Breathing Exercises versus Strength Exercises through Telerehabilitation in COVID-19 Patients in the Acute Phase: Randomized Controlled Trial

Introduction

After the first reported case of coronavirus disease 2019 (COVID-19), a global pandemic was declared. It was spread exponentially worldwide,[1] a severe and acute respiratory coronavirus syndrome (SARS-CoV-2), [1] provoking different clinical pictures in infected patients [2,3] and leading governments to implement isolation and quarantine measurements[4].

In this situation, home isolation could reduce physical activity and, therefore, notable deconditioning[5], in addition to changes in metabolic and immune function, which have been related to the risk of worsening in the clinical picture of COVID-19 patients[6,7]. Besides, patients with COVID-19 may develop different sequelae, such as lung injury, among others[8].

In that sense, exercise seems to be an excellent therapeutic strategy to face these problems. It has been demonstrated that exercise can improve immune function[9,10], and increasing aerobic capacity may have a preventive and curable role against respiratory infections and disorders[11,12]. Indeed, physical therapy has been suggested to improve respiratory function in elderly patients with COVID-19[13] and has also been recommended to manage critically ill patients with COVID-19[14]. There is evidence on the efficacy of domiciliary exercise-based interventions applied in patients with respiratory disorders [15] and in other health disorders [16]. For this reason, we hypothesize about applying for a telerehabilitation physical activity program to reduce the rate aggravation and hospital admissions for confined patients [17]. Therefore, we conducted a randomized controlled

trial to compare the effectiveness of two different exercise-based programs in COVID-19 versus control.

METHODS

A randomized, controlled, parallel, double-blinded, three-arm clinical trial was conducted in Spain from September 2020 to January 2021. The protocol version for this study was already published[17]. The trial is registered in the Brazilian Clinical Trial Register with the number RBR-6m69fc. The study was approved by the ethics committee of University Hospitals Virgen Macarena-Virgen del Rocio and also complied with the Helsinki Ethical Principles for Medical Research Involving Human Patients and its subsequent modifications. University of Seville, Spain, was responsible for the integrity and conduct of the study.

We have made some minor changes concerning the initially published protocol [17.] The reasons that have motivated these changes are related to the lack of resources and the social confinement of the Spanish population during the pandemic. Initially, our intervention was planned for 21 days, but later, we reduced it to 14 days to adjust it to the official quarantine period. A sham intervention was not carried out in the CG, as it could be considered inappropriate and associated with psychological effects. Finally, we decided to use a control group without intervention. To avoid ethical conflicts, all patients in the control group received the treatment after completing the intervention phase of the study. The variables FEV1 and PEF could not finally be evaluated due to a lack of economic resources and multiple logistical difficulties during social confinement.

Participants were recruited through social media (WhatsApp, Facebook, Instagram, Twitter, LinkedIn), radio programs, and newspapers. A general message about the possibility of participating in a physiotherapy study was distributed; all those interested were advised later in greater detail. The recruitment period was four months, and the initial screening was carried out by telephone. In terms of privacy, before being enrolled in the study, the patient signed the informed consent on the website www.fisiosurid.com/covid19/.

Eligible patients between 18 and 75 years old were positive diagnosed cases of COVID-19 through PCR (polymerase chain reaction) test or Antigen test by the epidemiology services and were at home confinement. All patients had to be in the acute phase of the disease and with no more than one week of evolution from the onset of the first symptom. It was not attended to the day that the test was positive due to the possible delay in the realization and analysis. Although it was initially planned to analyse the measurements on day 7 of the treatment period in all study groups, before the study, we observed significant difficulties due to great losses to follow-up and reduced adherence to treatment, so these measurements were not considered. Finally, we focused on evaluations on the baseline (day 1) and 14 days after the intervention (day 14), keeping a daily communication with patients by WhatsApp message, as a reminder (day 1 to 14), during the treatment period as an adherence control procedure.

The exclusion criteria were the following: patients with chronic lung conditions, chronic kidney disease, chronic neurological disorders, chronic mental and/or psychological or/and hypertension, and cardiovascular conditions without medical treatment if they were affected by grade III osteoporosis, acute phase of rheumatologic disorders, and acute phase of disc abnormalities. We also excluded those patients who suffered a respiratory

disease or musculoskeletal condition in the last 12 months, not fully recovered, and showed signs of serious illnesses or red flags (night pain, severe muscle spasm, loss of involuntary weight, symptom mismatch). Finally, those patients classified as severe cases based on the Spanish Society of Family and Community Medicine (SEMFYC)[18] were excluded. Therefore, our study only included patients diagnosed with COVID-19 who met the selection criteria.

Patients were randomized using balanced block randomization. We used a free software tool to randomize the study groups (http://www.randomized.org/), considering blocks of six elements according to the initials of the study groups (e.g., BSCCSB). The randomization sequence was obtained before starting the baseline evaluations. This randomization technique is advantageous when recruitment is slow, especially with small samples. There is a possibility that the trial will be interrupted prematurely for reasons of efficacy or safety.

The randomization sequence was obtained and guarded by the principal investigator and an external auditor exclusively. Patients and assessors were unaware of this randomization sequence and never had access to it. The sequence was hidden and guarded to guarantee correct randomization with security. The evaluators were unaware of patients' randomized distribution, so they were blinded during the entire process. Participants and therapists were not masked to treatment due to the nature of the interventions. Still, the assessors and patients were unaware of the allocation group, so the study design was double-blinded.

Participants were assessed the days 1 and 14 through a call by a study team member, who asked for possible adverse events. This follow-up was performed through a checklist translated and adapted from "Criteria for clinical evaluation during telephone follow-up

of home care", published by SEMYFC[18]. The data were collected by researchers assigned to our research group, who were previously instructed on all the details of the procedures they had to perform. All outcomes were recorded using WhatsApp or by email on days 1 and 14. Subjects and evaluators agreed on an appointment, and the evaluation was conducted through a videoconference to complete the assessment, with the following outcome measures.:

A. Visual Analog Scale Fatigue. This 0-10 self-reported scale is a valid and reliable instrument for the quantitative assessment of fatigue[19]. Minimal clinically significant differences are not available for patients with respiratory pathologies for VASF. A higher score indicated a worse score.

B. Six-Minute Walk Test. The patient's Smartphone recorded the number of steps through the App "StepsApp". The patients performed the test, wrote down the results, and later they were transferred to evaluators. This test can determine the functional state correctly[20]. The minimum clinically significant difference represents 54 meters or 75 steps[21]. A higher score indicates a better result on that test. The following procedure was performed to standardize the test: The evaluators asked the patient to walk as far as possible at home without generating 180º changes of direction, thus suppressing the variability in the distribution of households.

C. Thirty Seconds Sit-To-Stand Test. This test has been demonstrated to be a valid and reliable tool to assess peripheral muscle performance of lower limbs[22]. The patients performed the test, and the evaluator counted the number of repetitions, minimum clinically significant difference [23]. A higher score indicates a better result on that test. The following procedure was performed to standardize the test: Evaluators asked patients to place a straight-backed armless chair with a hard seat, which will be stabilized by placing it against a wall, considering floor to seat height will be between 45 and 50 cm. Seated

participants will be asked to come forward on the seat until their feet are flat on the floor and fold their upper limbs across the chest without moving them during all tests. Patients will then be instructed to stand up all the way and sit down once without using the upper limbs. Patients will start in the sitting position in the chair and, when instructed, through the online application, will stand up and then return to sitting as many times as possible within a 30 second period.

D. Multidimensional Dyspnoea-12. We used this test (already validated Spanish version) as a valid and reliable instrument to study dyspnoea's multidimensional nature[24]. The minimum clinically significant difference is represented by 2,83 points [25], and a higher score indicates a worse result on the test.

E. The modified Borg Scale [26] of perceived effort measures the entire range of activities that the individual perceives when exercising. The minimum clinically significant difference is represented by 0,9 points[27], and a higher score indicates a worse result on the test. This scale gives criteria to adjust to the intensity of exercise, that is, to the workload, and thus forecast and dictate the different powers of activity in sports and medical rehabilitation.

The assessment protocol was as follows: first, the Visual Analogue Fatigue Scale was evaluated to determine the patient's level of fatigue. After that, the patients performed the 6-minute walk test and the 30-second sit-and-stand test. Finally, Multidimensional Dyspnea-12 and the Borg Scale were evaluated. All patient information was stored and classified by the assessors, transferring the numerical values to an Excel file. Excel files were encrypted, and only evaluators and the leading researcher had access to them. This information was updated through a secure encrypted cloud located on a secure encrypted network. The rate of loss to follow-up and its reasons were also analysed.

Patients were contacted daily by therapists for any problems or doubts with the intervention; a complete description of our methods, including patients' management, can be checked in the previously published protocol[17]. The intervention lasted 14 days: interventions were applied at patients' homes through a mobile application so-called "WhatsApp". Day 1 was considered when the initial evaluation was performed (Baseline), and the patients performed their exercise protocol for the first time. The patients completed the assigned therapeutic exercises exclusively, according to their group assignment. They could not perform any other physiotherapy treatment or sports physical activity simultaneously, so any interference in the treatment led to exclusion.

a. Group 1: Breathing exercise program (Breathing Exercise Group – BG).

The breathing exercise program consisted of 10 exercises based on the active cycle of breathing techniques. It uses an alternate depth of breathing to move mucus and achieve more excellent ventilation throughout the lung. The activities are available at https://www.fisiosurid.com/exercises-covid-19/ .

It was carried out once a day, for 14 days, at the patient's home. Depending on the score obtained on the Borg scale during the assessment, patients performed one set of 4 (BS 7-10), 8 (BS 5-7), or 12 (BS 8-10) repetitions per exercise and day; these repetitions took 10, 20 and 30 minutes, respectively.

The exercise program was taught on day 1 through videoconference. It was reinforced by a physical therapist at least two times (1 time a week, if the patient does not require further attention) through telematic control during the treatment period of 14 days.

Additionally, patients received a text message daily, asking about the activities and improving adherence as a follow-up method.

Once the data from the evaluations were obtained, the patients were taught group 2 interventions.

b. Group 2: Strength exercise program (Strength Group – SG).

The strength exercise program consisted of 10 exercises based on strength exercise to improve the physical deconditioning and physiological deterioration. Also, it has been demonstrated that exercise therapy produces many benefits in the immune/defense system. The exercises are available at https://www.fisiosurid.com/ejercicios-proyecto-covid/.

It was carried out once a day, for 14 days, at the patient's home. Depending on the score obtained on the Borg Scale during the assessment, patients performed one set of 4 (Borg Scale 7-10), 8 (Borg Scale 5-7), or 12 (Borg Scale 8-10) repetitions per exercise and day; these repetitions took 10, 20 and 30 minutes, respectively.

The exercise program was taught on day 1 through videoconference. It was reinforced by a physical therapist at least two times (1 time a week, if the patient does not require further attention) through telematic control during the treatment period of 14 days. Additionally, patients received a text message daily, asking about the exercises and improving adherence as a follow-up method.

Once the data from the evaluations were obtained, the patients were taught group 1 interventions.

c. Group 3: Control group (CG).

The patients in this control group underwent the assessments on days 1 and 14. These assessments were carried out by a physiotherapist who was unaware of the patient's group. Once the data from the different evaluations had been obtained, the patients were taught group 1 and group 2 interventions.

Statistical analysis was carried out using SPSS v.26.0 (IBM, Armonk, N.Y., USA). As a baseline, we carried out the statistical analysis through a descriptive analysis of the data before the intervention, applying the Kolmogorov-Smirnov normality test for the quantitative or Chi-Square for qualitative variables. The between-groups analysis was performed by applying the ANOVA (one-way) test. The univariate (ANOVA) and multivariate analysis of variance (MANOVA) was used to assess differences between groups, as well as post hoc differences. The effect sizes were analysed through the R-square coefficient (R^2), considering effect sizes lower than 0.01 as small and upper than 0.06 are considered a medium. In contrast, an upper than 0.14 is considered as large. The statistical analysis was conducted at a 95% confidence level, and a p-value of less than 0.05 was considered statistically significant in our study.

Results

Of the 93 subjects assessed for eligibility, 88 were enrolled, and 77 completed the 14-days intervention and were included in the analysis. The CONSORT flow diagram is included in *figure 1*.

FIGURE 1. CONSORT FLOW DIAGRAM

Only 1 participant found incidences with telerehabilitation devices that could not be resolved, and he decided not to collaborate. Concerning the losses due to the disease's worsening, only two hospital admissions belonged to the control group; the experimental groups did not present losses.

Seventy-seven patients completed the 14-days intervention, were included in the analysis, and were allocated into three groups: 26 to SG (mean [SD] age 34.81 [11.82], 29 to BG (mean [SD] age 41.93 [10.19]), and 22 to CG (mean [SD] age 42.36 [11.84]). All groups were comparable at baseline, so there were no between-group differences in any outcome measures (all p-values > 0.05). *Table 1* summarizes descriptive baseline data for all groups.

The 14-day intervention resulted in a statistically significant improvement between groups, not only in the SG but also in the BG. We found a statistically significant improvement between SG and BG groups versus CG. The most remarkable between-groups differences (p<0,001) were found in the BS, MD12, and VAFS variables in the SG and all BG variables. The intergroup analysis shows significant differences between the study groups and CG in all variables (p<0,05). *Table 2* summarizes between-groups pre-post data.

TABLE 1. DESCRIPTIVE BASELINE DATA

A post hoc analysis, through the Bonferroni contrast, reveals that significant differences were observed between the CG and the SG ($p < 0,001$) for all variables except the 6-Minute Walking Test variable ($p > 0,05$). We attended the same behavior between the CG and BG, obtaining significant differences for all variables (*Table* 2).

TABLE 2. BETWEEN-GROUPS PRE-POST DATA

Regarding the effect size analysis, we observed that most of the values obtained were considered greater than large ($R^2 > 0,14$), with the exception of the variable 6-Minute Walking Test ($p=0,002$; $F_{1,75}= 6,251$; $R^2=0,123$), being the greatest effects obtained for the variables Borg Scale ($p=0,001$; $F_{1,75}= 42,430$; $R^2=0,548$) and Multidimensional Dyspnoea-12 ($p=0,001$; $F_{1,75}= 34,542$; $R^2=0,475$) and large effects for VAFS ($p=0,001$; $F_{1,75}= 15,732$; $R^2=0,280$) and 30STST ($p=0,001$; $F_{1,75}= 12,539$; $R^2=0,268$).

DISCUSSION

Our study found that two different telerehabilitation programs based on respiratory and strength exercise effectively improved fatigue, dyspnea, perceived effort, and physical state in patients affected by COVID19. The implementation of respiratory exercises seems to obtain a more significant clinical benefit concerning dyspnea and aerobic capacity than the strength exercise intervention. No complications were developed after implementing activities in patients with COVID19 in the acute phase, as found in our pilot studies[28,29]. Therefore, these findings align with the recommendation of using remote consultations or videos to manage respiratory problems due to SARS-CoV-2[30-32].

In this regard, other authors such as Sakai et al.[33] described the efficacy and risk management of remote rehabilitation of patients with coronavirus disease (COVID-19), demonstrating improved rehabilitation in COVID-19 areas. We have observed that patients affected with COVID-19 who perform an exercise protocol in their homes, telematically advised by physiotherapists, improve significantly, whether the protocol is integrated by breathing exercises or strength exercises, although the improvement is more significant in patients who perform breathing exercises. Thus, it can be suggested that other mechanisms might play a role in rehabilitation and improvement of symptomatology and function in these patients.

On the one hand, regular exercise has been demonstrated to improve immunity and reduce infectious diseases[34]. Also, metabolic dysfunction, which has been related to a worse

clinical course of the disease[35], could be prevented by exercise training. Moreover, it has been found that patients with COVID-19 in home confinement suffered a decline in physical function[36]. Thus, the benefits coming from our proposed strength exercise intervention could be due to all these mechanisms.

On the other hand, the exact respiratory pathophysiology remains unclear; nonetheless, it has been hypothesized that respiratory problems in COVID-19 patients could be associated with lung injury due to three different ways: diffuse alveolar damage, diffuse thrombotic alveolar microvascular occlusion, and inflammatory mediator-associated airway inflammation, which may lead to residual physical impairments of varying degrees[8]. Although we could not demonstrate changes in these disturbances, we proved that dyspnea, one of the most typical characteristics of patients with SARS-CoV-2, improved after 14 days of intervention, which could be related to strengthening respiratory muscles[13]. Indeed, one of the most important findings of our study is that we found statistical differences in Multidimensional Dyspnoea-12 at the end of both programs between respiratory and strength exercise groups. The level of dyspnea improves when compared with a control group but is also reduced, especially in the breathing group.

When we analyse the associated effect's size, high values are obtained for all variables, which would indicate critical clinical implications of the proposed interventions, suggesting that strength or respiratory exercises might be of interest in COVID-19 patients during home confinement. Moreover, we observed that our program was well-received, without considerable technical difficulties[37].

To the best of our knowledge, this is the first randomized controlled trial to test the efficacy of two different interventions (through telerehabilitation exercises) applied in confined COVID-19 patients in the acute phase.

Our results are in line with those reported by other authors such as Vasilopoulou M et al. [38] et al., who found that home-based maintenance telerehabilitation is as effective as inpatient and outpatient maintenance pulmonary rehabilitation in reducing the risk of acute, chronic obstructive pulmonary disease exacerbation and hospitalizations.

Besides, Hansen H[39] et al. found that pulmonary telerehabilitation was as effective as conventional pulmonary rehabilitation in 6-minute walking distance, respiratory symptoms, quality of life, physical activity, and lower extremity muscle function in patients with chronic obstructive pulmonary disease.

In terms of limitations, firstly, we observed that the studied sample has an average age of 39 ± 12 years; this implies a young selection that tends not to develop severe symptoms, limiting our study's capacity to assess the preventive role of exercise in the rate of hospitalization. In addition, the sample size was relatively small, and we did not achieve our estimated sample size, which could become a limitation. The main reasons we found for the recruitment and follow-up of the rehabilitation program were the insecurity of the patients regarding the disease and the beliefs that specific exercises could worsen the condition, and the lack of collaboration after starting the treatment. Studies with higher sample sizes are required. The difficulties encountered in the current pandemic concerning the limited information that the population received regarding the prognosis and evolution of the disease led to low reception to any external treatment. At present, there are still no published studies of telerehabilitation with large sample size, and this is a challenge posed by this study.

Physical exercise induced improvements in the patients' health status. Still, in clinical practice, it would be necessary to adapt the load, and the volume of training, since patients who tend to improve the implemented exercise program can assume too mild a stimulus. This factor is problematic since it is difficult to predict the degree of symptoms that patients affected by COVID19 will develop, and adaptation is necessary according to evolution. Therefore, load and volume become a limitation in our study.

Besides, we only evaluated subjects at baseline and the end of the 14-day program, without follow-up evaluation. Thus, based on our results, we could not investigate what happened after the exercise program, if patients in intervention groups achieved more physical benefits when compared to the control group in the long term, or if subjects in the control group had more possibilities to need hospital admission.

Finally, we would like to point out that although increasingly studied and accepted, remote assessments could become a limitation to extrapolate our findings to clinical practice and when facing telerehabilitation tools to face-to-face evaluations.

Remote assessments have the disadvantage of the researcher's dependence on the subject's praxis for self-assessment. Therefore, our results could not be extrapolated to some populations that could have some problems managing these tools, such as older people. Future studies comparing the same treatment protocols in person and at a distance would improve their reliability.

We consider that our findings could become a start point to implement strength and breathing exercises in COVID-19 patients since effectiveness and security have been demonstrated; in our opinion, since both interventions showed clinical improvements, combining both could be of interest. Nonetheless, future research should address the main limitations of our study. Higher sample sizes, adaptability of exercises' load and volume, and feasibility of telerehabilitation assessments should be deeply studied to confirm our findings. In addition, future research may be directed to clarify if the implementation of programs including both types of exercises is more beneficial for the management of these patients; in addition, investigating the possible correlation in clinical improvements and changes in respiratory pathophysiology could be of interest.

Clinical messages

· Breathing and strength exercises led to clinical benefits in confined patients with COVID-19.
· Respiratory exercises showed greater improvements in dyspnea and aerobic capacity than tonic intervention.
· Both interventions could be integrated with the management of these patients through telerehabilitation devices.

Authors contribution

This trial was coordinated by the clinical research group of the Junta de Andalucia *CTS-954: Innovations in Health and Quality of Life.* All the recruitment procedures,

intervening and evaluating the participants were carried out by personnel attached to this group. CRB provided clinical expertise and did the statistical analysis. CBU and EAL, and MSH contributed to manuscript development and guided evaluation and intervention procedures. MGM and MASF provided clinical expertise and collaborated in the development of the study. EDLBA contributed to manuscript development and provided clinical expertise. JJGG is the principal investigator and contributed to the manuscript development. All authors read and approved the final manuscript.

Clinical Trial Registration

The trial was registered at the Brazilian Trial Registry (RBR-6m69fc)

Data sharing

The study protocol and de-identified individual participant data generated during this study are available from the investigators on reasonable request with the publication. Requests should be directed to the corresponding author by email.

Disclosures and Presentations

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

Ethics Approval

The study was approved by the ethics committee of University Hospital Virgen Macarena-Virgen del Rocio and complied with the Helsinki Ethical Principles for Medical Research Involving Human Patients and its subsequent modifications.

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Figure 1. CONSORT Flow Diagram

Consort flow diagram. SG, strength group; BG, breathing exercise group; CG, control group.

TABLE 1. DESCRIPTIVE BASELINE DATA

	SG (n=26)	**BG** (n=29)	**CG** (n=22)
AGE (years)	34,81 ± 11,82 [30,03 to 39,58] *	41,93 ± 10,19 [37,98 to 45,88] *	42,36 ± 11,84 [37,11 to 47,61] *
GENDER (male/female)	14 / 12 **	13 / 16 **	10 / 12 **
HEIGHT (cm)	170,76 ± 9,65 [166,86 to 174,66] *	169,96 ± 7,64 [167,00 to 172,92] *	170,95 ± 8,09 [167,36 to 174,54] *
WEIGHT (kg)	75,71 ± 12,29 [70,75 to 80,68] *	74,91 ± 8,11 [71,76 to 78,05] *	72,54 ± 9,44 [68,36 to 76,73] *

Data expressed as mean ± standard deviation [95% CI Lower to Upper]. *SG: Strength Group; BG: Breathing Group; CG: Control Group;* **: p>0,05 (p-values come from the Chi-Square test); *: p>0,05 (p-values come from the Kolmogorov-Smirnov test).

TABLE 2. BETWEEN-GROUPS PRE-POST DATA

	GROUPS								
	SG (n=26)			**BG** (n=29)			**CG** (n=22)		
	PRE	POST	DIF	PRE	POST	DIF	PRE	POST	DIF
BS	4,58 (1,60) [3,93 to 5,22]	2,50 (0,99) [2,10 to 2,90]	-2,076 (1,128) [-2,532 to -1,621] **	5,71 (2,27) [4,83 to 6,60]	2,96 (1,45) [2,40 to 3,53]	-2,750 (1,205) [-3,217 to -2,282] **	4,45 (1,87) [3,63 to 5,28]	4,59 (1,68) [3,85 to 5,34]	0,136 (0,940) [-0,280 to 0,553]
MD12	7,85 (6,82) [5,09 to 10,60]	4,54 (4,82) [2,59 to 6,49]	-3,307 (2,541) [-4,334 to -2,281]**¥	11,04 (6,49) [8,52 to 13,55]	5,32 (3,63) [3,91 to 6,73]	-5,714 (3,408) [-7,036 to -4,392]** ¥	10,27 (6,49) [7,39 to 13,15]	10,59 (6,58) [7,67 to 13,51]	0,318 (0,994) [-0,122 to 0,759]
VAFS	4,15 (1,46) [3,56 to 4,74]	1,73 (2,18) [0,85 to 2,61]	-2,423 (1,579) [-3,060 to -1,785] **	7,25 (1,75) [6,56 to 7,93]	4,57 (3,40) [3,25 to 5,89]	-2,678 (2,735) [-3,739 to -1,617] **	4,18 (2,26) [3,18 to 5,18]	4,45 (2,19) [3,48 to 5,43]	0,272 (1,202) [-0,260 to 0,805]
6MWT	455,38 (150,46) [394,61 to 516,16]	520,58 (143,40) [462,65 to 578,50]	65,192 (112,662) [19,687 to 110,697]	400,86 (161,28) [338,32 to 463,40]	497,25 (141,55) [442,36 to 552,14]	96,392 (122,98) [48,702 to 144,083] *	392,14 (134,61) [332,45 to 451,82]	388,91 (138,13) [327,66 to 450,16]	-3,227 (13,948) [-9,411 to 2,957]
30STST	12,19 (4,42) [10,40 to 13,98]	13,58 (5,37) [11,41 to 15,75]	1,384 (2,041) [0,560 to 2,209] **	11,18 (3,42) [9,85 to 12,51]	12,79 (4,00) [11,23 to 14,34]	1,607 (1,594) [0,988 to 2,225] **	10,45 (2,15) [9,50 to 11,41]	9,86 (1,88) [9,03 to 10,70]	-0,590 (0,854) [-0,969 to - 0,212]

TABLE 2. BETWEEN-GROUPS PRE-POST DATA. Data expressed as mean (standard deviation) [95% CI Lower-Upper]. BS: Borg Scale; MD12: Multidimensional Dysphnoea-12; VAFS: Visual Analog Fatigue Scale; 6MWT: Six-Minute Walking Test; 30STST: 30-Seconds Sit to Stand Test; PRE: Preintervention Data; POST: Postintervention Data; DIF: Prepost Differences Data. *SG: Strength Group; BG: Breathing Group; CG: Control Group; p-values interaction with CG, come from MANOVA analysis* (*: p<0,05; **: p<0,01); *p-values interaction between intervention groups, come from MANOVA analysis* (¥: p<0,05).