Experimental Gerontology 135 (2020) 110884

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Osteosarcopenic obesity markers following elastic band resistance training: A randomized controlled trial

Ebrahim Banitalebi*,[1], Mohammad Faramarzi[1], Majid Mardaniyan Ghahfarokhi[1], Farideh SavariNikoo[1], Neda Soltani[1], Azita Bahramzadeh[1]

Department of Sport Sciences, Shahrekord University, Shahrekord, Iran

ARTICLE INFO

Section Editor: Emanuele Marzetti

Keywords:
Osteosarcopenic obesity markers
Resistance training
Randomized controlled trial

ABSTRACT

The main purpose of present study was to investigate the effects of elastic band resistance training (EBRT) on muscle quality (MQ), serum osteosarcopenic obesity (OSO) biomarkers, bone density and functional profile in women living with OSO syndrome. The eligible participants, aged 65 to 80 years, were selected by a physician. Accordingly, a total number of 63 women with OSO syndrome were recruited and assessed using a dual energy X-ray absorptiometry (DXA) instrument, body mass index (BMI) $>$ 30 kg/m^2, $-2.5 \leq$ T-score ≤ -1.0 of L1-L4, and/or total femur or femoral neck, and gait speed (10-meter walk test (10MWT)) $\leq$ 1 (m/s^2). The 12-week supervised EBRT was designed to train all major muscle groups for 3 times per week. In the first two sessions, the participants became familiar with targeted number of repetitions (TNRs) and OMNI-resistance exercise scale (OMNI-RES) to control exercise intensity. Following an adaptation phase of 4 weeks (1 set of 12 rep) using low resistance (yellow Thera-Band), exercise intensity progressively increased by adapting the resistance of the elastic band (based on the Thera-Band® force-elongation table) from yellow to red and further to black. The participants in the control group also received telephone contacts or face-to-face interviews on a weekly basis to maintain their typical diet and activity habits. A two-way repeated measures ANOVA was employed to determine the main changes (2 times × 2 groups) after 12 weeks of training. Partial eta-squared (ηp^2) was additionally used to determine ES in ANOVA tests. At all the stages of data analysis in this RCT, intention-to-treat (ITT) analysis was performed.

The results of two-way ANOVA showed significant elevations in E2 ($F = 7.881$, $p = 0.006$, ES = 0.079), MQ ($F = 4.225$, $p = 0.043$, ES = 0.044), OSO *Z*-score ($F = 7.091$, $p = 0.030$, ES = 0.069), 30-s chair stand test ($F = 4.599$, $p = 0.036$, ES = 0.063) and hand grip strength ($F = 6.411$, $p = 0.013$, ES = 0.065) in the experimental group compared with those in the controls. Besides, there were no significant differences in CAF ($F = 0.456$, $p = 0.501$, ES = 0.005), CTX-I ($F = 3.427$, $p = 0.067$, ES = 0.036), adiponectin ($F = 2.733$, $p = 0.102$, ES = 0.029), sTnT ($F = 3.245$, $p = 0.075$, ES = 0.034), sclerostin ($F = 2.927$, $p = 0.091$, ES = 0.034), gait speed (10MWT) ($F = 1.524$, $p = 0.220$, ES = 0.016), 6MWT ($F = 1.169$, $p = 0.284$, ES = 0.017) and TUG ($F = 1.502$, $p = 0.225$, ES = 0.022), BMI ($F = 0.354$, $p = 0.553$, ES = 0.004), BFP ($F = 2.888$, $p = 0.093$, ES = 0.030), body mass content (BMC) ($F = 0.030$, $p = 0.862$, ES = 0.001) and BMD ($F = 0.335$, $p = 0.564$, ES = 0.004) between study groups. Taken together, the results of this study illustrated significant differences only in some OSO markers between groups after 48 h of chronic EBRT in women affected with OSO syndrome. Further research is thus recommended to design machine-based and elastic band-based training regimes at different intensities and volumes.

1. Introduction

Aging is accompanied by major adverse and unfavourable changes in the body composition and primarily an increase in fat mass (FM) (i.e. fat redistribution in the abdominal region), a decrease in bone mineral density (BMD) (specifically, osteoporosis) and a decline in skeletal muscle mass index (SMI) (that is, sarcopenia) and also identified as a new triad geriatric syndrome termed osteosarcopenic obesity (OSO) (Ilich et al., 2014; Kim et al., 2017). It has been demonstrated that drop in physical activities and increased low-grade chronic inflammation are

* Corresponding author at: Department of Sport Sciences, Faculty of Humanities, Shahrekord University, P.O. Box: 34141-88186, Shahrekord, Iran.
E-mail address: banitalebi@sku.ac.ir (E. Banitalebi).
[1] Other authors contributed to this work according the order in which they are named.

https://doi.org/10.1016/j.exger.2020.110884
Received 14 November 2019; Received in revised form 25 January 2020; Accepted 19 February 2020
Available online 21 February 2020
0531-5565/

associated with OSO syndrome in elderly women (Szlejf et al., 2017). To the best of authors' knowledge, there were no studies assessing the prevalence rate of OSO syndrome in Iran although such values related to OSO syndrome among older adults have noticeably increased by 19% (Szlejf et al., 2017) and 6.79% (Perna et al., 2018) in Mexican middle-aged and Italian older women and elderly people, respectively.

Some identified OSO syndrome markers are muscle quality (MQ) (JafariNasabian et al., 2017a), *Z*-score of the muscular strength, percentage of body fat and bone mineral density (BMD) (Z-score OSO) (Cunha et al., 2018), C-telopeptides of type I collagen (CTX-I), skeletal muscle-specific troponin T (sTnT), sclerostin, leptin, adiponectin (JafariNasabian, 2017), C-terminal agrin fragment (CAF) (Fragala et al., 2014a; Landi et al., 2016; Marzetti et al., 2014), and estradiol (E2) levels. Given aging is related to loss of bone, loss of lean, mass and muscle strength, and gain in adiposity. Previous studies have reported that sclerostin is associated with low BMD and osteoporosis (Ardawi et al., 2012), inhibits the differentiation of osteoblasts, reduces the availability of calcium for bone mineralization (Ishimura et al., 2014). It has been shown that serum CTX was greater in the women with osteoporosis, and appears to be a good serum marker in the diagnosis of osteoporosis compared to bone alkaline phosphatase (Bouzid et al., 2010). In addition, sTnT may be considerate a skeletal muscle tissue turnover and sarcopenia biomarkers, since high levels sTnT increased following skeletal muscle injury and neuromuscular disorders (Casati et al., 2019). Researchers illustrated that leptin is also a major regulator of bone remodelling and obesity. There are similarities in the mechanism between estrogen and leptin in influencing bone remodelling and leptin may be involved in the pathogenesis of sarcopenic obesity and link obesity and sarcopenia obesity (Kohara et al., 2011). It has been reported that adiponectin improved aged ovariectomized (OVX)-induced osteosarcopenia in rats (China et al., 2017).

These OSO markers may provide an alternative clinical assessment of skeletal muscle, bone, and fat tissues and also predict functional responses to anabolic stimulations such as exercise training and nutrition supplements (Bhasin et al., 2009).

Although long-term aerobic training is effective for improving cardio-metabolic capacity, aerobic training fails to have significant effects on bone, fat, skeletal muscle, muscular fitness, and functional capacity in older adults living with OSO syndrome. On the other hand, resistance-type training is likely to induce changes in body FM, muscle mass, and BMD in the elderly (JafariNasabian, 2018). It seems that resistance training improves parameters of OSO syndrome risk factors through a variety of different mechanisms (Ormsbee et al., 2014). Nevertheless, the effects of resistance-type training on OSO syndrome have not been clearly quantified and just a few studies have evaluated the impact of chronic resistance training on sarcopenic obesity syndrome (Chen et al., 2017; Chiu et al., 2018; de Oliveira Silva et al., 2018; Fragala et al., 2014b; JafariNasabian et al., 2017a).Moreover; free weights and weight machines are not also generally portable, inexpensive, and easier to use and they take up more space. As well, they may not be practical and even cause damage if practiced without proper control(Yasuda et al., 2014).

Recently, Liao et al. (2018) conducted a randomized trial during a 12-week training program and concluded that elastic band-based training could improve MQ and physical function in older women with sarcopenic obesity (Liao et al., 2018). In Chinese older adults with sarcopenic obesity, Shen et al. (2016) also found that an 8-week EBRT had improved physical function and body composition (Shen et al., 2016). Furthermore, Chen et al. (2017) demonstrated that EBRT could reduce FM and improve BMD in elderly women with sarcopenic obesity (MEDICA, 2017).

With regard to complexity and variability in body composition responses to this exercise modality, sensitive OSO markers to muscle contraction can serve as promising markers for monitoring improvements of risk factors related to OSO syndrome. Interestingly, increasing evidence has suggested that such risk factors can be regulated in OSO state, and correspondingly have beneficial effects on therapeutic mechanisms following exercise training modalities (Goisser et al., 2015; Martínez-Amat et al., 2018).

Therefore, the present study was to evaluate the effects of theoretically-grounded elastic resistance-type training modality on some parameters of OSO syndrome risk factors and related functional profiles. It was thus hypothesized that MQ, serum biomarkers of OSO syndrome, and OSO *Z*-score would be improved following exercise training compared with those in a routine care control group in women with OSO syndrome. Secondly, it was hypothesized that EBRT would be associated with functional benefits compared with that in the control group. Finally, it was hypothesized that changes in OSO syndrome markers would be related to the magnitude of the body composition and functional profile benefits observed.

The primary objective of this randomized controlled trial (RCT) was to investigate the effects of a unique and targeted EBRT intervention on some OSO syndrome markers such as MQ, serum biomarkers of MQ, and OSO Z-score in older women with OSO syndrome. To meet this goal, a single-blind RCT was conducted on women living with OSO syndrome, randomized to either a control group or an experimental (i.e. EBRT) group for 3 months. The secondary objective of this study was to use 10-meter walk test (10MWT) to assess gait speed and to employ 6-minute walk test (6MWT), 30-second (30s) chair-stand test, and timed up and go test (TUG) to reflect on mobility and both static and dynamic balance, and hand grip strength.

2. Methods

2.1. Study design

This 12-week RCT (Iranian Registry of Clinical Trials, trial registration no.: IRCT20180627040260N1; https://www.irct.ir/trial/32463) was approved by Iranian Ethics Committee of Sport Sciences Research Center (IR.SSRC.REC.1398.040). All the study participants also provided written informed consent.

2.2. Study cohort

Based on patient recruitment rates in previous studies conducted by other researchers and along with comprehensive assessment protocols, the participants in this study were recruited via community-wide and general practitioner advertising in Shahrekord city. A detailed telephone screening process was thus conducted to identify those possible exclusions from participating in the study. This was followed by assessment tests and all the participants underwent medical screening to confirm their eligibility based on the following inclusion criteria.

The participants were enrolled on the basis of the Consolidated Standards of Reporting Trials (CONSORT) Statement for randomized trials of non-pharmacologic treatments (Boutron et al., 2017; Liao et al., 2017). The eligible participants, aged 65 to 80 years, were selected by a physician. Therefore, a total of 102 women with OSO syndrome were assessed using a dual energy X-ray absorptiometry (DXA) instrument, aged > 60–80 years, body fat percentage (BFP) > 32%, body mass index (BMI) > 30 kg/m^2, $-2.5 \leq$ T-score ≤ -1.0 of L1-L4, and/or total femur or femoral neck, gait speed (10-meter walk test (10MWT)) $\leq$ 1 (m/s^2), and SMI $\leq$ 28% or $\leq$7.76 kg/m^2 (Hita-Contreras et al., 2015; Ilich et al., 2016), not receiving hormonal therapies, participating in no regular exercise training > 30 min once a week in the last six months, taking no nutritional supplements within the past 3 months, and obtaining a Montreal Cognitive Assessment (MoCA) cut-off score $\geq$ 21 (Pinto et al., 2019). Participants were excluded if they had resting blood pressure $\geq$ 160/100 mmHg, fasting triglyceride $\geq$5.7 mmol/L, a history of cardiovascular disease, thyroid disorder, cancer, endocrine disorder such as diabetes, kidney or liver disease, surgery, smoking or using recreational drugs or any alcohol.

2.3. Sample size determination/power calculations

The sample size was calculated considering two-way repeated measures analysis of variance (ANOVA), two groups, type I error = 5%, type II error = 20%, statistical test power = 80%, and (6) effect size (ES) = 0.20. The effect size of the EBRT program was also estimated at 41 W for MQ index. Considering these parameters and the use of G*Power software (Version 3.1.9.2), a total sample size of 52 individuals (26 individuals per group) was calculated. The sample size was taken into account by 63 participants (experimental group, $n = 32$ and control group, $n = 31$) to accord with an anticipated 20% dropout rate.

2.4. Randomization and concealment strategy

Informed consent was sought from all participants followed by baseline assessment and randomization (Efird, 2010). The randomization was also fulfilled by an external researcher, not involved in testing or training programs, through the use of randomly permuted block allocation with a block size of 4. Participants were stratified according to two cut-offs for each stratification of age (60–70 or 70–85 yrs) and OSO-z score (-3 to 0 or 0 to $+3$). The allocation was further concealed from those responsible for designing the exercise training protocol or monitoring the control group until the beginning of the exercise training period. Neither participants nor researchers were blinded due to the nature of the intervention. Besides; exercise trainers, not involved in data collection, did the exercise session program and monitored the individuals in the control group. Participants in the control group also received no diet intervention or changes in their typical diet or physical activity habits during the study period. They received telephone calls or face-to-face interviews once a week to be sure, there has been no changes in their physical activity and diet habits during this study. During these weekly visits; health problems, functional problems, as well as medication use were recorded by a trained researcher. At the same time, the researchers reinforced the obligation to maintain their typical diet and activity habits.

2.5. Training protocol

The participants were instructed how to use two exercise devices during the first two sessions before beginning the training protocol. In addition, in the first two sessions, the participants became familiar with targeted number of repetitions (TNRs) and OMNI-resistance exercise scale (OMNI-RES) to control exercise intensity (Colado and Triplett, 2008; Lagally and Robertson, 2006). The participants also had to increase or decrease grip width to adjust the resistance easier. Additionally, they were asked to choose an elastic band grip width that allowed them to perform a 20 repetitions maximum (RM) (Colado and Triplett, 2008). The EBRT (using Thera-Band®, The Hygienic Corporation, Akron, OH, USA) was designed to train all major muscle groups (namely; legs, back, abdomen, chest, shoulder, and arms). Training volume and intensity were progressively increased and performed 3 times per week. Exercise training took place in small groups of not > 10 participants and supervised by trained and experienced sport scientists. Each exercise session consisted of a general warm-up of 10 min, followed by a resistance training session (60 min) incorporating one to two exercises (in a slow controlled manner, 2 s for concentric phase and 4 s for eccentric phase), and was completed by a cool-down routine. Following an adaptation phase of 4 weeks (1 set of 12 rep) using low resistance (yellow Thera-Band), exercise intensity progressively increased by adapting the resistance of the elastic band (based on the Thera-Band® force-elongation table) from yellow to red and further to black. Additionally, the exercise volume was enhanced by adding to the number of sets from one to two. Progression rate was based on individual improvements (band colour was changed if participants would have been able to perform two more repetitions in the second set and reported to be below seven on the OMNI-IR for active muscle scale (0: extremely easy to 10: extremely hard)) (Lagally and Robertson, 2006). Details of the exercise regime and exercise progression protocol are reported in Supplementary file.

The participants in the control group also received telephone contacts or face-to-face interviews on a weekly basis to maintain their typical diet and activity habits.

2.6. Nutritional status, physical activity levels and assessment of frailty

A food frequency questionnaire (FFQ) was used to assess individual intake of foods and nutrients (i.e. daily calorie, carbohydrate, fat, protein, vitamin D, calcium, phosphate) at baseline and end of study (Taylor et al., 2009).

Based on the sum five score of fried frailty criteria such as nutrition (weight loss), physical exhaustion (The 10-item Centre for Epidemiological Studies Depression Scale (CES-D-10)), low energy expenditure (Minnesota Leisure Time Activity questionnaire), mobility (5-meter walking test (5MWT)), and muscular strength (dominant hand handgrip strength) weight loss, exhaustion, weakness, slowness, and physical activity, subjects were divided into three frailty levels (non-frail (score 0), pre-frail (score 1–2) and frail (score 3–5)) (Furtado et al., 2019). In addition, The Edmonton Frail Scale (EFS) assesses nine domains of frailty (cognition, general health status, functional independence, social support, medication usage, nutrition, mood, continence, functional performance) was used to classify frailty severity: not frail (0–5), apparently vulnerable (6–7), mildly frail (8–9), moderately frail ($10-11$) and severely frail (12–17) (Perna et al., 2017).

The Iranian version of Barthel Index for Activities of Daily Living (ADL) was used to measure performance in activities of daily living (eating, bathing, getting dressed, toileting, transferring, and continence) (Asgharzadeh et al., 2014). The eight-item Persian version of Lawton Instrumental Activities of Daily Living Scale (IADL) was used to assess independent living skills (using the phone, transportation, shopping, meal preparation, light housework, taking medication and managing money) (Mehraban et al., 2014).

2.7. Adverse events

All defined adverse events that occurred during or up to 48 h after resistance training were recorded every session and reported to the local Ethics Committee.

2.8. Measurements

All pre- and post-measurements of the experiment were conducted by the same assessor who was blind to treatment allocation. Assessments were performed at baseline and at 48 h after last session in both groups. Demographic characteristics and medical history information was also collected through questionnaires. Additionally, the 3-m timed-up-and-go walking test (TUG) was used to assess clinical performance-based measure of lower extremity function, mobility, and fall risk (Barry et al., 2014). Briefly, the TUG test measures the time it takes to stand in a chair (without armchair). Walk 3 m, rotate one cone; return to sitting position as soon as possible. Attempts were made three times and the mean of these three was used as the representative GUG score (Stout et al., 2013).

6-minute walk test (6MWT) used as a tool to measure the functional status of the elderly population. 6MWT was performed previous guidelines. Subjects were asked to walk “as far as possible” in 6 min, and no runs allowed (Chan and Pin, 2019). 10-meter walk test (10MWT) was measured to obtain the gait speed of the subjects. The time began when the participants walked for the middle 10 m of the 15-meter corridor. The first three meters and the last two meters were reserved for acceleration and deceleration, respectively, and the speed of walking was calculated by dividing by 10 m at the time used

(meters/second) (Chan and Pin, 2019).

Lower body strength in older adults was measured by a 30s chair-stand test. During 30s chair-stand test, subjects seated in a chair (height: 43 cm) and asked to perform s many squats as possible during 30 s (de Oliveira Silva et al., 2018).

Hand grip strength test is a clinical indicator of overall muscle strength for elderly people. The participants asked to hold the dynamometer with the arm at right angles and elbows next to the body. The dynamometer handle was adjusted if necessary. When preparing the subject, compress the dynamometer with maximum isometric effort, which is maintained for about 5 s. No other body movement was allowed. The participants strongly encouraged to give a maximum effort.

MQ of the upper extremity was subsequently calculated by: (Leg length × 0.4 body mass × gravity × 10/time sit-stand) (Fragala et al., 2014b).

Besides, OSO *Z*-score was calculated as; a composite Z-score, derived from the average of the components calculated based on the following formula: (Muscular strength Z-score) + (SMM Z-score) + (−1 × body fat Z-score) + (BMD Z-score) / 4 (Cunha et al., 2017). E2 (Cat number: EKU03971, sensitivity 4.45 pg/mL), CTX-I (Cat number: EKU03502, sensitivity 52.9 pg/mL), sTnT (Cat number: EKE60125, sensitivity 9.38 pg/mL), leptin (Cat number: EKU05593, sensitivity 0.058 ng/ml), adiponectin (Cat number: EKU02153, sensitivity 0.069 ng/ml), and CAF (Cat number: MBS771072, sensitivity 0.01 ng/ml) in fasting serum were also evaluated via the commercial enzyme-linked immunosorbent assay (ELISA) kits. Blood samples were collected in the fasting condition at baseline and 48 h after last session in fasting status. All reagents were prepared room temperature and in accordance with the manufacturer's protocols. All samples were tested repeatedly. Each serum sample was diluted 40 fold with a serum diluent. 100 μl of serum was added to wells and then incubated with gentle shaking at room temperature for 2.5 h. The wells were washed 3 times with 300 μl of 1% wash solution. After that, antibody (100 μl) was added to each well, and the plate was incubated for 1 h with gentle shaking and washed again. The prepared streptavidin solution (100 μl) was added to each well and the wells were incubated at room temperature for 45 min with gentle shaking. The plate was decanted and washed again, and 100 μl of the substrate solution was added to wells. 50 μl of stop solution was added to each well. Finally, the plate was read on a microwell plate reader (450 nm).

2.9. Statistical analyses

Regardless of intervention adherence level, data analysis strategy was chosen. Assumption of data normality was also checked using Kolmogorov-Smirnov test prior to conducting parametric tests. Descriptive data included means, standard deviations (SDs), and percentage distributions. Independent-sample *t*-test was correspondingly used for baseline comparisons. A two-way repeated measures ANOVA was also employed to determine the main changes (2 times × 2 groups) after 12 weeks of training. Besides, Bonferroni's method was applied wherein a significant interaction effect was observed. Partial eta-squared (ηp^2) was additionally used to determine ES in ANOVA tests. The statistical significance was set at $p < 0.05$. Relationships between the mentioned variables were further calculated through simple and multiple linear regression models. At all the stages of data analysis in this RCT, intention-to-treat (ITT) analysis was performed. The data were analysed using the SPSS Statistics (Version 22.0) for Windows (SPSS Inc., Chicago, IL, USA) and then expressed as mean ± SD.

3. Results

Participant recruitment throughout this trial can be found in the CONSORT flowchart in Fig. 1. Among 102 patients screened, 63 met the inclusion criteria. The main reasons for exclusion were unwillingness to participate in the study, and not meeting some inclusion criteria such as age > 65–80 years, BFP > 32%, BMI > 30 kg/m^2, −2.5 ≤ T-score ≤ −1.0 of L1-L4 and/or total femur or femoral neck, and 10MWT ≤ 1 m/s^2 gait speed. The participants were also randomly assigned to the experimental (namely, EBRT) group ($n = 32$) or control group ($n = 31$). At the baseline, no differences were observed between both study groups (Table 1).

3.1. Dropout and adherence rates

Data from 29.03% ($n = 9$) and 18.75% ($n = 6$) participants from control and experimental groups who did not attend the post-test evaluation were excluded, respectively. Outcome data imputed for 15 patients were included in ITT. The main reasons given for dropout were personal problems, lack of interest, and moving to another city. The rate of adherence to training sessions was also by 85% in the experimental group. No significant adverse events were reported by investigators who were not blinded to group assignment during the 12-week intervention. However, a few patients reported muscle soreness, knee pain, and shoulder pain in experimental group (25%) in the first three sessions of training. No adverse events were reported by the control group.

3.2. OSO syndrome markers

The results of two-way ANOVA showed a significant elevation in E2 ($F = 7.881$, $p = 0.006$, ES = 0.079) and a noticeable decline in leptin ($F = 12.586$, $p = 0.001$, ES = 0.123) in the experimental group compared with those in the controls. Besides, there were no significant differences in CAF ($F = 0.456$, $p = 0.501$, ES = 0.005), CTX-I ($F = 3.427$, $p = 0.067$, ES = 0.036), adiponectin ($F = 2.733$, $p = 0.102$, ES = 0.029), sTnT ($F = 3.245$, $p = 0.075$, ES = 0.034), and sclerostin ($F = 2.927$, $p = 0.091$, ES = 0.034) between study groups. However, a significant increase was observed in MQ ($F = 4.225$, $p = 0.043$, ES = 0.044) and OSO *Z*-score ($F = 7.091$, $p = 0.030$, ES = 0.069) in the experimental group compared with that in the control one (Fig. 2).

3.3. Functional profile

After 12 weeks of EBRT by the experimental group, the results of 30-s chair stand test ($F = 4.599$, $p = 0.036$, ES = 0.063) and hand grip strength ($F = 6.411$, $p = 0.013$, ES = 0.065) significantly increased compared with those in the control group. However, there were no significant differences in gait speed (10MWT) ($F = 1.524$, $p = 0.220$, ES = 0.016), 6MWT ($F = 1.169$, $p = 0.284$, ES = 0.017), and TUG ($F = 1.502$, $p = 0.225$, ES = 0.022) tests between study groups (Fig. 3).

3.4. Body composition and dietary assessment

There were no significant differences between groups in terms of height ($F = 0.019$, $p = 0.889$, ES = 0.001), weight ($F = 0.602$, $p = 0.440$, ES = 0.007), BMI ($F = 0.354$, $p = 0.553$, ES = 0.004), BFP ($F = 2.888$, $p = 0.093$, ES = 0.030), body mass content (BMC) ($F = 0.030$, $p = 0.862$, ES = 0.001), and BMD ($F = 0.335$, $p = 0.564$, ES = 0.004). But, there were significant improvement in Freid Frailty ($F = 7.760$, $p = 0.007$, ES = 0.088), ADL ($F = 7.868$, $p = 0.009$, ES = 0.092), IADL ($F = 5.774$, $p = 0.024$, ES = 0.077), EFS ($F = 9.631$, $p = 0.003$, ES = 0.107) and GFST ($F = 7.402$, $p = 0.008$, ES = 0.085). As well, no significant differences were observed between groups in daily calorie ($F = 0.199$, $p = 0.678$, ES = 0.002), carbohydrate ($F = 0.211$, $p = 0.606$, ES = 0.003), FM ($F = 0.055$, $p = 0.808$, ES = 0.001), protein ($F = 0.986$, $p = 0.196$, ES = 0.010), vitamin D ($F = 0.603$, $p = 0.448$, ES = 0.006), calcium ($F = 0.346$, $p = 0.507$, ES = 0.004), and phosphate ($F = 0.244$, $p = 0.645$,

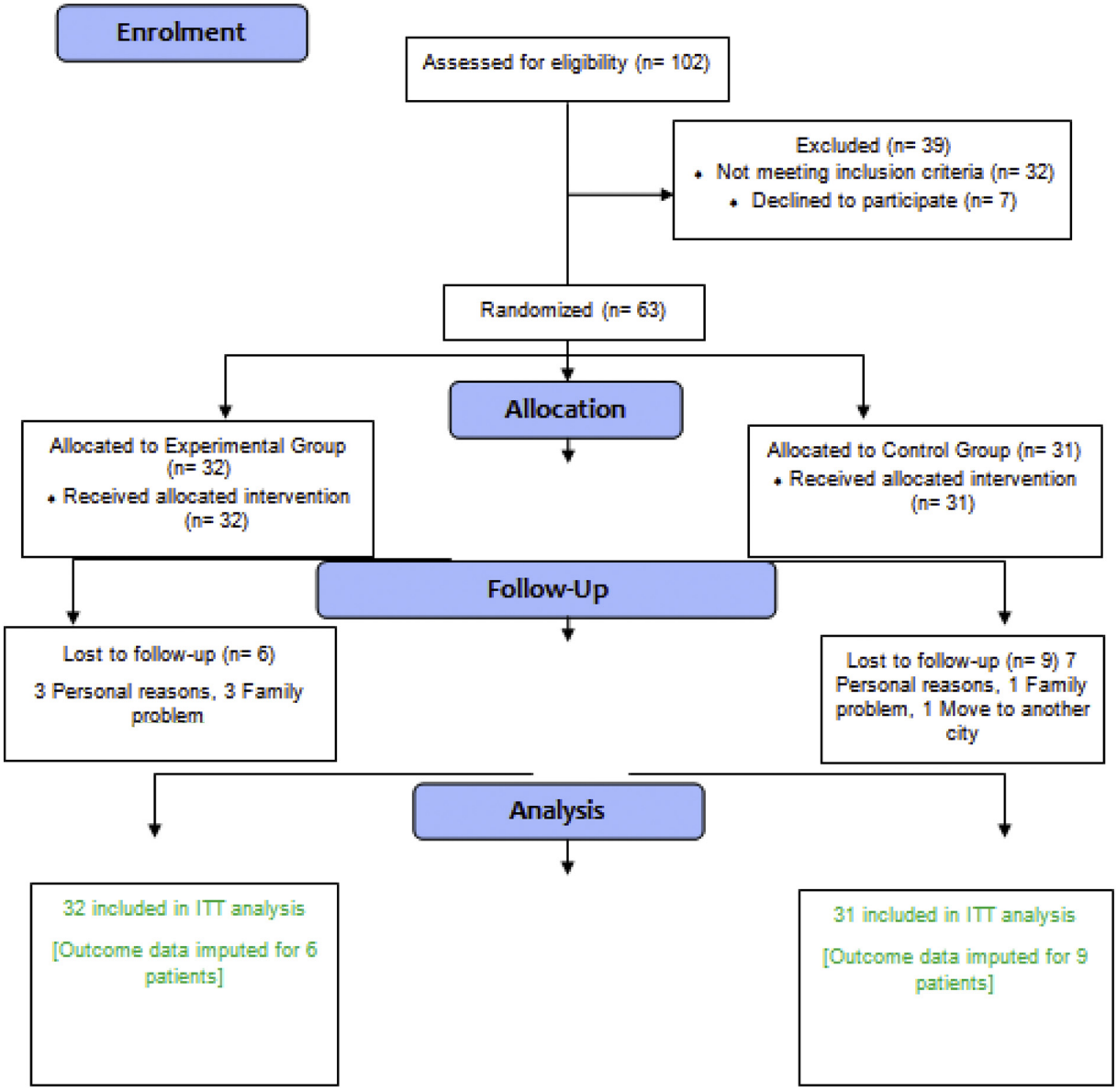

Fig. 1. CONSORT flow diagram. Flow diagram representing study design.

ES = 0.003) following almost a normal diet (Table 2).

3.5. Relationships between OSO syndrome markers and other variables

Significant correlations were found between changes in serum CAF levels and those in OSO *Z*-score (R^2 = 0.076, p = 0.032), SBBP (R^2 = 0.084, p = 0.026), gait speed (10MWT) (R^2 = 0.114, p = 0.011), 30s chair-stand test (R^2 = 0.084, p = 0.026), and TUG (R^2 = 0.085, p = 0.025). There was also a significant relationship between changes in serum CTX-I levels and MQ (R^2 = 0.116, p = 0.010). After running liner regression, significant relationships were also observed between serum leptin concentration and MQ (R^2 = 0.127, p = 0.007), gait speed (10MWT) (R^2 = 0.136, p = 0.006), and hand grip strength (R^2 = 0.097, p = 0.018). Similarly, there were significant relationships between adiponectin and MQ (R^2 = 0.149, p = 0.004) and hand grip strength (R^2 = 0.129, p = 0.007). Significant correlations were also found between E2 and MQ (R^2 = 0.096, p = 0.018) and gait speed (10MWT). There were additionally significant correlations between serum sTnT levels and MQ (R^2 = 0.296, p = 0.0001) and hand grip strength (R^2 = 0.096, p = 0.018). Considering sTnT, significant correlations were observed between serum sclerostin levels and MQ (R2 = 0.311, p = 0.0001), and hand grip strength and sclerostin levels (R2 = 0.099, p = 0.014). In addition, there were significant correlations between OSO *Z*-score, MQ (R^2 = 0.210, p = 0.001), hand grip strength (R^2 = 0.065, p = 0.045), 6MWT (R^2 = 0.448, p = 0.0001), 30s chair-stand test (R^2 = 0.659, p = 0.0001), and TUG (R^2 = 0.661, p = 0.0001) (Supplementary file).

4. Discussion

Contrary to the research hypotheses raised in this cohort, EBRT had affected chronic levels of some serum OSO biomarkers in women with OSO syndrome. Accordingly, changes in OSO syndrome biomarkers had significantly decreased in leptin and increased in E2 after 12 weeks. However, it was notable that the changes in leptin and E2 were directly associated with variations in MQ, OSO Z-score, 30s chair-stand test, and hand grip strength in experimental group. Therefore, even greater body FM and SMI adaptations than those observed in the experimental group would be required to demonstrate a significant change in these OSO

Table 1
Comparison of baseline characteristics of participants in experimental and control groups.

Variable	Group	Baseline	T	*p*-Value
Age (years)	Con (n = 31)	64.05 ± 3.35	−0.067	0.947
	Ex (n = 32)	64.11 ± 3.81		
Height (cm)	Con (n = 31)	155.77 ± 4.14	−0.239	0.812
	Ex (n = 32)	155.59 ± 4.38		
Weight (kg)	Con (n = 31)	78.73 ± 7.52	−1.121	0.268
	Ex (n = 32)	81.81 ± 8.03		
BMI (kg/m^2)	Con (n = 31)	32.53 ± 2.01	−0.761	0.451
	Ex (n = 32)	33.72 ± 3.15		
Body fat %	Con (n = 31)	43.60 ± 2.66	−1.887	0.067
	Ex (n = 32)	46.29 ± 3.42		
BMC (gr)	Con (n = 31)	2.13 ± 0.50	−0.885	0.381
	Ex (n = 32)	2.24 ± 0.38		
BMD (gr/cm^2)	Con (n = 31)	1.005 ± 0.450	0.897	0.374
	Ex (n = 32)	0.929 ± 0.245		
MQ (W)	Con (n = 31)	578.42 ± 100.46	0.757	0.453
	Ex (n = 32)	563.90 ± 101.92		
OSO *Z*-score	Con (n = 31)	0.022 ± 1.281	0.192	0.844
	Ex (n = 32)	−0.275 ± 1.601		
FF	Con (n = 31)	1.78 ± 1.11	−0.540	0.592
	Ex (n = 32)	1.96 ± 1.04		
ADL	Con (n = 31)	13.89 ± 0.47	0.111	0.912
	Ex (n = 32)	13.87 ± 0.34		
IADL	Con (n = 31)	16.22 ± 2.07	0.879	0.385
	Ex (n = 32)	15.67 ± 1.99		
EFS	Con (n = 31)	5.11 ± 1.97	−1.869	0.052
	Ex (n = 32)	6.41 ± 2.02		
Daily calorie	Con (n = 31)	1778.05 ± 91.44	−0.276	0.797
	Ex (n = 32)	1802.19 ± 88.54		
Carbohydrate (%)	Con (n = 31)	55.13 ± 6.73	−0.752	0.398
	Ex (n = 32)	56.38 ± 4.95		
Fat (%)	Con (n = 31)	28.23 ± 4.82	0.644	0.522
	Ex (n = 32)	27.66 ± 3.44		
Protein (%)	Con (n = 31)	16.96 ± 2.09	0.981	0.334
	Ex (n = 32)	15.92 ± 1.86		
Vitamin D (IU/day)	Con (n = 31)	91.11 ± 6.53	−1.034	0.273
	Ex (n = 32)	93.35 ± 8.11		
Calcium (mg/day)	Con (n = 31)	733.08 ± 400.30	0.485	0.618
	Ex (n = 32)	729.29 ± 288.24		
Phosphate (mg/day)	Con (n = 31)	1411 ± 524.81	0.398	0.689
	Ex (n = 32)	1368.7 ± 363.93		
E2 (pg/ml)	Con (n = 31)	180.75 ± 44.70	−1.911	0.056
	Ex (n = 32)	191.47 ± 51.58		
CAF (pg/ml)	Con (n = 31)	3.14 ± 0.58	−0.238	0.813
	Ex (n = 32)	2.89 ± 0.44		
CTX-I (ng/ml)	Con (n = 31)	0.526 ± 0.097	1.076	0.287
	Ex (n = 32)	0.543 ± 0.081		
Leptin (ng/ml)	Con (n = 31)	18.67 ± 1.41	−1.129	0.265
	Ex (n = 32)	20.41 ± 2.10		
Adiponectin (μg/ml)	Con (n = 31)	6.02 ± 0.91	0.279	0.782
	Ex (n = 32)	5.56 ± 0.80		
sTnT (pg/ml)	Con (n = 31)	26.10 ± 3.05	−1.132	0.098
	Ex (n = 32)	27.33 ± 4.42		
Sclerostin (ng/ml)	Con (n = 31)	269.48 ± 23.96	0.289	0.802
	Ex (n = 32)	270.99 ± 23.74		
Gait speed (10MWT) (m/s)	Con (n = 31)	0.883 ± 0.62	0.875	0.386
	Ex (n = 32)	0.864 ± 0.61		
6MWT (m)	Con (n = 31)	306.57 ± 58.86	−1.364	0.184
	Ex (n = 32)	302.93 ± 42.45		
30s chair-stand test (Reps)	Con (n = 31)	7.64 ± 1.28	−0.919	0.364
	Ex (n = 32)	8.71 ± 1.44		
TUG (s)	Con (n = 31)	15.91 ± 4.47	0.455	0.652
	Ex (n = 32)	13.49 ± 2.95		
Hand grip strength (kg)	Con (n = 31)	20.48 ± 4.12	1.174	0.247
	Ex (n = 32)	20.54 ± 3.37		

BMI: body mass index; BMC: bone mass content; BMD: bone mass density; MQ: muscle quality: MQ; OSO Z-score: Osteosarcopenic obesity Z-score; E2: estradiol; C-terminal agrin fragment: CAF; C-telopeptides of type I collagen: CTX−I; sTnT: skeletal muscle-specific troponin T; 10MWT: 10-min walk test: 10-MWT; 6MWT: six-minute walk test; TUG: Timed Up and Go; FF: Fried Frailty; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living Scale; EFS: Edmonton Frail Scale.

syndrome biomarkers after training. In addition, E2 and leptin remnants increased and decreased 48 h after chronic EBRT compared with those in control group in aged women with OSO syndrome, respectively. Furthermore, functional outcomes such as 30s chair-stand test, hand grip strength, OSO Z-score, and MQ outcomes improved by group × time following the trainings. However, there were no significant changes in weight, BMI, BFP, BMC, and BMD over time in all study groups.

There have been so far a few studies on the effect of EBRT on MQ markers and functional outcomes in elderly people (Fragala et al., 2014b; Fragala et al., 2014a; J Kelly and C Gilman, 2017; Ribeiro et al., 2016; Scanlon et al., 2014). However, to the best of authors' knowledge, this RCT was the first study to evaluate the effects of some parameters of OSO syndrome biomarkers and functional outcomes in elderly women living with this disorder. There are different reasons why the EBRT resulted in significant increase in estradiol levels. Previous study reported that resistance training can significantly change estrogen metabolism in premenopausal women. It seems that 12 weeks EBRT may lead to significant increases the ratio of the estradiol metabolites 2-OHE1/16α-OHE1 in premenopausal women (Smith et al., 2013), even though we did not evaluate estrogen metabolism in current study. Although primary source of estradiol is adipose tissue (Judd et al., 1982), it is possible that EBRT exerts a body composition-independent effect on hormone exposure by disrupting hypothalamic function (Campbell et al., 2007). In our study, although we observed no significant within- or between-group changes in body composition, it is possible that EBRT intervention resulted in changes estrogen metabolism. Finally, it is possible that the absence of body composition change or obvious menstrual cycle disruption, three sessions per week of EBRT leads to reductions in sex hormone concentrations such as estradiol in women with OSO.

Possible mechanisms for significant decreasing in serum leptin following EBRT regardless of no change in adiposity may related to improved leptin sensitivity (Beavers et al., 2010; Fedewa et al., 2018), as it has been shown that obese people have leptin resistance, and decrease in leptin following chronic resistance training observed in the present study may be due to improved leptin sensitivity (Guadalupe-Grau et al., 2009). As only a little portion of the variation in the change in leptin following exercise training is weight loss dependent (Gleeson et al., 2011; Miller et al., 2004a).

In contrast to the research hypotheses, this type of resistance training did not have any effects on changes in serum CAF, CTX-I, adiponectin, and sTnT concentrations. In this respect, a previous study had revealed that the levels of these serum biomarkers of OSO syndrome were different in older people with OSO syndrome compared with osteopenic obese and obese-only groups (JafariNasabian et al., 2017b).

Bondocet et al. (Bondoc et al., 2015) had also demonstrated no significant decrease in serum CAF protein levels following 12-month intervention via moderate physical activities (i.e. walking, resistance training, flexibility, balance training, and home-based training) in mobility-limited older adults (mean age 76.7 ± 4.21 years). Furthermore; a study on healthy older males and females, aged 60–85 years, had reported that circulating CAF had increased by 10.4% (3.59 to 4.00 pg/ml) following 6 weeks of machine-based resistance training protocol which had involved all muscles (Fragala et al., 2014a). In contradiction of the present study, Drey et al. (Bondoc et al., 2015) had reported that resistance exercise training plus consuming vitamin D was associated with a significant reduction in CAF levels in adults aged 65–94 years. Nevertheless, the results of the present study were similar to findings from Fragala et al. (2014a), indicating improved MQ by 28% despite no significant changes in lean body mass. In connection with the different result in our study versus previous studies, there is a possibility that may be different depending on the duration of exercise intervention. The participants in this study performed EBRT during 12 weeks, while a duration of exercise in previous studies that have

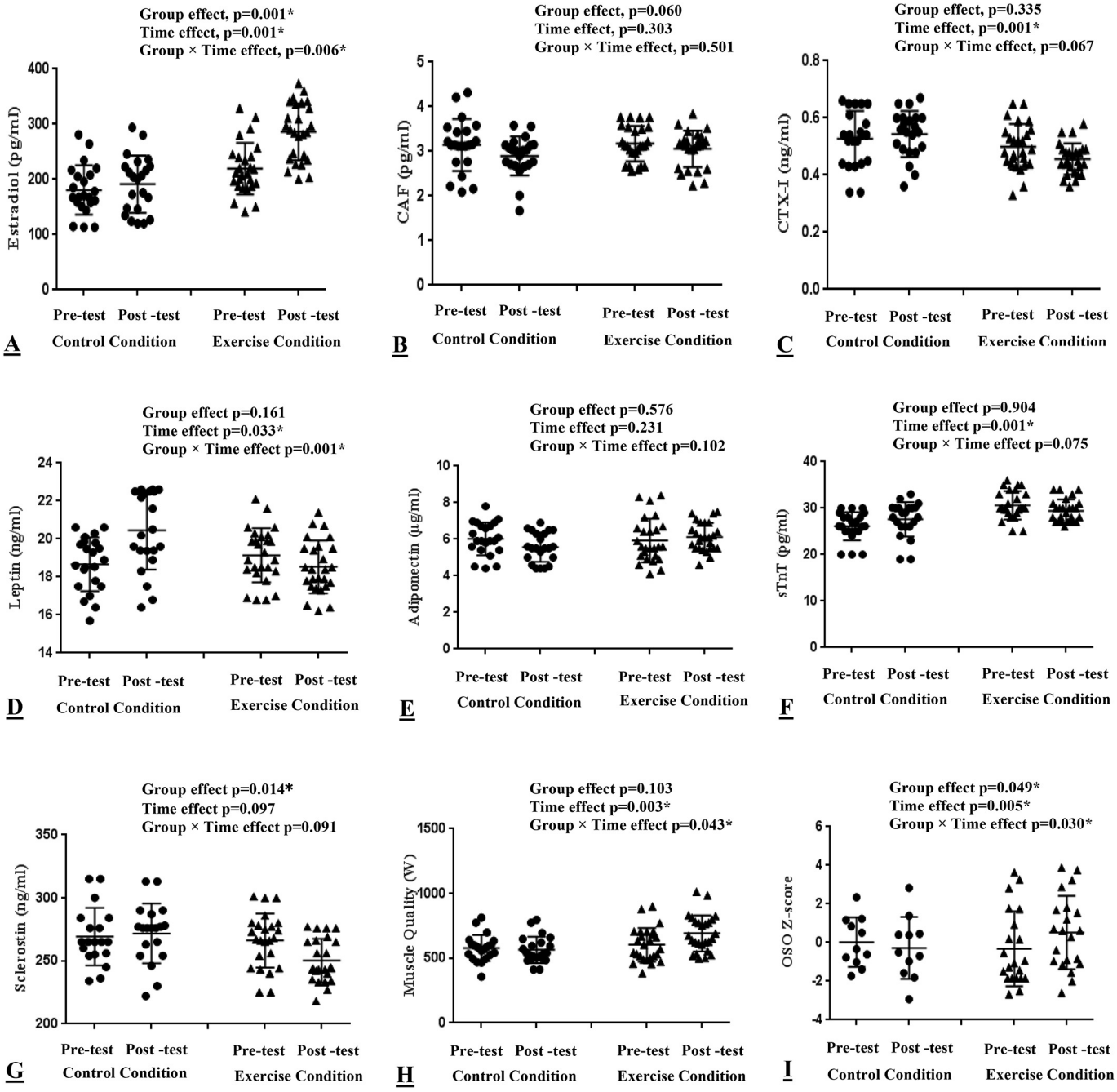

Fig. 2. OSO markers change following 12 weeks of supervised elastic band resistance training.
* Indicate significant effect based on $p < 0.05$. CAF: C-terminal agrin fragment; CTX-I: C-telopeptides of type I collagen; sTnT: skeletal muscle specific troponin T.

alteration on the theses biomarker levels conducted at least 6 month or more. In our study, 12 weeks of EBRT, 3 sessions per week did not lead to significant changes in serum CTX-I levels in women with OSO syndrome. However, the findings of other studies in response to different exercise training are somewhat contradictory. For example, Toriola et al. illustrated that 6 and 12 months diet and exercise training interventions led to lack of CTX change in obese or overweight females. Likewise, Evans and co-workers illustrated that 9 months of aerobic training led to a reduction in serum CTX levels in postmenopausal women. The unchanged serum CTX-I concentration in our study may be attributed to the moderate intensity of EBRT. In addition, lack of measurement of other bone metabolism biomarkers such as osteocalcin, alkaline phosphatase, calcitonin and parathyroid hormone are other limitations of present study.

Though an association was observed between changes of serum CAF levels and gait speed (10MWT), 30s chair-stand test, and TUG; this study showed that serum CAF concentrations were associated with more functional outcomes. These results illustrated that serum CAF might be a strong predictor biomarker of functional improvements in this population following EBRT. These results were consistent with the ones reported in other studies, indicating that gait speed (Drey et al., 2013) was not significantly associated with serum CAF concentrations. This RCT was the first study to measure the relationships between these OSO markers and physical performance outcomes. Briefly, multiple possibilities could explain the differences in results between previous research and those reported in the present study. First, Drey et al. utilized a quantitative Western blot method to detect CAF protein levels while ELISA kits were utilized in the present study and that conducted

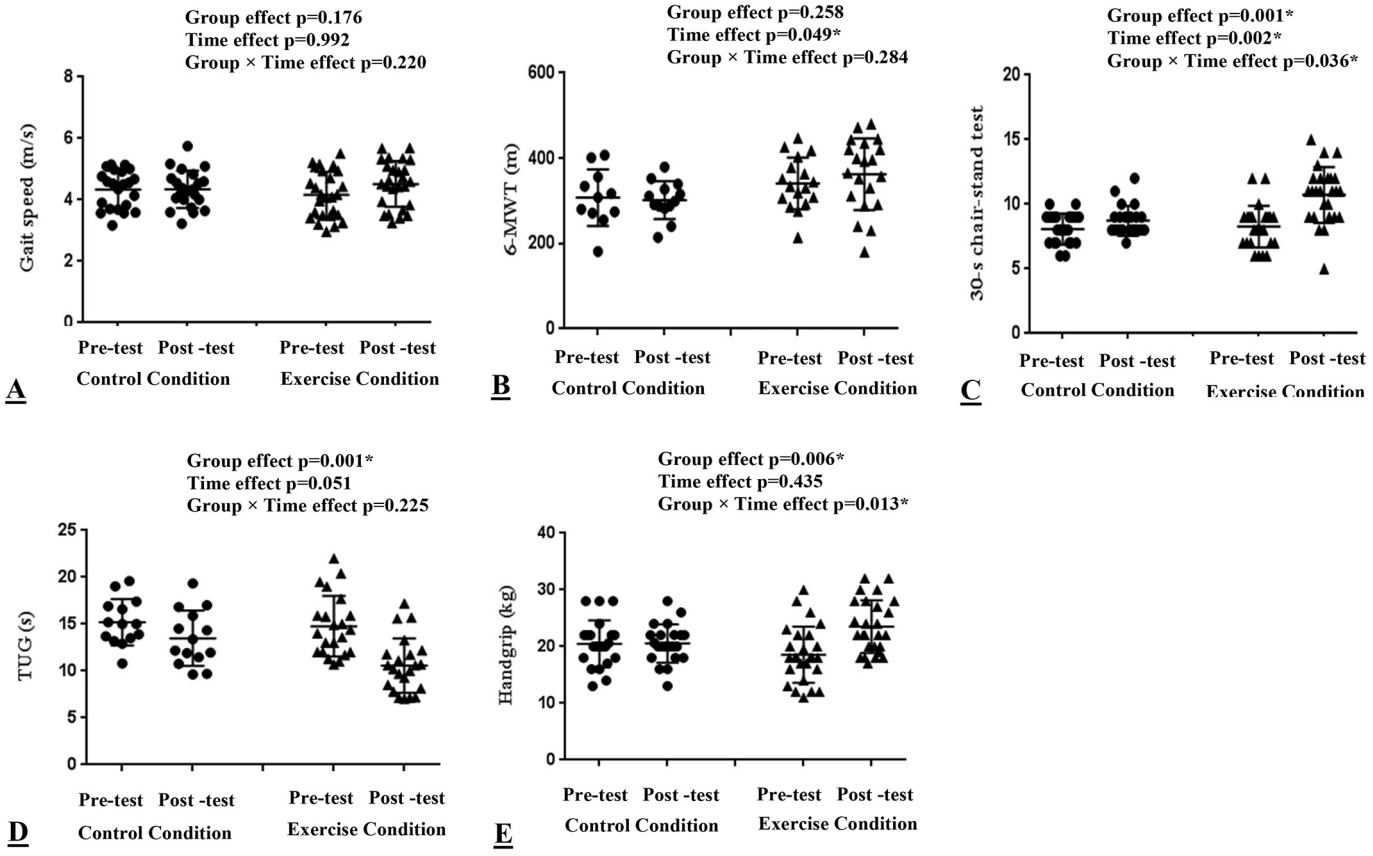

Fig. 3. Functional profile change following 12 weeks of supervised elastic band resistance training.
* Indicate significant effect based on $p < 0.05$. 6-MWT: 6 minute walking test; TUG: timed up and go test.

by Bondocet et al. Secondly, previous studies had employed machine-based resistance-type exercise training and multimodal protocols whereas the present study had benefitted from EBRT intervention with an emphasis on moderate resistance training as the primary modality. As the third possibility, longer duration of the present study could have influenced the results though the sample size in this RCT was significantly larger. Fourthly, longer period of resistance training was required to change CAF concentrations since previous studies had illustrated that sarcopenic elderly populations could have greater serum CAF levels than non-sarcopenic age-matched controls (Bondoc et al., 2015; Landi et al., 2016).

In line with the research hypotheses, a significant elevation was observed in serum E2 hormone in the experimental group after EBRT compared with that in the controls. So, it is necessary to consider hormonal status such as E2 when evaluating exercise modality responses in females (Wingfield et al., 2015). In addition, it had been shown that the number of falls and fractures could be associated with a decrease in serum E2 levels (Ribom et al., 2002). Interestingly, in previous studies, interventions including exercise training had resulted in an overall decrease of free E2 levels, but none of them had included a resistance-type exercise training (Ennour-Idrissi et al., 2015). The rise in E2 levels in response to EBRT was consistent with previous studies reporting similar findings following endurance and resistance-type training programs (ElDeeb et al., 2018). However, there were research studies illustrating opposite results (Atkinson et al., 2004; Chan et al., 2007; Tartibian and Zarneshan, 2008). Contradicting results had also occurred because of differences in exercise intensity and duration, which might affect adaptations of E2 levels to exercise training (Consitt et al., 2001). It seems that increased metabolic clearance rates during exercise training may explain E2 elevation (Devries et al., 2005).

Leptin is known as an adipokine that is epidemiologically associated with OSO syndrome, and also mechanistically with bone, adipose, and sarcopenia dysregulation (JafariNasabian, 2017). It has been also illustrated that there are complex biologic networks involved in leptin signaling in OSO syndrome (JafariNasabian et al., 2017b). Thus, therapeutic exercise training interventions are necessary for aging individuals at risk for OSO syndrome to lower their leptin concentrations (J Kelly and C Gilman, 2017; JafariNasabian et al., 2017a). The relationship between resistance training and leptin levels had been also examined in only a few studies in older populations (Fatouros et al., 2005; Fatouros et al., 2009; Prestes et al., 2018). Previous studies had thus reported divergent results in the serum levels of leptin. A recent study had further reported a decrease in leptin levels following a 16-week resistance training (2 sessions per week/6-14 RM) (Prestes et al., 2018). Furthermore, 12 months of resistance training program (6-14 RM) for three times a week had decreased the serum levels of leptin in elderly post-menopausal women (mean age of 63.02 ± 4.42 years, mean BMI of 28.01 ± 1.02 kg/m^2) (Botero et al., 2013). The findings of the present study were not in line with other investigations reflecting on the effects of exercise and changes in body composition on leptin levels. The decline of serum leptin concentrations induced by EBRT in the present study was not accompanied by changes in BMI and BFP. In fact, EBRT-induced leptin responses did not correlate with BMI and BFP changes, indicating an irrelevant association between leptin and body composition parameters, as it had been shown that body FM changes could explain only a portion of variations in serum leptin levels following exercise training (Miller et al., 2004b). The reduction of serum leptin levels in response to 12-month of resistance training in the present RCT was verified, which was in agreement with previous studies; (Botero et al., 2013; Fatouros et al., 2005; Kanaley et al., 2001; Prestes et al., 2018) however, others had found no effects of resistance training on leptin (Lau et al., 2010; Prestes et al., 2009). These conflicting

Table 2
Secondary outcomes; anthropometric profile, nutritional status, physical activity levels and assessment of frailty.

Variable	Group	Time		%Δ	*p*-Value	F,T	Effect size
		Pre	Post				
Age (years)	Con (n = 31)	64.05 ± 3.35			0.947	−0.067	
	Ex (n = 32)	64.11 ± 3.81					
Height (cm)	Con (n = 31)	155.77 ± 4.14	155.08 ± 4.59	−0.44	Group = 0.964	0.002	0.001
	Ex (n = 32)	155.59 ± 4.38	156.15 ± 4.89	0.36	Time = 0.641	0.218	0.002
					Group × time = 0.889	0.019	0.001
Weight (kg)	Con (n = 31)	78.73 ± 7.52	81.66 ± 10.09	3.72	Group = 0.409	0.687	0.007
	Ex (n = 32)	81.81 ± 8.03	81.87 ± 9.82	0.07	Time = 0.422	0.650	0.007
					Group × time = 0.440	0.602	0.007
BMI (kg/m^2)	Con (n = 31)	32.53 ± 2.01	33.33 ± 4.05	0.73	Group = 0.317	1.012	0.011
	Ex (n = 32)	33.72 ± 3.15	33.65 ± 3.67	−0.06	Time = 0.614	0.256	0.003
					Group × time = 0.553	0.354	0.004
Total fat %	Con (n = 31)	43.60 ± 2.66	47.60 ± 2.65	9.17	Group = 0.400	0.714	0.008
	Ex (n = 32)	46.29 ± 3.42	47.35 ± 3.86	2.29	Time = 0.001	22.046	0.193
					Group × time = 0.093	2.888	0.030
BMC (g)	Con (n = 31)	2.13 ± 0.50	2.11 ± 0.53	−0.94	Group = 0.175	1.868	0.020
	Ex (n = 32)	2.24 ± 0.38	2.26 ± 0.44	0.89	Time = 0.985	0.001	0.001
					Group × time = 0.862	0.030	0.001
BMD (g/cm^2)	Con (n = 31)	1.005 ± 0.450	0.947 ± 0.274	−5.77	Group = 0.550	0.360	0.004
	Ex (n = 32)	0.929 ± 0.245	0.945 ± 0.271	1.72	Time = 0.779	0.079	0.001
					Group × time = 0.564	0.335	0.004
FF	Con (n = 31)	1.78 ± 1.11	1.72 ± 1.18	−3.37	Group = 0.052	3.888	0.046
	Ex (n = 32)	1.96 ± 1.04	0.67 ± 0.70	−65.82	Time = 0.003	9.218	0.103
					Group × time = 0.007	7.760	0.088
ADL	Con (n = 31)	13.89 ± 0.47	13.33 ± 2.35	−4.03	Group = 0.036	4.048	0.066
	Ex (n = 32)	13.87 ± 0.34	17.50 ± 2.06	26.17	Time = 0.014	7.196	0.082
					Group × time = 0.009	7.868	0.092
IADL	Con (n = 31)	16.22 ± 2.07	14.94 ± 2.34	−7.89	Group = 0.033	4.433	0.068
	Ex (n = 32)	15.67 ± 1.99	18.67 ± 2.30	19.14	Time = 0.077	3.011	0.040
					Group × time = 0.024	5.774	0.077
EFS	Con (n = 31)	5.11 ± 1.97	5.89 ± 2.08	15.26	Group = 0.702	0.147	0.002
	Ex (n = 32)	6.29 ± 2.20	5.33 ± 2.14	−16.85	Time = 0.193	1.721	0.021
					Group × time = 0.003	9.631	0.107
Daily calorie	Con (n = 31)	1778.05 ± 91.44	1746.35 ± 101.66	−1.78	Group = 0.616	0.205	0.003
	Ex (n = 32)	1802.19 ± 88.54	1738.61 ± 90.21	−3.52	Time = 0.547	0.358	0.005
					Group × time = 0.678	0.199	0.002
Carbohydrate (%)	Con (n = 31)	55.13 ± 6.73	55.64 ± 5.14	0.92	Group = 0.550	0.348	0.005
	Ex (n = 32)	56.38 ± 4.95	55.92 ± 6.08	−0.81	Time = 0.484	0.585	0.007
					Group × time = 0.606	0.211	0.003
Fat (%)	Con (n = 31)	28.23 ± 4.82	28.55 ± 4.18	1.13	Group = 0.789	0.072	0.001
	Ex (n = 32)	27.66 ± 3.44	28.02 ± 5.01	1.30	Time = 0.718	0.102	0.002
					Group × time = 0.808	0.055	0.001
Protein (%)	Con (n = 31)	16.96 ± 2.09	15.77 ± 2.47	−7.01	Group = 0.029	5.623	0.077
	Ex (n = 32)	15.92 ± 1.86	16.94 ± 2.06	6.40	Time = 0.112	1.436	0.017
					Group × time = 0.196	0.986	0.010
Vitamin D (IU/day)	Con (n = 31)	91.11 ± 6.53	93.6 ± 6.01	2.73	Group = 0.676	0.198	0.002
	Ex (n = 32)	93.35 ± 8.11	96.80 ± 7.33	4.13	Time = 0.219	1.612	0.018
					Group × time = 0.448	0.603	0.006
Calcium (mg/day)	Con (n = 31)	733.08 ± 400.30	716.94 ± 319.44	−2.20	Group = 0.292	0.707	0.007
	Ex (n = 32)	729.29 ± 288.24	742.25 ± 297.85	1.77	Time = 0.330	1.009	0.010
					Group × time = 0.507	0.346	0.004
Phosphate (mg/day)	Con (n = 31)	1411 ± 524.81	1465.23 ± 497.35	3.84	Group = 0.426	0.653	0.007
	Ex (n = 32)	1368.7 ± 363.93	1422.47 ± 428.71	3.92	Time = 0.718	0.088	0.001
					Group × time = 0.645	0.244	0.003

BMI: body mass index; BMC: bone mass content; BMD: bone mass density; FF: fried frailty; ADL: activities of daily living; IADL: Instrumental Activities of Daily Living Scale; EFS: Edmonton Frail Scale.

results could be attributed to different training regimes (i.e. participants' gender as well as intensity, volume, and duration of training) and initial physical fitness. The decrease in leptin following EBRT may be of clinical relevance, regardless of the non-responsiveness to body composition. Moreover, it seems that leptin triggers pro-inflammatory effects through activating macrophage and producing pro-inflammatory adipokine (Procaccini et al., 2012).

Contrary to the research hypotheses, no significant changes were observed in adiponectin in the experimental group after EBRT compared with that in the controls. By contrast, Abbenhardt et al. (2013) performed 12 months of moderate-to-vigorous intensity aerobic exercises at 70–85% maximum heart rate for 45 min in overweight or obese post-menopausal women (mean age of 58.0 ± 5.0 years) and reported that adiponectin levels had increased in diet and diet + exercise groups compared with controls by 9.5% and 6.6%; respectively (Abbenhardt et al., 2013). In agreement with the findings in the present study, Figueroa et al. (2013) reported that a hypocaloric diet and supervised low-intensity resistance exercise training (LIRET) comprised of 4 machine-based resistance exercises (namely; leg press, leg extension, leg flexion, and calf raise), 3 exercise sessions per week, 2 sets of 18–22 repetitions in each set on obese post-menopausal women (aged 54 ± 6 years, BMI of 33.8 ± 0.5 kg/m^2) had not changed adiponectin concentrations after intervention (Figueroa et al., 2013). In contrast, a 24-week study with different intensity resistance (low, moderate, and high intensities) groups and sets of 2–4 of 6–12 repetitions in overweight inactive elderly men (aged 65–78 years, BMI of 28.7–30.2 kg/

m^2) showed that moderate- and high-, but not low-intensity resistance training had elevated adiponectin circulating levels (Fatouros et al., 2005). The disparate results regarding adiponectin responses might be due to intensity and duration of exercises (De Salles et al., 2010) as well as insignificant changes observed in body composition in the present study, so it may be necessary to improve adiponectin levels (Zoico et al., 2004).

In the present study, there were no statistically significant changes in sTnT levels between groups. In this respect, a previous study (JafariNasabian et al., 2017b) had indicated that sTnT levels, as a marker for muscle turnover, were higher in individuals with OSO compared with obese-only elderly. Therefore, the presence of sTnT in the blood is a potentially valuable biomarker for MQ, which is an important risk factor for falls (King et al., 2016). In fact, a previous study (Abreu et al., 2014) had revealed a significant drop in serum sTnT following 10 weeks of strength-training regimen for 60 min, 2 sessions per week with and without free weights exercises in old men and women aged 64–94 years. In contrast, a 5-month resistance trial using 3 sets of 10 repetitions (70% 1-RM) had shown a significant elevation in skeletal muscle troponin I mRNA in the human vastus lateralis muscle (Zhang et al., 2013). It seems that body composition changes and resistance training regimes may also play pivotal roles in regulating skeletal muscle troponin (Pihlajamäki et al., 2011). In the present study, obesity status could interfere with normal skeletal muscle troponin regulation in patients with OSO syndrome. Similar to these results, Abreu et al. reported that an increase in hand grip strength test was correlated with a significant reduction in serum sTnT levels and a significant reduction in sTnT levels (Abreu et al., 2014). Furthermore, King et al. (2016) illustrated a significant association between balance scores and strength, and serum sTnT levels (King et al., 2016).

Furthermore, no significant changes were found in CTX-I between study groups. An acute study on older adults with low bone mass (59.1 ± 7.1 years) divided into a control group with BMI (28.1 ± 3.9 kg/m2), a resistance exercise group with BMI (26.3 ± 5.4 kg/m2), and a walking group with BMI (27.2 ± 6.1 kg/m^2), with a moderate intensity brisk walking (3–6 METs) and resistance training (30 min of exercises that included large muscle groups and core exercise training) also showed changes in CTX-I levels in the resistance training but not in the walking group) (Gombos et al., 2016). Based on these analyses, exercise training regime did not change some OSO markers, except for leptin, MQ, and OSO *Z*-score. The dissociation in patterns of training-induced changes in these OSO markers might be due to the fact that circulating leptin had significantly decreased, whereas other OSO biomarkers such as CAF, adiponectin, and sTnT had not changed modestly in response to muscle contraction in women with OSO syndrome. It seems that unchanged OSO markers after 12-week resistance training and discrepancies in reports were probably due to different metabolic states, discrepancy between applied exercise intensities, (Jedrychowski et al., 2015) as well as different analytical and pre-analytical conditions (JafariNasabian et al., 2017b).

The current study has some limitation that are worthy of note. First, given the nature of the design, we cannot control or determine the effect of social interactions as part of exercise training on outcomes; therefore, probably social interactions could affect our outcomes. Secondly, our training program included 12 weeks of EBRT. The short duration of the intervention may be a reason for non-significant effect of exercise on some study markers or lack of moderator effect of disability status. Another limitation is the absence of long-term follow-up which could indicate a lasting effect of the intervention. Additionally, elevating time-course response of the biomarkers to a single session of exercise can also useful to interpret current results; therefore, it is recommended that in future studies the moderator role of OSO syndrome investigated in this issue. Furthermore, it is possible that studies with larger sample size would be more effective to detect small effect sizes of this kind of intervention. Finaly, due to the specific natures of sarcopenia, SO and OSO which include aspects of inflammation, obesity, osteoporosis, sarcopenia and other factors that may decrease different tissues responses to exercise, it is debatable whether results evaluated in OSO subjects can be simply generalized to OSO cohorts. This suggests, however, that future studies should compare the effect of dedicated different exercise programs in older cohorts with and without sarcopenia, OS and SO to allow a generalization of data to the field of sarcopenic, SO and OSO cohorts.

4.1. Perspectives

Based on the above-mentioned analyses, MQ was significantly associated with all OSO markers and functional performance variables, except for CAF. Taken together, the results of the present study showed significant differences only in some OSO markers between groups after 48 h of chronic EBRT in women with OSO syndrome. EBRT provoke only minor and non-significant improvements in total serum OSO biomarkers, some functional abilities and body composition parameters, which indicates that the responsibility potential of women with OSO is blunted at OSO syndrome status. From a physiological perspective, this results could be useful for the application of EBRT in OSO people may be required to maximize functional gains in elderly women with OSO, although it has been suggested that greater training duration and volume may largely compensate for lower intensity in this study.

The present EBRT protocol could facilitate tailoring decision-making regarding the optimal treatment protocol for elderly women with OSO. However, the information available has been limited and insufficient to characterize precise functions and activities in response to different exercise programs in humans for many of the OSO markers identified to date. Further research is thus recommended to design machine- and elastic band-based resistance training regimes at different intensities and volumes.

Ethics approval

This trial was approved by Iranian Ethics Committee of Sport Sciences Research Center (IR.SSRC.REC.1398.140).

CRediT authorship contribution statement

Ebrahim Banitalebi: Methodology, Supervision, Investigation, Data curation, Writing - original draft, Writing - review & editing.**Mohammad Faramarzi:** Methodology, Investigation, Writing - review & editing.**Majid Mardaniyan Ghahfarokhi:** Methodology, Data curation, Writing - original draft, Writing - review & editing.**Farideh SavariNikoo:** Methodology, Supervision, Data curation, Writing - review & editing.**Neda Soltani:** Methodology, Supervision, Data curation, Writing - review & editing.**Azita Bahramzadeh:** Methodology, Supervision, Data curation, Writing - review & editing.

Declaration of competing interest

The authors declared no competing interests.

Acknowledgements

The authors would like to express their gratitude to all participants contributing to this study.

Funding

This study was supported by a grant from Shahrekord University (grant no: 96INT8M895).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2020.110884.

References

Abbenhardt, C., McTiernan, A., Alfano, C.M., Wener, M.H., Campbell, K.L., Duggan, C., Foster-Schubert, K.E., Kong, A., Toriola, A.T., Potter, J.D., 2013. Effects of individual and combined dietary weight loss and exercise interventions in postmenopausal women on adiponectin and leptin levels. J. Intern. Med. 274, 163–175.

Abreu, E.L., Cheng, A.-L., Kelly, P.J., Chertoff, K., Brotto, L., Griffith, E., Kinder, G., Uridge, T., Zachow, R., Brotto, M., 2014. Skeletal muscle troponin as a novel biomarker to enhance assessment of the impact of strength training on fall prevention in the older adults. Nurs. Res. 63, 75–82.

Ardawi, M.S.M., Rouzi, A.A., Al-Sibiani, S.A., Al-Senani, N.S., Qari, M.H., Mousa, S.A., 2012. High serum sclerostin predicts the occurrence of osteoporotic fractures in postmenopausal women: the Center of Excellence for Osteoporosis Research Study. J. Bone Miner. Res. 27, 2592–2602.

Asgharzadeh, S., Zaeri, M., Holakouie Naeini, K., Rahimi Foroushani, A., 2014. The Quality of Life and its effective factors in the elderly living population of Azerbaijan District, Tehran, Iran. Iran. J. Epidemiol. 9, 66–74.

Atkinson, C., Lampe, J.W., Tworoger, S.S., Ulrich, C.M., Bowen, D., Irwin, M.L., Schwartz, R.S., Rajan, B.K., Yasui, Y., Potter, J.D., 2004. Effects of a moderate intensity exercise intervention on estrogen metabolism in postmenopausal women. Cancer Epidemiology and Prevention Biomarkers 13, 868–874.

Barry, E., Galvin, R., Keogh, C., Horgan, F., Fahey, T., 2014. Is the Timed Up and Go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. BMC Geriatr. 14, 14.

Beavers, K.M., Brinkley, T.E., Nicklas, B.J., 2010. Effect of exercise training on chronic inflammation. Clin. Chim. Acta 411, 785–793.

Bhasin, S., He, E.J., Kawakubo, M., Schroeder, E.T., Yarasheski, K., Opiteck, G.J., Reicin, A., Chen, F., Lam, R., Tsou, J.A., 2009. N-terminal propeptide of type III procollagen as a biomarker of anabolic response to recombinant human GH and testosterone. The Journal of Clinical Endocrinology & Metabolism 94, 4224–4233.

Bondoc, I., Cochrane, S.K., Church, T.S., Dahinden, P., Hettwer, S., Hsu, F.-C., Stafford, R.S., Pahor, M., Buford, T.W., Investigators, L.S., 2015. Effects of a one-year physical activity program on serum C-terminal Agrin Fragment (CAF) concentrations among mobility-limited older adults. J. Nutr. Health Aging 19, 922–927.

Botero, J.P., Shiguemoto, G., Prestes, J., Marin, C., Do Prado, W., Pontes, C., Guerra, R., Ferreia, F., Baldissera, V., Perez, S., 2013. Effects of long-term periodized resistance training on body composition, leptin, resistin and muscle strength in elderly postmenopausal women. J Sports Med Phys Fitness 53, 289–294.

Boutron, I., Altman, D.G., Moher, D., Schulz, K.F., Ravaud, P., 2017. CONSORT statement for randomized trials of nonpharmacologic treatments: a 2017 update and a CONSORT extension for nonpharmacologic trial abstracts. Ann. Intern. Med. 167, 40–47.

Bouzid, K., Bahlous, A., Kalaï, E., Fellah, H., Sahli, H., Sellami, S., Abdelmoula, J., 2010. C-telopeptides of type I collagen in postmenopausal women: an experience in a Tunisian Clinical Laboratory. Tunis Med 88, 467–469.

Campbell, K.L., Westerlind, K.C., Harber, V.J., Bell, G.J., Mackey, J.R., Courneya, K.S., 2007. Effects of aerobic exercise training on estrogen metabolism in premenopausal women: a randomized controlled trial. Cancer Epidemiology and Prevention Biomarkers 16, 731–739.

Casati, M., Costa, A.S., Capitanio, D., Ponzoni, L., Ferri, E., Agostini, S., Lori, E., 2019. The biological foundations of sarcopenia: established and promising markers. Frontiers in medicine 6, 184.

Chan, W.L., Pin, T.W., 2019. Reliability, validity and minimal detectable change of 2-minute walk test, 6-minute walk test and 10-meter walk test in frail older adults with dementia. Exp. Gerontol. 115, 9–18.

Chan, M.-F., Dowsett, M., Folkerd, E., Bingham, S., Wareham, N., Luben, R., Welch, A., Khaw, K.-T., 2007. Usual physical activity and endogenous sex hormones in postmenopausal women: the European Prospective Investigation into Cancer–Norfolk Population Study. Cancer Epidemiology and Prevention Biomarkers 16, 900–905.

Chen, H.T., Chung, Y.C., Chen, Y.J., Ho, S.Y., Wu, H.J., 2017. Effects of different types of exercise on body composition, muscle strength, and IGF-1 in the elderly with sarcopenic obesity. J. Am. Geriatr. Soc. 65, 827–832.

China, S.P., Pal, S., Chattopadhyay, S., Porwal, K., Kushwaha, S., Bhattacharyya, S., Mittal, M., Gurjar, A.A., Barbhuyan, T., Singh, A.K., 2017. Globular adiponectin reverses osteo-sarcopenia and altered body composition in ovariectomized rats. Bone 105, 75–86.

Chiu, S.-C., Yang, R.-S., Yang, R.-J., Chang, S.-F., 2018. Effects of resistance training on body composition and functional capacity among sarcopenic obese residents in long-term care facilities: a preliminary study. BMC Geriatr. 18, 21.

Colado, J.C., Triplett, N.T., 2008. Effects of a short-term resistance program using elastic bands versus weight machines for sedentary middle-aged women. The Journal of Strength & Conditioning Research 22, 1441–1448.

Consitt, L.A., Copeland, J.L., Tremblay, M.S., 2001. Hormone responses to resistance vs. endurance exercise in premenopausal females. Can. J. Appl. Physiol. 26, 574–587.

Cunha, P.M., Ribeiro, A.S., Tomeleri, C.M., Schoenfeld, B.J., Silva, A.M., Souza, M.F., Nascimento, M.A., Sardinha, L.B., Cyrino, E.S., 2017. The effects of resistance training volume on osteosarcopenic obesity in older women. J. Sports Sci. 1–8.

Cunha, P.M., Ribeiro, A.S., Tomeleri, C.M., Schoenfeld, B.J., Silva, A.M., Souza, M.F., Nascimento, M.A., Sardinha, L.B., Cyrino, E.S., 2018. The effects of resistance training volume on osteosarcopenic obesity in older women. J. Sports Sci. 36, 1564–1571.

De Salles, B., Simao, R., Fleck, S., Dias, I., Kraemer-Aguiar, L., Bouskela, E., 2010. Effects of resistance training on cytokines. Int. J. Sports Med. 31, 441–450.

Devries, M.C., Hamadeh, M.J., Graham, T.E., Tarnopolsky, M.A., 2005. 17β-estradiol supplementation decreases glucose rate of appearance and disappearance with no effect on glycogen utilization during moderate intensity exercise in men. The Journal of Clinical Endocrinology & Metabolism 90, 6218–6225.

Drey, M., Sieber, C., Bauer, J., Uter, W., Dahinden, P., Fariello, R., Vrijbloed, J., 2013. C-terminal Agrin Fragment as a potential marker for sarcopenia caused by degeneration of the neuromuscular junction. Exp. Gerontol. 48, 76–80.

Efird, J., 2010. Blocked randomization with randomly selected block sizes. Int. J. Environ. Res. Public Health 8, 15–20.

ElDeeb, A.M., Elsisi, H.F., Lasheen, Y.R., 2018. Response of lipids, estradiol level, and liver size to diet and high-intensity interval training in postmenopausal women with fatty liver. Bulletin of Faculty of Physical Therapy 23, 69.

Ennour-Idrissi, K., Maunsell, E., Diorio, C., 2015. Effect of physical activity on sex hormones in women: a systematic review and meta-analysis of randomized controlled trials. Breast Cancer Res. 17, 139.

Fatouros, I., Tournis, S., Leontsini, D., Jamurtas, A., Sxina, M., Thomakos, P., Manousaki, M., Douroudos, I., Taxildaris, K., Mitrakou, A., 2005. Leptin and adiponectin responses in overweight inactive elderly following resistance training and detraining are intensity related. The Journal of Clinical Endocrinology & Metabolism 90, 5970–5977.

Fatouros, I.G., Chatzinikolaou, A., Tournis, S., Nikolaidis, M.G., Jamurtas, A.Z., Douroudos, I.I., Papassotiriou, I., Thomakos, P.M., Taxildaris, K., Mastorakos, G., 2009. Intensity of resistance exercise determines adipokine and resting energy expenditure responses in overweight elderly individuals. Diabetes Care 32, 2161–2167.

Fedewa, M.V., Hathaway, E.D., Ward-Ritacco, C.L., Williams, T.D., Dobbs, W.C., 2018. The effect of chronic exercise training on leptin: a systematic review and meta-analysis of randomized controlled trials. Sports Med. 48, 1437–1450.

Figueroa, A., Vicil, F., Sanchez-Gonzalez, M.A., Wong, A., Ormsbee, M.J., Hooshmand, S., Daggy, B., 2013. Effects of diet and/or low-intensity resistance exercise training on arterial stiffness, adiposity, and lean mass in obese postmenopausal women. Am. J. Hypertens. 26, 416–423.

Fragala, M.S., Jajtner, A.R., Beyer, K.S., Townsend, J.R., Emerson, N.S., Scanlon, T.C., Oliveira, L.P., Hoffman, J.R., Stout, J.R., 2014a. Biomarkers of muscle quality: N-terminal propeptide of type III procollagen and C-terminal agrin fragment responses to resistance exercise training in older adults. J. Cachexia. Sarcopenia Muscle 5, 139–148.

Fragala, M.S., Fukuda, D.H., Stout, J.R., Townsend, J.R., Emerson, N.S., Boone, C.H., Beyer, K.S., Oliveira, L.P., Hoffman, J.R., 2014b. Muscle quality index improves with resistance exercise training in older adults. Exp. Gerontol. 53, 1–6.

Furtado, G., Letieri, R., Caldo, A., Patricio, M., Loureiro, M., Hogervorst, E., Ferreira, J., Teixeira, A., 2019. The role of physical frailty independent components on increased disabilities in institutionalized older women. Translational medicine@ UniSa 19, 17.

Gleeson, M., Bishop, N.C., Stensel, D.J., Lindley, M.R., Mastana, S.S., Nimmo, M.A., 2011. The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat. Rev. Immunol. 11, 607–615.

Goisser, S., Kemmler, W., Porzel, S., Volkert, D., Sieber, C.C., Bollheimer, L.C., Freiberger, E., 2015. Sarcopenic obesity and complex interventions with nutrition and exercise in community-dwelling older persons—a narrative review. Clin. Interv. Aging 10, 1267.

Gombos, G.C., Bajsz, V., Pék, E., Schmidt, B., Sió, E., Molics, B., Betlehem, J., 2016. Direct effects of physical training on markers of bone metabolism and serum sclerostin concentrations in older adults with low bone mass. BMC Musculoskelet. Disord. 17, 254.

Guadalupe-Grau, A., Perez-Gomez, J., Olmedillas, H., Chavarren, J., Dorado, C., Santana, A., Serrano-Sanchez, J.A., Calbet, J.A.L., 2009. Strength training combined with plyometric jumps in adults: sex differences in fat-bone axis adaptations. J. Appl. Physiol. 106, 1100–1111.

Hita-Contreras, F., Martínez-Amat, A., Cruz-Díaz, D., Pérez-López, F.R., 2015. Osteosarcopenic obesity and fall prevention strategies. Maturitas 80, 126–132.

Huang, S.W., Ku, J.W., Lin, L.F., Liao, C.D., Chou, L.C., Liou, T.H., 2017. Body composition influenced by progressive elastic band resistance exercise of sarcopenic obesity elderly women: a pilot randomized controlled trial. Eur J Phys Rehabil Med. 53, 556–563.

Ilich, J.Z., Kelly, O.J., Inglis, J.E., Panton, L.B., Duque, G., Ormsbee, M.J., 2014. Interrelationship among muscle, fat, and bone: connecting the dots on cellular, hormonal, and whole body levels. Ageing Res. Rev. 15, 51–60.

Ilich, J.Z., Kelly, O.J., Inglis, J.E., 2016. Osteosarcopenic obesity syndrome: what is it and how can it be identified and diagnosed? Current gerontology and geriatrics research 2016.

Ishimura, E., Okuno, S., Ichii, M., Norimine, K., Yamakawa, T., Shoji, S., Nishizawa, Y., Inaba, M., 2014. Relationship between serum sclerostin, bone metabolism markers, and bone mineral density in maintenance hemodialysis patients. The Journal of Clinical Endocrinology & Metabolism 99, 4315–4320.

J Kelly, O., C Gilman, J., 2017. Can unconventional exercise be helpful in the treatment, management and prevention of osteosarcopenic obesity? Current aging science 10, 106–121.

JafariNasabian, P., 2017. Analyzing Bone, Muscle and Adipose Tissue Biomarkers to Identify Osteosarcopenic Obesity Syndrome in Older Women. The Florida State University.

JafariNasabian, P., 2018. How exercise and dietary intervention affect the outcome of osteosarcopenic obesity syndrome? Journal of Functional Morphology and Kinesiology 3, 31.

JafariNasabian, P., Inglis, J.E., Kelly, O.J., Ilich, J.Z., 2017a. Osteosarcopenic obesity in

women: impact, prevalence, and management challenges. Int. J. Women's Health 9, 33.
JafariNasabian, P., Inglis, J.E., Ave, M.P., Hall, K.J., Nieto, S.E., Kelly, O.J., Ilich, J.Z., 2017b. Metabolic profile of osteosarcopenic obesity syndrome: identifying biomarkers for diagnostic criteria. FASEB J. 31, 151–155.
Jedrychowski, M.P., Wrann, C.D., Paulo, J.A., Gerber, K.K., Szpyt, J., Robinson, M.M., Nair, K.S., Gygi, S.P., Spiegelman, B.M., 2015. Detection and quantitation of circulating human irisin by tandem mass spectrometry. Cell Metab. 22, 734–740.
Judd, H.L., Shamonki, I.M., Frumar, A.M., Lagasse, L.D., 1982. Origin of serum estradiol in postmenopausal women. Obstet. Gynecol. 59, 680–686.
Kanaley, J., Fenicchia, L., Miller, C., Ploutz-Synder, L., Weinstock, R., Carhart, R., Azevedo Jr, J., 2001. Resting leptin responses to acute and chronic resistance training in type 2 diabetic men and women. Int. J. Obes. 25, 1474.
Kim, J., Lee, Y., Kye, S., Chung, Y.S., Lee, O., 2017. Association of serum vitamin D with osteosarcopenic obesity: Korea National Health and Nutrition Examination Survey 2008–2010. J. Cachexia. Sarcopenia Muscle 8, 259–266.
King, G.W., Abreu, E.L., Cheng, A.-L., Chertoff, K.K., Brotto, L., Kelly, P.J., Brotto, M., 2016. A multimodal assessment of balance in elderly and young adults. Oncotarget 7, 13297.
Kohara, K., Ochi, M., Tabara, Y., Nagai, T., Igase, M., Miki, T., 2011. Leptin in sarcopenic visceral obesity: possible link between adipocytes and myocytes. PLoS One 6, e24633.
Lagally, K.M., Robertson, R.J., 2006. Construct validity of the OMNI resistance exercise scale. The Journal of Strength & Conditioning Research 20, 252–256.
Landi, F., Calvani, R., Lorenzi, M., Martone, A.M., Tosato, M., Drey, M., D'angelo, E., Capoluongo, E., Russo, A., Bernabei, R., 2016. Serum levels of C-terminal agrin fragment (CAF) are associated with sarcopenia in older multimorbid community-dwellers: results from the ilSIRENTE study. Exp. Gerontol. 79, 31–36.
Lau, P.W., Kong, Z., Choi, C.-r., Clare, C., Chan, D.F., Sung, R.Y., Leung, B.W., 2010. Effects of short-term resistance training on serum leptin levels in obese adolescents. Journal of Exercise Science & Fitness 8, 54–60.
Liao, C.-D., Tsauo, J.-Y., Lin, L.-F., Huang, S.-W., Ku, J.-W., Chou, L.-C., Liou, T.-H., 2017. Effects of elastic resistance exercise on body composition and physical capacity in older women with sarcopenic obesity: a CONSORT-compliant prospective randomized controlled trial. Medicine 96.
Liao, C.-D., Tsauo, J.-Y., Huang, S.-W., Ku, J.-W., Hsiao, D.-J., Liou, T.-H., 2018. Effects of elastic band exercise on lean mass and physical capacity in older women with sarcopenic obesity: a randomized controlled trial. Sci. Rep. 8, 2317.
Martínez-Amat, A., Aibar-Almazán, A., Fábrega-Cuadros, R., Cruz-Díaz, D., Jiménez-García, J.D., Pérez-López, F.R., Achalandabaso, A., Barranco-Zafra, R., Hita-Contreras, F., 2018. Exercise alone or combined with dietary supplements for sarcopenic obesity in community-dwelling older people: a systematic review of randomized controlled trials. Maturitas 110, 92–103.
Marzetti, E., Calvani, R., Lorenzi, M., Marini, F., D'Angelo, E., Martone, A.M., Celi, M., Tosato, M., Bernabei, R., Landi, F., 2014. Serum levels of C-terminal agrin fragment (CAF) are associated with sarcopenia in older hip fractured patients. Exp. Gerontol. 60, 79–82.
Mehraban, A.H., Soltanmohamadi, Y., Akbarfahimi, M., Taghizadeh, G., 2014. Validity and reliability of the persian version of Lawton instrumental activities of daily living scale in patients with dementia. Med. J. Islam Repub. Iran 28, 25.
Miller, G.D., Nicklas, B.J., Davis, C.C., Ambrosius, W.T., Loeser, R.F., Messier, S.P., 2004a. Is serum leptin related to physical function and is it modifiable through weight loss and exercise in older adults with knee osteoarthritis? Int. J. Obes. 28, 1383–1390.
Miller, G., Nicklas, B., Davis, C., Ambrosius, W., Loeser, R., Messier, S., 2004b. Is serum leptin related to physical function and is it modifiable through weight loss and exercise in older adults with knee osteoarthritis? Int. J. Obes. 28, 1383.
de Oliveira Silva, A., Dutra, M.T., de Moraes, W.M.A.M., Funghetto, S.S., de Farias, D.L., dos Santos, P.H.F., Vieira, D.C.L., da Cunha Nascimento, D., Orsano, V.S.M., Schoenfeld, B.J., 2018. Resistance training-induced gains in muscle strength, body composition, and functional capacity are attenuated in elderly women with sarcopenic obesity. Clin. Interv. Aging 13, 411.
Ormsbee, M.J., Prado, C.M., Ilich, J.Z., Purcell, S., Siervo, M., Folsom, A., Panton, L., 2014. Osteosarcopenic obesity: the role of bone, muscle, and fat on health. J. Cachexia. Sarcopenia Muscle 5, 183–192.
Perna, S., Francis, M.D.A., Bologna, C., Moncaglieri, F., Riva, A., Morazzoni, P., Allegrini, P., Isu, A., Vigo, B., Guerriero, F., 2017. Performance of Edmonton Frail Scale on frailty assessment: its association with multi-dimensional geriatric conditions assessed with specific screening tools. BMC Geriatr. 17, 2.
Perna, S., Spadaccini, D., Nichetti, M., Avanzato, I., Faliva, M.A., Rondanelli, M., 2018. Osteosarcopenic visceral obesity and osteosarcopenic subcutaneous obesity, two new phenotypes of sarcopenia: prevalence, metabolic profile, and risk factors. Journal of aging research 2018.
Pihlajamäki, J., Lerin, C., Itkonen, P., Boes, T., Floss, T., Schroeder, J., Dearie, F., Crunkhorn, S., Burak, F., Jimenez-Chillaron, J.C., 2011. Expression of the splicing factor gene SFRS10 is reduced in human obesity and contributes to enhanced lipogenesis. Cell Metab. 14, 208–218.
Pinto, T.C., Santos, M.S., Machado, L., Bulgacov, T.M., Rodrigues-Junior, A.L., Silva, G.A., Costa, M.L.G., Ximenes, R.C., Sougey, E.B., 2019. Optimal cutoff scores for dementia and mild cognitive impairment in the Brazilian version of the Montreal cognitive assessment among the elderly. Dementia and Geriatric Cognitive Disorders Extra 9, 44–52.
Prestes, J., Shiguemoto, G., Botero, J.P., Frollini, A., Dias, R., Leite, R., Pereira, G., Magosso, R., Baldissera, V., Cavaglieri, C., 2009. Effects of resistance training on resistin, leptin, cytokines, and muscle force in elderly post-menopausal women. J. Sports Sci. 27, 1607–1615.
Prestes, J., da Cunha Nascimento, D., de Sousa Neto, I.V., Tibana, R.A., Shiguemoto, G.E., de Andrade Perez, S.E., Botero, J.P., Schoenfeld, B.J., Pereira, G.B., 2018. The effects of muscle strength responsiveness to periodized resistance training on resistin, leptin, and cytokine in elderly postmenopausal women. The Journal of Strength & Conditioning Research 32, 113–120.
Procaccini, C., Jirillo, E., Matarese, G., 2012. Leptin as an immunomodulator. Mol. Asp. Med. 33, 35–45.
Ribeiro, A.S., Schoenfeld, B.J., Souza, M.F., Tomeleri, C.M., Venturini, D., Barbosa, D.S., Cyrino, E.S., 2016. Traditional and pyramidal resistance training systems improve muscle quality and metabolic biomarkers in older women: a randomized crossover study. Exp. Gerontol. 79, 8–15.
Ribom, E.L., Piehl-Aulin, K., Ljunghall, S., Ljunggren, Ö., Naessén, T., 2002. Six months of hormone replacement therapy does not influence muscle strength in postmenopausal women. Maturitas 42, 225–231.
Scanlon, T.C., Fragala, M.S., Stout, J.R., Emerson, N.S., Beyer, K.S., Oliveira, L.P., Hoffman, J.R., 2014. Muscle architecture and strength: adaptations to short-term resistance training in older adults. Muscle Nerve 49, 584–592.
Shen, S.-S., Chu, J.-J., Cheng, L., Zeng, X.-K., He, T., Xu, L.-Y., Li, J.-R., Chen, X.-J., 2016. Effects of a nutrition plus exercise programme on physical function in sarcopenic obese elderly people: study protocol for a randomised controlled trial. BMJ Open 6, e012140.
Smith, A.J., Phipps, W.R., Thomas, W., Schmitz, K.H., Kurzer, M.S., 2013. The effects of aerobic exercise on estrogen metabolism in healthy premenopausal women. Cancer Epidemiology and Prevention Biomarkers 22, 756–764.
Stout, J.R., Smith-Ryan, A.E., Fukuda, D.H., Kendall, K.L., Moon, J.R., Hoffman, J.R., Wilson, J.M., Oliver, J.S., Mustad, V.A., 2013. Effect of calcium β-hydroxy-β-methylbutyrate (CaHMB) with and without resistance training in men and women 65+ yrs: a randomized, double-blind pilot trial. Exp. Gerontol. 48, 1303–1310.
Szlejf, C., Parra-Rodríguez, L., Rosas-Carrasco, O., 2017. Osteosarcopenic obesity: prevalence and relation with frailty and physical performance in middle-aged and older women. J. Am. Med. Dir. Assoc. 18, 733. e1–733. e5.
Tartibian, B., Zarneshan, A., 2008. Effect of 10 week chosen aerobic training program in serum 17 beta estradiol and menopause women overweight. Bull Olympic 3, 43.
Taylor, C., Lamparello, B., Kruczek, K., Anderson, E.J., Hubbard, J., Misra, M., 2009. Validation of a food frequency questionnaire for determining calcium and vitamin D intake by adolescent girls with anorexia nervosa. J. Am. Diet. Assoc. 109, 479–485 (e3).
Wingfield, H.L., Smith-Ryan, A.E., Melvin, M.N., Roelofs, E.J., Trexler, E.T., Hackney, A.C., Weaver, M.A., Ryan, E.D., 2015. The acute effect of exercise modality and nutrition manipulations on post-exercise resting energy expenditure and respiratory exchange ratio in women: a randomized trial. Sports medicine-open 1, 11.
Yasuda, T., Fukumura, K., Uchida, Y., Koshi, H., Iida, H., Masamune, K., Yamasoba, T., Sato, Y., Nakajima, T., 2014. Effects of low-load, elastic band resistance training combined with blood flow restriction on muscle size and arterial stiffness in older adults. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences 70, 950–958.
Zhang, T., Choi, S.J., Wang, Z.-M., Birbrair, A., Messi, M.L., Jin, J.-P., Marsh, A.P., Nicklas, B., Delbono, O., 2013. Human slow troponin T (TNNT1) pre-mRNA alternative splicing is an indicator of skeletal muscle response to resistance exercise in older adults. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences 69, 1437–1447.
Zoico, E., Di Francesco, V., Mazzali, G., Vettor, R., Fantin, F., Bissoli, L., Guariento, S., Bosello, O., Zamboni, M., 2004. Adipocytokines, fat distribution, and insulin resistance in elderly men and women. J. Gerontol. Ser. A Biol. Med. Sci. 59, M935–M939.