Research Article

The effects of an elastic-band resistance training on hepatic steatosis and osteosarcopenic adiposity

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Abstract

Osteosarcopenic adiposity (OSA) syndrome significantly impacts hepatic disorders more than each of the tissues alone. The purpose of this study is to evaluate the effects of elastic resistance training modality on hepatic health markers, including fatty liver index (FLI), lipid accumulation product (LAP), hepatic steatosis index (HSI), and Framingham steatosis index (FSI)), in the elderly with OSA. Sixty-three eligible patients aged 60-80 years meet the inclusion criteria, including a) body fat percentage (BFP) ≥32%; b) body mass index (BMI) ≥30 kg/m²; c) T-score of L1-L4, and/or total femur or femoral neck -2.5≤T-score ≤-1.0; d) gait speed (10-meter walk test (10MWT) ≤1 (m/s²); and e) skeletal muscle index (SMI) ≤28% or ≤7.76 kg/m². The participants were randomly assigned to experimental (n=32) or control (n=31) groups. The experimental group completed a 12-week elastic-band resistance training program [3x/week; 60 min/session]. The results showed a statistically significant benefit from the elastic-band resistance training on LAP (P=0.033), FLI (P=0.001), HSI (P=0.008), and FSI (P=0.001). Our findings show that an elastic-band resistance exercise training program can improve hepatic function. This relatively low-cost, highly accessible form of exercise can be easily implemented to enhance the health of this population across a wide range of settings.

Key Words: **Exercise training, Fatty liver index, Obesity, Older adults, Sarcopenia**

Introduction

Maintenance of the systemic homeostasis in the older individual and chronic hepatic diseases requires the coordination and crosstalk (Priest & Tontonoz, 2019) between main endocrine tissue-organs such as liver, adipose (Azzu et al., 2020), bone (Musso et al., 2013; Yilmaz, 2012), and skeletal muscle (Chakravarthy et al., 2020) Each of these tissues can affect metabolic pathways in distant tissues with beneficial or non-beneficial effects on the pathophysiology of hepatic disorders (Kashiwagi et al., 2021). It has been suggested that bone, muscle, and adipose tissues may act synergistically, and may have a greater impact on hepatic disorders than each of the tissues alone (Kashiwagi et al., 2021; Lee et al., 2021). In that context and with the deterioration of each tissue, the best model to examine would be the osteosarcopenic adiposity (OSA) syndrome. It is a condition characterized by simultaneous unfavourable changes in bone, muscle, and adipose tissue, resulting in osteoporosis, sarcopenia, and overweight/adiposity (Ilich, 2020; Ilich et al., 2020). The prevalence of OSA varies due to the different diagnostic cut-off points but it is clinically related to several cardiometabolic diseases including hepatic disorders like dyslipidaemia, insulin resistance and hyperglycaemia. Given its detrimental effects clinical effects (Ilich et al., 2024).

Expanding our understanding of the relations between OSA and hepatic disorders might help identify potential therapeutic targets that delay the development of OSA as well as its progression to hepatic disorders (Ilich, 2020; Ilich et al., 2020; Poggiogalle et al., 2021). Exercise training is one of the safest, most inexpensive, and most feasible therapeutic interventions for adipose, bone, and skeletal muscle tissues related disorders (Biolo et al., 2014; JafariNasabian et al., 2017), as well as for hepatic disorders (Banitalebi et al., 2019). Resistance training offers a wide range of physiological benefits to skeletal muscle, bone and fat tissues (Banitalebi et al., 2020; Banitalebi et al., 2021; Cunha et al., 2018). Similarly, both aerobic and resistance exercise reduce hepatic steatosis. However, resistance training may be more feasible than aerobic exercise

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for older population with poor cardiorespiratory capacity or for those who cannot tolerate or participate in aerobic exercise (Hashida et al., 2017; Schranz et al., 2013).

Although long-term aerobic training is effective for improving cardio-metabolic capacity, aerobic training fails to result in significant effects on bone, fat, skeletal muscle, muscular fitness, and functional capacity in older adults living with OSA syndrome model. Performing resistance training by the use of elastic bands or tubes can control tension during loading, provide the proper individualized load beneficial for body composition compartments, and enhance hepatic benefits (Souza et al., 2019). For many years researchers have focused on identifying and introducing a clinical risk scoring for predicting hepatic steatosis for evaluating and monitoring responses to therapeutic strategies. Several risk prediction equations useful in the primary prevention of hepatic steatosis at the individual and clinical level have been developed in recent years. For example, it has been shown that Fatty Liver Index (FLI) (Leutner et al., 2017), Lipid Accumulation Product (LAP) (Mazidi et al., 2017; Pineda et al., 2017), Hepatic Steatosis Index (HSI) (Lee et al., 2010), Framingham Steatosis Index (FSI) (Shen et al., 2017) have been utilized to screen hepatic steatosis identify potential patients for further examination in clinical practice (Zhu et al., 2018) Therefore, the primary objective of this randomized controlled trial (RCT) was to investigate the effects of unique and targeted resistance training with elastic band on traditional hepatic steatosis risk markers, as well as on some novelty combined markers. The secondary objective was to evaluate the changes in body composition because of resistance training in older women with OSA syndrome. We hypothesized that traditional hepatic steatosis risk factors such alkaline phosphatase (ALP). Alanine transaminase (ALT). Aspartate transaminase (AST) gamma-glutamyl transferase (GGT) would be improved following the resistance training intervention compared with those in a routine care control group, Moreover this group would be associated with greater gains in the novel hepatic steatosis biomarkers (FLI, LAP, HSI, and FSI) compared with the control group. To our knowledge, the present study is the first clinical trial to evaluate the effects of elastic resistance-type training modality on traditional and novel composite hepatic health outcomes, as well as on body composition compartments in older women with OSA.

Materials and Methods

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 Centre (IR.SSRC.REC. 1398.040). All the st-udy participants also provided written informed consent.

Based on patient recruitment rates in previous studies, the participants in this study were recruited via community-wide and general practitioner advertising in the city of Shahrekord. A detailed telephone screening was conducted to identify eligibility of each participant who responded to the advertisement. The enrolment and the study procedures occurred based on the Consolidated Standards of Reporting Trials (CONSORT) Statement for randomized trials of non-pharmacologic treatments (Boutron et al., 2017; Liao et al., 2017). A total of 102 eligible women between 60 and 80 years were evaluated by anthropometric measurements and by dual energy X-ray absorptiometry (DXA) instrument to identify those who met the body composition criteria for OSA. The inclusion criteria were: body mass index (BMI) ≥30 kg/m2, body fat percentage (BFP) ≥32%, T-scores for L1-L4, and/or total femur or femoral neck of -2.5≤T-score≤-1.0, gait speed (10-meter walk test (10MWT)) ≤ 1 (m/s2), and skeletal muscle index (SMI) ≤28% or ≤7.76 kg/m2 (Hita-Contreras et al., 2015; Ilich et al., 2016). Participants were excluded: a) if received hormonal therapies, b) participated in regular exercise training (more than 30 min once a week) in the last six months: toke nutritional supplements within the past 3 months. In addition, participants were excluded if they had resting blood pressure ≥ 160/100 mmHg, fasting triglyceride ≥ 5.7 mmol/L, a history of cardiovascular disease, thyroid disorder, cancer, endo crine disorder such as diabetes, kidney or liver disease, surgery, smoking or using recreational drugs or any alcohol. 63 older women met all criteria and were enrolled in the study (Figure 1).

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 effect size (ES)=0.20. The ES of the elastic band resistance training program was also estimated at 41 Watt for muscle quality (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 to assure for a possible 20% dropout rate (Banitalebi et al., 2020).

Randomization and concealment strategy

All participant provided their written informed consent. After signing the informed consent form, participant performed their baseline assessment and were afterwards randomized The randomization was performed by an external researcher, not involved in testing or training programs, using randomly permuted block allocation with a block size of 4 (Efird, 2010). Participants

were stratified according to two cut-offs for each stratification of age (60-70 or 70-85 years) and OSA-z score (-3 to 0 or 0 to +3). The allocation was 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. Exercise trainers, not involved in data collection, conducted the exercise sessions and monitored the individuals in the control group. The control group received telephone calls or face-to-face interviews once a week to ensure that there were 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. The researchers reinforced the obligation to maintain typical diet and physical activity habits for all participants through the study.

Training protocol

The participants were instructed on how to use the 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 & Triplett, 2008; Lagally & Robertson, 2006). The participants also had to increase or decrease grip width to adjust easier the resistance. Additionally, they were asked to choose an elastic band grip which allowed them to perform 20

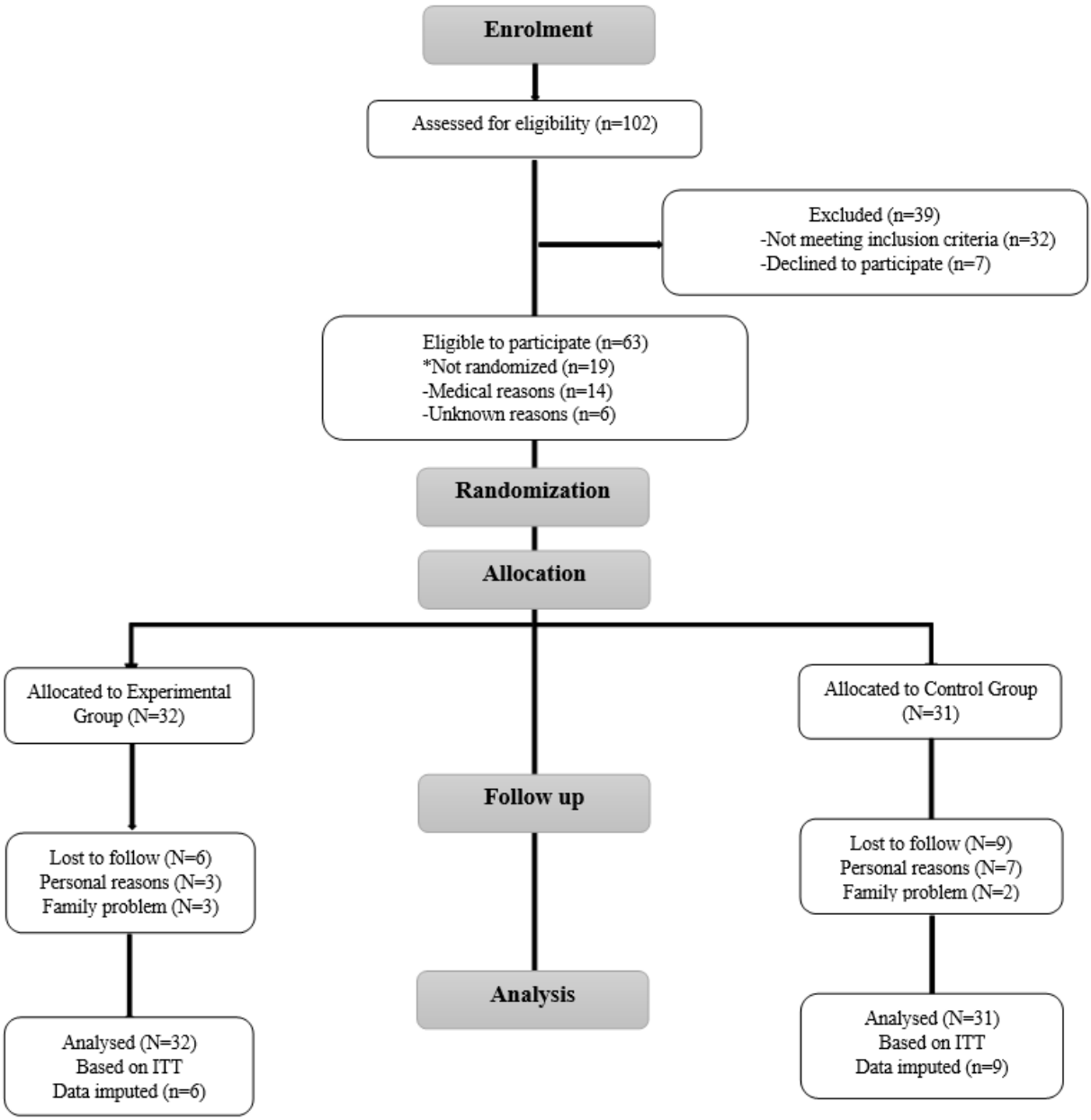

Table 2. Figure 1. Flow diagram representing study design.

repetitions maximum (RM) (Colado & Triplett, 2008). The elastic band resistance training (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 more than 10 participants, 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 seconds 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 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 & Robertson, 2006).

Anthropometric and hemodynamic measurements

All pre- and post-measurements of the experiment were conducted by the same assessor who was blinded to treatment allocation. Assessments were performed at baseline and at 12 weeks within 48 hours after last session in both groups. Demographic and medical history information was collected by questionnaires. Anthropometric measurements, including weight, height (to calculate BMI), waist and hip circumferences were conducted by standard procedures and equipment. Body composition, including measurements of total body, lumbar spine and femur, were performed to assess bone lean and adipose tissues by dual energy x-ray absorptiometry (DXA) (DXA, Discovery WI, Hologic Inc., USA; CV = 1% for whole body values). Systolic and diastolic blood pressure was evaluated as the average of three consecutive measures using an electronic oscillometer device (Rossmax International Ltd., Taiwan).

Clinical markers

Peripheral venous blood was drawn from the antecubital vein after ten hours overnight fasting at the same time under the same conditions before and after 12 weeks exercise training intervention. Fasting blood glucose (FBG) was measured using glucose oxidase method kit (Pars Azmoon, Tehran, Iran), through auto-analyser devices (Hitachi®, model 704, 902, Japan). Serum insulin concentrations were determined by ELISA technique usi-ng a microplate reader. Serum levels of ALT, AST, GGT, TG and high-density lipoprotein cholesterol (HDL-C) were subsequently measured by Pars Azmoon kits (Pars Azmoon Co., Tehran, I.R. Iran). HOMI-IR was calculated by computing the following equation: (fasting glycemia [mmol/l] × fasting insulin [MIU/l]) / 22.5 (Ahmadizad et al., 2007). Participants who used insulin injection were excluded for the HOMA-IR analysis.

Novel hepatic steatosis indices

Novel hepatic steatosis indices included the fatty liver index (FLI) lipid accumulation product (LAP) hepatic steatosis index (HIS) Framingham steatosis index (FSI) and Homeostasis model assessment (HOMA-IR) were calculated as follow:

1. FLI = (E0.953 × log (triglycerides) + 0.139 × BMI + 0.718 × log (GGT) + 0.053 × waist circumference - 15.745) / (1 + e 0.953 × loge (triglycerides) + 0.139 × BMI + 0.718 × loge (GGT) + 0.053 × waist circumference - 15.745) × 100 (Leutner et al., 2017).
2. LAP= (waist circumference [cm] −65) × (triglyceride concentration [mM]) for men, and (waist circumference [cm] −58) × (triglyceride concentration [mM]) for women (Mazidi et al., 2017; Pineda et al., 2017).
3. HSI = 8 (ALT/AST) ratio + BMI (+2 if male +2 if female) (Lee et al., 2010).
4. FSI = -7.981 + 0.011 x age (years) – 0.146 x sex (female=1, male=0) + 0.173 x BMI (kg/m2) + 0.007 x triglycerides (mg/dl) + 0.593 x hypertension (yes=1, no=0) + 0.789 x diabetes (yes=1, no=0) + 1.1 x ALT/AST ratio ≥1.33 (yes=1, no=0) (Shen et al., 2017).
5. HOMA-IR was calculated using the formula: HOMA-IR= [fasting concentrations of glucose (mg/dl) × insulin (mU/L)] /405 (Shabkhiz et al., 2021).

Statistical analyses

Data were initially inspected for normality of distribution using the Kolmogorov-Smirnov test. Both the Mann-Whitney U Test (when data were not normally distributed) and independent-sample t-test were used to compare baseline characteristics of the groups relative to the baseline values. Within group baseline/ follow-up assessments were made using paired sample t-tests or Wilcoxon (when data were not normally distributed). Independent-sample t-test was used to compare group differences. The magnitude of the effect within and between group comparisons were made using Cohen's D as modified by Sawilosky et al. and interpreted as very small (0.01), small (0.20), medium (0.50), large (0.80), very large (1.20) and huge (2.0). The statistical significance was set at $p<0.05$.the primary analysis in this RCT, were performed using the intention-to-treat (ITT) approach. All analyses were performed using SPSS software (version 25; IBM Corp., Armonk, NY, USA). Data are presented as mean (SD) and mean change from baseline (95% CI) unless otherwise noted. Effect sizes, their respective 95% CI and effect interpretation as proposed by Sawilowsky et al. are also presented.

Results

Participants flow throughout this trial is presented on Figure 1. Among 102 patients screened for eligibility, N= 63 met the inclusion criteria. The main reasons for exclusion were unwillingness to participate in the study, and not meeting some of the inclusion criteria such as age, or other body composition parameters. Eligible participants were randomized into the experimental group (n=32) and the control group (n=31). Fifteen participants dropped out prior to the post-test evaluation. Missing data from 29.03% (n=9) and 18.75% (n=6) participants from control and experimental groups, respectively, were imputed in the ITT analysis. The main reasons given for the dropout were personal problems, lack of interest, and moving to another city. The rate of adherence to the exercise training sessions was 85%. No significant adverse events were reported, however, 16 patients reported muscle soreness, knee pain, and shoulder pain in the elastic band resistance training group (25%) in the first three sessions of training. No adverse events were reported by the control group.

Table 1. Baseline demographic and clinical characteristics of the study participants.

Characteristics	Experimental (n=32)	Control (n=31)	P-value
Age (years)	64.11±3.81	64.05±3.35	0.947
Height (cm)	155.59±4.38	155.77±4.14	0.812
Body mass (kg)	81.81±8.03	78.73±7.52	0.268
BMI (kg/m^2)	33.7±3.2	32.5±2.0	0.451
WC (cm)	103.0±9.1	102.3±8.0	0.418
HC (cm)	102.6±8.7	101.8±7.2	0.366
Lean mass (kg)	45.7±4.55	46.1±3.8	0.515
Body fat (%)	46.29±3.42	43.60±2.66	0.067
BMC (gr)	2.24±0.38	2.13±0.50	0.381
BMD (gr/cm^2)	0.929±0.245	1.005±0.450	0.374
SBP (mmHg)	137.7±12.6	135.4±15.6	0.533
DBP (mmHg)	83.9±2.2	82.1±3.1	0.294

Data presented as Mean ± SD. BMI: body mass index; WC: waist circumference; HC: Hip circumference; WHR: waist-to-hip ratio; BMC: bone mass content; BMD: bone mass density; SBP: systolic blood pressure; DBS: diastolic blood pressure.

Baseline demographic and clinical measurements

Table 1 presents the baseline characteristics for demographic and clinical measures. There was no statistical difference in any of the parameters measured between the experimental and the control groups at baseline. Overall, participants had an average (±SD) age of 64.08 (±3.58) years, were obese 32.96 (±3.39) kg/m2, and had a mean body fat percentage of 44.52 (±3.18) %.

Anthropometric and standard clinical measurements

Table 2 presents the anthropometric and standard clinical measures at baseline and follow-up. Between-group comparisons demonstrated that body mass (T= 3.807, P= 0.001, ES=1.36), BMI (T= 2.149, P= 0.037, ES=0.85) and body fat (T= 4.106, P= 0.001, ES=-1.07) significantly increased in control group but not in the experimental group. The effect size estimates demonstrated that in control group these changes were “small,” while the non-significant changes for body mass in the experimental group were deemed “trivial”, except in body fat where the effect size in the control group were considered “large” and in the experimental group were deemed “small”.

Regarding the standard clinical measures, the HDL-C presented a significant increase (T= 2.831, P= 0.022, ES=1.26) in experimental versus the control group. We observed a significant increase in HDL-C within- groups in the experimental [0.62, 95% CI, 0.44, 0.53 (P=0.001)], but not in the control group [-0.03, 95% CI, -0.20, -0.11, (P=0.737)]. This effect size was “moderate” while the non-significant changes in the control group were deemed “trivial.” In contrast, LDL (T= 3.327, P= 0.008, ES=-1.12) and FBG (T= 2.048, P= 0.046, ES=-1.06) significantly decreased in the experimental versus the control group. We also observed a significant decrease within the experimental group [LDL: -0.34, 95% CI, -0.52, -0.43 (P=0.012); FBG: [-1.01, 95% CI, -1.20, -1.10 (P=0.009)], but not in the control group. The effect size estimates were “large,” while the non-significant changes in the control group were deemed “small.”

Similar trends were observed in the glycemic measures, that is, on insulin (T= 3.445, P= 0.004, ES=-1.32) and HOMA-IR (T= 3.009, P= 0.017, ES=-1.14). We observed a significant withing-group decrease in the experimental [insulin: -0.55, 95% CI, -0.73, -0.64 (P=0.002); HOMA-IR: -0.66, 95% CI, -0.84, -0.75 (P=0.001)], but not in control. The effect size estimates were “moderate,” while the non-significant changes in the control group were deemed “trivial.”

Regarding the hepatic markers, between group comparisons presented a significant increase in AST (T= 2.420, P= 0.034, ES=1.18) and ALT (T= 2.918, P= 0.014, ES=1.23) in the experimental versus the control group. We observed a significant within- group increase in the experimental [AST: 0.31, 95% CI, 0.22, 0.40 (P=0.011); ALT: 1.39, 95% CI, 1.29, 1.49 (P=0.001)], but not in the control group. The effect size for AST was “small,” while the non-significant changes in the control group were deemed “trivial” whereas for the ALT effect size was “large,” and the non-significant changes for ALT in the control group were deemed “small.” In contrast, the AST/ALT ratio (T= 2.668, P= 0.028, ES=-1.12) decreased in the experimental [-0.85, 95% CI, -0.94, -0.76 (P=0.001)], but not in control [-0.43, 95% CI, -0.52, -0.34, (P=0.118)]. This effect size was “large,” and in the control group were deemed “small.”

Novel hepatic steatosis risk indices

Table 3 presents the novel composite hepatic steatosis risk indices at baseline and follow-up. Overall, there were significant decreases in LAP (T= 2.259, P= 0.033, ES=-1.52), FLI (T= 3.618, P= 0.001, ES=-1.44), HSI (T= 3.229, P= 0.008, ES=-1.13) and FSI (T= 3.904, P= 0.001, ES=-1.45) in experimental versus the

Table 2. Anthropometry and standard clinical measures at baseline and follow-up.

Variables	Test	Experimental (n=32)	Control (n=31)	P-value between group	T	Effect size
Anthropometry						
Body mass (kg)	Pretest	81.81±8.03	78.73±7.52	0.001*	3.807	1.36
	Posttest	81.87±9.82	81.89±10.09			
	Within Group Sign.	0.923	0.001*			
BMI ($kg.m^2$)	Pretest	33.72±3.15	32.53±2.01	0.037*	2.149	0.85
	Posttest	33.65±3.67	33.72±4.05			
	Within Group Sign.	0.808	0.003*			
Body Fat (%)	Pretest	46.29±3.42	43.60±2.66	0.001*	4.106	-1.07
	Posttest	47.35±3.86	47.92±2.65			
	Within Group Sign.	0.477	0.001*			
WHR (cm)	Pretest	1.02±0.27	1.04±0.33	0.293	1.058	-0.14
	Posttest	1.01±0.33	1.04±0.25			
	Within Group Sign.	0.242	0.891			
WC (cm)	Pretest	102.29±7.98	103.05±9.11	0.547	0.358	0.35
	Posttest	102.77±6.21	102.97±7.65			
	Within Group Sign.	0.758	0.592			
Standard clinical measures						
MAP (mmHg)	Pretest	9.21±1.19	9.38±1.33	0.484	0.585	-0.61
	Posttest	9.08±0.94	9.36±1.29			
	Within Group Sign.	0.566	0.678			
HDL-C (mg.dl)	Pretest	47.93±6.42	46.97±6.88	0.022*	2.831	1.26
	Posttest	51.94±8.53	46.10±8.41			
	Within Group Sign.	0.001*	0.737			
LDL (mg.dl)	Pretest	95.40±23.82	92.25±21.41	0.008*	3.327	-1.12
	Posttest	85.37±22.65	98.70±25.32			
	Within Group Sign.	0.012*	0.052			
TG (mg/dl)	Pretest	185.75±65.38	178.86±57.54	0.212	1.273	-0.43
	Posttest	143.09±56.90	173.27±48.60			
	Within Group Sign.	0.001*	0.433			
FBG (mg/dl)	Pretest	191.94±21.76	198.72±14.17	0.046*	2.048	-1.06
	Posttest	163.53±29.18	194.92±22.69			
	Within Group Sign.	0.009*	0.324			
Insulin (µU/mL)	Pretest	10.02±4.78	9.87±5.56	0.004*	3.445	-1.32
	Posttest	7.42±3.25	10.11±4.86			
	Within Group Sign.	0.002*	0.212			
HOMA-IR	Pretest	24.11±3.38	23.66±4.16	0.017*	3.009	-1.14
	Posttest	21.32±4.01	24.23±5.09			
	Within Group Sign.	0.001*	0.532			
AST (IU/L)	Pretest	17.82±6.72	16.64±5.14	0.034*	2.420	1.18
	Posttest	20.17±8.32	16.63±5.48			
	Within Group Sign.	0.011*	0.889			
ALT (IU/L)	Pretest	5.47±3.30	4.90±2.59	0.014*	2.918	1.23
	Posttest	11.73±5.43	6.08±6.52			
	Within Group Sign.	0.001*	0.058			
AST/ALT	Pretest	3.25±2.03	3.39±1.98	0.028*	2.668	-1.12
	Posttest	1.72±1.53	2.73±0.84			
	Within Group Sign.	0.001*	0.118			
GGT (IU/L)	Pretest	28.42±21.84	28.19±13.74	0.460	0.652	-0.26
	Posttest	26.26±14.56	29.36±13.61			
	Within Group Sign.	0.176	0.404			

Data presented as Mean ± SD. BMI: body mass index; WC: waist circumference; HC: Hip circumference; WHR: waist-to-hip ratio; BMC: bone mass content; BMD: bone mass density; SBP: systolic blood pressure; DBS: diastolic blood pressure; MAP: mean arterial pressure; HOMA-IR: homeostasis model assessment of insulin resistance; FBG: fasting blood glucose; HbA1c: hemoglobin A1c; AST: aspartate transaminase; ALT: alanine transaminase; GGT: gamma-glutamyl transferase; LDL: Low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; TG: triglyceride; FBG: fasting blood glucose. * showed significant difference. Effect sizes are presented as Cohen's D and interpreted as very small (0.0-0.20), small (0.20-0.50), medium (0.50-0.80), large (0.80-1.20), very large (1.20-2.0) and huge (>2.0).

Table 3. Composite hepatic steatosis indices at the baseline and follow-up.

Variables	Test	Experimental (n=32)	Control (31)	P-value between group	T	Effect size
Novel hepatic steatosis indices						
LAP	Pretest	81.73±18.52	80.57±20.11	0.033*	2.259	-1.52
	Posttest	64.06±15.63	77.92±17.84			
	Within Group Sign.	0.001*	0.213			
FLI	Pretest	48.33±10.69	46.54±12.44	0.001*	3.618	-1.44
	Posttest	33.26±12.02	44.68±11.94			
	Within Group Sign.	0.001*	0.544			
HIS	Pretest	52.50±12.62	53.44±12.08	0.008*	3.229	-1.13
	Posttest	39.22±10.04	48.98±13.65			
	Within Group Sign.	0.001*	0.339			
FSI	Pretest	0.82±0.13	0.68±0.12	0.001*	3.904	-1.45
	Posttest	0.29±0.11	0.64±0.18			
	Within Group Sign.	0.001*	0.611			

Data are presented as Mean ±SD. * showed significant difference. Effect sizes are presented as Cohen's D and interpreted as very small (0.01), small (0.20), medium (0.50), large (0.80), very large (1.20) and huge (2.0).

control group. Likewise, we observed a significant decrease within the experimental [LAP: -0.94, 95% CI, -1.12, -1.03 (P=0.001); FLI: -1.32, 95% CI, -1.42, -1.23 (P=0.001); HIS: -1.16, 95% CI, -1.26, -1.07 (P=0.001); FSI: -4.40, 95% CI, -4.57, -4.24 (P=0.001)], but not in control group. The effect size estimates were "large," while the non-significant changes in the control group were deemed "trivial" or "small" among all measures.

Discussion

Our results indicate that elastic band resistance training has beneficial effects on traditional and composite hepatic health-related indices in older women with OSA, after 12 weeks of training. In addition, this exercise type intervention promotes significant improvements in several indices of body composition and hepatic function including body mass, BMI, body fat percent, LDL-C, HDL-C, insulin, FBG, HOMA-IR, ALT, AST, AST/ALT ratio, LAP, FLI, HIS and FSI. These results support the hypothesis that elastic band resistance training can improve standard hepatic health-related indices in older female patients with OSA as well as novel composite hepatic risk scores.

To date there are only a limited number of studies evaluating the impact of resistance-type exercise on hepatic steatosis-related indices in older woman. For instance Barsalani et al., showed that 6-month combined aerobic and resistance training intervention contributed to favorable changes in the level of hepatic enzymes in postmenopausal women (Barsalani et al., 2012) whereas, Kelardeh et al. using 12-week non-linear resistance training alone found hepatic biochemical marker beneficial effects on non-alcoholic fatty liver disease in older obese women (Kelardeh et al., 2020). Despite consistent with our results, these studies vary on the clinical condition [non- alcoholic fatty liver disease versus sarcopenia/obesity/osteoporosis] and the type of exercise training interventions [combined versus res-istance exercise only] and thus, a direct comparison with our findings is difficult (Banitalebi et al., 2020). It has been suggested that the mechanism of elastic band resistance training benefit on hepatic steatosis are muscle-induced, regardless of the co exercise of the fat infiltration into skeletal muscle (Pasco et al., 2022). However, this traditional belief of a generally beneficial effect of muscle tissue on hepatic steatosis risk (Bayol et al., 2014) is vague and reductionist. Reductions of BF% and BMI, which are considered valid determinants of obesity, and parameters closely related to fatty liver (Fan et al., 2018), are also important mechanistic markers mediating the effects of isolated elastic band resistance training on the LAP, FLI, HSI, and FSI. Furthermore, resistance training improves metabolism, and metabolic capacity (Batacan et al., 2017; Kessler et al., 2012) enhancing insulin resistance, hyperglycaemia and dyslipidaemia which is consistent with our results on FBG, HDL-c, LDL, HOMA-IR, AST, ALT, and insulin indicators of a reduction on the severity of the hepatic steatosis in our participants.

LAP predicts visceral obesity and non-alcoholic fatty liver disease making it a useful biomarker with a high diagnostic accuracy for identifying non-alcoholic fatty liver disease (NAFLD) (Dai et al., 2017). Another aspect of our study that we consider important is our examination of the LAP index, which has not been studied in response to exercise. Improvements in LAP index correlate with reductions in ectopic fat, and lowering of improved insulin resistance in older women with OSA (Mirmiran et al., 2014). Consistent with this finding, we also observed significant reductions in LAP, BMI and body fat, the latter being a surrogate estimate of abdominal fat as well as on FBG and HOMA-IR. Reductions in LAP were considered "large" in our study, with resistance training group experiencing "large" reductions in insulin resistance markers (FBG, HOMA-IR). Improvements in LAP after resistance training likely reflects decreases in ectopic

fat, which further associate with the changes seen in insulin resistance (Briganti et al., 2015).

Variations in FLI have been observed in women with type 2 diabetes after both sprint interval training and combined aerobic and resistance exercise (Banitalebi et al., 2019), which is in line with our findings. Postmenopausal women experienced reductions in FLI after a 6-month training program (Barsalani et al., 2012). Similarly, Reverter-Masia et al. (2021) reported that FLI improved after 10 weeks of exercise and/or whole-body electro-myostimulation in postmenopausal women. Other studies have demonstrated significant changes in FLI response following lifestyle interventions including exercise training and diets. These benefits are likely related to effect of an increment in the activity of oxidative enzymes, higher fatty acid oxidation rates, and lower lipogenesis in the liver (Balducci et al., 2015; Barsalani et al., 2012). In addition, exercise training may reduce FLI, through reduction of insulin resistance, increasing mitochondrial biogenesis, and body strength (Balducci et al., 2015). This is consistent with the observations that skeletal muscle mass is inversely associated with FLI values (Moon et al., 2013).

A novel finding of our study is that the elastic band resistance training reduced variables associated with hepatic steatosis such as HIS and FSI in older women with OSA. We report that a 12-week resistance training program reduced risk scores of hepatic steatoses in older female patients, supporting the importance of monitoring hepatic steatosis risk scores in secondary prevention. To date, there are few randomized controlled trials reporting effects of exercise training on hepatic steatosis indices. For instance, Banitalebi et al., showed that both sprint interval training and combined training had no effect of FSI and HSI. Similarly, in another randomized controlled trial, the same authors showed no significant differences in FSI and HSI following elastic resistance band training with green coffee supplementation in obese women (Mardaniyan Ghahfarrokhi et al., 2020).

This RCT is the first to investigate the effects of resistance training on hepatic steatosis risk indices in elderly female patients with OSA, including emerging measures of hepatic health and function. We compared the benefits of resistance training with “usual care”. The major strength of our study is the examination of a sample of female participant, a high-risk population that is not always considered in RCT. However, despite the promise findings seen in our study, we cannot generalize the results into the male population given the biological and physiological differences in both sexes. In addition, the elevated missing data post-intervention may have limited the statistical analysis and the interpretation of the results. Nonetheless, we used several statistical procedures to reduce its impact by imputing the missing values. Despite these limitations, the present study proposes that an elastic band resistance exercise program is an affordable and versatile exercise intervention and can be carried out in any loca-tion for management of fatty liver risk in OSA women. However, future studies should compare aerobic training versus the elastic-band resistance exercise training because other exercise type modalities may have a similar or even greater benefits than ours on hepatic risk indices in older women with OSA syndrome.

Conclusion

In summary, our findings highlight the importance of elastic resistance-type training modality in improving hepatic function in older female patients with OSA. Importantly, in addition to potentially reducing falls risk and managing sarcopenia in this population, resistance exercise can improve hepatic function and body composition. This relatively low cost, highly accessible form of exercise can be easily implemented for this population in a wide range of settings.

What is already known on this subject?

Osteosarcopenic adiposity (OSA) syndrome significantly impacts hepatic disorders more than each of the tissues alone.

What this study adds?

Our findings highlight the importance of elastic resistance-type training modality in improving hepatic function in older female patients with OSA.

Organ Cross-Talk Tips:

- Improved mechanical loading from resistance exercise may restore bone-muscle crosstalk, indirectly benefiting hepatic metabolism.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was conducted in accordance with the Declaration of Helsinki and approved by Iranian Registry of Clinical Trials, trial registration no.: IRCT20180627040260N1; https://www.irct.ir/trial/32463) and was approved by Iranian Ethics Committee of Sport Sciences Research Center (IR.SSRC.REC.1398.040). Informed consent was obtained from all subjects involved in the study.

Informed consent Animal study

Author contributions

Conceptualization, S.T, M.MG..; methodology, M.MG.; formal analysis, M.MG.,S.T and L.CB.; resources, S.T; data curation, M.MG.,L.CB.; writing—original draft preparation, S.T, M.MG.,L.CB.; writing-review and editing, M.MG. L.CB. funding acquisition L.CB authors have read and agreed to the published version of the manuscript.

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