwCOVID showed poor dynamic balance and increased sway oscillation during quite stance. Indeed, the Mini-BESTest score was below the cutoff of 23, which identifies subjects with severe balance impairments [17]; similarly, the time necessary for performing the TUG test was higher than the cutoff of 8 s found for community-dwelling elderly (60–69 years) [18]. Both these results suggest an increased risk of falls for PwCOVID. The magnitude of the differences, quantified with the effect size between PwCOVID and healthy subjects for both the tests and the stabilometric measures, was greater than the value of 0.8, corresponding to a relevant clinical difference. Similar behavior was observed in the comparison of PwAECOPD with healthy subjects, with the exception of the sway path at eyes closed. Interestingly, while it is well known that people with the chronic obstructive pulmonary disease have deficits in balance not explained by the age-related processes alone [19], this is the first study which quantify the impairments of PwCOVID in both static and dynamic balance. Our findings highlight that these two diseases involve similar balance impairments, though underlying mechanisms for reduced postural control remain unclear. Therefore, we could hypothesize that balance impairment may be added to the other characteristics in common between PwCOVID and PwAECOPD, that is respiratory symptoms as cough and breathlessness [20].

Consequently, because American Thoracic Society/European Respiratory Society statement recommends to include balance as one of the outcome assessments in pulmonary rehabilitation [19] and specific component of balance training are effective on balance of PwAECOPD [7], we would recommend it also for PwCOVID to prevent today's PwCOVID from becoming tomorrow's fallers.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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