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Efficacy of a rehabilitation protocol on pulmonary and respiratory muscle function and ultrasound evaluation of diaphragm and quadriceps femoris in patients with post-COVID-19 syndrome: a series of cases

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Abstract

This study assessed the efficacy of a pulmonary rehabilitation (PR) on pulmonary and respiratory muscle function and thickness of quadriceps femoris and diaphragm of patients with post-COVID-19 syndrome. This series of cases followed nine patients who performed PR twice a week for six weeks. Patients received the following PR program: lung expansion therapy; respiratory muscle training; upper limb strength exercises; aerobic exercises on a treadmill. After the program, we observed increased peak expiratory flow (26.03%), forced vital capacity (FVC) (7.14%), forced expiratory volume in the first second (FEV_1) (9.55%), and ratio between FEV_1/FVC (6.19%). All parameters of respiratory muscle strength and endurance were improved. Diaphragmatic thickening fraction and thickness of quadriceps femoris also improved, whereas echo intensity of quadriceps reduced. Thus, RP protocol improved pulmonary function, respiratory muscle strength and endurance, and thickness of diaphragm and quadriceps femoris, and reduced echo intensity of quadriceps in patients with post-COVID-19 syndrome.

Introduction

Healthcare services strive to reduce COVID-19 mortality risk, however, they need to develop strategies that promote physical functional recovery and social reintegration of patients post-COVID-19, such as pulmonary rehabilitation (PR) [1]. Long-term follow-up studies observed persistent symptoms in patients with post-COVID-19 syndrome, such as fatigue, dyspnea, impaired pulmonary function, and physical and psychological alterations. This syndrome also reduces functional capacity and health status [2], even in non-hospitalized patients.

PR is essential for patients hospitalized for long periods in the intensive care unit and under mechanical ventilation [3]. It may also improve dyspnea, fatigue, respiratory function, anxiety, depression, and quality of life of patients with post-COVID-19 syndrome [2]. The benefits of PR programs on respiratory symp-

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toms of patients with post-COVID-19 syndrome are still poorly described in the literature. Therefore, this study aims to evaluate the efficacy of a PR protocol on pulmonary and respiratory muscle function of patients with post-COVID syndrome [1] and ultrasound evaluation of diaphragm and quadriceps femoris.

Case Reports

This series of cases followed nine patients with different degrees of COVID-19 pulmonary involvement, according to chest computed tomography (CT) [4]. Patients presented respiratory complaints of post-COVID-19 syndrome, such as: dry cough, dyspnea and chest pain [5] and participated in a PR program between May and September 2021. The study was conducted according to the Declaration of Helsinki and approved by the human research ethics committee of the Health Sciences Center of Federal University of Paraiba (number 4.867.074). All patients signed the informed consent form.

Case #1

A 56-year-old female, with body mass index (BMI) of 31.3 kg/m^2 and a pathological history of thyroid cancer and fibromyalgia. On April 7, 2021, presented the following symptoms: dyspnea on exertion, cough, anosmia and ageusia, where went to the emergency room, underwent a chest CT that showed a 40% pulmonary impairment and a positive nasal swab for COVID-19. She did not need to be hospitalized and received guidance on social isolation. After recovering from COVID-19, she continued to complain of chest pain, dyspnea on medium exertion and dry cough, seeking the PR.

Case #2

A 74-year-old male, with a BMI of 27 kg/m^2 and a pathological history of arterial hypertension. On February 25, 2021, presented the following symptoms: dry cough, fever, tiredness, body pain, diarrhea and dyspnea, with this he sought the emergency room, underwent a chest CT that showed a pulmonary impairment of 25% and the positive nasal swab for COVID-19. He was admitted to a public hospital for 8 days, used low-flow oxygen therapy through a nasal cannula and was referred to physical therapy at hospital discharge. After recovering from COVID-19, he continued to complain of chest pain, dyspnea on minimal exertion and dry cough, seeking PR.

Case #3

A 48-year-old female, with a BMI of 35.8 kg/m^2 and a pathological history of endometriosis, depression, anxiety, panic syndrome and arterial hypertension. On May 13, 2021, presented the following symptoms: dry cough, fever, fatigue, pain and discomfort in the body, diarrhea, headache, dyspnea, anosmia, ageusia and chest pain, where went to the emergency room, underwent a chest CT that showed a pulmonary impairment of 30% and a positive nasal swab for COVID-19. She did not need to be hospitalized and received guidance on social isolation. After recovering from COVID-19, he continued to complain of chest pain and fatigue, seeking PR.

Case #4

A 49-year-old male, with a BMI of 47.2 kg/m^2 and a pathological history of diabetes mellitus. On May 9, 2021, presented the following symptoms: dry cough, fever, fatigue, body aches, diarrhea, dyspnea, where went to the emergency room, underwent a chest CT that showed pulmonary impairment of more than 50% and a positive nasal swab for COVID-19. He was admitted to a private hospital for three days, using low-flow oxygen therapy through a nasal cannula and non-invasive ventilation (NIV), and was not referred to physical therapy. After recovering from COVID-19, he continued to complain of dyspnea on exertion and pain in the lower limbs, seeking PR.

Case #5

A 54-year-old female, with a BMI of 36.1 kg/m^2 and a pathological history of arterial hypertension. On February 27, 2021, presented the following symptoms: dry cough, fever, fatigue, asthenia, pain in the body and throat, headache, dyspnea, anosmia, ageusia and chest pain, where went to the emergency room, underwent a chest CT that showed pulmonary involvement of more than 50% and a positive nasal swab for COVID-19. She was admitted to a public hospital for 19 days, using high-flow oxygen therapy with oxygen rebreathing mask. After hospital discharge, she was not referred to physical therapy and upon recovering from COVID-19, she continued to complain of dyspnea on exertion and chest pain, seeking PR.

Case #6

A 52-year-old female, with a BMI of 32.1 kg/m^2 and a pathological history of arterial hypertension. On April 3, 2021, presented the following symptoms: headache, fatigue and dyspnea, where sought the emergency room, underwent a CT scan of chest that showed pulmonary involvement of more than 15% and a positive nasal swab for COVID-19. She was admitted to a public hospital for 5 days, using low-flow oxygen therapy. After hospital discharge, she continued to complain of chest pain, fatigue and dyspnea on minimal exertion, seeking the PR.

Case #7

A 30-year-old male, with a BMI of 27.1 kg/m^2 and a pathological history of revascularization in the right lower limb. On June 28, 2021, presented the following symptoms: fever, dry cough and dyspnea, where sought emergency care, performed a chest CT that showed pulmonary involvement of more than 60% and a positive nasal swab for COVID-19. He was admitted to a public hospital for 9 days. After hospital discharge, he was not referred to physical therapy and upon recovering from COVID-19, he continued to complain of dyspnea on exertion, seeking the PR service.

Case #8

A 52-year-old female, with a BMI of 28.5 kg/m^2 and pathological history of removal of the module in the right breast, former smoker and undergoing varicose vein surgery. On July 11, 2021, presented the following symptoms: headache, fatigue and dyspnea, where he went to the emergency room, underwent a chest CT that showed a pulmonary impairment of 10% and a positive nasal swab for COVID-19. She was admitted to a private hospital for 10 days, using low-flow oxygen therapy resources. After being discharged from the hospital, she remained with the complaint of dyspnea on exertion and fatigue, seeking PR.

Case #9

A 60-year-old male, with a BMI of 25.2 kg/m^2 and a pathological history of lymphoma with lymph node emptying. On August 5, 2021, presented the following symptoms: fever, dry cough, headache, pain in the body and dyspnea, where looked for the emergency room performed a chest CT that showed pulmonary impairment of more than 50% and a positive nasal swab for COVID-19. He was hospitalized for 5 days in a private hospital, using low-flow oxygen therapy resources with oxygen rebreathing mask and NIV. After hospital discharge, he was referred to physical therapy and upon recovering from COVID-19, he continued to complain of dyspnea on exertion and shortness of breath, seeking PR.

Intervention

All patients completed the PR program, performed twice a week for six weeks. Pulmonary and respiratory muscle function and ultrasound of diaphragm and quadriceps femoris were before and after the six weeks of rehabilitation. Patients received the following rehabilitation program (Table 1):

a) Initial and at six-week assessment of pulmonary function, respiratory muscle function, and diaphragmatic and quadriceps femoris ultrasound:

Pulmonary function: patients performed at least three maneuvers seated, with a nose clip, and mouthpiece coupled to the mouth [6]. Patients were instructed to perform maximal inspiration to total lung capacity, followed by forced maximal and continuous expiration for six seconds until residual volume. Forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, and peak expiratory flow (PEF) were included for analysis [7].

Respiratory muscle function: MIP, sustained maximal inspiratory pressure (SMIP), and fatigue resistance index (FRI) were assessed using an electronic device (KH2; PowerBreathe International Ltd., UK) with Breath-Link software. Patients were seated with arms supported and nose clip to prevent air leakage. During MIP assessment, patients were instructed to expire to residual volume and perform a maximum inspiration for as long as possible. Maximum inspiration values were ignored when less than 1.5 s. The test was repeated three to eight times for a variation of less than 10% between repetitions. We considered the highest value measured for analysis [8]. Respiratory muscle endurance was assessed using SMIP. Patients were instructed to sustain maximum inspiratory pressure for at least one minute using an initial load of 10 cmH_2O. If sustained, patients should rest for one minute and perform a new sustained maneuver with an increment of 10 cmH_2O. The highest load sustained for at least one minute was considered as SMIP value [9]. MIP was evaluated before (initial MIP) and after the maximum incremental load (final MIP) to verify muscle fatigue. The ratio between final and initial MIP was defined as FRI. Respiratory muscle endurance was reduced when FRI was <88% [10].

Ultrasound of diaphragm and quadriceps femoris: diaphragmatic thickening fraction (TF) was obtained using ultrasound (Mindray, model DP30; São Paulo, Brazil) and a linear transducer placed between eighth and ninth intercostal spaces and anterior and midaxillary lines (apposition zone). Images were acquired in B-mode to identify the diaphragm followed by M-mode [11]. TF

Table 1. Cardiopulmonary rehabilitation protocol.

Protocol		Post-COVID-19 pulmonary rehabilitation
Initial assessment		Pulmonary and respiratory muscle function and diaphragmatic and quadriceps ultrasound.
Lung expansion therapy - EPAP	Charge	EPAP (5 to 20 cmH_2O) pressure increase according to the modified Borg Scale (0-10) between 4 and 6.
	Volume	3 sets of 2 min with a 1 min rest interval.
Inspiratory muscle training - threshold	Charge	40% of PIM in the 1st, 2nd and 3rd weeks. 50% of PIM in the 4th , 5th and 6th weeks.
	Volume	3 sets of 10 reps.
Strengthening exercises of the upper limbs	Charge	Initial load: 50% of the load obtained in the incremental test of upper limbs. Load increase according to modified Borg Scale (0-10), between 4 and 6.
	Volume	3 sets of 1 min.
Treadmill	Charge	60% to 70% of the maximum HR obtained in the exercise test in the 1st, 2nd and 3rd weeks. 70 to 80% of the HR obtained in the exercise test in the 4th, 5th and 6th weeks. Modified Borg scale (0-10) between 4 and 6.
	Volume	10 to 20 min.
Reassessment after 6 weeks		Pulmonary and respiratory muscle function and diaphragmatic and quadriceps ultrasound.

COVID-19, coronaviruses; EPAP, positive airway expiratory pressure; MIP, maximum inspiratory pressure; HR, heart rate.

was calculated considering inspiratory and expiratory thickness obtained from functional residual capacity:

$$TF = (\text{inspiratory thickness} - \text{expiratory thickness}) / \text{expiratory thickness} \times 100$$

The transducer was placed perpendicular to the limb, two-thirds between the anterior superior iliac spine and lateral condyle of the knee [12]. Ultrasound coupling gel was applied to minimize the distortion caused by underlying tissues [13]. Thickness of rectus femoris (RF) and vastus intermedius (VI) were assessed by the same evaluator in the lateral view of the thigh with minimal pressure on the skin. The same positioning and points were assessed before and after pulmonary rehabilitation. This measure has high intra- and inter-examiner reliability [14].

Four analyzes were performed in each image from the right thigh of patients:

i) lateral image, transducer positioned perpendicular to the limb and two-thirds between anterior superior iliac spine and lateral condyle of the knee;
ii) anterior image, total thickness of quadriceps femoris with tracing from the highest point of the femur to the end of the rectus femoris fascia;
iii) anterior image, thickness of VI was measured from the highest point of the femur to the end of muscle thickness; whereas for RF, the straight line starting at the central point and with a straight line (muscle fascia was excluded in both measurements);
iv) anterior image for region of interest (ROI), positioned by the square method in the most voluminous region of RF muscle for echo intensity analysis.

Echo intensity was analyzed using grayscale analysis after determining ROI, a reliable method for analyzing skeletal muscles (11,14). ROI (50 mm of height and width) was determined in the most voluminous region of muscles according to muscular architecture of patients. Values were given in pixels by the grayscale histogram analysis (0 corresponded to black and 255 to white), and highest values indicated possible muscle infiltration and myofibril depletion. Images were analyzed using Image J software (NIH, Bethesda, MD), and each pixel was equivalent to 1 mm [14].

b) lung expansion therapy using expiratory positive airway pressure (EPAP), performed in 3 sets of 2 min with a rest interval of 1 min between them, starting with a positive expiratory end pressure (PEEP) at 5cmH_2O, increment of 5cmH_2O in each session, up to a maximum PEEP of 20cmH_2O, maintaining a score between 4 and 6 on the modified Borg Perceived Effort Scale. All patients at the end of the rehabilitation program were able to reach the maximum pressure of the EPAP device.
c) inspiratory muscle training using the threshold valve for 3 sets of 10 repetitions with a load of 40% of the maximum inspiratory pressure (MIP), maintained in the first three weeks and increased to 50% of the IMP in the last three weeks of the program [15].
d) upper limb strength exercises with anterior elevation of shoulders for 3 sets of 1 min and rest interval of 1 min between sets, with an initial load of 50% of the maximum load obtained in the incremental test of the upper limbs and increment of the weight of 0.5 kg according to a score between 4 and 6 on the modified Borg Perceived Effort Scale [16].
e) aerobic exercises on a treadmill, using the staggered protocol with a steady state of 60 to 70% of the heart rate (HR) obtained in the effort test in the first three weeks and increment to 70 to 80% in the last three weeks [3].

Patients were continuously monitored through measurements of respiratory rate (RR), heart rate (HR), peripheral oxygen saturation (SPO_2) and the Borg's perceived exertion scale during assessments and PR. One patient presented SPO_2 of ≤88% while using the treadmill during the first two rehabilitation sessions and needed low-flow supplemental oxygen at 2L/min in the nasal cannula.

Results

Table 2 shows the mean and standard deviation of the assessment of respiratory muscle function and kinesiological ultrasound of

Table 2. Baseline and reassessment after six (6) weeks of respiratory muscle function, kinesiological ultrasound and pulmonary function in the nine cases included.

Variables	Baseline Average±SD	6 weeks Average±SD
Respiratory muscle function		
MIP (cmH_2O)	84.18±27.15	113.58±31.02
MSIP (cmH_2O)	35.55±22.16	68.88±15.23
FRI (%)	0.87±0.12	1.03±0.17
Kinesiological ultrasound		
Diaphragmatic TF (%)	32.78±10.79	35.88±12.65
Special VI (mm)	13.9±2.2	15.0±2.4
Eco. VI (AU)	47.53±15.13	40,23±11.89
Special RF (mm)	15.7±2.5	16.8±1.8
Eco. RF (AU)	68.36±20.31	53.07±15.34
Special Q (cm)	30.9±4.5	31.8±4.4
Pulmonary function test		
PEF (%)	41.84±12.51	67.87±12.90
FLC (%)	55.10±17.72	62.24±13.65
FEV_1 (%)	66.85±21.18	76.40±13.60
FEV_1/FLC (%)	85.71±7.48	91.90±8.86

MIP, maximum inspiratory pressure; MSIP, maximum sustained inspiratory pressure; FRI, fatigue resistance index; SD, standard deviation; TF, diaphragmatic thickening fraction; special VI, thickness of the vastus intermedium; Eco. VI, ecointensity of vast intermediate; special RF, thickness of the rectus femoris; eco. RF, ecointensity of rectus femoris; special Q, quadriceps thickness; UA, arbitrary units; PEF, peak expiratory flow; FLC, forced vital capacity; FEV_1, forced expiratory volume in the first second; FEV_1/FLC, forced expiratory volume in the first second/forced vital capacity.

the diaphragm and femoral quadriceps and the percentage values of the pulmonary function test at baseline and after six weeks of PR (Table 2). Regarding respiratory muscle function, we can observe that all parameters of respiratory muscle strength and endurance improved after PR. Mean of the maximal inspiratory pressure (MIP) increased by 29.4 cmH_2O after six weeks of rehabilitation [8]. Regarding sustained maximal inspiratory pressure (SMIP) [9] we observed an increase of 33.33 cmH_2O in the mean sustained load, with the lowest non-baseline sustained load of 10 cmH_2O (patient #5) and the highest sustained load of 90 cmH_2O at the end of six weeks (patient #7). The mean fatigue resistance index (FRI) [10] of patients changed from values representing reduced FRI=0.87 for the general population to a value considered normal, FRI=1.03, at the end of six weeks. With regard to kinesiological ultrasound of the diaphragm and femoral quadriceps, the pulmonary rehabilitation program decreased echo intensity of vastus intermedius (VI) by (7.3 AU) and of rectus femoris (RF) (15.29 AU) and increased mean thickening fraction (TF) of diaphragm by 3.1% and the thickness of VI in 1.1 mm of RF in 1.1 mm and quadriceps femoris in 0.9 mm (Table 2) (11-14). In this same Table 2, comparing the percentage values of peak expiratory flow (PEF), forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1) and FEV_1/FVC obtained at baseline and after six weeks of the pulmonary recovery program [7]. After the PR program, we observed a mean increase of 26.03% of PEF, 7.14% of FVC, 9.55% of FEV_1 and 6.19% in FEV_1/FVC ratio compared to baseline.

Discussion

We presented nine cases of patients with different COVID-19 severity (according to chest tomography) and sequelae post-COVID-19. PR was conducted to reverse respiratory sequelae, such as dyspnea on exertion, dry cough, chest pain, and fatigue. Our patients showed promising results in pulmonary function, respiratory muscle strength and endurance, and diaphragmatic and peripheral ultrasound after a six-week PR program. These results are important with regard to PR in this population [2,17].

A considerable proportion of patients with post-COVID-19 syndrome have reduced lung function and diffusing capacity associated with the severity of the disease in the acute phase [18]. Lewis *et al.* observed a trend of worsening pulmonary function in critically ill but not in non-critically ill patients. Moreover, authors suggested patients who recover without orotracheal intubation or positive pressure ventilation are more likely to return to pre-infection diffusion capacity values [18].

In all our patients, after six weeks of rehabilitation, we observed improvement in lung volumes and capacities. Our findings corroborate the studies of Liu *et al*. [2] and Chikhanie et *al*. [19], who showed significant gains in pulmonary function of patients post-COVID-19 after rehabilitation. We suggest that lung expansion therapy using EPAP associated with other interventions applied during our rehabilitation program significantly improved outcomes in this population.

Our patients improved respiratory muscle strength and endurance (expressed by MIP and SMIP and FRI, respectively). This may be due to respiratory muscle training (RMT), an important respiratory muscle reconditioning strategy that positively impacts respiratory muscle strength and endurance [20] and correlates with PEF [21,22]. It is important to highlight that RMT and aerobic and endurance training probably favored these gains. Crimi et al. evaluated the effects of PR in 25 patients with chronic obstructive pulmonary disease (COPD) using ultrasound of diaphragm and quadriceps. They described this test as adequate to assess PR and accurate to predict the response to therapy [23].

Ultrasound analysis of quadriceps femoris indicated increased thickness of VI, RF, and quadriceps and reduced echo intensity of VI and RF. To date, there are few studies that have evaluated the effects of PR in patients with post-COVID-19 syndrome; Menon *et al*. [24] evaluated quadriceps on the dominant side of 45 patients with COPD and 19 healthy individuals using ultrasound before, during, and after an eight-week high-intensity knee extensor resistance training. Authors observed that serial ultrasound measurements of quadriceps detected changes in muscle mass of patients with COPD in response to resistance training [24].

Conclusion

PR based on rehabilitation principles reduced echo intensity of quadriceps and improved pulmonary function, respiratory muscle strength and endurance, and thickness of diaphragm and quadriceps femoris in patients with post-COVID-19 syndrome.

References

1. Santana AV, Fontana AD, Pitta F. Pulmonary rehabilitation after COVID-19. J Bras Penumol 2021;47:e20210034.
2. Liu K, Zhang W, Yang Y, et al. Respiratory rehabilitation in elderly patients with COVID-19: a randomized controlled study. Complement Ther Clin Pract 2020;39:101166.
3. França EET, Junior UE, Schwingel PA, et al. Distinct phenotypes in COVID-19 may require distinct pulmonary rehabilitation strategies. Monaldi Arch Chest Dis 2020;90:1523.
4. Song F, Shi N, Shan F, et al. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology 2020;295:210-7.
5. Goertz YMJ, Herck MV, Delbressine JM, et al. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? ERJ Open Res 2020;6:00542-2020.
6. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur Respir J 2005;26:319-38.
7. Pereira CAC, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. J Bras Pneumol 2007;33:397-406.
8. Neder JA, Andreoni S, Lerario MC, et al. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. Braz J Med Biol Res 1999;32:719-27.
9. Dias FD, Sampaio LMM, Silva GA, et al. Home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomized clinical trial. Int J Chron Obstruct Pulmon Dis 2013;8:537-44.
10. Chang AT, Boots RJ, Brown MG, et al. Reduced inspiratory muscle endurance following successful weaning from prolonged mechanical ventilation. Chest 2005;128:553-9.
11. Guarracino F, Vetrugno L, Forfori F, et al. Lung, heart, vascular, and diaphragm ultrasound examination of COVID-19 patients: A comprehensive approach. J Cardiothorac Vasc Anesthesia 2021;35:1866-74.
12. Lima RVSA, Fernandes JS, Sousa ASL, et al. Ultrasound analysis of the quadriceps femoris of critically ill patients on mechanical ventilation. Conscientiae Saude 2020;19:1-14, e17090.

13. Annetta MG, Pittiruti M, Silvestri D, et al. Ultrasound assessment of rectus femoris and anterior tibialis muscles in young trauma patients. Ann Intensive Care 2017;7:104.
14. Paris MT, Mourtzakis M, Day A, et al. Validation of bedside ultrasound of muscle layer thickness of the quadriceps in the critically ill patient (VALIDUM study) a prospective multicenter study. JPEN J Parenter Enteral Nutr 2017;41:171-80.
15. Abodonya AM, Abdelbasset WK, Awad EA, et al. Inspiratory muscle training for recovered COVID-19 patients after weaning from mechanical ventilation. A pilot control clinical study. Medicine (Baltimore) 2021:100:13.
16. Silva CM, Neto MG, Saquetto MB, et al. Effects of upper limb resistance exercise on aerobic capacity, muscle strength, and quality of life in COPD patients: a randomized controlled trial. Clin Rehabil 2018;32:1636-44.
17. Tozato C, Ferreira BFC, Dalavina JP, et al. Cardiopulmonary rehabilitation in post-COVID-19 patients: case series. Rev Bras Ter Intens 2021;33:167-71.
18. Lewis KL, Helgeson SA, Tatari MM, et al. COVID-19 and the effects on pulmonary function following infection: A retrospective analysis. EClinicalMedicine 2021;39:101079.
19. Chikhanie YA, Veale D, Schoeffler M, et al. Effectiveness of pulmonary rehabilitation in COVID-19 respiratory failure patients post-ICU. Respir Physiol Neurobiol 2021;287:103639.
20. Nepomuceno BRV Junior, Gomes-Neto M. [Treinamento muscular inspiratório no ambiente hospitalar: protocolo para um ensaio clínico randomizado].[Article in Portuguese]. Rev Pesquisa Fisioter 2016;6:896.
21. Lima EVNCL, Lima WL, Nobre A, et al. Inspiratory muscle training and respiratory exercises in children with asthma. J Bras Pneumol 2008;34:552-8.
22. Nascimento LP, Andrade ALM, Faria TCC, et al. [Treinamento muscular respiratório em Distrofia Muscular de Duchenne: Série de casos].[Article in Portuguese]. Rev Neurocien 2015;23:9-15.
23. Crimi C, Heffler E, Augelletti T, et al. Utility of ultrasound assessment of diaphragmatic function before and after pulmonary rehabilitation in COPD patients. Int J Chron Obstruct Pulmon Dis 2018;13:3131-9.
24. Menon MK, Houchen L, Harrison S, et al. Ultrasound assessment of lower limb muscle mass in response to resistance training in COPD. Respir Res 2012;13:119.