

Combined training (strength plus aerobic) potentiates a reduction in body fat but only functional training reduced low-density lipoprotein cholesterol in postmenopausal women with a similar training load

Fabício Eduardo Rossi^{1,2,*}, Ana Claudia S. Fortaleza¹, Lucas M. Neves³, Tiego A. Diniz⁴, Marcela R. de Castro⁵, Camila Buonani⁶, Jorge Mota⁷, Ismael F. Freitas Junior⁶

¹Department of Physical Education, Federal University of Piauí, Teresina, Brazil

²Institute of Bioscience, São Paulo State University, Rio Claro, Brazil

³School of Physical Education and Sport, University of São Paulo, São Paulo, Brazil

⁴Department of Cell and Developmental Biology, Institute of Biomedical Sciences, University of São Paulo, São Paulo, Brazil

⁵Department of Physical Education, Federal University of Maranhão (UFMA), São Luis, Brazil

⁶Department of Physical Education, University Estadual Paulista, Presidente Prudente, Brazil

⁷Faculty of Sport Sciences and Physical Education, Porto University, Porto, Portugal

The aim of this study was to compare the effects of combined (CT; strength plus aerobic) and functional training (FT) on the body composition and metabolic profile with a similar training load in postmenopausal women. The participants were divided into three groups: CT (n = 20), FT (n = 17), and control group (CG, n = 15). The trunk FM, fat mass (FM), percentage of FM (FM%), and fat-free mass were estimated by dual-energy X-ray absorptiometry. The metabolic profile, glucose, triacylglycerol, total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol (LDL-c) were assessed. There were main effects of time in trunk fat, FM, and FM% ($P < 0.05$). There were statistically significant interaction for FM ($P = 0.015$), FM% ($P = 0.017$) with lower values

for CT group. For LDL-c, there was significant interaction ($P = 0.002$) with greater values for FT group in relation to CG and CT. Furthermore, when performed the *post hoc* test on the "mean absolute differences" (Δ), it can be observed statistically significant difference between FT, CT, and CG (-13.0 ± 16.5 mg/dL vs. 4.8 ± 18.4 mg/dL vs. 9.2 ± 18.8 mg/dL, $P < 0.05$). In conclusion, when training loads are equivalent CT potentiated a reduction in FM and FM%, however, only FT reduced LDL-c in postmenopausal women.

Keywords: Aerobic training, Strength training, Body composition, Lipid profile

INTRODUCTION

The menopause involves psychological, hormonal and physical alterations (Stojanovska et al., 2014) which can lead to a marked reduction in lean body mass and an increase in total adipose and trunk fat (TF) (Sims et al., 2013). These changes contribute to reduced mobility and functionality (Bannerman et al., 2002), in addition to the development of cardiovascular diseases, type 2 diabe-

tes, hypertension, dyslipidemia, and metabolic syndrome (Kueht et al., 2009). On the other hand, physical activity is considered an important strategy for tackling these changes (Stojanovska et al., 2014), avoiding an increase in fat mass (FM) (Peterson et al., 2011; Sims et al., 2013), improvements in metabolic profile (Park et al., 2015) and quality of life (de Souza Santos et al., 2011).

Several studies from our group had showed the benefits of different kinds of training on the body composition and metabolic

*Corresponding author: Fabício Eduardo Rossi

 <http://orcid.org/0000-0002-0594-2529>

Department of Physical Education, Paulista State University "Júlio Mesquita Filho", Roberto Simonsen Street, n° 305 – Educational Center, Presidente Prudente, 19060-900, São Paulo, Brazil

Tel: +55-18-3229-5828, Fax: +55-18-3221-4391, E-mail: rossifabicio@yahoo.com.br

Received: February 15, 2017 / Accepted: June 6, 2017

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profile in postmenopausal women (Diniz et al., 2016; Neves et al., 2017; Rossi et al., 2013; Rossi et al., 2015; Rossi et al., 2016). Diniz et al. (2016) demonstrated that only 8 weeks of aerobic training prescribed by the critical velocity was sufficient in reduced total FM, percentage of fat and low-density lipoprotein cholesterol (LDL-c) in postmenopausal women. Rossi et al. (2013, 2015) showed that resistance plus aerobic training in the same session (combined training, CT) was effective in improving fat-free mass (FFM) and decreased whole and trunk adiposity after short period and post-16 weeks of training.

More recently, new programs of training have used at the literature, such as vibrating platforms (Emerenziani et al., 2014), elastic bands (Chang et al., 2012), and unstable bases (Chulvi-Medrano et al., 2012). Neves et al. (2017) investigated the effects of functional training (FT), which had used activities aimed at developing strength, endurance, agility, proprioception and neuromuscular control (Beckham and Harper, 2010) and observed improved on the body composition, lipid profile, and functional fitness in postmenopausal women, and suggested that the FT, using implements such as elastic bands, free weights and unstable bases could be an interesting strategies to improve healthy in postmenopausal women.

However, defining which strategy is the most effective in promoting changes in body composition constitutes a problem which has yet to be solved because the training protocols are compared without equal parameters concerning the quantification of training load (TL). One alternative that has been used to quantify TL is based on the training impulses (TRIMP), which it has been applied in recent studies (Akubat et al., 2012; Borresen and Lambert, 2008; Scott et al., 2013) and it is notable for its low cost and easy implementation.

Our group conducted a recently study and verified the effects of 16 weeks of aerobic and aerobic plus resistance training on the body composition and lipid profile of obese postmenopausal women and to analyzed which of these models were more effective after equalizing the TL using the TRIMP and demonstrated that CT potentiated a reduction in FM but there were no difference on the metabolic profile in postmenopausal women when a similar TL was used (Rossi et al., 2016).

Therefore, in order to ascertain the best training program to improve body composition and metabolic profile in postmenopausal women, and if FT is more effective than strength plus aerobic after equalizing the TL is not clear. Thus, this study aimed to compare the effects of 8 weeks of combined and FT on the body composition and metabolic profile with a similar TL in postmenopausal women. It was hypothesized that CT, as it contains ele-

ments of traditional strength training (dumbbells, machines) would be the more effective in reducing FM, increase FFM as well as in improve metabolic profile than FT, using elastic bands, free weights and unstable bases.

MATERIALS AND METHODS

Subjects

Subjects were invited through television and newspaper advertising to participate in the study. The participants contacted the researchers by telephone and an appointment was made in order to carry out a more detailed interview. The inclusion criteria were: (a) postmenopausal women (having had no menstrual cycle for one or more years) (World Health Organization, 1996) and follicle-stimulating hormone ≥ 26.72 mUI/mL; (b) not presenting any physical limitations or health problems that could prevent the completion of the assessments and exercise intervention (uncontrolled diabetes, hypertension, or rheumatoid arthritis); (c) presenting a medical certificate to participate in the training; (d) not having participated in any systematic physical exercise for, at least, 6 months prior to the study; (e) not receiving hormone replacement therapy. All participants signed the consent form and the present project was approved by the Ethics Research Group of the University (Protocol 64/2011).

Out of a total of 207 women who participated in the first screening, only 75 met all the inclusion criteria and agreed to participate in the study protocol. The subjects were randomly allocated into three groups: CT ($n=25$), FT ($n=25$), and control group (CG, $n=25$). The final sample consisted of 52 participants: CT ($n=20$), FT ($n=17$), and CG ($n=15$). The reasons for drop-outs included personal/family problems; unspecified reasons, absence of blood sample data or an accumulation of three consecutive absences or four nonconsecutive absences during 1 month.

Procedures

Evaluations were performed at baseline and after 8 weeks of training at the Science and Technology Department of the São Paulo State University (FCT/UNESP), Presidente Prudente Campus and involved screening for inclusion in the study, anthropometric, body composition and metabolic profile measurements.

The anthropometric measurements were conducted on the same morning as the dual-energy X-ray absorptiometry (DXA) scan, after a 4-hr fasting and subjects barefoot and wearing light clothing. Body composition was assessed between 8:00 a.m. and 12:00 p.m., by the same evaluator. Blood samples were collected after an

overnight fast (12 hr).

Two weeks prior to evaluating, the participants performed one sets of 12–15 repetition in each exercise, 3 times per week (Monday, Wednesday, and Friday) for familiarization with equipment and training routine. The control group maintained 8 weeks of a sedentary lifestyle without participating in any regular physical exercise—essentially maintaining their habits. All training sessions were conducted under the supervision of physical education professionals.

Anthropometric measurements and body composition

Anthropometry was composed of body weight and height measurements. Height was measured on a fixed stadiometer of the Sanny brand, with an accuracy of 0.1 cm and length of 2.20 m. Body weight was measured using an electronic scale (Filizola PL 50, Filizzola Ltda., Brazil), with a precision of 0.1 kg. Body composition was estimated using a DXA scanner ver. 4.7 (Lunar DPX-NT, General Electric Healthcare, Buckinghamshire, England). The participants were positioned in the supine position and remained motionless throughout the examination. FM, percentage of FM (FM%), FFM, and TF were assessed and expressed in absolute values by the DXA software. TF was estimated in the abdominal region, and was defined as 20% of the length from a circumference line at the pelvis to a circumference line at the neck (Bhupathiraju et al., 2011). All measurements were carried-out at the University laboratory, in a temperature controlled room. Each morning, before the beginning of the measurements, the equipment was calibrated by the same researcher, according to the manufacturer's instructions.

Blood samples

The blood samples were taken at the baseline and postintervention. After an overnight fast (12 hr), venous blood samples were collected to measure glucose (mg/dL) total fasting cholesterol (Chol, mg/dL), high-density lipoprotein cholesterol (HDL-c, mg/dL) using the colorimetric technique and dry chemicals, with equipment of the Johnson and Johnson brand, model Vitro 250. The Friedewald formula (Friedewald et al., 1972) was used to calculate LDL-c (mg/dL) concentration.

Dietary intake assessment

Twenty-four hour dietary recalls were conducted at 2-time points, on three nonconsecutive days (one weekend and two weekdays): 1 week before the beginning and in the first week after the intervention. The participants were oriented by a nutritionist as to how to complete the food records. Data were analyzed by the

same nutritionist using the software NutWin, version 1.5 (Nutritional Program, Federal University of São Paulo, Brazil, 2002).

CT procedures

CT (strength plus aerobic) was performed by strength training plus aerobic training, including 10 min of warm-up and stretching at the end of the training session.

The determination of the intensity of the aerobic training was performed using the critical velocity protocol proposed by Wakayoshi et al. (1993) and used in our previous studies with postmenopausal women (Diniz et al., 2016; Neves et al., 2017). The studied group traveled three distances (400, 800, and 1,200 m) on a running track on separate, nonconsecutive days. The participants were instructed to cover the distance in the shortest possible time, which was recorded using a digital stopwatch (model S810i or RS800, Polar Electro, Espoo, Finland). The relationship between the distance (m) and the exercise time (s) was linearly adjusted and the critical velocity was assumed to be the slope of this model (Zagatto et al., 2013) which is the intensity of aerobic training (Takahashi et al., 2009; Wakayoshi et al., 1993).

The resistance exercises used in the program were: 45° leg press, leg extension, leg curl, bench press, seated row, arm curl, triceps extension, side elevation with dumbbells, and abdominal exercises. The resistance training program consisted of two progressive phases: phase 1, 1st to 4th weeks, 12–15 repetitions, three sets per exercise, 60 sec between sets; phase 2, 5th to 8th weeks, 10–12 repetitions, three sets per exercise, 60 sec between sets. The TL was adjusted every four training weeks in order to maintain the prescribed number of repetitions (Table 1).

The intensity of the resistance training was controlled through the zone of maximum repetitions. The series were executed until momentary exhaustion, meaning that when participants performed the training with repetitions varying from 12 to 15 repetition maximum, they were always stimulated to execute at least 12 and no more than 15 repetitions. In the case of the participants executing more than 15 repetitions, the overload was increased in order to have the training zone respected (Rossi et al., 2015).

FT procedures

FT was performed by FT plus aerobic training, including 10 min of warm-up and stretching at the end of the training session. The intensity of the aerobic training was determined by the critical velocity, similar to the model described in the CT and applied in our previous study with FT and postmenopausal women (Neves et al., 2017). The FT was composed of 11 exercise stations devel-

Table 1. Summary of interventions

Intervention	Exercise	Session details	Session time	Rest interval	Training load
Combined training	Strength	11 Exercises for strength training exercise	40 min	1 min	Week 1 to 4: 3 × 12–15 repetitions 65%–70% 1RM each exercise (RPE 12–13) Week 5 to 8: 3 × 10–12 repetitions 70%–75% 1RM (RPE 12–13)
	Aerobic	Walking in athletics track (400 m)	30 min	None	100% Critical velocity
Functional training	Functional	11 Exercises for strength training, agility, coordination, and balance exercise	40 min	30 sec	Week 1 to 4: 3 series circuit - stimulus 40 sec each exercise (RPE 12–13) Week 5-8: 3 circuit series - stimulus 50 sec each exercise (RPE 12–13)
	Aerobic	Walking in athletics track (400 m)	27–30 min	None	100% Critical velocity

RPE, rating of perceived exertion; 1RM, one-repetition maximum.

oped in circuit format, which the participants completed three times with a pause of 30 sec between each station. At the end of the exercise the participants performed a 28- to 30-min walk, depending on the overload performed (Table 1).

The functional exercises were performed with elastic bands and free weights and consisted of sit-ups, arm curls, lateral raises, seated rows, knee flexions, crucifixes, handle triceps and squats. The agility drills were conducted using movement between cones, agility ladders were used for coordination and unstable bases such as a Bosu ball, swissball, boards and balance discs were used for balance exercises. There were also variations in the support base and movement of the upper body in the upright position. The exercises are illustrated in Fig. 1.

The FT program consisted of two progressive phases: phase 1, 1st to 4th weeks, 40 sec of execution and 30-sec pause between exercises; phase 2, 5th to 8th weeks, 50 sec of execution and 30-sec pause between exercises. The training intensity was monitored by rating of perceived exertion (RPE), due to the variations in tension/overload of the equipment used (Table 1).

Session RPE

A previous pilot study was performed to equalize the load of the training groups, which involved a session of combined and FT in different day. For load equalization, the 20-point scale as standardized by Borg et al. (1987) was used to determine the RPE at the end of each training and the time of sessions was modified to induce similar values of RPE between groups [RPE = 13–14 (arbitrary units)⁻¹].

The pilot study indicated the necessity of 27 min of resistance exercises and 30 min of aerobic exercise for the CT. For FT, the pilot study indicated the necessity of 33 min of functional exercises and 27 min of aerobic exercise.

The monitoring impulse training (TRIMP) for each session was calculated by multiplying the duration of the session and the RPE (i.e., TRIMP [a.u.] = Duration [min] × RPE [arbitrary units]⁻¹) as proposed by Foster et al. (2001). This model was chosen because it

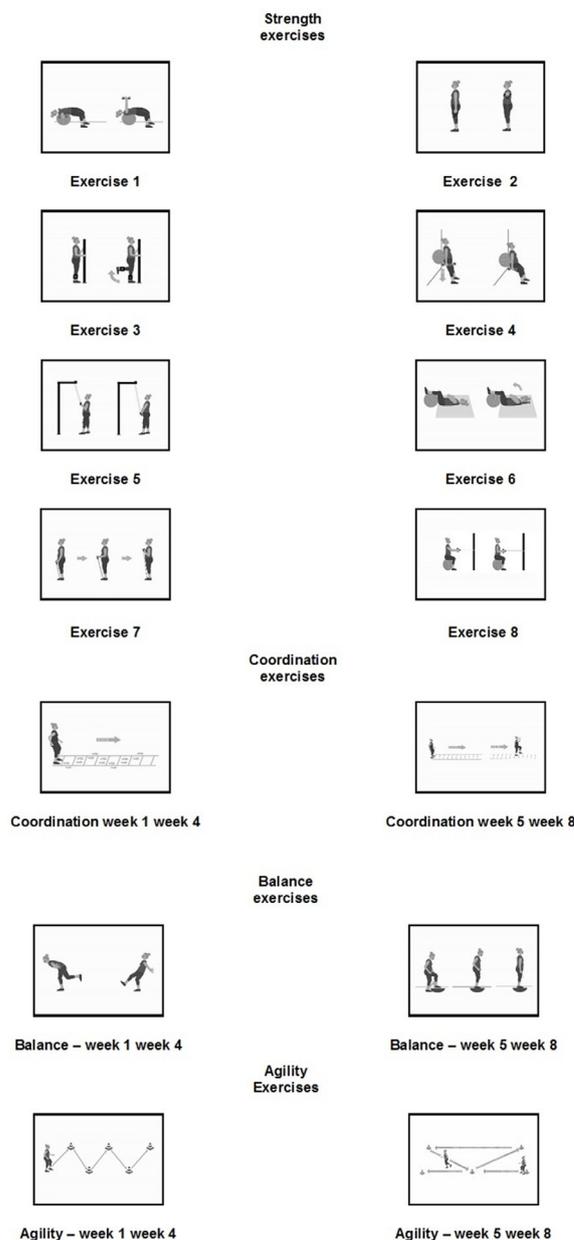


Fig. 1. Functional training program.

allows the assessment of internal TL in both continuous efforts (i.e., aerobic stimuli) and intense efforts of short duration (i.e., resistance training). Thus, the TRIMP for the CT was taken as the sum of the impulses calculated for the strength training and the aerobic training (TRIMP [a.u.] = [27 × RPE of resistance⁻¹] + [30 × RPE of aerobic⁻¹]). The TRIMP for the FT was equivalent to the sum of the calculated impulses for the FT and aerobic training (TRIMP [a.u.] = [33 × RPE of functional⁻¹] + [27 × RPE of aerobic⁻¹]).

The weekly TL was assumed as the average TRIMP observed in the three sessions per week, on condition that no significant difference was presented in the comparison between the two training models during the period (Table 2).

Statistical analysis

To compare the TRIMP between two training models the Mann-Whitney test was used and the median values and inter-

quartile range were presented. In the longitudinal analysis, the two-way analysis of variance (ANOVA) (time × group) was conducted. When a significant difference in group or interaction was observed, a Tukey *post hoc* test was conducted. Finally, the “mean absolute differences” (post exercise value minus baseline value = Δ) were calculated and one-way ANOVA with Tukey *Post hoc* was used, which complementary analysis. The effect size (eta-squared; η²) of each test was calculated for all analyses. All analysis was performed using the statistical software SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA) and the significance level adopted was P < 0.05.

RESULTS

The weekly TRIMP behavior was not significantly different in the two experimental groups during the eight weeks (Table 2). In addition, the median of TRIMP during the training period also presented no significant differences between groups (FT = 6,203 [381] a.u.; CT = 6,384 [716]; P = 0.151).

Table 3 presents the mean values of body weight, body composition, metabolic profile and dietary intake in the pre- and post-intervention period in the three groups studied. In relation to the age (CG = 61.9 ± 7.2 years; FT = 60.1 ± 5.4 years; CT = 62.2 ± 6.3 years; P = 0.575), high (CG = 154.6 ± 6.1 cm; FT = 157.8 ± 5.7 cm; CT = 155.8 ± 5.3 cm; P = 0.274) and all variables investigated, there were no statistical differences between groups at the baseline.

When performing the comparison on the body composition, there were main effects of time in trunk FM (F = 8.003, P = 0.007, η² = 0.140), FM (F = 16.401, P < 0.001, η² = 0.25) and FM% (F =

Table 2. Median values and interquartile range of the TRIMP per week

Moment	FT (n=17)	CT (n=20)	P-value
Week 1	763.5 (57)	798.0 (60)	0.091
Week 2	769.5 (84)	798.0 (101)	0.060
Week 3	780.0 (67)	798.0 (101)	0.709
Week 4	777.0 (60)	798.0 (114)	0.278
Week 5	780.0 (69)	798.0 (114)	0.444
Week 6	780.0 (44)	795.0 (96)	0.421
Week 7	780.0 (60)	798.0 (101)	0.137
Week 8	771.0 (61)	798.0 (114)	0.558

Mann-Whitney test.
TRIMP, training impulses; FT, functional training; CT, combined training.

Table 3. Comparison on the body composition, metabolic profile, and dietary intake in control group, functional, and combined training after 8 weeks

Variable	CG (n=15)			FT (n=17)			CT (n=20)			Interaction (time × group)
	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ	P-value
Weight (kg)	61.4 ± 8.4	61.4 ± 8.5	-0.020 ± 1.1	64.1 ± 8.5	63.5 ± 8.6	-0.565 ± 1.2	59.7 ± 5.8	59.4 ± 5.8	-0.370 ± 1.4	0.469
TF (kg)	14.0 ± 3.2	14.1 ± 3.2	0.077 ± 0.6	13.8 ± 3.2	13.3 ± 3.2	-0.467 ± 0.5	13.3 ± 2.7	12.8 ± 2.8	-0.489 ± 0.9	0.059
FM (kg)	26.3 ± 6.3	26.3 ± 6.3	0.028 ± 1.0	26.1 ± 5.2	25.3 ± 5.4	-0.711 ± 0.8	24.9 ± 4.8	24.0 ± 4.8*	-0.941 ± 1.0 ^b	0.015
FM (%)	42.4 ± 6.4	42.4 ± 6.3	0.025 ± 1.2	40.4 ± 4.0	39.6 ± 4.2	-0.812 ± 1.4	41.5 ± 5.5	40.2 ± 5.5*	-1.3 ± 1.3 ^b	0.017
FFM (kg)	33.0 ± 4.5	32.9 ± 4.3	-0.079 ± 0.8	35.7 ± 4.0	35.8 ± 3.8	0.164 ± 1.5	32.7 ± 3.6	33.3 ± 3.5	0.600 ± 1.0	0.230
Glucose (mg/dL)	95.3 ± 22.2	94.6 ± 18.8	0.00 ± 7.7	96.9 ± 17.8	98.3 ± 26.1	1.4 ± 15.0	90.5 ± 10.4	88.8 ± 10.6	-1.7 ± 6.8	0.662
TAG (mg/dL)	131.9 ± 58.9	128.6 ± 57.0	-3.3 ± 35.1	119.6 ± 47.7	110.3 ± 45.5	-9.3 ± 36.1	146.2 ± 60.2	128.9 ± 53.0	-17.3 ± 62.7	0.688
Chol (mg/dL)	198.5 ± 38.7	209.2 ± 41.6	10.7 ± 22.7	198.5 ± 35.8	184.5 ± 30.7	-14.0 ± 19.0 ^b	204.9 ± 26.6	205.2 ± 21.3	0.3 ± 24.9	0.079
HDL-c (mg/dL)	51.1 ± 8.6	51.8 ± 9.0	0.7 ± 3.7	55.7 ± 15.8	56.6 ± 14.1	0.9 ± 7.8	55.5 ± 14.6	54.8 ± 10.3	-0.7 ± 10.9	0.822
LDL-c (mg/dL)	121.5 ± 30.6	130.7 ± 32.1	9.2 ± 18.8	118.8 ± 29.2	105.8 ± 26.7	-13.0 ± 16.5 ^{ab}	120.2 ± 20.8	125.1 ± 20.7	4.8 ± 18.4	0.012
Dietary intake (kcal)	1639.0 ± 384.6	1661.1 ± 123.1	22.0 ± 297.9	1529.6 ± 347.2	1634.3 ± 260.5	102.9 ± 389.4	1779.6 ± 378.8	1697.6 ± 469.5	-82.0 ± 416.3	0.477

Values are presented as mean ± standard deviation.
CG, control group; FT, functional training; CT, combined training; Δ, mean absolute differences (post exercise value minus baseline value); TF, trunk fat; FM, fat mass; FFM, fat-free mass; TAG, triacylglycerol; Chol, total cholesterol; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol.
*Statistic significant difference from pre. ^aP < 0.05 compared to control group, Tukey *post hoc* test. ^bP < 0.05 compared to concurrent training, Tukey *post hoc* test with.

14.305, $P < 0.001$, $\eta^2 = 0.23$). There were significant interactions in FM and FM% with lower values for CT group, according demonstrated on Table 3. In addition, *post hoc* analysis performed on the “mean absolute differences” (Δ) showed statistically significant difference between CT and CG group in FM ($P = 0.013$) and FM% ($P = 0.012$). There were no main effects of time, group and interaction for TF and FFM ($P > 0.05$).

In relation to the metabolic profile, there were statistically significant interaction (time \times group) for LDL-c ($F = 7.152$, $P = 0.002$, $\eta^2 = 0.23$) with greater concentration for FT group. When performed the *post hoc* test on the “mean absolute differences” (Δ), it can observed statistically significant difference between FT and GC ($P = 0.003$) and FT and CT ($P = 0.011$). There were no main effect of time or significant differences between group and interaction for glucose, TAG and HDL-c ($P > 0.05$).

DISCUSSION

There is no consensus in the literature regarding the best training model for reducing body and TF and increasing FFM in postmenopausal women. Although studies have been conducted to find the most effective model, both in young people (Schwingshackl and Hoffmann, 2013) and middle-aged and elderly adults (Bales et al., 2012; Sanal et al., 2013; Seo et al., 2010), the majority of these studies made comparisons by standardizing only the total time of the training session, not carrying out appropriate load adjustments, and thus were unable to discern whether the changes in body composition were caused by the training stimulus or whether they were the consequence of the total quantity of work performed.

In the present study, when comparing the training protocols in the equalizing load model, it was observed that only 8 weeks of CT (strength plus aerobic) decreased FM and FM%, however, FT was more effective in reduced LDL-c than CT and CG.

In accordance with these results, in previous study developed by our group (Rossi et al., 2016) verified the effects of isolated aerobic training and CT on the body composition and metabolic profile of postmenopausal women after equalizing the TLs using TRIMP and demonstrated that after 16 weeks both training programs induced an “antiatherogenic” profile, however, CT was more efficient in decreased FM and increased FFM. In this present study, although CT induced to increased FFM ($\Delta = 0.600$ kg) there was not statistically significant difference in relation to the FT.

It is known that in women the period of menopause is associated with a reduction in FFM, and an increase in body fat, of up to

2.5 kg, principally in the trunk region (Sims et al., 2013). Excessive accumulation of central fat is considered the best predictor of cardiovascular risk, as it is associated with diabetes mellitus, hypertension and dyslipidemia, which contribute to the development of cardiovascular diseases (Kueht et al., 2009). In this sense the identification of effective measures to combat this situation are of great importance.

In relation to the metabolic profile, the improvement observed in the TF group, maybe have been favored the training format (circuit training). Several studies demonstrated benefits on metabolic profile during circuit training (Miller et al., 2014; Neves et al., 2017; Paoli et al., 2013).

Neves et al. (2017) verified the effect of circuit training format with eight stations related to the development of resistance force (using elastic bands for resistance) plus four stations focused on balance, coordination, and agility plus 18- to 30-min walk and observed that 16 weeks of FT performed using circuit training improved body composition, lipid profiles and functional fitness. However, a recent study has shown that the concurrent exercise can also promote the improvement in LDL-c (Atashak et al., 2016). Thus, despite there is no consensus at the literature regarding the intervention that produces greater improvements on metabolic profile, in this study TF group showed significant difference when compared to CG and CT for LDL-c.

It has been shown that a decrease of 1.0 mmol/L in LDL concentrations reduces by around 5% the incidence of major vascular events (Cholesterol Treatment Trialists' (CTT) Collaboration et al. 2010). In this way, exercise program has been well established as a way to improves serum lipoprotein and lipid profiles and thereby, reduces cardiovascular risk (Lira et al., 2010). Indeed, a meta-analysis of 51 exercise training studies showed an average decrease of 3.7% in triacylglycerol and 5.0% in LDL-c, and an increment of 4.6% in HDL-c (Leon and Sanchez, 2001), confirming the importance of exercise in the improvement of vascular health.

Despite these results being of great relevance, it is necessary to mention some limitations; there was no standardization of the diet, however the subjects maintained the same dietary intake during the study. In addition, it is suggested that other studies are needed which compare the effects of different physical exercise protocols, conducted over a longer period of time and using other variables, such strength and functional capacity.

In conclusion, when TLs are equivalent CT (strength plus aerobic) potentiated a reduction in FM and FM%, however, only FT reduced LDL-c in postmenopausal women.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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