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Additional Information

- 1 Effects of Resistance Training of Peripheral Muscles versus Respiratory Muscles in
- 2 Institutionalized Older Adults with Sarcopenia: A Randomized Controlled Trial
- 3

## 1 Abstract

2 This study compares the effects of two resistance training programs in peripheral and  
3 respiratory musculature on muscle mass and strength and physical performance, and identify  
4 the appropriate muscle mass parameter for assessing the intervention effects. Thirty-seven  
5 institutionalized older Spanish adults with sarcopenia were analyzed: Control Group (n=17),  
6 Respiratory Muscle Training Group (n=9) and Peripheral Muscle Training Group (n=11). Pre  
7 and post-intervention, participants were assessed for Appendicular Skeletal Mass  
8 (ASM/height<sup>2</sup>; ASM/weight; ASM/BMI), isometric knee-extension, arm-flexion and handgrip  
9 strength, Inspiratory and Expiratory Maximal Pressures (MIP and MEP), and gait speed.  
10 Trained groups participated in a 12-week program and improved in MIP, MEP, knee-  
11 extension and arm-flexion ( $p<.05$ ), while nonsignificant changes were showed in gait speed  
12 and ASM indexes between pre and post-intervention in the three groups. In conclusion,  
13 resistance training improved skeletal muscle strength in the studied population, and any ASM  
14 index was found to be appropriate in detecting changes after physical interventions.

15

16 *Keywords:* aging, nursing homes, muscle strength, exercise training, prevention

17

18

1           The presence of comorbidity and other factors such as physical inactivity in older  
2 people favor the onset of sarcopenia (Cruz-Jentoft et al., 2010). The prevalence of this  
3 geriatric syndrome in institutionalized older adults is around 14-33% in Europe (Cruz-Jentoft  
4 et al., 2014), and even higher in Spain (37%) (Salvà et al., 2016).

5           The European Working Group on Sarcopenia in Older People (EWGSOP) defines this  
6 syndrome as a gradual and widespread loss of skeletal muscle mass and strength. As a result,  
7 mobility disorders appear, such as an increased risk of falls and fractures, impaired ability to  
8 perform daily living activities, loss of independence, a worsening of comorbidity and an  
9 increased risk of death (Cruz-Jentoft et al., 2010). Recently, the International Working Group  
10 on Sarcopenia (IWGSP) and Asian Working Group for Sarcopenia (AWGSP) shared this  
11 definition but both groups suggested working towards a more appropriate selection of  
12 diagnostic cut-off values (Wei-Ju, Li-Kuo, Li-Ning, Ming-Hsien & Liang-Kung, 2013; Chen  
13 et al., 2014). In this respect, recent studies (Meng et al., 2015; Ethgen et al., 2016; Kim et al.,  
14 2016) emphasize the need to personalize the cut-off values according to the characteristics of  
15 the studied population (anthropometrics, ethnic and clinical setting).

16           Previous literature points out that this loss affects the skeletal muscles involved in both  
17 mobility (limb or peripheral muscles, PMs) and ventilation (respiratory muscles, RMs).  
18 Enright et al. (1994) and Neder et al. (1999) corroborate the association between the strength  
19 of the PMs and RMs. In studies of institutionalized older adults, the prevalence of decreased  
20 strength of the PMs and RMs is clear (Simões, Castello, Auad, Dionísio & Mazzonetto, 2009;  
21 Simões, Dias, Marinho, Pinto & Britto, 2010; Cruz-Jentoft et al., 2010). Authors such as  
22 Newman et al. (2003) suggest that during aging the decline in lower limb muscle strength is  
23 greater than in upper limbs, and is associated with lower gait speed and increased risk of  
24 disability. Moreover, dysfunction of the RMs is accompanied by a reduced tolerance

1 requirement associated with the basic activities of daily living, and in some extreme cases  
2 with respiratory failure (Bahat et al., 2014).

3         In addition, most Systematic Reviews and Meta-Analysis for Sarcopenia in older  
4 adults (Cruz-Jentoft et al., 2014; Beaudart, Zaaria, Pasleau, Reginster & Bruyère, 2017)  
5 suggest exercise interventions (mainly resistance exercises) can improve muscle strength and  
6 physical performance, with the majority of these studies being carried out in older adults  
7 living in the community. In this respect, it is worth considering extending the research to  
8 older adult groups living in other settings, such as hospitals and nursing homes. Currently,  
9 studies show high prevalence of sarcopenia in older adults residing in nursing homes (Landi  
10 et al., 2012; Henwood, Keogh, Reid, Jordan & Senior, 2014) and initial results regarding  
11 resistance training on sarcopenia in nursing care facilities are emerging. These are mainly  
12 focused on the improvement in the strength of only the peripheral muscles (Hassan et al.,  
13 2016) or of the respiratory muscles (Cebrià i Iranzo, Arnall, Igual Camacho, Tomás &  
14 Meléndez, 2013), but there is a lack of studies which compare both resistance training  
15 interventions.

16         It is assumed that the physical intervention in the institutionalized older adults is  
17 accompanied by lower benefits (Cruz-Jentoft et al., 2011). The clinical novelty of this study is  
18 showing that resistance exercise interventions in nursing homes may improve, or at least  
19 control, the deterioration that sarcopenia entails in older adults, as well as reduce the risk of  
20 mortality associated to muscle strength (Newman et al., 2006). On the other hand, it  
21 highlights the use of this exercise intervention as a routine in the socio-sanitary planning of  
22 nursing homes.

23         In light of the above, and considering the importance of preventing sarcopenia effects  
24 in institutionalized older people, the main objective of this study was to compare the effects of  
25 two resistance training programs in peripheral and respiratory musculature on muscle mass

1 and strength and physical performance. And a secondary objective was to compare and  
2 identify which parameters relative to muscle mass are the appropriate for assessing the effects  
3 of resistance training programs in institutionalized older adults in Spain. We hypothesize that  
4 resistance training would improve muscle mass and strength, and physical performance in  
5 older adults with sarcopenia, although these effects would depend on the specific resistance  
6 training program (PM or RM training).

## 7 **Method**

### 8 **Study design**

9 This study was designed as a parallel group randomized controlled trial in which 81  
10 institutionalized older Spanish adults with sarcopenia were randomized on a single sequence  
11 (simple randomization) to one of three balanced groups: One Control Group (CG) and two  
12 resistance training groups (Peripheral Muscle Training Group (PMTG) and Respiratory  
13 Muscle Training Group (RMTG)). A flow diagram (Figure 1) describes the participant  
14 eligibility, randomization, lost to follow-up and data analysis. A statistician who had no  
15 contact with the participants and/or the health care professionals who undertook the  
16 measurements and the intervention performed the random allocation sequence (random  
17 number generator in SPSS; SPSS, Inc, Chicago, Illinois). The three groups were followed in  
18 the same way and the only difference between them was the received care. CG participants  
19 obtained standard treatment and were asked to maintain their usual care and daily life  
20 activities at the nursing home (lying down, sitting, and walking short distances between  
21 rooms). Participants of the intervention groups (PMTG and RMTG) also carried out a  
22 resistance training program for 12 weeks.

23 INSERT FIGURE 1 ABOUT HERE

24 The University of XXXX Ethics Committee for Human Research (H1382044172319)  
25 approved this study. All participants were informed of the risks and benefits, and agreed to

1 participate by signing a consent form. This study was performed between 2013 and 2016, and  
2 has been registered in the ClinicalTrials.gov (NCT ID: NCT02120586).

### 3 **Participants**

4         The sample was made up of all eligible older adults from four nursing homes located  
5 in XXXX, Spain. The nursing homes involved met similar criteria in relation to classification  
6 of the participants and had similar professional health services. Participants met the following  
7 inclusion criteria: (1) Older than 65 years; (2) clinically stable at least two months before the  
8 study; and (3) compliance of the sarcopenia diagnostic criteria proposed by Tyrovolas et al.  
9 (2015) which include: (a) Skeletal Muscle Mass Index (SMI = Appendicular Skeletal Muscle  
10 Mass/Body Mass Index) with cut-off points for Spanish population ( $\leq 0.93$  for male and  $\leq$   
11  $0.57$  for female) and (b) gait speed with cut-off points according to sex, height and age  
12 (between  $0.95$ - $0.66$  m/s for male and  $0.80$ - $0.48$  m/s for female). Exclusion criteria were as  
13 follows: (1) Those clinical situations (signs and/or symptoms) that could interfere in the  
14 proper performance of assessment and/or training protocols (i.e.: presence of edema or severe  
15 disorder of hydration status that could interfere in Bioelectrical Impedance Analysis  
16 (Rubbieri, Mossello, & Di Bari, 2014), malnutrition, muscle-joint pain, tremor or dyspnea at  
17 rest, recent fracture or surgery, etc.); (2) a terminal disease diagnosis; and (3) moderate or  
18 severe cognitive deterioration that could affect their proper collaboration (Mini-Mental State  
19 Examination score  $\leq 20$  points) (Lobo, Saz, & Marcos, 2002).

### 20 **Measurements**

21         Participants were assessed at enrollment phase (T1), after a 2-week familiarization  
22 (T2, baseline or pre-intervention) and at 12 weeks (T3, post-intervention). The reason for  
23 repeating two close assessments (T1 and T2) was to avoid the possible learning effect of tests.  
24 These assessments were conducted by researchers who were trained in the procedures by an  
25 expert before the data collection period and who were blind to the purpose of the study and

1 the participants' group membership. Tests were performed over two consecutive days to  
2 avoid participant fatigue and to get the highest value.

### 3 **Outcomes and Procedures**

4 Each time-point measurements (T1-T3) recorded the following outcomes:

5 ***Skeletal Muscle Mass.*** Bioimpedance Analysis (BIA) technique was used to assess muscle  
6 mass (Kg) using a Bodystat<sup>®</sup> 1500MDD (Bodystat Ltd., Douglas, Isle of Man, UK).

7 Measurements were obtained under recommended standard conditions (NIH, 1996):

8 participants in supine position on their bed, on waking up and with an empty stomach, upper  
9 and lower limbs of predominant side abducted at least 30-degree angle from the medium line,  
10 and controlled bedroom temperature of 25 degree. The equipment calibration, individual data  
11 introduction (sex, age, height and weight) and skin preparation for the placement of the  
12 adhesive electrodes on the wrist and the ankle of the predominant side were prepared  
13 previously. According to Meng et al. (2015) and Kim, Jang & Lim (2016) the skeletal mass  
14 index was defined as Appendicular Skeletal Muscle Mass (ASM), after being adjusted in  
15 different ways: height ( $ASM/height^2$ ), weight ( $ASM/weight$ ) or Body Mass Index  
16 ( $ASM/BMI$ ).

17 ***Peripheral Muscle Strength.*** Maximal isometric muscle strength (Kg) was assessed with the  
18 dynamometer MicroFet 2<sup>®</sup> (Hoggan Health industries, West Jordan, UT, USA) on the  
19 predominant side for three consecutive trials with at least a 1 minute resting period between  
20 them. Previous strength testing, a 5-minute warm-up for lower and upper limbs on the  
21 Monark<sup>®</sup> Rehab Ergometer Trainer (Monark 881E; Vansbro, Sweden) was performed.

22 Participants remained in a seated position with the muscle to be evaluated in relative  
23 shortening position, maintaining a maximal and sustained contraction for at least 3 seconds.

24 The movements tested were: knee-extension (*Quadriceps Femoris*) and elbow-flexion (*Biceps*  
25 *Brachii*) (Bean et al., 2002).



1           The maximal handgrip strength (Kg) was measured with a hydraulic hand  
2 dynamometer Jamar Plus+<sup>®</sup> (Patterson Medical, Sammons Preston, Bolingbrook, IL, USA).  
3 Participants remained seated, the dynamometer in the dominant hand, with the elbow locked  
4 at 90° and at their side. Predicted values (%) for handgrip strength were also registered (Luna-  
5 Heredia, Martín-Peña & Ruiz-Galiana, 2005). Three consecutive measurements were made on  
6 the predominant side upper limb with a between-measurement interval of 1 minute.

7 ***Respiratory Muscle Strength.*** Maximum static inspiratory pressure (MIP, cmH<sub>2</sub>O) and  
8 maximum static expiratory pressure (MEP, cmH<sub>2</sub>O) were measured using a MicroRPM<sup>®</sup>  
9 (Respiratory Pressure Meter, CareFusion, Hoechberg, Germany) according to the Black &  
10 Hyatt technique (1969). These strength measurements followed the standard guidelines  
11 established by the ATS/ERS Statement on respiratory Muscle Testing (2002). Predicted  
12 values (%) for both MIP and MEP were also registered by using the reference values reported  
13 by Enright, Kronmal, Manolio, Schenker & Hyatt (1994).

14 For peripheral and respiratory muscle strength data, the highest value was recorded.

15 ***Respiratory Muscle Endurance.*** Maximum Voluntary Ventilation test (MVV, L/min) was  
16 measured following the standard guidelines established by the ATS/ERS Statement on  
17 respiratory Muscle Testing (2002), using a portable Jaeger<sup>®</sup> spirometer as referred to above.

18 ***Physical Performance.*** Maximal gait speed (m/s) was collected as participants walked as fast  
19 as they safely could on a marked 14 m walkway. Participants started and finished walking two  
20 meters before and after the walkway to ensure the participants reached a steady state gait  
21 speed across the middle 10 meters (Tilson et al., 2010). Each participant performed two  
22 consecutive trials with a one minute resting period between them, and the highest value was  
23 recorded. Pulse oximetry was registered during the test and the participants were asked about  
24 their subjective effort perception by the Borg CR10 Scale (Borg, 2004).

## 25 **Interventions**

1 Both intervention groups participated in a 12-week training program, three times a  
2 week on alternate days, in groups of eight to ten participants. All training sessions were  
3 supervised by two physiotherapists not involved in assessments (T1-T3). Previously,  
4 familiarization consisted of six sessions to guarantee appropriate realization was performed  
5 with low training workload (5-10% of maximal muscle strength (Kg) for PMTG and 7-9  
6 cmH<sub>2</sub>O for RMTG). Since some of the participants could not remain standing, the training  
7 was performed in a sitting position. Each session was structured in four phases: (1) Record of  
8 resting blood pressure, heart frequency and oxygen saturation (SpO<sub>2</sub>); (2) an initial 5-minutes  
9 warm-up; (3) resistance exercises with workload during 20 to 30 minutes; and (4) a final 5-  
10 minute cool-down to recover baseline condition. Individual training journals were kept on the  
11 progress of each participant documenting the increases in training workload as well as  
12 recording their perceived exertional efforts (Borg CR10 Scale) and any complaints related to  
13 training program reported by the participants. In order to ensure that each participant was  
14 training with the appropriate workload, a monthly measurement was performed. Participants  
15 who attended less than 80% of the sessions in both programs were dropped from the analyses.

16 ***Peripheral Muscle Training (PMT)*** consisted of ten isotonic resistance exercises, 12  
17 repetitions for each one, completing the maximum mobility at a slow speed, working both  
18 concentric and eccentric phases and with two minutes recovery time between them.

19 Resistance exercises were performed with a workload adjusted to 40- 60% of maximal  
20 isometric muscles strength (Kg), except when participants did not complete the maximum  
21 mobility, in which case the workload was reduced. Exercises were performed with dumbbells  
22 and ankle/wrist weights: four lower limb exercises (ankle flexion/extension, knee extension,  
23 and hip flexion/abduction/adduction) and six upper limb exercises (handgrip, wrist  
24 flexion/extension, forearm pronation/supination, elbow flexion/extension, and shoulder  
25 flexion/extension/adduction/abduction).

1 **Respiratory Muscle Training (RMT)** was carried out using a Threshold Inspiratory Muscle  
2 Trainer device (Respironics<sup>®</sup> Health Scan Inc. Cedar Grove, NJ, USA) with working range of  
3 7–41 cmH<sub>2</sub>O. An interval-based Inspiratory Muscle training program was performed  
4 consisting of seven 2-minute cycles of loaded breathing interspersed with a 1 minute period of  
5 rest between cycles (Hill, Cecins, Eastwood & Jenkins, 2010). The workload was adjusted to  
6 40-60% of MIP (cmH<sub>2</sub>O), except when participants did not complete the interval-training  
7 program, in which case the workload was reduced. The physiotherapists monitored the  
8 participants throughout the training session with a pulse oximeter (SpO<sub>2</sub> and heart frequency).  
9 In this way, each participant adopted their own and comfortable respiratory rate, avoiding  
10 undesirable desaturations and/or heart rate increases, as well as the occurrence of symptoms  
11 due to hyperventilation.

## 12 **Statistical Analyses**

13 A priori sample size calculations were obtained with the statistical program G\*power  
14 3.1 (Faul, Erdfelder, Lang & Buchner, 2007), with an expected effect size (f) from medium to  
15 large, alfa of .05 and statistical power of .80. This resulted in an a priori total sample size of  
16 72 participants, or 24 per group.

17 Analyses were conducted using the statistical software Statgraphics Centurion XVI.II.  
18 All data were checked for outliers, normal distributions (Shapiro-Wilk test), and homogeneity  
19 of variance (Levene's test).

20 Descriptive statistics were conducted for all variables at pre-intervention (T2).  
21 Moreover, pre-intervention differences of the variables between groups were examined to test  
22 whether any clinical or anthropometric variable could be included as a covariate in the  
23 analysis of variance (ANOVA). For this purpose, one-way ANOVA was conducted for all  
24 continuous variables and chi-square tests were used for categorical variables.

1 Treatment effects between the three groups (PMTG, RMTG, CG) were determined using one-  
2 way ANOVA on change from pre-intervention, defined as post-intervention (T3) minus pre-  
3 intervention (T2) values for each variable. Change analysis was used to offset possible  
4 differences of participants at pre-intervention and to minimize group data variability. Within-  
5 group differences were assessed using paired t tests to compare mean change values.  
6 Between-group differences were calculated using a three-way ANOVA with group  
7 cardiovascular disease and endocrine disease as factors. Cardiovascular disease and endocrine  
8 disease were included as (categorical) covariates to eliminate the variability attributable to  
9 these variables. *Post-hoc* analyses were performed using Tukey's highly significant difference  
10 test when a significant effect was found. Statistical significance was set at  $p < .05$  for all tests.

## 11 **Results**

### 12 **Participants**

13 The analyzed sample was made up of 37 older adults. The flow diagram (Figure 1)  
14 shows 44 drop-outs, the main reasons being: deaths, exacerbations, attendance less than 80%  
15 of sessions in trained groups, and withdraws (i.e. changing to another nursing home, falls,  
16 personal reasons and complaints). Deaths during the study development were as a result of the  
17 participants' illnesses, and not from factors related to the measurements and/or training  
18 programs. Main complaints reported by participants occurred within the first two weeks of  
19 training and the most common were: difficulty in keeping the lips constrained in the  
20 mouthpieces of IMT device and nasal discomfort from nose clip placement during the session,  
21 in the RMTG; mild muscular discomfort and generalized fatigue that disappeared between  
22 sessions, in the PMTG.

### 23 **Descriptive**

#### 24 *Baseline characteristics*

1 Pre-intervention characteristics of the three groups are presented in Table 1. Initially,  
2 the three groups did not show differences, except for cardiovascular ( $p = 0.02$ ) and endocrine  
3 ( $p = .04$ ) diseases. PMTG participants presented a higher number of cardiovascular and  
4 endocrine dysfunctions in comparison with the other two groups.

5 INSERT TABLE 1 ABOUT HERE

## 6 **Effects of the training programs**

7 Results from the within-group and the between-group effects over the main outcomes  
8 are summarized in Table 2. No effects were found from endocrine and cardiovascular disease  
9 in any variables between pre and post-intervention in the three groups.

10 INSERT TABLE 2 ABOUT HERE

### 11 ***Skeletal Muscle Mass***

12 No significant changes were detected in any of the skeletal muscle mass measures  
13 (ASM /height<sup>2</sup>, ASM/weight and ASM/BMI) between pre and post-intervention in the three  
14 groups.

### 15 ***Peripheral Muscle Strength***

16 A significant decrease occurred from pre to post-intervention in CG for *Quadriceps*  
17 *Femoris* (13.1%;  $t(11) = -2.33$ ;  $p = .040$ ) and *Biceps Brachii* (23.8%;  $t(11) = -2.84$ ;  $p = .016$ ).  
18 Nevertheless, results for the PMTG showed a significant increase in *Quadriceps Femoris*  
19 (51.9%;  $t(6) = 3.66$ ;  $p = .011$ ) and *Biceps Brachii* (17.4%;  $t(7) = 2.40$ ;  $p = .048$ ). For the  
20 RMTG, *Quadriceps Femoris* showed an increasing trend (9.1%;  $t(7) = .18$ ;  $p = .859$ ) while  
21 *Biceps Brachii* showed a significant decrease (16.7%;  $t(8) = -2.34$ ;  $p = .048$ ).  
22 Moreover, significant differences in peripheral muscle strength between groups were also  
23 observed for both *Quadriceps Femoris* ( $p = .009$ ) and *Biceps Brachii* ( $p = .003$ ). Post hoc  
24 analysis for *Quadriceps Femoris* strength showed that increases were greater in PMTG than

1 for CG participants. For *Biceps Brachii* strength, changes for the PMTG were greater than  
2 changes for the other two groups.

3 No significant changes were seen in dominant handgrip strength values between pre  
4 and post-intervention. The same effects were detected for handgrip strength predicted values.

### 5 ***Respiratory Muscle Strength***

6 The within-group ANOVA revealed significant differences in MIP and MEP values  
7 for CG between pre and post-intervention. CG subjects decreased their MIP and MEP with a  
8 mean of 8.2% ( $t(12) = -2.62, p = .022$ ) and 15.6% ( $t(12) = -2.32, p = .039$ ), respectively.

9 PMTG showed a nonsignificant ascending trend of 13.5% in MIP ( $t(8) = 1.86, p = .100$ ) and  
10 of 3.9% in MEP ( $t(8) = 0.63, p = .548$ ). Likewise, changes from pre to post-intervention in  
11 these variables for RMTG were also found to be statistically nonsignificant.

12 ANOVA comparisons between groups revealed significant differences for MIP ( $p = .007$ ) and  
13 MEP ( $p = .040$ ). Post hoc analysis showed greater changes for PMTG and RMTG compared  
14 to CG.

15 Similar effects were detected for MIP and MEP predicted values.

### 16 ***Respiratory Muscle Endurance***

17 Changes in MVV were statistically significant in the CG ( $t(12) = -3.22, p = .007$ ),  
18 showing a 19.6% reduction from pre to post-intervention, while no significant changes were  
19 detected for both intervention groups (RMTG and PMTG). However, ascending trend values  
20 of 8.8% were seen for MVV in the PMTG ( $t(8) = 1.80, p = .110$ ).

21 Between-group ANOVA showed significant differences for MVV ( $p = .020$ ). Post hoc  
22 analysis showed that changes in MVV for the PMTG and RMTG were greater than changes  
23 in the CG.

### 24 ***Physical Performance***

25 Gait speed remained unchanged from pre to post-intervention in the three groups.

### 1 **Training load**

2 Training loads in RMTG (Table 3) significantly improved during the training sessions both  
3 for absolute values ( $F_{11,220} = 130.2, p < .001, \eta^2 = .867$ ) and the percentages ( $F_{11,220} = 33.3, p$   
4  $< .001, \eta^2 = .625$ ). Similar findings were obtained for PMTG (Table 3) in *Biceps Brachii*  
5 (absolute values  $F_{11,55} = 14.9, p = .005, \eta^2 = .749$ ; percentages  $F_{11,55} = 19.7, p = .002, \eta^2 =$   
6  $0.797$ ) and *Quadriceps Femoris* (absolute values  $F_{11,44} = 50.6, p < .001, \eta^2 = .927$ ;  
7 percentages  $F_{11,44} = 41.0, p < .001, \eta^2 = .911$ ).

### 8 **Discussion**

9 This study revealed that resistance training mainly improved the skeletal muscle  
10 strength in institutionalized older people, while there were no significant changes in physical  
11 performance and muscle mass for both training groups. Therefore, the most relevant finding  
12 of this study remained in counteracting the loss of muscle strength in this population. This  
13 result suggests that muscle strength was more sensitive to change, which declines  
14 significantly in the Control Group throughout the 3-month intervention. The improvement in  
15 muscle strength is more remarkable in the peripheral muscles (where there is a significant  
16 increase in the specifically trained group) than in the respiratory ones. Moreover, there was no  
17 evidence to suggest that one specific muscle mass index ( $ASM/height^2$ ,  $ASM/weight$  and  
18  $ASM/BMI$ ) was more appropriate than another when assessing the effects of the 3-month  
19 resistance training.

20 These results, as stated in a recent systematic review about sarcopenia by Cruf-Jentoft  
21 et al. (2014), reinforce the need to perform peripheral muscle resistance training in older  
22 adults. For example, Binder et al. (2005) obtained an improvement in voluntary knee-  
23 extension force through progressive resistance training in frail older adults living in the  
24 community. In our study, the peripheral muscle strength was assessed by maximal isometric  
25 *Quadriceps Femoris* and *Biceps Brachii* strength and also showed an improvement, while

1 there was no significant effect seen in handgrip strength. In this respect, a recent pilot study  
2 implemented in nursing home participants (Hassan et al., 2016) demonstrated an  
3 improvement in muscle strength (dominant handgrip measurement) as a consequence of a  
4 longer period of intervention (six months), including balance training. Tieland et al. (2015)  
5 doubt if handgrip is a good measurement to detect changes in muscle strength derived from  
6 resistance training in frail older people because measurements could vary depending on age,  
7 sex and nutrition, as also pointed out by Budziareck, Roig, & Barbosa (2008). In the present  
8 study, the improvement in *Quadriceps Femoris* and *Biceps Brachii* strength was important for  
9 two reasons; firstly, because there was a substantial reversion of the muscle strength loss in  
10 Control Group, and secondly because there was a significant increase in the peripheral trained  
11 group.

12         The present study demonstrated nonsignificant improvement in RM functioning in the  
13 RMTG. However, when compared with the CG values, it showed a significant improvement.  
14 This result suggests that respiratory muscle training has a preventive function as RM values  
15 were maintained in institutionalized older adults with sarcopenia. This is relevant, bearing in  
16 mind the high prevalence of RM strength decline in this group of the population (Simões,  
17 Castello, Auad, Dionísio & Mazzonetto, 2009; Simões, Dias, Marinho, Pinto & Britto, 2010).  
18 According to Bahat and colleagues (2014), the decline affects more inspiratory than  
19 expiratory muscle strength in sarcopenic older adults. Another explanation for this  
20 nonsignificant improvement in RM functioning in the trained group could be the short  
21 program duration or amount of sessions (Cebrià i Iranzo, Arnall, Igual Camacho, Tomás &  
22 Meléndez, 2013). Despite following recommendations for an Inspiratory Muscle Training  
23 program (intensity, frequency and duration) for Chronic Obstructive Pulmonary patients  
24 proposed by Hill, Cecins, Eastwood & Jenkins (2010) and Gosselink et al. (2011), these have  
25 been insufficient for the characteristics of our study population. Moreover, Current



1 recommendations for resistance training in sarcopenic older adults (Cruz-Jentoft et al., 2014)  
2 point out that the time of intervention should be at least 3 months.

3         As it has been commented in the Results section, the rise in the training load was  
4 observed both for the inspiratory muscle strength (MIP) and for peripheral muscle strength  
5 (maximal isometric muscle strength of *Biceps Brachii* and *Quadriceps Femoris*). This shows  
6 that the intensity of training increased progressively. Moreover, this increase has exceeded the  
7 percentage of load that has been considered high enough to achieve the training adaptations.  
8 Although the planning contemplated training at loads between 40 and 60%, the participants  
9 trained with the load they were able to lift.

10         The current study revealed a maintenance of gait speed after training, as was also  
11 demonstrated in the study carried out by Hassan et al. (2016). A possible explanation could be  
12 that our training program did not include specific exercises to improve mobility, such as  
13 aerobic training and balance reeducation. These authors combine resistance and balance  
14 training without obtaining significant gain in the gait speed. Nevertheless, there was an  
15 improvement in standing capacity.

16         As mentioned above, the evolution of the muscle mass indexes along time (pre-post-  
17 intervention) was similar in both the control group and the trained ones. That is, it remained  
18 relatively stable for all three groups. In this respect, a pilot study implemented in nursing  
19 home participants also obtained similar results (Hassan et al., 2016). Though the result in  
20 muscle mass after training was unexpected, the improvement of muscle strength is a positive  
21 result because this could help prevent disability in institutionalized older adults. Ivey et al.  
22 (2000) and Hassan et al. (2016) suggest that the resistance training might induce functional  
23 (consequence of neural and/or metabolic muscle responses) versus structural (muscle cross  
24 sectional area) adaptations.

1           Sarcopenia is related to factors such as comorbidity, mobility disorders and  
2 malnutrition, thus experts (EWGSOP, IWGSP, AWGSP y el FNIH) recommend combining  
3 exercise and nutrition interventions. Recent literature reviews (Denison, Cooper, Sayer &  
4 Robinson, 2015; Yu, Khaw, Jadcak & Visvanathan, 2016) highlight inconsistent results  
5 mainly due to heterogeneity of population (age, sex, anthropometrics, settings, etc.) and  
6 intervention characteristics (resistance versus aerobic, diversity in nutrition supplementation,  
7 etc.). The majority of published trial findings were carried out on healthy older adults living  
8 in the community (Bell et al., 2017) and in sarcopenic older adults (Rondanelly et al., 2016).  
9 In settings such as nursing homes or hospitals there is still a lack of these combined  
10 interventions (Bauer, Kaiser & Sieber, 2008), and their results are also inconsistent (Carlsson  
11 et al., 2011).

12           The EWGSOP (Cruz-Jentoft et al., 2010) define sarcopenia as low muscle mass and  
13 /or both low muscle strength and low gait. Nowadays, there is an important debate on muscle  
14 mass cut-off (Pagotto y Silveira, 2014; Studensky et al., 2014; Moon et al., 2016), arguing  
15 that they should be considered and adapted to older population characteristics and settings  
16 (Tyrovolas et al., 2015; Meng et al., 2015; Kim, Jang & Lim, 2016), in order to avoid the  
17 infra-diagnostic of sarcopenia. For this reason, our study has included different muscle mass  
18 parameters (ASM/height<sup>2</sup>; ASM/weight; ASM/BMI) as proposed by Tyrovolas et al., (2015).  
19 With regards to the characteristics of our studied population (Spanish, institutionalized and  
20 obese, BMI > 30 Kg/m<sup>2</sup>), we considered the appropriate parameters to be those related to  
21 weight (ASM/weight; ASM/BMI) instead of the one usually applied (ASM/height<sup>2</sup>). We  
22 assessed which of these parameters was more sensitive for showing an improvement after  
23 resistance training in sarcopenic institutionalized older adults, and the findings were unclear  
24 because all parameters behaved similarly.

1           Our study has several limitations. The analyzed sample diminishes considerably with  
2 respect to the participants' characteristics (Table 1) such as high comorbidity and advanced  
3 age ( $M_{\text{age}} > 80$  years), functional impairment and whether they live in a nursing home. This  
4 lost in the follow-up is common in other nursing home research studies (Mody et al., 2008;  
5 Hassan et al., 2016). We consider only the sarcopenia status for inclusion criteria and  
6 outcomes rather than the Fragility status, which contemplates additional functional  
7 parameters. We did not include follow-up of maintenance of resistance training effects.  
8 Despite ASM being a variable used infrequently in previous clinical trials, which makes it  
9 difficult to make direct comparison with our trial, we decided to use ASM indexes proposed  
10 by Tyrovolas et al. (2015) which are specific cut-offs for Spanish population. Furthermore,  
11 ASM might be more appropriate for detecting possible changes in upper and lower limbs  
12 muscles. Finally, this trial did not collect physical activity as outcome.

13           Nonetheless, this study has some distinctive strengths. We compared two resistance  
14 training protocols: One in respiratory muscles and one in peripheral muscles, both skeletal  
15 muscles affected by sarcopenia syndrome. Following the current international debate on  
16 reviewing the definition of sarcopenia, we have used the criteria of Tyrovolas et al. (2015) for  
17 muscle mass measurement (ASM/BMI) specific for older Spanish people. Finally, as a  
18 relevant clinical finding, the improvement of muscle strength may be associated to a lower  
19 risk of mortality, as suggested by Newman and colleagues (2006). In this line, the  
20 improvement of peripheral muscle strength, as well as the absence of loss of this in the  
21 respiratory musculature in our study, may lead to a lower risk of mortality.

22           Mainly this clinical trial shows an improvement in the skeletal muscle strength in  
23 institutionalized older adults with sarcopenia. This benefit can be extended to the older  
24 population with sarcopenia, both at the community and nursing homes. To achieve this, health  
25 professionals' collaboration might be necessary in order to inform, encourage and supervise

1 the training programs (health promotion programs in primary care and the improvement of  
2 rehabilitation programs in nursing homes).

### 3 **Conclusion**

4 This resistance training has demonstrated an improvement in skeletal muscle strength  
5 (MR and MP) in institutionalized older adults with sarcopenia, indicating its preventive  
6 character and the potential benefit in carrying out the training in presarcopenic  
7 institutionalized older adults. However, there was no significant improvement in muscle mass,  
8 in spite of measuring it through different parameters to avoid sarcopenia infra-diagnosis and  
9 detect the training effects appropriately. Consequently, there are two fundamental  
10 considerations rising from this study: Firstly, the necessity to adapt the physical exercise  
11 program by taking into account the specificity of the population and the desired functional  
12 outcome (improvement in muscle strength, walking speed, transfers, etc.); secondly, to  
13 combine physical exercise intervention with nutritional supplementation.  
14 Finally, regarding the debate around cut-offs, this study does not clarify which muscle mass  
15 parameter is the appropriate for detecting changes after physical interventions. As a result, the  
16 discussion continues on how to propose interventions and how to measure their effects on  
17 sarcopenia in the institutionalized older adult population.

18

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