

High intensity interval resistance training (HIIRT) in older adults: Effects on body composition, strength, anabolic hormones and blood lipids



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1. Introduction

The aging process induces significant changes in skeletal muscle morphology and functionality. If not counteracted, this process, termed sarcopenia, can lead to progressively greater disability, frailty and loss of independence. Whilst determining the prevalence of sarcopenia at the population level is complicated by different diagnostic criteria and methodologies used to assess muscle mass, a large percentage of older adults will suffer from this condition in their lifetime (von Haehling et al., 2010). Additionally, longer life expectancy is producing a growing number of elderly individuals worldwide (Beard et al., 2016). Therefore, age-related diseases, such as sarcopenia, are an increasingly important public health concern, and optimal strategies for combatting the progressive loss of muscle mass and function are needed.

It is well known that performing regular resistance training (RT) can counteract sarcopenia and improve fitness and body composition

(Raymond et al., 2013; Steib et al., 2010). The American College of Sports Medicine (ACSM) and American Heart Association (AHA) physical activity recommendations for older adults encourage progressive weight training at least 2 days per week at a subjective intensity corresponding to “moderate” to “vigorous” (i.e. an intensity of 5–6 to 7–8 on a scale of 0 to 10) (Chodzko-Zajko et al., 2009). ACSM has also put forth a position stand advocating the usage of loads corresponding to 60–80% of the 1-repetition maximum (1RM) for 8–12 repetitions with 1–3 min of rest between sets in healthy older adults (The American College of Sports, 2009).

In addition to counteracting sarcopenia through maintaining or increasing muscle mass and strength, RT can improve functional abilities and combat a variety of other disease states, including cardiovascular and metabolic diseases, depression, and osteoporosis (Chodzko-Zajko et al., 2009). Implementing a RT program can lead to beneficial modifications of blood lipid components in the elderly, such as reduc-

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tions in LDL cholesterol and increases in HDL cholesterol (Chodzko-Zajko et al., 2009). Whilst a variety of RT programs may be beneficial, most previous investigations have not employed direct comparisons of the efficacy of different RT programs in the elderly. Although it seems that higher intensities (> 80% 1RM) lead to greater improvements in muscular strength and muscle mass in the elderly (Csapo and Alegre, 2016), the effects on other physiological parameters are less clear. Perhaps due to the numerous variables involved in RT programming, the differences between training styles in the elderly are not completely understood and warrant further investigation (Paoli, 2012b). Although utilizing 60–80% of the 1-repetition maximum (1RM) for 8–12 repetitions with 1–3 min of rest between sets is the suggested training protocol for healthy older adults (The American College of Sports, 2009), other methods utilizing shorter incomplete rest periods could be a more time-efficient strategy. A recent meta-analysis has demonstrated that lack of time and interest, as well as post-exercise soreness, is a major factor contributing to attrition of elderly individuals undergoing exercise training (Raymond et al., 2013). Developing a training protocol that is feasible enough to keep older adults training consistently, but intense enough to promote muscular improvements, should be a goal of researchers interested in the prevention of sarcopenia and the related functional limitations. A resistance training based technique that fits these requirements is the rest-pause technique and its variants (Korak et al., 2017). Rest-pause techniques involve a pause (that may vary in duration) between a certain number of repetitions within a set (Keogh et al., 1999; Korak et al., 2017; Marshall et al., 2012). We previously investigated the effect of a variant of the rest-pause technique, called high-intensity interval resistance training (HIIRT), on metabolism in young adult males (Paoli et al., 2012).

The aim of this study was to assess the effects of two different RT programs on muscle strength, body composition, anabolic hormones and blood lipids in older adults. Specifically, a traditional resistance training (TRT) program conforming to ACSM recommendations (i.e. 3 sets of 8 repetitions at 75% 1RM with 90 s rest periods) was compared to high-intensity interval resistance training (HIIRT; 2 sets of 6/2/2 repetitions with incomplete rest periods of 20 s within the set).

2. Methods

2.1. Participants

2.1.1. Recruitment

Fifty subjects were recruited through advertisement in newspaper and medical studios in the metropolitan area surrounding the University of Padova. Screening procedures included a health history questionnaire and a medical visit, and individuals with any musculoskeletal, cardiovascular, metabolic, inflammatory or neurodegenerative diseases were excluded. Subjects undertaking hormonal replacement therapy were also excluded. Only individuals who were between the ages of 60 and 80 years, with a BMI lower than 30 and no prior resistance training experience were allowed to participate.

After providing written informed consent and completing the medical history visit, all subjects performed a stress test under the supervision of a cardiologist to evaluate any cardiac abnormalities that would prevent their participation in the study.

Thirty-five older adults (15 female and 20 male) were included in the study (Fig. 1).

2.1.2. Randomization

The participants (males and females) were randomized to either TRT ($N = 17$) or HIIRT ($N = 18$) using on-line QuickCalcs ([http://www.](http://www.graphpad.com/quickcalcs/randomize1.cfm)

[graphpad.com/quickcalcs/randomize1.cfm](http://www.graphpad.com/quickcalcs/randomize1.cfm)) by GraphPad Software, San Diego, California.

2.1.3. Ethics

All subjects were informed about the purpose and risks of the study and provided written informed consent in accordance with the Declaration of Helsinki. The study was approved by the local ethical committee of the Department of Biomedical Sciences (University of Padova).

2.2. Experimental approach and study design

The intervention was divided in two phases (Fig. 2). During the first 4 months, all the subjects performed the same progressive resistance training program, starting with 3 sets of 15 repetitions at 60% of 1RM for each exercise and progressing to 3 sets of 10 repetitions at 70% 1RM. After the 4-month familiarization period, subjects started the intervention period, which lasted 2 months. Subjects were randomized into high intensity interval resistance training group (HIIRT) or traditional resistance training group (TRT) group. Subject characteristics after the randomization are shown in Table 1.

The rationale behind the long (4 months) period before randomization comes from necessity of gradually progressing through the neuroadaptation stage that normally occurs in the first weeks or months of resistance training in previously untrained individuals (Moritani and Vries, 1979; Seynnes et al., 2007) and to let all the subjects achieve the experience necessary to complete the higher intensity experimental protocol without muscular injury.

Before and after the training period, Bioelectrical Impedance Analysis (BIA), blood test analysis and strength tests (1RM) were performed. Muscular strength tests were also repeated before the randomization process to ensure equivalent baseline strength between groups prior to the intervention period.

2.3. Measurements

Before and after the training period, all subjects participated in the same testing visit. All subjects were instructed to arrive fasted and not to perform any exercise for 8 h before the testing. On the test day, participants arrived at the laboratory around 8:00 am.

2.3.1. Anthropometry and body composition

Height and body weight were measured with a digital electronic scale (Tanita BWB-800 Medical Scales, Tanita Co. Arlington Heights, IL, USA), and body composition was assessed using bioelectrical impedance analysis (BIA, Akern Bioresearch, Pontassieve, FI, Italy). BIA is a reliable, safe, convenient, and non-invasive method that provides estimations of fluid compartments, fat and fat-free mass in healthy subjects (Frisard et al., 2005; Kushner et al., 1990; Paoli et al., 2013a; Piccoli et al., 2007; Stewart and Hannan, 2000). Through the analysis software, we obtained the values of fat free mass (FFM) and fat mass (FM).

2.3.2. Blood biochemistry

Blood samples were taken from antecubital vein and collected into BD Vacutainers Tubes (SST™ II Advance, REF 367953). After blood sampling, samples were centrifuged (4000 RPM at 4 °C using centrifuge J6-MC by Beckman), and the serum was aliquoted and stored at – 80 °C. All samples were analysed in the same analytical session for each test using the same reagent lot, and the intraassay CV was < 7% for all analyses. Before the analytical session, the serum samples were thawed overnight at 4 °C and

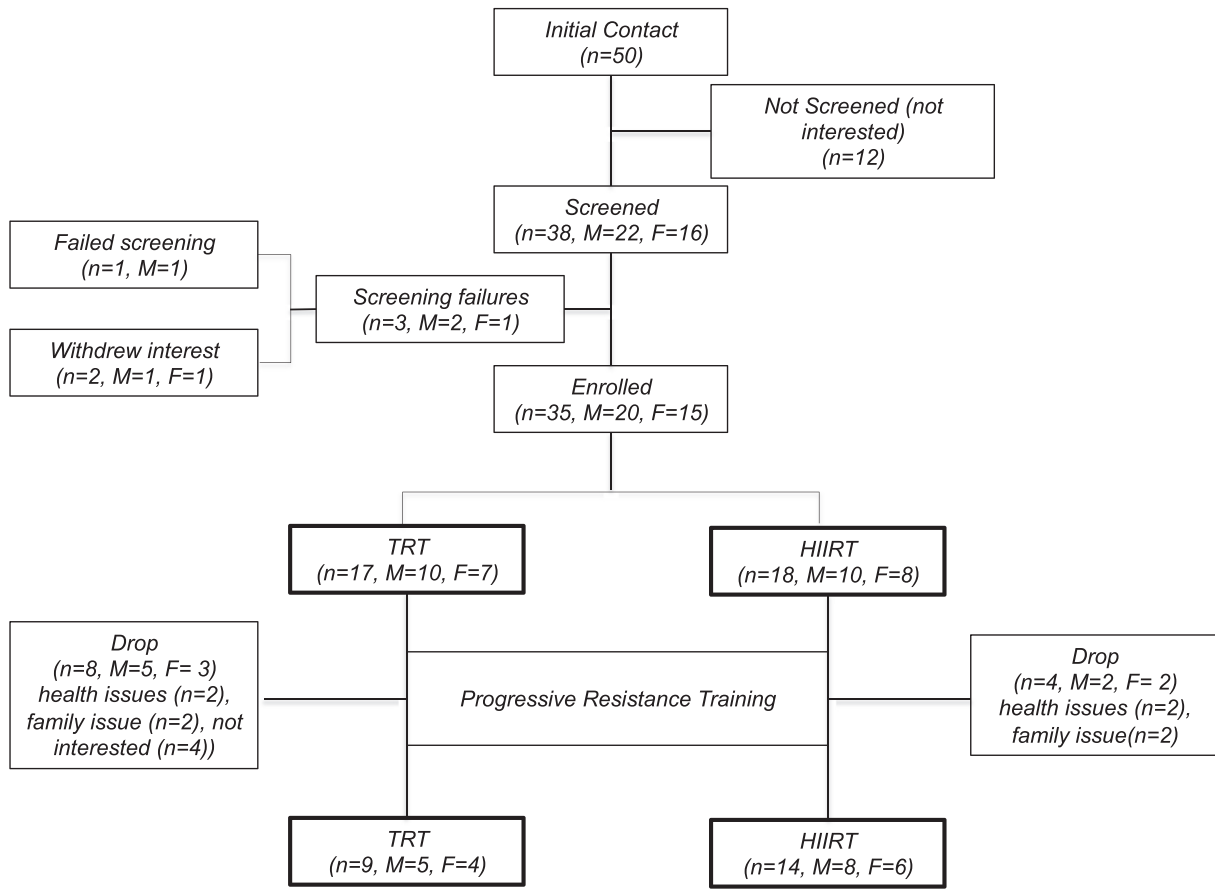


Fig. 1. CONSORT (Consolidated Standards of Reporting Trials) diagram of study recruitment, enrollment, randomization follow-up, and analysis.

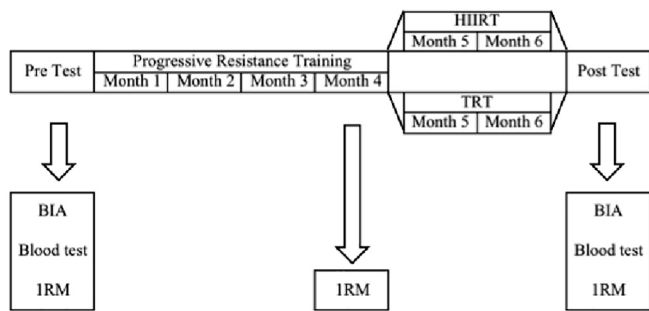


Fig. 2. Study design. After 4 months of progressive resistance training subjects were randomly divided in the two experimental groups: high intensity interval resistance training (HIIRT) and traditional resistance training (TRT). BIA = Bioelectrical Impedance Analysis, 1 RM = 1 repetition maximum.

Table 1

Anthropometric characteristics of subjects after randomization to the specific RT protocols. Data are presented as mean ± SD. BMI = Body Mass Index, FFM = Fat Free Mass.

	TRT (N = 17)	HIIRT (N = 18)
Age (years)	61.7 ± 4.2	64.1 ± 2.3
Weight (kg)	72.4 ± 14.6	70.3 ± 10.5
BMI (kg/m ²)	25.7 ± 3.6	25.5 ± 2.5
FFM (kg)	36.8 ± 5.9	36.5 ± 7.2

then mixed. Testosterone, cortisol, growth hormone (GH), insulin-like growth factor-1 (IGF-1), IGF-binding protein-1 and 3 (IGFBP1 and IGFBP3), lipoproteins, insulin, glycaemia, alanine aminotransferase (ALT), aspartate transaminase (AST), gamma-glutamyl transferase (GGT), creatine kinase (CK), creatinine, uric acid and urea were determined. Total testosterone was measured by immunochemiluminescent method (Roche Cobas e601, Roche Diagnostics, Mannheim, Germany), blood glucose by enzymatic method with esokinase (Roche Cobas e702, Roche Diagnostics, Mannheim, Germany), total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL) and GGT by enzymatic colorimetric in homogenous phase (Roche Cobas e702, Roche Diagnostics, Mannheim, Germany), triglycerides (TGs) and uric acid by an enzymatic colorimetric method (Roche Cobas e702, Roche Diagnostics, Mannheim, Germany). ALT and AST were measured by pyridoxal phosphate activation according to IFCC, GGT was measured by a IFCC and Szasz standardized enzymatic colorimetric method, CK and Urea by kinetic enzymatic method, creatinine by enzymatic (Roche Cobas e702, Roche Diagnostics, Mannheim, Germany). Apolipoprotein A-1 (APOA1) and Apolipoprotein B (APOAB) were measured by immunophelometric system (Dimension VISTA, Siemens, Healthcare Diagnostics Ltd., Camberley, UK). Free testosterone was determined by RIA (radioimmunological manual method) (Beckman Coulter) and IGFBP3 and IGFBP1 by IRMA (Dia Source). IGF-I was measured using the analyzer Liaison XL (DiaSorin S.p.A, Vercelli- Italy). The test is a sandwich immunoassay based on a chemiluminescent revelation. Insulin was measured with a chemiluminescent immunoassay (Siemens Immulite 2000).

After the blood draw, subjects were then familiarized with the strength testing protocol and the exercises used in the training program.

2.3.3. Strength

Strength was measured via a 3–6 RM strength test for the major trained muscle groups (leg extension, chest press, latissimus pull down and arm curl). After an appropriate warm up for each test, weight was gradually increased until failure occurred between a range of 3–6 repetitions, which were performed using correct technique and without assistance. A 3–6 RM test was chosen because it is suitable to test maximal strength in subjects with little or no previous resistance training experience (Reeves et al., 2004), and this technique has been shown to have a high reproducibility ($r = 0.99$) in our lab (Paoli et al., 2012; Paoli et al., 2013b). Using the results of the strength testing, 1RMs were estimated with Brzycki formula (Brzycki, 1993): $1 \text{ RM (estimated)} = \text{load (kg)} / [1.0278 - (0.0278 \times \text{number of repetitions})]$. Data obtained from initial strength testing was used to determine appropriate loads at the beginning of the resistance training program.

2.4. Training protocol

Training sessions were performed twice a week and included: chest press, lat pulldown, military press, bicep curls, triceps extensions, leg press, leg curls and sit-ups. During the first 4 months, training intensity gradually increased to reach 70% of 1RM, as estimated by the first strength test. After the 4-month training period, a new 3–6 RM strength test was performed to determine the appropriate level for the two intervention protocols. One group used a modified rest-pause method called HIIRT, as previously described (Paoli et al., 2012; Paoli et al., 2011; Paoli et al., 2010; Paoli et al., 2013b). For each exercise, the HIIRT technique consisted of two series of the following: 6RM at 80% 1RM followed by 20" of rest, repetitions to failure with the same weight, another 20" of rest, and repetitions to failure (2–3 repetitions) using the same weight again (Paoli et al., 2012). After 2'30" rest, subjects repeated the entire sequence a second time (i.e. the second series was performed). The entire training session lasted approximately 45 min, including the warm up and cold down periods.

The TRT group performed three sets of eight repetitions at 75% of 1RM, with 2'30" of rest between sets. The training session lasted approximately 65 min, including the warm up and cold down periods. Training volume of the two different protocols was similar. For example, assuming that the 1RM of the subjects was 100 kg, with HIIRT protocol the total volume of training (set \times reps \times load) was about 1760 kg ($2 \times 6 + \sim 3 + \sim 2 \times 80$ kg), whilst with TRT was 1800 kg ($3 \times 8 \times 75$ kg). HIIRT volume may have differed slightly from subject to subject, as participants were requested to perform repetitions to failure (typically 2–4 repetitions) after the first six reps at 80% 1RM (Fig. 3).

A certified personal trained supervised all sessions in order to ensure safety and proper execution of the training program.

2.5. Statistical analysis

Data are expressed as means \pm SD. Statistical analysis was performed with GraphPad Prism 6.0 software (GraphPad Software, San Diego, California). Through the Shapiro-Wilk's W test, we assessed the normality between groups. An independent samples *t*-test was used to test baseline differences between groups. Within-group effects were analysed using one-way ANOVA. The effects of training were analysed using a two-way repeated measures ANOVA (time \times treatment); in case of significant main effects or interactions, Bonferroni post hoc test was performed. Standardized differences between pre-post interventions were obtained through Cohen's effect size. Significance was set at $p < 0.05$.

3. Results

A total of 35 subjects were included in the study and divided randomly into two groups: traditional training (TRT; $N = 17$) and high intensity interval resistance training (HIIRT; $N = 18$). During the two-month intervention period, 8 subjects dropped out of the study from TRT (-47%) whilst only 4 subjects dropped out of the study from HIIRT (-22%), indicating superior retention with the high intensity protocol compared to traditional resistance training.

Strength increased with both training protocols ($p < 0.001$), without any significant difference between the two programs (Table 2). HIIRT and TRT both showed large Cohen's effect size (ES) for leg extension strength (0.818 and 1.138, respectively). For chest press strength, ES were also large in HIIRT (0.957) and TRT (0.736). Lat pulldown strength ES was large in HIIRT (1.103) and small in TRT (0.455). Arm curl strength ES were large in both cases (1.840 in HIIRT and 1.787 in TRT).

Bioelectrical impedance analysis showed a significant decrease of total FFM (-5%) and a significant increase of FM ($+5\%$) only of TRT groups, whilst HIIRT showed no significant changes (Table 2). Body weight showed a small ES for both groups TRT (0.0145) and HIIRT (0.0181), also fat free mass showed a small ES for TRT (0.2588) and HIIRT (0.1523). Finally, fat mass ES resulted also small (0.0702) in TRT and small (0.1108) in HIIRT.

Concentrations of hormones in the blood are displayed in Table 3. Cortisol concentrations were higher after training in both groups (TRT $+8\%$ and HIIRT $+14\%$), although this was only statistically significant in HIIRT. IGF-1 decreased in both groups but without differences between groups, whilst insulin decreased significantly only in the HIIRT group (-29% vs. -11% in TRT). Basal GH levels decreased significantly in TRT (-78%), but not HIIRT (-30%). Circulating concentration of testosterone was also analysed by gender: no significant differences were observed in males (TRT $+6\%$, HIIRT $+7\%$), whilst females experienced a significant improvement from basal condition without differences between training groups (TRT $+64\%$, HIIRT $+24\%$) (Fig. 4).

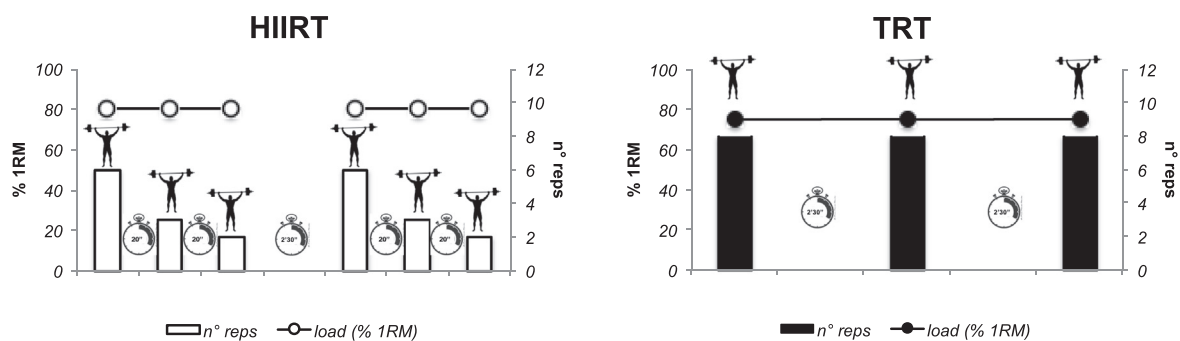


Fig. 3. Training protocols. HIIRT protocol consisted of 2 series at 80% 1RM in which subjects were instructed to perform repetitions to exhaustion three different times in each series, with 20" rest between the 1st and 2nd efforts and the 2nd and 3rd efforts. Subjects were allowed to rest 2'30" before starting the second series. TRT protocol consisted of 3 series of 8 repetitions at 75% 1RM, with 2'30" rest between sets. Both resistance training protocols utilized the same methods for progression.

Table 2
Strength test and body composition results. Values are presented as mean \pm SD.

	TRT (N = 9)			HIIRT (N = 14)		
	Pre	Post	%	Pre	Post	%
Strength test 1RM						
Leg extension (kg) [#]	50.8 \pm 13.8	67.7 \pm 15.8*	+ 36%	54.7 \pm 14.2	68.5 \pm 19.1*	+ 27%
Chest Press (kg)	38.7 \pm 15.4	49.9 \pm 14.9*	+ 33%	46.4 \pm 14.5	59.1 \pm 12.1*	+ 32%
Lat Pulldown (kg)	51.8 \pm 13.1	58.2 \pm 15.1*	+ 12%	54.6 \pm 11.3	66.9 \pm 11.0*	+ 24%
Arm Curl (kg)	16.7 \pm 5.3	25.7 \pm 4.7*	+ 51%	22.6 \pm 4.5	30.4 \pm 4.4*	+ 40%
Body composition						
Body Weight (kg)	70.4 \pm 13.8	70.2 \pm 13.6	- 0.3%	69.5 \pm 11.1	69.3 \pm 10.9	- 0.3%
Fat Free Mass (kg)	37.6 \pm 7.2	35.8 \pm 6.7*	- 5%	36.5 \pm 5.1	35.7 \pm 5.4	- 2%
Fat Mass (kg)	37.7 \pm 12.2	38.6 \pm 13.4*	+ 5%	33.0 \pm 7.7	33.8 \pm 6.7	+ 3%

* Significantly different from baseline.

Significantly different between groups, $p < 0.05$.

Interestingly, both groups improved their lipid profile (Table 4), but only HIIRT elicited a significant ($p < 0.05$) improvement of total cholesterol (HIIRT - 9%), cholesterol LDL (HIIRT - 11%) and triglycerides (HIIRT - 18%).

4. Discussion

We have previously demonstrated that, in an acute setting, high intensity interval resistance training (HIIRT) is able to increase EPOC in the 22 h following the training session in young healthy adults (Paoli et al., 2012). These promising data were confirmed subsequently in a group of overweight middle-aged subjects performing HIIRT alternating with a HIT-like protocol (8' of endurance on cycloergometer performed for 3' at 50% and 1' at 75% of HRR) in a 12-week study (Paoli et al., 2013b). We demonstrated that the high intensity circuit exerted a greater positive effect on blood lipids compared to a constant endurance protocol or lighter circuit training. Moreover Romero-Arenas and colleagues (Romero-Arenas et al., 2013) showed that a high-resistance circuit training improves cardiovascular system variables and decreases fat mass. Thus, in the present study we sought to investigate the effects of an HIIRT in an elderly population. Our data showed that HIIRT protocol was at least as beneficial as a traditional resistance protocol for strength improvement and body composition, whilst HIIRT produced a greater increase of testosterone in females, a less pronounced decrease of GH and superior modulation of blood lipids.

The lack of significant differences between groups for body composition is somewhat surprising considering our previous results. Nevertheless, an examination of our data indicates that TRT lost muscle but also increased fat mass whilst changes were not significant in the HIIRT group. The population in the present study was somewhat

different from our previous subjects (e.g. lower body mass). Regarding fat mass, it seems that the intensity performed by our older adults during HIIRT may not have been great enough to elicit significant fat loss (contrary to our previous studies (Paoli et al., 2012; Paoli et al., 2013b)), but was intense enough to prevent fat gain compared to TRT group.

Regarding muscle, it is well known that muscle mass is difficult to maintain during the aging process (Csapo and Alegre, 2016). The total training volume was similar between the two groups: 1760 kg for TRT and 1800 kg for HIIRT. This fact could explain the lack of significant differences between HIIRT and TRT in terms of muscle mass, even though some authors suggest a role of high intensity RT on muscle hypertrophy (Seynnes et al., 2007). Anyway it should be taken into account that it could be a relative reduced response of older individuals to high intensity resistance training. Indeed, our data are in accordance with Kumar and colleagues (Kumar et al., 2009), supporting the idea that protein synthesis is blunted at higher training intensity (> 60% 1 RM) in older adults, although recent research has suggested otherwise (Bechshoft et al., 2017). Although the classical anabolic pathway (IGF1/AKT/mTOR) seems to be unaffected, other protein synthesis/degradation machineries could be key factors involved in the process of muscle loss (Sandri et al., 2013). Our recent data suggest that drastic activation of the IGF1-Akt pathway may be counterproductive in the elderly (Sandri et al., 2013). The present research showed a decrease of basal IGF-1 in both groups without a difference between groups, a significant decrease in both groups of IGFBP3 and a significant increase of IGFBP1 only in HIIRT group. In older adults, low levels of IGF-1 and GH are correlated to a high risk of metabolic syndrome (Ren and Anversa, 2015), but in our subjects the lowering of IGF-1 was counterbalanced by a significant decrease of IGF-1 BP3. Higher levels of

Table 3

Hormonal results. Values are presented as mean \pm SD. GH = Growth Hormone, IGF-1 = Insulin Growth Factor 1, IGF-BP1 = Insulin Growth Factor Blinding Protein 1, IGF-BP3 = Insulin Growth Factor Blinding Protein 3.

	TRT		HIIRT	
	Pre	Post	Pre	Post
Cortisol (nmol/L)	395.44 \pm 97.51	425.11 \pm 100.96	390.21 \pm 100.00	443.36 \pm 85.13*
GH (ng/ml)	2.39 \pm 2.57	0.53 \pm 0.59*	3.05 \pm 4.74	2.13 \pm 4.41
Insulin (uU/ml)	7.32 \pm 3.81	6.51 \pm 3.06	8.50 \pm 5.95	6.01 \pm 2.79*
IGF-1 (ng/ml)	160.00 \pm 40.23	135.26 \pm 36.34*	155.80 \pm 25.93	132.08 \pm 20.38*
IGF-BP1 (ng/ml)	3.93 \pm 2.87	4.17 \pm 2.49	2.91 \pm 3.32	4.33 \pm 2.50*
IGF-BP3 (ng/ml)	4269 \pm 1000.69	3634.67 \pm 1236.98*	4553.93 \pm 685.73	4127.36 \pm 876.45*
Free Testosterone (ng/ml)				
Male	25.60 \pm 8.08	28.20 \pm 7.82	27.25 \pm 7.87	30.38 \pm 8.72
Female	3.40 \pm 0.73	5.18 \pm 1.52*	4.78 \pm 0.92	6.05 \pm 0.99*
Total Testosterone (ng/ml)				
Male	12.57 \pm 2.38	13.34 \pm 3.57	14.52 \pm 4.93	15.55 \pm 6.19
Female	0.32 \pm 0.23	0.52 \pm 0.31*	0.68 \pm 0.46	0.84 \pm 0.41*

* $p < 0.05$ pre vs. post (main time effect).

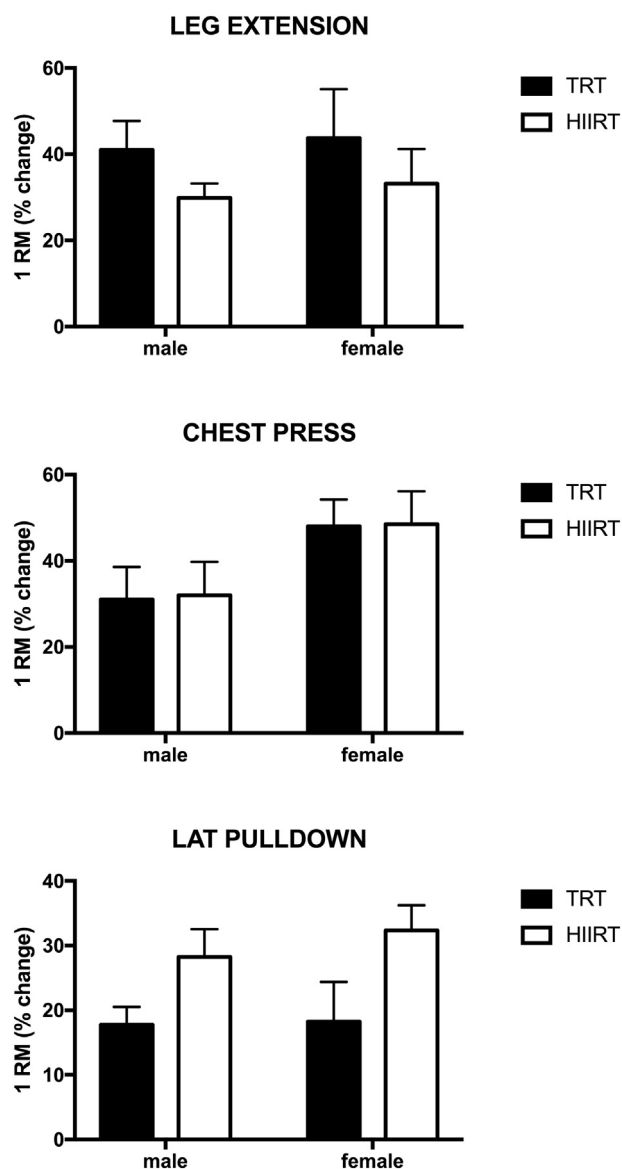


Fig. 4. Changes in estimated 1 RM after 6 months of training, divided by male and female. Changes are showed as percent change from baseline.

Table 4

Blood biochemistry results. Values are presented as mean \pm SD. APOA1 = Apolipoprotein A-1, APOB = Apolipoprotein B, CHOL = total cholesterol, HDL = high-density lipoprotein cholesterol, LDL = low-density lipoprotein cholesterol, TG = triglycerids, ALT = alanine aminotransferase, AST = aspartate transaminase.*

	TRT		HIIRT	
	Pre	Post	Pre	Post
APOA1 (g/L)	1.66 \pm 0.32	1.63 \pm 0.34	1.73 \pm 0.22	1.65 \pm 0.22*
APOAB (g/L)	1.05 \pm 0.23	0.94 \pm 0.19*	1.00 \pm 0.17	0.88 \pm 0.16*
CHOL (mmol/L)	5.73 \pm 1.19	5.30 \pm 1.02	5.56 \pm 0.65	5.07 \pm 0.78*
HDL (mmol/L)	1.56 \pm 0.53	1.54 \pm 1.02	1.66 \pm 0.37	1.63 \pm 0.40
LDL (mmol/L)	3.87 \pm 1.02	3.47 \pm 0.82	3.65 \pm 0.66	3.24 \pm 0.66*
TG (mmol/L)	1.51 \pm 0.87	1.42 \pm 0.55	1.20 \pm 0.66	0.99 \pm 0.44
Glucose (mmol/L)	5.61 \pm 1.09	5.89 \pm 2.66	5.62 \pm 0.81	5.07 \pm 0.50
ALT (U/L)	22.33 \pm 10.20	22.33 \pm 5.83	30.57 \pm 21.54	25.07 \pm 8.64
AST (U/L)	27.22 \pm 5.93	24.00 \pm 3.28	31.79 \pm 13.59	23.29 \pm 5.34*
Gamma GT (U/L)	19.22 \pm 11.07	20.33 \pm 12.67	26.93 \pm 9.61	26.79 \pm 10.40
Creatine kinase (umol/L)	119.11 \pm 62.03	113.44 \pm 39.83	110.08 \pm 42.73	127.85 \pm 57.63
Creatinine (umol/L)	70.78 \pm 8.29	74.56 \pm 8.80	75.71 \pm 9.19	81.29 \pm 6.27*
Uric acid (mg/L)	0.29 \pm 0.05	0.31 \pm 0.06	0.31 \pm 0.08	0.33 \pm 0.08*
Urea (mg/L)	6.09 \pm 1.68	6.13 \pm 2.07	5.92 \pm 0.82	6.29 \pm 1.09

* $p < 0.05$ pre vs post (main time effect).

IGFBP3, which reduce bioavailability of IGF1, have been correlated with higher cardiovascular risks (Colangelo et al., 2004). However, HIIRT produced a significant increase of IGFBP1. Reductions in IGFBP1 have been suggested as a marker of insulin resistance, and have been correlated with a greater carotid media thickness in type 2 diabetes (Leinonen et al., 2002). Integrating the body composition and hormonal data, the results of our research seem to suggest that the effects of the IGF1 reduction was blunted by a decrease of IGFBP3 with a maintenance of fat free mass (superior in the HIIRT group) and fat mass.

Both groups increased strength after 6 months of training without any significant differences between treatments and between gender.

A major result of the present investigation confirmed our previous findings, which indicated beneficial effects of HIIRT on blood lipids parameters (Paoli et al., 2013b). HIIRT subjects experienced significant improvements in total cholesterol (-9%) and LDL (-11%) compared to TRT (Table 3). Even though it has been demonstrated that total cholesterol, HDL and triglyceride levels can be improved through regular resistance training in middle-aged subjects (Hurley and Roth, 2000), the precise dosage of RT intensity necessary to produce these changes is still unclear (Paoli, 2012a; Paoli and Bianco, 2012). Exercise intensity might be a key factor in blood lipids' exercise response (Paoli et al., 2014). The total energy expenditure seems to have a direct correlation with the changes in lipids and lipoproteins, i.e. changes in blood lipid and lipoprotein concentration depends on total amount of calories expended (Durstine et al., 2002). We demonstrated higher excess post exercise oxygen consumption (EPOC) after a HIIRT session compared to traditional resistance training (Paoli et al., 2012). In general, RT seems to positively affect the blood lipids parameters HDL, LDL and TG (Bemben and Bemben, 2000; Dalleck et al., 2009; James et al., 2016; Kelley and Kelley, 2009; Pitsavos et al., 2009; Ribeiro et al., 2016), even though the exact underlying mechanisms are not well understood (Gordon et al., 2014). A recent 1-year study showed significant improvements of cholesterol values, specifically LDL cholesterol, total cholesterol and non-HDL cholesterol, as a result of resistance training (James et al., 2016). Stimulation of PPAR- γ and PGCI- α pathways has been suggested as possible mechanisms for the improvement in lipid profile (Ruschke et al., 2010), as well as reduced LDL formation from VLDL precursors or an improved hepatic removal activity. In accordance with James et al.'s data (James et al., 2016), we did not find a significant decrease of TG, suggesting an increased hepatic uptake and clearance. HDL showed no modification, but its response to RT appears to be quite variable considering conflicting results in literature with no change (James et al., 2016; Kim and Kim, 2013), increases (Fahlman et al., 2002; Paoli et al., 2013b) or decreases (Arnanson et al., 2014) reported. In the present study, no significant

changes of HDL were observed, which could be explained by the absence of aerobic training, such as was performed during our previous study (Paoli et al., 2013b). The HIIRT group showed a significant decrease of APOA1, whilst both interventions produced a decrease of APOAB. The APOB/APOA1 ratio decreased significantly by 8% in TRT and 7% in HIIRT, without any statistical significant difference between the two groups, suggesting a general positive effects of resistance training on this parameter. No differences in basal blood glucose were observed after the training period, but this result is not surprising considering that our subjects were not diabetics. However, insulin decreased significantly in HIIRT group after 6 months of training, which may suggest an improvement in insulin sensitivity (IS) related to RT intensity. Indeed, other researchers found no effect of RT alone on IS (Bateman et al., 2011; James et al., 2016), whilst improvement of IS has been reported after combined training (i.e. aerobic plus resistance training) (Hurley et al., 2011). The impact of RT intensity remains an open question: it is possible, as suggested in a previous discussion (Paoli and Bianco, 2012), that low intensity RT (Bateman et al., 2011) may not elicit an adequate stimulus for some adaptations. Instead, a higher intensity RT may lead to the related physiological responses such as an increase of myokines, cytokines (Pedersen, 2011) and other proinflammatory molecules, or to the downstream molecule AMPK (Jensen and O'Rahilly, 2017). RT could also stimulate AMPK and proteins regulating glucose uptake (p-AS160) (Ahtiainen et al., 2015). These mechanisms could explain the improvement of IS observed in HIIRT group.

Whilst testosterone concentration (both free and total) did not differ when all participants were analysed together, HIIRT females showed a significant increase of both free testosterone and total testosterone (respectively +26% and +23%) compared to TRT females (see Table 4). An appropriate level of testosterone in postmenopausal women has protective effects against depressed mood, decreased muscle mass, reduced bone density, and decreased sense of well-being (Yasui et al., 2012). No correlations were found between basal free testosterone level or testosterone/cortisol ratio and strength gains, unlike other data from Hakkinen (Hakkinen et al., 2002) who showed that the individual basal testosterone/cortisol ratios correlated with 1RM increases in response to RT. Our data failed to find such correlations in all tested exercises. Our study has some limitations: the first is the lack of biochemical measurements at 4th month (before the split of the groups); however, considering that our aim was to investigate the effects of HIIRT vs TRT and not the simple effect of a traditional training period, blood parameters were evaluated at the end of the study. The second is the use of BIA which, although a widely used and reliable methods for this kind of investigation, is not the gold standard for body composition analysis. Thus, long term physiological and anthropometric changes during HIIRT protocol warrant further investigation.

5. Conclusions

Our data suggest that high intensity interval resistance training (HIIRT) can be safely performed by older individuals. No differences were detected in strength performance, whilst HIIRT produced slightly better body composition changes these results should be interpreted with care considering the methodology used ~~by maintaining fat free mass and preventing fat mass gain~~. Moreover, HIIRT significantly reduced basal insulin levels, suggesting an effect on insulin sensitivity. The reduction of total cholesterol and LDL, together with the significant increase of IGFBP1, observed in the HIIRT groups suggest a direct relationship between the intensity of RT and improvement of blood lipids parameters and associated cardiovascular risks. HIIRT could be implemented as an efficient training method to improve blood lipids and other cardiovascular risk factors.

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