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Effect of high-intensity interval training on body composition and inflammatory markers in obese postmenopausal women: a randomized controlled trial

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Abstract

Objectives: This study tested whether high-intensity interval training is a time-efficient strategy for improving visceral adiposity tissue and inflammatory markers in obese postmenopausal women when compared with combined training. Moreover, we tested whether change in visceral adiposity tissue is associated with alterations in these inflammatory markers.

Methods: Postmenopausal women were randomized in two groups: combined training (n = 13) and high-intensity interval training (n = 13). The combined training group performed 60 minutes of walking at 70% of maximum heart rate and resistance exercises at 70% of one repetition maximum. The high-intensity interval training group performed 28 minutes of high-intensity exercises (> 80% of maximum heart rate). Both groups trained three times a week for 12 weeks. Body composition and inflammatory markers were analyzed with dual-energy x-ray absorptiometry scanning and enzyme-linked immunosorbent assay, respectively.

Results: All groups reduced body fat percentage ($P = 0.026$), visceral adiposity tissue ($P = 0.027$), leptin ($P = 0.043$), and increased interleukin (IL)-1 receptor antagonist ($P < 0.01$). The high-intensity interval training group reduced visceral adiposity tissue ($P = 0.021$) in a greater magnitude and increased interleukin-6 ($P = 0.037$) level when compared with the combined training group. Moreover, the visceral adiposity tissue changes explained the changes in IL-6 (56%; $P = 0.002$) only in the high-intensity interval training group.

Conclusions: These results suggest that high-intensity interval training is a time-efficient strategy for improving visceral adiposity tissue and inflammatory markers in obese postmenopausal women. Moreover, we observed that serum cytokine changes, at least in part, depend on visceral adiposity tissue alterations.

Key Words: Adipokines – Calisthenics – Menopause – Obesity.

The link between menopause and excess visceral adiposity tissue (VAT) leads to an imbalance between increased pro-inflammatory and decreased anti-inflammatory markers (eg, cytokines) in postmenopausal women (PW), termed as low-grade inflammation.[1] In PW, VAT excess and increased level of inflammatory markers[1] are associated with increased risk of breast cancer,[2] cardiovascular disease,[3] and mortality.[4] Supervised exercise training, aerobic and resistance training, and more recently high-intensity interval training (HIIT) have been shown to reduce VAT[5,6] and inflammatory markers.[7] However, there is little evidence concerning which supervised-training modality (ie, aerobic and resistance training or HIIT) is better for reducing VAT and inflammatory markers in PW.

Public health guidelines recommend 150 minutes per week of moderate-intensity training, combining aerobic training with resistance training.[8] While the aerobic training increases oxidative capacity, the resistance training increases postexercise oxygen consumption and muscle mass. These combined effects increase energy expenditure and reduce body adiposity, contributing to inflammatory marker improvements.[8] Moreover, resistance training increases muscle strength and power, and aerobic training increases muscle endurance. These adaptations improve exercise performance and tolerance, which may further increase exercise energy expenditure.[8] Thus, combined training (CT) is considered an efficient

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and well-accepted treatment strategy for improving body adiposity and low-grade inflammation in PW.[8-10] However, a lack of time has been cited as a barrier for people not to comply with public health guideline recommendations.[11] Hence, more recently, HIIT has been suggested as a time-efficient alternative strategy to 150 minutes of moderate-intensity training for reducing body adiposity[12,13] due to a low time commitment (60-75 minutes).[8] HIIT effects are based on similar energy expenditure when compared with aerobic training,[8] although there is evidence that HIIT induces a greater reduction in VAT than moderate-intensity aerobic training when total work is equated in obese PW.[12,13] Although the HIIT effectiveness has been compared with aerobic training, studies are still needed to establish that HIIT is an alternative time-efficient strategy when compared with CT for improving body adiposity.

In addition, it has been suggested that exercise-induced changes in inflammatory markers may be an indirect effect of improvement in total body adiposity,[9,10] particularly in VAT.[9,10] However, whereas a reduction in VAT with HIIT has been well observed,[5,6,12,13] the HIIT effect on interleukin (IL)-6 in overweight/obese populations is not so evident.[6] Studies have shown an increase,[14] maintenance,[6,15] or decrease of IL-6[15] after HIIT. These HIIT effects on IL-6 may be due to pleiotropic characteristics of IL-6[7] and also due to few studies with a varied population.[6] Moreover, the potential benefits of HIIT on other inflammatory markers associated with obesity-related diseases, such as IL-1 receptor antagonist (ra), monocyte chemoattractant protein (MCP)-1, intercellular adhesion molecule (ICAM)-1, leptin, and adiponectin, have yet to be established due to a lack of studies. Thus, more studies are needed to elucidate the impact of HIIT on inflammatory markers in obese PW.

Therefore, the present clinical trial was designed to test whether HIIT is a time-efficient strategy for improving VAT and inflammatory markers (IL-6, IL-1ra, MCP-1, ICAM-1, leptin, and adiponectin) in obese PW when compared with CT. Furthermore, we determined whether alterations in VAT are associated with changes in these inflammatory markers, using a coefficient of correlations adopting a within-subject model.

METHODS

Study design

A randomized, controlled, and parallel study (trial registration: NCT03200639) was performed over 12 weeks. The groups were randomized (CT or HIIT) using statistical software (MedCalc) after all the women fulfilled the inclusion criteria (Fig. 1). The outcomes were assessed at the baseline and at the end of the training interventions in the following

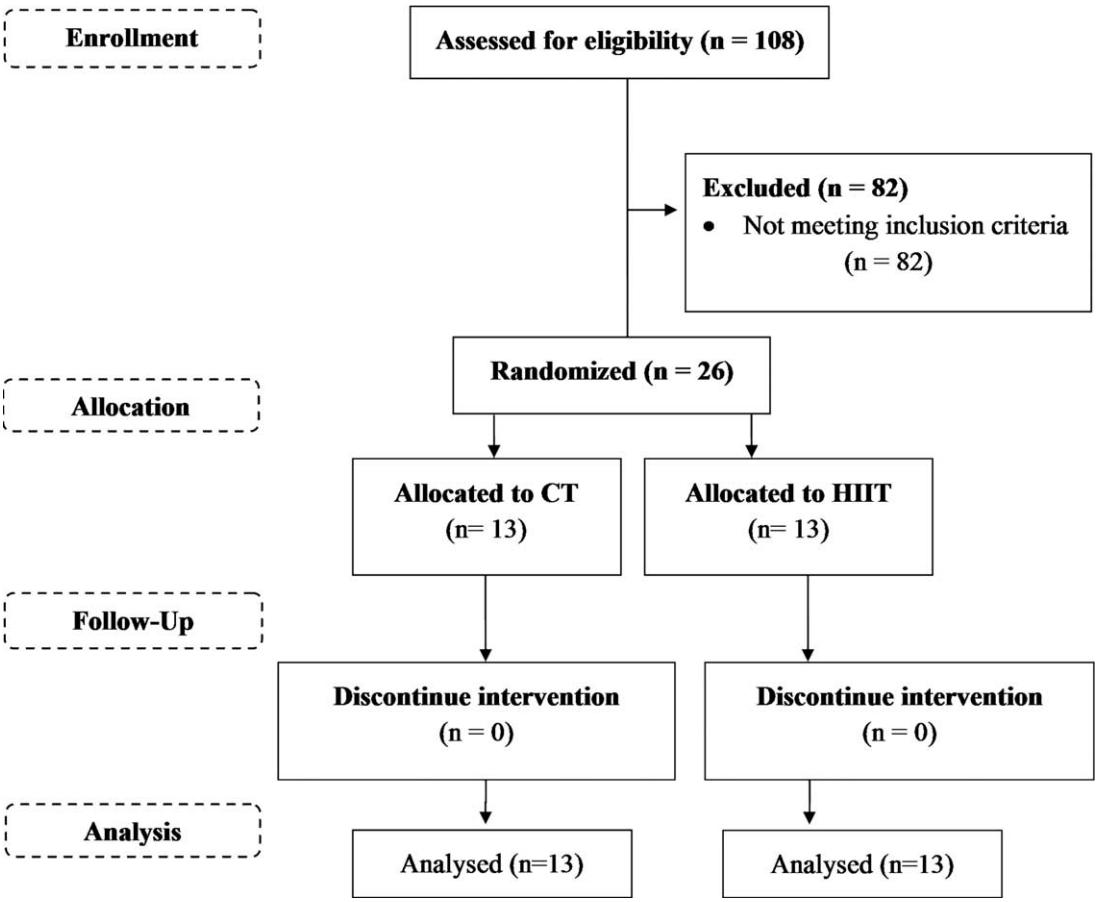

FIG. 1. Participant flow diagram. CT, combined training; HIIT, high-intensity interval training.

TABLE 1. *Trainings protocols and characteristics of the obese postmenopausal women by group*

	CT (n = 13)	HIIT (n = 13)	*P*
Adherence, %	90.5 (86.1-95.1)	87.0 (78.9-96.0)	0.446
Heart rate, beats per minute	111.5 (107.6-115.4)	133.3 (125.8-141.3)	<0.001
Heart rate zone, %	71.0 (69.1-73.1)	84.7 (80.8-88.7)	<0.001
Adapted Borg scale, score (0-10)	5.6 (5.3-6.0)	6.7 (6.5-7.0)	<0.001
Body squats, number	—	19.1 (17.1-21.1)	—
Step climbs, number	—	18.4 (15.9-20.9)	—
Total resistance training volume, kg	6277.0 (5668.3-6885.6)	—	—

Data are presented in means and CI of 95%. Independent *t* test was performed to compare groups ($P < 0.05$).
CI, confidence interval; CT, combined training; HIIT, high-intensity interval training; resistance training volume = load × set × repetitions.

order: serum inflammatory markers (ELISA) and body composition (DEXA). The final sample consisted of 26 PW divided into two groups: CT (n = 13) and HIIT (n = 13) (Fig. 1). Both groups trained for 12 weeks and performed a 3-day-a-week (no consecutive days) routine (Table 1). After the training interventions, all the assessments were performed 48 hours after the last training session. The study was approved by the local Research Ethics Committee and was conducted in accordance with the Declaration of Helsinki. All women gave written informed consent.

Women

All the women were housewives and reported no history of physical training practice before the study. They were aged >50 years and amenorrhea had occurred at least 12 months before the study. All the women were selected from a neighborhood association near the local university. The inclusion criteria consisted of: obesity (baseline body fat percentage >40%)[16]; controlled blood pressure; absence of myopathies, arthropathies, and neuropathies; absence of muscle, thromboembolic, and gastrointestinal disorders; absence of cardiovascular and infection diseases; nondrinker (no alcohol intake whatsoever in their diet), and nonuse of nutritional supplements which could affect the body composition or inflammatory serum markers. Thus, after applying the inclusion criteria to avoid bias in the study outcomes, 82 out of 108 women were excluded, and 26 eligible women participated in the study (Fig. 1).

Nutritional and sedentary behavior assessments

All women were submitted to a 3-day food record (2 days in the middle of the week and 1 day on the weekend). Energy and macronutrients (carbohydrate, protein, and lipid) were quantified. Data were calculated by a trained nutritionist using the Dietpro software (version 5.7i, Agromídia Softwares , Minas Gerais, Brazil) and the US Department of Agriculture (USDA) food composition table. To quantify the sedentary behavior, we used the International Physical Activity Questionnaire (IPAQ), which questions were about time spent on sitting time. All women were submitted to a 3-day sitting time record (2 days in the middle of the week and 1 day on the weekend). Afterwards, we calculated the mean of the week (7 days). The women were advised to maintain these nutritional habits and habitual physical activity until the end of the study.

Anthropometric, body composition, and blood sample assessments

To standardize the level of body hydration, all women were instructed to ingest 2 L of water and were oriented to perform an overnight fast (10-12 hours) before (24 hours) the anthropometric, body composition, and blood sample assessments. The assessment data were collected between 7:30 a.m. and 9:00 a.m. To minimize interobserver variations, all analyses were performed by the same evaluator at the same time of day.

For anthropometric assessment, the body weight and height were measured with a digital scale (Lider, Brazil) and a stadiometer fixed to the scale, respectively. Body mass index (BMI = weight [kg]/height [m^2]) was calculated. For body composition assessment, the whole-body adiposity and regional adiposity (trunk and VAT) was assessed via dual-energy x-ray absorptiometry scanning (iDXA; GE Healthcare-Lunar, Madison, WI) and quantified using the standard option of the Encore software, version 14.10. The coefficient of variation (CV) was 0.5% for fat mass. All women dressed in lightweight clothing and no shoes during the anthropometric and body composition assessments.

For blood sample assessments, the samples (venous) were collected in a dry tube with gel separator or EDTA (vacuum-sealed system; Vacutainer, England). The sample was centrifuged for 10 minutes (3,000 rpm), and samples were separated and stocked (−80°C) for future analysis. The blood markers were measured as follows: estradiol, follicle-stimulating hormone, insulin, glucose, glycated hemoglobin, and total cholesterol with Cobas 6000 equipment and Roche kit; IL-6 (CV of 4.5%), IL-1ra (CV of 8.5%), ICAM-1 (CV of 6.8%), MCP-1 (CV of 5.7%), leptin (CV of 6.5%), and total adiponectin (CV of 6.5%) (enzyme-linked immunosorbent assay method) with Spectra Max Plus 384 equipment (Molecular Devices, San Jose, CA) and R&D Systems kits (Minneapolis, MN).

Exercise training protocols

All training sessions were performed in the university gym facility adopting a 3-day-a-week (no consecutive days) routine for 12 weeks and were supervised by fitness professionals. Before and after each training session, a warm-up of 5 minutes walking and a cool down of 3 minutes walking at 60% of maximum heart rate (MHR) was provided, respectively. To ensure the relative intensity training zone of each protocol (HIIT or CT), the women were stimulated by the

fitness professionals to decrease or increase the exercise intensity if they surpassed or did not reach the intensity zone.

High-intensity interval training

The HIIT protocol followed the recommendation of previous studies in obese and diabetic PW.[12,13] HIIT (total session length time ~28 minutes) was composed by 10 sets of 60 seconds of high-intensity exercises, >80% of MHR, or adapted Borg scale >6 (30 seconds of step climbing plus 30 seconds of free body weight squats), interspersed with a recovery period of 60 seconds of low-intensity exercise at 60% of MHR or adapted Borg scale at <5 (light walk).[8] The height of the steps was about 16 cm and the angle of free body weight squats (without the help of arms) was about 90-degree knee flexion on a chair to ensure safety. All women were advised to perform the maximum number of step climbing and free body weight squats during the high-intensity exercises (Table 1).

The HIIT progression was separated as described: week 1—four sets of high-intensity exercise (1 minute) interspersed with four sets of low-intensity exercise (4 minutes); week 2—six sets of high-intensity exercise (1 minute) interspersed with six sets of low-intensity exercise (3 minutes); week 3—eight sets of high-intensity exercise (1 minute) interspersed with eight sets of low-intensity exercise (2 minutes); week 4 to 12—10 sets of high-intensity exercise (1 minute) interspersed with 10 sets of low-intensity exercise (1 minute).

Combined training

The CT protocol followed the recommendation of the American College of Sports Medicine Guidelines.[8] The CT protocol (total length time ~60 minutes) consisted of 30 minutes of moderate-intensity walking at 70% of MHR around a sports court plus five resistance exercises at 70% of 1RM with three sets of 8 to 12 repetitions and 1.5-minute rest interval between sets and exercises. The resistance exercises were performed with muscle-building machines (Buick Fitness, Brazil) in the following order: 45-degree half squat (smith machine), bench press, leg curl, rowing machine, and unilateral leg extension. If the women performed more than 12 repetitions in resistance exercise, the load was increased between 5% to 15% to maintain the repetition zone between 8 and 12 repetitions and to ensure the 70% of 1RM (Table 1).

The CT progression was separated as described: week 1—walking 15 minutes plus one set of the five total body resistance exercises; week 2—walking 20 minutes plus two sets of the five total body resistance exercises; week 3—walking 25 minutes plus two sets of the five total body resistance exercises; week 4 to 12—walking 30 minutes at plus three sets of the five total body resistance exercises.

Statistical analysis

Medicine intake and smokers are presented as the absolute and perceptual number of women of the sample and the chi-square test was used to compare the groups. Continuous data

TABLE 2. *Baseline characteristics of the obese postmenopausal women by group*

	CT (n = 13)	HIIT (n = 13)	*P*
Age, y	62.9 (57.6-68.2)	62.3 (58.2-66.5)	0.863
Menopause time, y	18.3 (12.3-24.2)	16.1 (10.0-22.2)	0.586
Week sitting time, min	2915.0 (2325.8-3504.3)	2776.8 (2038.3-3515.3)	0.752
SBP, mm Hg	127.4 (118.9-135.8)	122.9 (113.5-132.3)	0.446
DBP, mm Hg	79.4 (73.4-85.5)	78.7 (72.2-85.3)	0.863
Smokers, number	2 (15.3%)	2 (15.3%)	1.000
E_2, pg/mL	9.7 (4.6-14.7)	14.0 (3.5-24.5)	0.449
FSH, mUI/mL	73.0 (47.3-98.7)	59.3 (44.7-73.9)	0.299
Glucose, mg/dL	99.7 (91.8-107.6)	103.6 (91.6-115.6)	0.560
Hb1Ac, %	6.1 (5.6-6.6)	5.9 (5.5-6.2)	0.413
HOMA-IR	3.7 (2.4-5.0)	3.8 (2.3-5.3)	0.930
Insulin, μU/mL	15.0 (10.2-19.8)	14.2 (10.1-18.3)	0.785
Total cholesterol, mg/dL	235.0 (208.4-261.6)	224.4 (189.3-259.4)	0.602
Medicine intake			
Antihyperglycemic	0 (0%)	0 (0%)	0.844
Antihypertensive	1 (7.6%)	4 (30.7%)	0.319
Antiasmatic	1 (7.6%)	0 (0%)	1.000
Anti-inflammatory	0 (0%)	2 (15.3%)	0.461
Antiallergic	1 (7.6%)	0 (0%)	1.000
Antidepressives	1 (7.6%)	1 (7.6%)	0.461
Antianxiolytics	1 (7.6%)	1 (7.6%)	0.461
Antihypercholesterolemia	2 (15.3%)	0 (0%)	0.461
Antiulcers	2 (15.3%)	1 (7.6%)	1.000
Calcium	1 (7.6%)	0 (0%)	1.000
Analgesics	1 (7.6%)	1 (7.6%)	0.461
Estrogen therapy	0 (0%)	2 (15.3%)	0.461
Thyroxin therapy	1 (7.6%)	1 (7.6%)	0.461

Continuous data are presented in means and CI of 95%—independent *t* test was performed to compare groups ($P < 0.05$). Categorical data are presented in number of women and percent of sample—chi-square test was performed to compare groups ($P < 0.05$).
CI, confidence interval; CT, combined training; DBP, diastolic blood pressure; E_2, estradiol; FSH, follicle-stimulating hormone; Hb1Ac, glycated hemoglobin; HIIT, high-intensity interval training; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; SBP, systolic blood pressure.

TABLE 3. *Dietary intake of the obese postmenopausal women by group at baseline and after 12 weeks of training*

	CT (n = 13)			HIIT (n = 13)					
	Pre	Post	Δ	Pre	Post	Δ	*P* group	*P* time	*P* time vs group
EI, kcal	1449.8 (1209.4-1690.3)	1559.8 (1255.6-1864.0)	109.9 (−179.3-399.3)	1277.6 (1184.9-1370.4)	1289.1 (1073.3-1504.8)	11.4 (−219.2-242.1)	0.078	0.482	0.567
CHO, g	190.5 (159.5-221.6)	187.9 (148.9-226.9)	−2.6 (−35.7-30.4)	166.2 (150.7-181.6)	171.5 (147.8-195.3)	5.3 (−21.1-31.8)	0.212	0.891	0.685
CHO, %	53.2 (49.1-57.3)	48.4 (43.1-53.7)	−4.8 (−9.4 to −0.1)	52.3 (47.7-57.0)	53.9 (50.9-56.8)	1.5 (−3.9-6.9)	0.321	0.326	0.066
PTN, g	52.8 (42.6-63.0)	64.0 (48.4-79.5)	11.1 (−6.0-28.3)	47.4 (40.5-54.3)	51.7 (40.2-63.1)	4.2 (−8.1-16.7)	0.128	0.126	0.486
PTN, %	14.7 (12.6-16.8)	16.4 (14.0-18.8)	1.7 (−0.9-4.3)	14.9 (12.8-16.9)	15.9 (14.1-17.6)	0.9 (−1.4-3.4)	0.867	0.114	0.672
LPD, g	50.7 (41.4-60.1)	60.7 (46.8-74.7)	10.0 (−4.3-24.3)	46.8 (38.1-55.5)	44.4 (34.4-54.4)	−2.3 (−16.9-12.1)	0.058	0.425	0.199
LPD, %	31.4 (28.9-33.8)	35.1 (32.0-38.3)	3.7 (0.4-7.1)	32.5 (28.2-36.7)	30.5 (28.0-33.1)	−1.9 (−7.8-3.9)	0.213	0.566	0.079

Data are presented in means and CI of 95%. Repeated-measures ANOVA was used to compare groups ($P < 0.05$).
Δ, Final value minus baseline value; CHO, carbohydrate intake; CI, confidence interval; CT, combined training; EI, energy intake; HIIT, high-intensity interval training; LPD, lipid intake; PTN, protein intake.

are presented as the mean and 95% confidence interval (95% CI). The independent *t* test was used to compare the baseline characteristics of the groups (Tables 2 and 3). Pre to post changes (Δ) were calculated as the final value minus baseline value. Repeated analysis of variance (ANOVA) measures were used to compare the groups during the follow-up (time vs group; Tables 3–5). The effect size was measured by partial eta squared (η_p^2). Cohen (1988) provided benchmarks to define small ($\eta_p^2 = 0.01$), medium ($\eta_p^2 = 0.06$), and large ($\eta_p^2 = 0.14$) effects.[17] To determine whether a Δ in serum inflammatory markers across the intervention within the individual was associated with a Δ in body adiposity (body fat percentage and VAT) across the intervention, we used multiple regression as recommended by Bland and Altman:

$$\sqrt{\frac{\text{sum of square for serum inflammatory markers}}{\text{sum of square for serum inflammatory markers} + \text{residual sum of square}}}$$

The observed power was calculated for this study. The significant level was set at $P < 0.05$.

RESULTS

No differences between the groups were observed for the baseline values. Both groups were considered as an unhealthy metabolic profile (insulin resistance, high glycated hemoglobin levels, and hypercholesterolemia) and had normal levels of blood pressure (Table 2).

After 12 weeks of intervention, no differences were observed for the nutritional indicators (Table 3). Both groups reduced the body fat percentage and the VAT (ANOVA time effect; $P < 0.05$). However, a higher magnitude of reduction in the VAT was observed in the HIIT group when compared with the CT group (ANOVA time vs group effect; $P < 0.05$). There were no statistical differences between groups for the other body composition and the anthropometric variables (Table 4).

As shown in Table 5, both groups increased the IL-1ra level and decreased the leptin level (ANOVA time effect; $P < 0.05$) without any difference between them. Moreover, only the CT reduced the adiponectin levels (ANOVA time vs group effect; $P < 0.05$) and only the HIIT group increased the IL-6 level (ANOVA time vs group effect; $P < 0.05$) when groups were compared with each other. There were no statistical differences between the groups and time for the MCP-1 and the ICAM-1.

The body fat percentage changes explained the leptin changes in 20% ($r = 0.44$, $P = 0.018$, power = 0.67) in both groups. The VAT changes explained ($P < 0.05$) the IL-6 changes in 56% only in the HIIT group. The IL-6 changes explained ($P < 0.05$) the IL-1ra changes in 46% only in the HIIT group (Table 6).

DISCUSSION

The main findings of the current study were that HIIT reduces VAT and increases IL-6 in obese PW when compared with CT. Moreover, the increase in IL-1ra and the decrease in leptin and body fat percentage observed after intervention

TABLE 4. *Anthropometric and body composition markers of the obese postmenopausal women by group at baseline and after 12 weeks of training*

	CT (n = 13)			HIIT (n = 13)									
	Pre	Post	Δ	Pre	Post	Δ	*P* group	*P* time	η_p^2	Power	*P* time vs group	η_p^2	Power
Anthropometry													
Weight, kg	70.9 (63.4-78.4)	69.7 (61.4-77.9)	−1.2 (−3.5-1.0)	75.5 (65.3-85.7)	74.3 (64.1-84.5)	−1.2 (−2.4-0.0)	0.437	0.056	0.14	0.48	0.977	0.00	0.05
BMI, kg/m	30.6 (28.2-32.9)	30.0 (27.4-32.5)	−0.6 (−1.6-0.4)	31.4 (27.4-35.4)	30.9 (27.0-34.8)	−0.5 (−1.1-0.1)	0.673	0.065	0.13	0.45	0.800	0.00	0.05
Body composition													
F%	44.5 (42.7-46.4)	44.2 (42.3-46.1)	−0.3 (−0.8-0.2)	46.2 (43.0-49.4)	45.5 (42.3-48.7)	−0.7 (−1.5-0.0)	0.405	0.026	0.19	0.62	0.423	0.02	0.12
Android FM, kg	2.9 (2.4-3.4)	2.9 (2.4-3.3)	0.0 (−0.1-0.0)	3.3 (2.5-4.2)	3.2 (2.4-4.1)	−0.1 (−0.2-0.0)	0.363	0.107	0.10	0.36	0.176	0.08	0.26
Trunk FM, kg	17.0 (14.6-19.4)	17.0 (14.7-19.4)	0.0 (−0.3-0.5)	19.5 (14.6-24.3)	18.7 (14.3-23.2)	−0.8 (−1.6-0.0)	0.391	0.123	0.10	0.33	0.076	0.13	0.42
VAT, kg	1.3 (1.0-1.6)	1.3 (1.0-1.6)	0.0 (−0.1-0.1)	1.6 (1.2-2.0)	1.5 (1.1-1.9)	−0.1 (−0.2 to −0.1)	0.334	0.027	0.18	0.62	0.021	0.20	0.65

Data are presented in means and CI of 95%. Repeated-measures ANOVA was used to compare groups ($P < 0.05$). The effect size was measured by η_p^2.
Δ, Final value minus baseline value; η_p^2, partial eta squared; BMI, body mass index; CI, confidence interval; CT, combined training; F%, body fat percentage; FM, fat mass; HIIT, high-intensity interval training; VAT, visceral adipose tissue.

TABLE 5. *Inflammatory markers of the obese postmenopausal women by group at baseline and after 12 weeks of training*

	CT (n = 13)			HIIT (n = 13)									
	Pre	Post	Δ	Pre	Post	Δ	*P* group	*P* time	η_p^2	Power	*P* time vs group	η_p^2	Power
IL-6, pg/mL	1.8 (0.6 to 3.1)	1.7 (1.0 to 2.4)	−0.1 (−1.1 to 0.9)	1.4 (0.7 to 2.0)	2.6 (1.4 to 3.9)	1.2 (0.4 to 2.1)	0.676	0.083	0.12	0.41	0.037	0.17	0.56
IL-1 ra, pg/mL	459.3 (231.6 to 687.1)	672.7 (400.7 to 944.6)	213.3 (103.1 to 323.5)	397.4 (272.5 to 522.4)	589.1 (408.5 to 769.7)	191.6 (95.7 to 287.6)	0.584	<0.001	0.60	0.99	0.749	0.00	0.06
MCP-1, pg/mL	360.7 (276.2 to 445.3)	329.9 (233.2 to 426.7)	−30.7 (−147.8 to 86.3)	367.1 (319.3 to 414.9)	403.4 (343.6 to 463.2)	36.2 (−50.5 to 123.1)	0.267	0.935	0.00	0.05	0.326	0.04	0.16
ICAM-1, pg/mL	184.2 (141.4 to 227.0)	175.5 (127.6 to 223.4)	−8.6 (−56.5 to 39.1)	198.3 (160.4 to 236.1)	207.0 (167.5 to 246.5)	8.7 (−36.0 to 53.5)	0.329	0.999	0.00	0.05	0.568	0.01	0.08
Adiponectin, ng/mL	5121.9 (4017.8 to 6225.9)	3002.7 (1955.7 to 4049.7)	−2119.1 (−3588.1 to −650.1)	4352.4 (3022.3 to 5682.6)	4706.0 (3592.9 to 5819.0)	353.5 (−964.9 to 1671.9)	0.441	0.063	0.14	0.46	0.012	0.24	0.74
Leptin, pg/mL	21328.3 (15168.3 to 27488.2)	17417.0 (12912.8 to 21921.2)	−3911.2 (−11621.4 to 3798.9)	22573.8 (16125.6 to 29022.0)	17591.3 (11160.1 to 24022.6)	−4982.4 (−9778.8 to −186.0)	0.828	0.043	0.16	0.53	0.799	0.00	0.05

Data are presented in means and CI of 95%. Repeated-measures ANOVA was used to compare groups ($P < 0.05$). The effect size was measured by η_p^2.
Δ, Final value minus baseline value; η_p^2, partial eta squared; CI, confidence interval; CT, combined training; HIIT, high-intensity interval training; ICAM, intercellular adhesion molecule; IL, interleukin; MCP, monocyte chemoattractant protein; ra, receptor antagonist.

TABLE 6. *Coefficient of correlations and determinations of visceral adipose tissue and inflammatory markers changes after 12 weeks of training utilizing the within-subject model*

	CT group				HIIT group			
	r	R^2	*P*	Power	*r*	R^2	*P*	Power
Δ VAT								
Δ IL-6	−0.24	0.06	0.402	0.12	−0.74	0.56	0.002	0.94
ΔIL-6								
Δ IL-1ra	−0.10	0.01	0.714	0.06	0.67	0.46	0.007	0.84

Δ, Final value minus baseline value; CT, combined training; HIIT, high-intensity interval training; IL, interleukin; ra, receptor antagonist; VAT, visceral adipose tissue.

were not different between the training modalities. We also observed that IL-6 changes were associated with VAT changes. The findings from this randomized controlled trial highlight the important role of HIIT as a time-efficient strategy for improving VAT and cytokines in obese PW. Thus, within the relationship among menopause, VAT, and low-grade inflammation, HIIT was found to reduce, in a time-efficient way, the burden of VAT and low-grade inflammation state in PW.

Although HIIT is efficient in decreasing VAT, the need for expensive specific equipment (ie, a treadmill or bike) and high motor skill level (ie, running at high speed) required for the majority of HIIT protocols[6,12,13,18] are common barriers concerning regular physical activity, especially in developing countries and in older adults.[11,19-21] Unlike most HIIT studies, we used alternative HIIT protocols performed with body weight (30 seconds of step climbing plus 30 seconds of free body weight squats), termed as functional HIIT.[22,23] This functional HIIT does not incur high costs (ie, specific expensive equipment), it does not require a specific place to be performed, and may be configured for a lower motor skill level (ie, step climbing and free body weight squats), allowing people to perform HIIT regardless of their motor skill level and socioeconomic status. A previous study has shown that this functional HIIT improves body composition, peak oxygen uptake, and strength, and alters certain dimensions of the quality of life in young overweight women.[22] In the present study, we showed that this functional HIIT improves VAT in obese PW. Collectively, these data show that this functional HIIT is an accessible treatment strategy to improve body composition in obese PW.

High-intensity interval training-induced reductions in VAT are well-documented.[6,18] However, there is little evidence about which supervised-training modality (ie, aerobic and resistance training or HIIT) is better for reducing VAT in PW. Previous studies have demonstrated that HIIT induces a greater reduction in VAT than moderate-intensity aerobic training in obese PW.[12,13] Although the HIIT effectiveness on VAT has been compared with moderate-intensity aerobic training, studies are still needed to establish that HIIT is an alternative time-efficient strategy when compared with other exercise modalities for improving VAT. Finding the best supervised-training modality to reduce VAT is important due to the obesity epidemic worldwide, which would improve public health guideline recommendations regarding training strategies to improve VAT, particularly in PW. To the best of our knowledge, ours is the first study which compared the HIIT effects with CT—an efficient and well-accepted treatment strategy for improving body adiposity in PW.[8-10] In the present study, we demonstrate that the HIIT reduced VAT in a time-efficient manner, when compared with the CT (HIIT −0.1 kg vs CT 0.0 kg; Table 4). These findings are relevant considering that the comparison between the groups was an effect size (η_p^2) of 0.20, which is a large effect. Moreover, this difference is clinically important because epidemiological evidence has shown that a reduction in ∼0.06 kg of VAT is associated with a reduction in metabolic risk factors for all-cause mortality.[24,25] Collectively, these data suggest that HIIT is a time-efficient treatment strategy to improve VAT in PW.

The underlying mechanism of exercise-induced reductions in VAT is unclear, but they may involve the IL-6. It has been well-demonstrated that skeletal muscles secrete IL-6 into the circulation during intense exercise.[7,26] Furthermore, a dose-response relationship of exercise intensity (>70% of MHR) with VAT reductions in overweight/obese people has been demonstrated.[5,13] Petersen et al[27] showed that a single infusion of recombinant human IL-6 at physiological concentrations increases lipolysis and fat oxidation in humans regardless of increases in growth hormone and/or cortisol. Indeed, in the current study, the HIIT group showed a slight increase in IL-6 level (∼1.2 pg/mL) and a reduction in VAT, whereas the CT group (moderate intensity; Table 1) did not (Tables 4 and 5). Moreover, the IL-6 changes explained the VAT changes (56%) only in the HIIT group (Table 6) after intervention. Thus, although our results may not state cause and effect, to the best of our knowledge, our study is the first to provide support for the hypothesis that increased IL-6 may be the underlying mechanism of HIIT-induced reductions in VAT.

The increased basal IL-6 level after HIIT observed in our study differs from a meta-analysis, which has observed no HIIT effect on the basal IL-6 level.[6] However, this meta-analysis reported that a small number of studies combined with the varied populations limits their conclusion, and therefore the effects of HIIT on IL-6 are not clear. Recently, Windsor et al have observed greater circulating IL-6 concentrations in older adults with high levels of cardiorespiratory fitness compared with older adults with low levels of cardiorespiratory fitness (higher fit ∼3.4 pg/mL vs lower fit ∼1.9 pg/mL).[28] Thus, it would seem reasonable to assume

that HIIT (eg, efficient training to increase cardiorespiratory fitness) increases the basal IL-6 level in the long term. However, more studies addressing this issue are needed.

IL-6 is considered a pro-inflammatory cytokine, and high serum concentrations of IL-6 have been associated with obesity and aging/menopause.[1] Our results showed that the increase in IL-6 did not affect the IL-1ra, leptin, adiponectin, and VAT responses negatively (Tables 4 and 5). These results corroborate the findings of the previous work that exercise-induced increased IL-6 may act as an anti-inflammatory property.[7] IL-6 secreted by the contracting muscle serve as an adaptive mechanism in an attempt to improve the increase in anti-inflammatory cytokines (IL-1ra and IL-10), decrease pro-inflammatory cytokines (TNF-α), and further improves the fat and glucose metabolism in chronic disease conditions.[7] Indeed, we observed an association between IL-6, IL-1ra, and VAT in the HIIT group (Table 6). Thus, it seems that HIIT-induced increase in IL-6 is not harmful to health in PW.

IL-1 is a well-known inflammatory cytokine related with type II diabetes and cardiovascular diseases.[7,26] IL-1 signal transduction is inhibited by IL-1ra, which acts as an anti-inflammatory cytokine. The exercise-induced increased IL-6 induces macrophages to release IL-1ra (ie, cross-talk between muscle and macrophages) in circulation.[7,26] Indeed, in the present study, the HIIT group increased IL-6 and IL-1ra (Table 5) and the IL-6 changes explained the IL-1ra changes in 46% (Table 6). These results corroborate the findings of the previous work in this area linking IL-6 with IL-1ra.[7,26] However, the CT group did not change the IL-6, but increased the IL-1ra (Table 5). This result is in agreement with those obtained by Forti et al,[29] which observed an increase in IL-1ra, but not in IL-6, after 9 weeks of resistance training. Thus, it would seem reasonable to assume that other factors may regulate synthesis and secretion of IL-1ra after different exercise types.[26] However, there are still many unanswered questions about the effects of exercise on IL-1ra.[26] This is an important issue for future research.

High serum concentrations of leptin have been associated with obesity[30] and increased risk of breast cancer in PW.[2] On the contrary, aerobic training, resistance training, and CT decrease leptin levels regardless of age and sex.[31] This training-dependent decrease in leptin is associated with a training-dependent decrease in body adiposity.[31] Although the HIIT effect on leptin is scarce, Trapp et al[32] showed that 15 weeks of HIIT significantly reduced resting leptin levels and body fat when compared with moderate-intensity continuous training (60% of VO_{2max}), and the leptin level changes were positively correlated with the body weight changes among young women. To the best of our knowledge, no study has investigated the HIIT effect on leptin in PW. In the current study, both groups reduced the body fat percentage and leptin in PW (Table 5). Moreover, the training-dependent decrease in leptin was associated with a training-dependent decrease in body fat percentage in both groups. Thus, HIIT is comparable with CT in changes in leptin in PW.

In the current study, we observed a reduction in the adiponectin level after CT. Although low serum adiponectin levels are associated with obesity and metabolic syndrome,[30] the adiponectin changes after exercise training seem to be dependent on some factors. Previous studies have suggested that an increase in adiponectin is observed with high-intensity training (>70% of MHR)[33] and with robust weight reduction (~10%).[34] However, a coordinate regulation of the expression of adiponectin and its receptors has been observed, in which adiponectin serum level changes can be inversely correlated with adiponectin receptor changes in muscle and adipose tissue.[35-37] In addition, the adiponectin level is increased in some inflammatory conditions (eg, arthritis[38]) and different isoforms of adiponectin (high molecular weight adiponectin and globular adiponectin) may express pro-inflammatory actions.[39] If this inflammatory condition is improved, there may be a reduction in adiponectin levels. Hence, the increase in adiponectin after training has not been observed in some studies (ie, HIIT, aerobic and resistance training, and weight loss dietary intervention) even after weight and VAT loss, and metabolic profile improvements.[35-37,40,41] For instance, a study carried out by Langleite et al[36] showed that 12 weeks of CT reduced adiponectin (total and high molecular weight) levels, despite reduced body adiposity in middle-aged men. Thus, adiponectin outcomes after training (increase or decrease) seem to depend on the biological context.

The strengths of this study are related to the following: this was a controlled and randomized study, and women inclusion criteria provided a homogenous sample of PW, reducing bias. All training variable measures (intensity, volume, specific training exercises such as resistance training volume and number of steps climbed, and body weight squats) were taken to ensure that specificity and diet monitoring were recorded to reduce bias. All women in the present study were followed closely by skilled fitness professionals, and they completed the interventions with high compliance. To determine whether a Δ in serum inflammatory markers across the intervention within the individual was associated with a Δ in body adiposity (body fat percentage and VAT) across the intervention, we used a within-subject model to remove the difference between subjects and analyzed the changes within. The weaknesses of the study are related to the following: a small number of participants due to the nature of the intervention, which may have weakened the statistical analyses; however, we performed the power and effect-size analyses which demonstrated moderate to high power and large effect sizes.

CONCLUSIONS

To sum up, this study showed that this functional HIIT is an accessible time-efficient treatment strategy to improve body composition, especially VAT, in obese PW. Moreover, although our results may not state cause and effect, our study provides support for the hypothesis that increased IL-6 may be the underlying mechanism of HIIT-induced reductions in VAT. Moreover, our study provides support for an

anti-inflammatory effect of HIIT similar to CT, increasing IL-1ra and decreasing leptin, regardless of the increase in IL-6. These findings further support the important role of HIIT as a time-efficient strategy for healthy aging, reducing the burden related with VAT and low-grade inflammation state in PW. Thus, for obese PW who need to improve inflammatory markers and body adiposity and have little time to exercise or do not have easy access to physical facilities, HIIT is an alternative time-efficient treatment strategy.

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