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1 **MICT or HIIT ± RT programs for altering body composition in postmenopausal women**

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31

32 **ABSTRACT**

33 **Purpose:** To compare body composition changes induced by moderate-intensity continuous  
34 training (MICT), high-intensity interval training (HIIT), or HIIT + resistance training (RT)  
35 programs (3 days/week, 12 weeks) in postmenopausal women with overweight/obesity, and to  
36 determine whether fat mass reduction is related to greater fat oxidation (FatOx).

37 **Methods:** Participants (n=27) were randomized in three groups: MICT (40min at 55-60% of  
38 peak power output, PPO), HIIT (60 x 8s at 80-90% of peak heart rate, 12s active recovery),  
39 and HIIT + RT (HIIT + 8 whole-body exercises: 1 set of 8-12 repetitions). DXA was used to  
40 measure whole-body and abdominal/visceral fat mass (FM) and fat-free mass (FFM). FatOx  
41 was determined at rest, during a moderate-intensity exercise (40min at 50% of PPO), and for  
42 20 minutes post-exercise, before and after training.

43 **Results:** Overall, energy intake and physical activity levels did not vary from the beginning to  
44 the end of the intervention. Body weight and total FM decreased in all groups over time, but  
45 significant abdominal/visceral FM losses were observed only in HIIT and HIIT + RT groups.  
46 When expressed in percentage, total FM, FFM, and muscle mass were significantly modified  
47 only by HIIT + RT training. FatOx did not change at rest, but increased similarly in the three  
48 groups during and after exercise. Therefore, the HIIT-induced greater FM loss was not related  
49 to higher FatOx during or after exercise.

50 **Conclusions:** MICT or HIIT  $\pm$  RT could be proposed to non-dieting postmenopausal women  
51 with overweight/obesity to decrease weight and whole-body FM. The HIIT programs were  
52 more effective than MICT in reducing abdominal/visceral FM. RT addition did not potentiate  
53 this effect, but increased the percentage of muscle mass.

54

55 **Key words:** Menopause, (intra)-abdominal fat mass, high intensity interval training, resistance  
56 training, fat oxidation rate.

57

58

## 59 INTRODUCTION

60 In women, the incidence of obesity, type 2 diabetes and cardiovascular diseases (CVD)  
61 significantly increases after menopause and is related to an increase of fat mass (FM) (1–3),  
62 loss of fat-free mass (FFM) (especially muscle mass) (3), and body fat distribution alterations  
63 (1, 4). The increase of subcutaneous and particularly intra-abdominal FM (*i.e.*, visceral FM)  
64 after menopause partly explains the higher CVD risk in postmenopausal women (5).

65 Menopause is associated with a decrease of the resting metabolic rate (RMR) (6) and fat  
66 oxidation (FatOx) during physical activity (7, 8) and a lower total energy expenditure (EE) (8,  
67 9). Although literature data show that the diet and physical activity combination promotes  
68 longer-term weight and/or FM loss, exercise alone also might have positive effects, particularly  
69 on subcutaneous and intra-abdominal FM (10), if the training program is well supervised and  
70 if the EE leads to a negative energy balance (11).

71 The American College of Sports Medicine (ACSM) has recommended moderate intensity  
72 continuous training (MICT) in patients with obesity for losing weight and/or FM (11). This  
73 strategy is efficient in pre- and post-menopausal women with overweight or obesity (12, 13).  
74 Currently, high-intensity interval training (HIIT), which includes repeated bouts of high  
75 intensity effort followed by varied recovery times (14), is considered a time-efficient and safe  
76 strategy to reduce total FM and particularly subcutaneous and intra-abdominal FM in people  
77 with overweight/obesity (15). Our group demonstrated that in postmenopausal non-dieting  
78 women with type 2 diabetes, HIIT is more effective for reducing central obesity than MICT,  
79 and can be proposed as an alternative exercise program in this population (16). Resistance  
80 training (RT) does not enhance weight loss, but may increase FFM and decrease FM, and is  
81 associated with health risk reduction (11). Although several previous publications have focused  
82 on RT or MICT + RT effects on body composition (17, 18), only few randomized trials  
83 compared the impact of a combined HIIT + RT program in overweight/obese adults (19, 20),

84 and no study has been performed on postmenopausal women. The effects of HIIT  $\pm$  RT  
85 programs on fat mass losses may be partly due to the increase of RMR, total EE and FatOx  
86 (21). No study has thoroughly evaluated the impact of HIIT or HIIT + RT on these parameters  
87 in postmenopausal women, but limited post-training muscle mass gain in the female population  
88 could alter these adaptations (22).

89 Therefore, the aim of this study was to compare the effects of 12-week MICT, HIIT and HIIT  
90 + RT programs on body composition and FatOx in postmenopausal women with  
91 overweight/obesity. We hypothesized that compared with the traditional MICT, HIIT programs  
92 could be more efficient in reducing whole-body and abdominal/visceral FM and to favor  
93 FatOx, and that HIIT + RT, by also improving FFM and RMR, could offer the best benefits.

94

## 95 **METHODS**

96

97 The study was approved by the relevant ethics committee (Comité de Protection des Personnes  
98 Sud Est VI, CPPAU1303) and was registered on ClinicalTrials.gov via the Protocol  
99 Registration System (ClinicalTrials.Gov: NCT 03357016). After receiving detailed  
100 information on the study objectives and protocol, all participants signed a written informed  
101 consent.

102

### 103 **Participants**

104 Thirty-five women (mean age  $62.4 \pm 6.7$  yr) were recruited according to the following inclusion  
105 criteria: postmenopausal women, body mass index (BMI)  $>25 \text{ kg/m}^2$  and  $\leq 40 \text{ kg/m}^2$ , and stable  
106 eating habits and physical activity for at least 3 months. Non-inclusion criteria were: medical  
107 contraindications to intense physical activity, painful joints, and taking hormone replacement  
108 therapy. Finally, 30 postmenopausal women with overweight/obesity were selected for the

109 three 12-week interventional programs (Fig. 1). None of the participants had history of chronic  
110 arterial or respiratory disease, CVD, or endocrine disorders. All participants reported low levels  
111 of physical activity, based on the Global Physical Activity Questionnaire (GPAQ) results (23).  
112 Upon recruitment, participants were randomly assigned to an exercise modality [HIIT ( $n = 10$ ),  
113 MICT ( $n = 10$ ), HIIT + RT  $n = 10$ ]. A familiarization period of at least 10 days allowed  
114 participants to get accustomed with the exercise equipment before training.

115

## 116 **EXPERIMENTAL DESIGN**

117

118 **Anthropometric and body composition measurements.** Body weight was measured to the  
119 nearest 0.1 kg on a Seca 709 scale (Balance Seca 709, France) in fasting conditions, with the  
120 subjects wearing only underwear. Height was measured to the nearest 0.5 cm with a wall-  
121 mounted stadiometer. Body mass index (BMI) was calculated as body weight (kg) divided by  
122 the square of height ( $m^2$ ). Waist circumference (cm) was measured midway between the last  
123 rib and upper iliac crest, and hip circumference at the level of the femoral trochanters. Both  
124 measures were taken in standing position with a measuring tape. Sagittal abdominal diameter  
125 (supine abdominal height) was measured with a Holtain–Kahn abdominal caliper (Holtain  
126 Limited, Crymych, Pembrokeshire, UK) to the nearest mm in the sagittal plane at the level of the iliac  
127 crests (L4–L5) during normal expiration, with the subject lying supine on a firm bench with  
128 knees bent. Abdominal skinfold thickness was measured at four different sites (at 15 cm and 7  
129 cm to the right and left of the navel) with a Harpenden Skinfold Caliper (Mediflex Corp., Long  
130 Island, NY, USA), and the mean subcutaneous abdominal skinfold thickness was then  
131 calculated (16). The same experienced investigator took all anthropometric measurements at  
132 baseline and after 12 weeks of training.

133

134 **Adipose and fat-free mass tissue localization.** Total body and regional FM as well as FFM  
135 (expressed as kg and % of body mass) were measured with a dual-energy X-ray absorptiometry  
136 (DXA) scanner (QDR-4500A, Hologic, Inc., Marlborough, MA, USA). Two regions of interest  
137 were manually isolated and analyzed by an experienced technician: the area from L1–L2 to the  
138 pubic rami to determine the total abdominal FM (kg), and the area from the iliac crest to the  
139 feet to calculate the lower-body FM (kg). The same operator performed all analyses. Total  
140 visceral FM (kg) was estimated from the total abdominal FM on DXA, mean subcutaneous  
141 abdominal skinfold thickness and abdominal height, as previously described (16).

142

143 **Preliminary visit-maximal exercise testing.**  $VO_{2max}$  was measured during a graded  
144 exhaustive exercise test on a cycle ergometer (Ergoline, Bitz, Germany). After a 3min warm-  
145 up at 30 W, power output was increased by  $10\text{ W}\cdot\text{min}^{-1}$  until the participant's exhaustion (the  
146 test lasted between 10 and 15 minutes after warm-up). Participants were strongly encouraged  
147 by the experimenters throughout the test to perform a maximal effort. Respiratory gases ( $VO_2$   
148 and  $VCO_2$ ) were measured breath-by-breath through a mask connected to  $O_2$  and  $CO_2$  analyzers  
149 (Oxycon pro-Delta, Jaeger, Hoechberg, Germany).  $VO_{2max}$  was determined as the highest  
150 oxygen uptake during a 15s period. Ventilatory parameters were averaged every 30s. Heart  
151 activity was monitored by ECG throughout the test, and heart rate (HR) recorded continuously.  
152 The achievement of  $VO_{2max}$  criteria were: 1) oxygen uptake reaching a plateau with increasing  
153 work rate; 2) RER values higher than 1.1; and 3) peak heart rate (PHR) within 10% of the age-  
154 predicted maximal values (24). The peak power output (PPO), expressed in watts or  $\text{watts}\cdot\text{kg}^{-1}$ ,  
155 was considered the highest power measured at  $VO_{2max}$ .

156

157 **Training programs.**



158 We made the choice to have similar energy expenditure (EE) between MICT and HIIT sessions  
159 and to have the same session duration between MICT and HIIT + RT, because lack of time is  
160 a barrier to exercise for people with overweight/obesity. Thus, before the beginning of the  
161 training programs, the EE induced by a HIIT session (20 min duration) was measured in four  
162 subjects using a Metamax 3B apparatus (Matsport, France), and the time needed to spend the  
163 same energy was calculated during the MICT session. The mean EE spent for each HIIT or  
164 MICT session was  $180 \pm 22$  kcal and the time required for a MICT session was established to  
165 40 minutes. Therefore, each HIIT + RT session lasted 40 minutes (20 min of HIIT and 20 min  
166 of RT).

167 Participants performed three exercise sessions per week for 12 weeks (total = 36 sessions).  
168 Sessions were generally in the morning on Monday, Wednesday and Friday, to allow a  
169 sufficient recovery period, and were supervised by an experienced physical activity instructor.  
170 Each session included also 5 min warm-up and 2 min cool-down periods, in addition to the  
171 formal training.

172

173 **Moderate-intensity continuous training (MICT).** The MICT session consisted of 40min at  
174 55-60% of the participant's PPO performed continuously on a C-Max Club Fitness bike.  
175 During the first 6 weeks, the intensity was set at 55% of the PPO and was increased to 60% for  
176 the last 6 weeks to take into account the participants' aerobic fitness improvement. Each  
177 participant's resistance, pedal cadence (50-70 rpm), and power (watts) were controlled to reach  
178 the expected intensity.

179

180 **High-intensity interval training (HIIT).** The HIIT training program was based on the  
181 protocol by Maillard et al. (2016) (16), an attractive and feasible cycling program for  
182 postmenopausal women with overweight/obesity. The HIIT protocol consisted of repeated

183 cycles of sprinting/speeding for 8s followed by slow pedaling (20–30 rpm) for 12s on a  
184 WattBike pro Concept2 (with a freewheel and a double air and magnetic braking system).  
185 Resistance was very low to facilitate acceleration and limit bicycle-wheel inertia. Resistance  
186 was controlled to reach ~ 80% of each participant's PHR during the 20min session. All  
187 participants could complete the full 20min exercise program at this intensity after two or three  
188 sessions. HR was continuously monitored (A300, Polar, Finland) to control the intensity.  
189 Overall, the mean intensity during a HIIT session corresponded to  $85 \pm 4\%$  of PHR.

190

191 **High-intensity interval training and resistance training (HIIT + RT).** HIIT was always  
192 performed before RT to normalize the concurrent training effects (25). The HIIT session was  
193 the same as for the HIIT alone group. The upper and lower body muscular strength was  
194 measured using the one-repetition maximum (1 RM) method with bench press and leg press  
195 exercises on Universal™ weight machines, as previously described (26). Briefly, a warm-up  
196 of 5–10 repetitions at 40–60% of the perceived maximum was performed, followed by 3–5  
197 repetitions at 60–80% of the perceived maximum. Three to four subsequent attempts were then  
198 made to determine the 1 RM for each exercise. Rest periods (3-5min) were introduced between  
199 lifts to ensure optimal recovery.

200 The RT program included two different training circuits with ten exercises/each and was based  
201 on the program by Marx et al. (27). Circuit 1 included leg press, bench press, knee extension,  
202 cable row, dumbbell calf raise, elbow flexion, abdominal muscle, triceps exercises with upper  
203 pulley, plank and bum exercises. Circuit 2 included knees extension, pullover, leg press, side  
204 raise with dumbbells, dumbbell calf raise, triceps exercises with upper pulley, hip thrust, chin  
205 rowing, and plank to upright row. Participants performed a single-set circuit, with a load of 8–  
206 12 repetitions at around 80% of 1RM, with 1- to 1.5min rest period between exercises. The  
207 workouts were individually supervised by the same certified personal trainer. When

208 participants achieved more than 12RM, the load was adjusted to remain in the planned intensity  
209 zone. Participant alternated between circuits every 3 weeks to minimize boredom and to create  
210 some variation in the exercise choice.

211

212 **Resting metabolic rate (RMR) and substrate oxidation.** Subjects arrived at the laboratory  
213 at 7.30 am after overnight fast (12h). Participants were asked to eat a similar dinner for the pre-  
214 and post-training session the evening before, and to avoid any kind of strenuous exercise the  
215 day before. The experiment was conducted in a ventilated room at a temperature of 19–20°C.  
216 RMR and substrate oxidation were determined from respiratory gases using a Metamax 3B  
217 apparatus (Matsport, France). Carbohydrate oxidation and FatOx were measured at rest, during  
218 moderate-intensity prolonged exercise, and during the recovery period. Exercise consisted in  
219 40min of cycling at 55% of their PPO determined before and after training on a cycle ergometer  
220 (Ergoline, Bitz, Germany). Cadence was maintained between 60 and 70 rpm. HR was  
221 continuously monitored (A300, Polar, Finland). Resting gas exchange data were recorded for  
222 10 minutes, with the subject sitting on the bicycle. The last 2min of gas exchange data from  
223 each stage were averaged to calculate  $VO_2$  and  $VCO_2$  that were then used to determine the  
224 RER ( $RER = VCO_2/VO_2$ ). Recording was continued during the recovery period for 20 minutes.  
225 RMR assessment was considered valid in the presence of a minimum of 10min of steady state  
226 with less than 10% of fluctuations in oxygen consumption ( $VO_2$ ). RMR ( $kcal.day^{-1}$ ) was  
227 calculated using the Weir equation (28), and substrate oxidation ( $g.min^{-1}$ ) was calculated using  
228 the Frayn's equations (29), as follows:

229 -  $RMR = [(3.941 \times VO_2) + (1.1106 \times VCO_2)] \times 1440$

230 - Carbohydrate (CHO) oxidation =  $[(4.55 \times VCO_2) - (3.21 \times VO_2)]$

231 - FatOx =  $[(1.67 \times VO_2) - (1.67 \times VO_2)]$

232

233 **Physical activity and dietary assessments.** Participants were asked to maintain their normal  
234 levels of physical activity during the 12-week study period. Their usual weekly level of  
235 physical activity was determined at baseline and after 12 weeks using the French version of the  
236 GPAQ (23). They were also asked to maintain their normal eating habits for the study period.  
237 At baseline and at week 12 of training, each participant filled in a 7-day food-intake diary that  
238 was evaluated by a dietician using a nutrition analysis software program (Nutrilog®, Marans,  
239 France).

240

241 **Biochemical Assays.** Blood samples were taken the week before starting the training (pre-  
242 intervention) and then 2–4 days after the last exercise session (post-intervention), depending  
243 on the participants' availability and to avoid any potential effect of the last exercise session on  
244 the results. After overnight fasting, a cannula was inserted in the antecubital vein, and whole  
245 blood was collected in EDTA- and fluoride-containing vacutainers tubes. The plasma  
246 concentration of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and  
247 triglycerides (TG) was immediately measured, using a Synchron Clinical System UniCel Dx-C  
248 analyzer (Beckman Coulter, Brea, CA, USA) and a cholesterol oxidase method for TC (CHOL  
249 reagent), a direct homogeneous method for HDL-C (HDL-D reagent), and a lipase/glycerol  
250 kinase method for TG (GPO reagent). The low-density lipoprotein cholesterol (LDL-C)  
251 fraction was indirectly quantified using the equation described by Friedewald et al. (30).  
252 Plasma glucose concentration was immediately determined using the hexokinase method  
253 (UniCel Dx-C analyzer, Synchron). Plasma insulin concentration was measured by enzyme-  
254 linked immunosorbent assay from Sigma-Aldrich Insulin Elisa kit (Paris, France). HbA1c  
255 values were evaluated with a high-performance liquid chromatography (HPLC) Variant II  
256 analyzer equipped with the new 270-2101 NU Kit (Bio-Rad Laboratories, Hercules, CA, USA).

257 The HOMA-IR index was calculated using the formula:  $\text{HOMA-IR} = [\text{Fasting glucose}$   
258  $(\text{mmol.L}^{-1}) \times \text{Fasting insulin } (\mu\text{U.mL}^{-1})] / 22.5$ .

259

260 **Statistical analyses.** Before the study start, the sample size required for a statistical power of  
261 80% was calculated based on previous results on FM loss after HIIT training in women (31).  
262 Based on a two-sided type I error of 5%, a minimum difference of  $1.5 \pm 0.88$  kg, as described  
263 by Tremblay et al. (32), for FM loss could be detected with seven women per group. Our sample  
264 was increased to ten women per group at the beginning of the intervention to take into account  
265 participants lost to follow-up.

266 All statistical analyses were carried out with the STATISTICA version 12.00 software (StatSoft  
267 Inc., Tulsa, OK, USA). Data are presented as the mean  $\pm$  standard deviation (SD). The data  
268 normal distribution was tested using the Kolmogorov–Smirnov test, and the homogeneity of  
269 variance was tested with the F-test. Data were log-transformed, when appropriate, prior to  
270 statistical analyses. Two-way analysis of variance (ANOVA) with repeated measures was used  
271 to determine group and time effects, and group  $\times$  time interactions. When a significant effect  
272 was found, post-hoc multiple comparisons were performed using the Newman-Keuls test. The  
273 effect size was reported when significant main or interaction effects were detected. The effect  
274 size was assessed using the partial eta-squared ( $\eta^2$ ) and ranked as follows:  $\sim 0.01$  = small effect,  
275  $\sim 0.06$  = moderate effect,  $\geq 0.14$  = large effect (33). Baseline values and changes between  
276 baseline and the study end [delta change:  $(12 \text{ weeks} - \text{baseline} / \text{baseline}) \times 100$ ] were also  
277 compared among groups, using one-way ANOVA. Differences with a P-value  $\leq 0.05$  were  
278 considered statistically significant.

279

## 280 **RESULTS**

281

282 **Participants' Characteristics.** Of the 30 postmenopausal females randomized in the three  
283 training groups (n=10/group), 27 were retained for the analysis (n=3 left the study for different  
284 reasons listed in Fig. 1). At baseline, the mean age was not significantly different among groups  
285 (MICT:  $67.1 \pm 7.2$  y; HIIT:  $59.9 \pm 5.9$  y; HIIT + RT:  $61.1 \pm 5.4$  y) as well as total body weight  
286 (MICT:  $80.4 \pm 7.1$  kg; HIIT:  $81.6 \pm 12.7$  kg; HIIT + RT:  $75.6 \pm 8.9$  kg) and total FM (MICT:  
287  $30.6 \pm 5.3$  kg; HIIT:  $27.6 \pm 10.7$  kg; HIIT + RT:  $28.1 \pm 5.8$  kg) (Table 1). The participants'  
288 compliance with the training program was  $97\% \pm 1\%$ . No adverse event was reported during  
289 testing or training in any group.

290

291 **Habitual Energy Intake and Energy Expenditure.** Physical activity levels (GPAQ scores)  
292 were comparable between pre- and post-training in all groups. For all participants, the daily  
293 energy intake and the percentage of energy contribution from macronutrients did not  
294 significantly change during the intervention period. No significant dietary intake difference  
295 was observed in the three groups at baseline and after 3 months (mean values:  $1563 \text{ kcal} \pm 276$   
296 pre-intervention vs  $1557 \text{ kcal} \pm 255$  post-intervention).

297

298 **Aerobic Fitness.**  $\text{VO}_{2\text{max}}$  ( $\text{ml}\cdot\text{min}\cdot\text{kg}^{-1}$ ) and PPO (watts or  $\text{watts}\cdot\text{kg}^{-1}$ ) were not different in the  
299 three groups at baseline (Table 1). Overall, aerobic fitness ( $\text{VO}_{2\text{max}}$  and PPO) significantly  
300 increased after the 12-week intervention (time effect,  $p < 0.0001$ ,  $\eta^2 = 0.71$ ). A group effect was  
301 noted concerning  $\text{VO}_{2\text{max}}$  ( $\text{ml}\cdot\text{min}\cdot\text{kg}^{-1}$ ) and PPO (when expressed in watts, but not in  $\text{watts}\cdot\text{kg}^{-1}$ )  
302 with lower values in the MICT group than in the HIIT and HIIT + RT groups ( $p = 0.042$ ,  $\eta^2$   
303  $= 0.24$ ).

304

305 **Anthropometric Measurements and Whole Body Composition.** Overall, body weight (kg),  
306 total FM (kg) and waist and hip circumferences (cm) were significantly decreased after the 12-

307 week intervention (time effect,  $p=0.02$ ,  $\eta^2 = 0.21$ ;  $p=0.002$ ,  $\eta^2 = 0.34$ ;  $p=0.01$ ,  $\eta^2 = 0.44$ ;  $p =$   
308  $0.001$ ,  $\eta^2 = 0.37$ , respectively) (Table 1). When the absolute values were expressed in  
309 percentage (%), total FM decreased and FFM and muscle mass increased only in the HIIT +  
310 RT group ( $p = 0.02$ ,  $\eta^2 = 0.20$ ). The percentage of total FM loss (kg) was higher (but not  
311 significant,  $p=0.07$ ) in the HIIT and HIIT + RT groups than in the MICT group ( $-3.06 \% \pm 4.2$ ,  
312  $-4.43 \% \pm 3.1$  and  $-0.05 \% \pm 3.9$  respectively), but with a large size effect ( $\eta^2 = 0.19$ ) (Fig. 2).

313

314 **Abdominal and Visceral Fat Mass.** Baseline total abdominal (kg) and visceral FM (kg) were  
315 similar in the three groups. At the end of the training period, total abdominal FM (kg) was  
316 significantly reduced only in the HIIT and HIIT+RT groups (group  $\times$  time interaction;  $p$   
317  $<0.008$ ,  $\eta^2 = 0.48$ ) (Table 1). When expressed as delta change values, abdominal and visceral  
318 FM changes were reduced only in the HIIT and HIIT + RT groups and were significantly  
319 different from MICT (Fig. 2). No significant difference was noted after training between the  
320 HIIT and HIIT + RT groups.

321

322 **Resting Metabolic Rate, Substrate Oxidation and Energy Expenditure.** None of the  
323 training modes altered RMR ( $\text{kcal}\cdot\text{day}^{-1}$ ) and substrate oxidation at rest (Table 2). Overall, all  
324 training programs increased FatOx during moderate intensity exercise (expressed as percentage  
325 of EE or  $\text{g}\cdot\text{min}^{-1}$ ) and during the recovery period (time effect,  $p < 10^{-4}$ ,  $\eta^2 = 0.47$ ) (Fig. 3).  
326 Concomitantly, carbohydrate oxidation decreased. No group effect was noted. EE (kcal) during  
327 exercise and during recovery did not change between pre- and post-intervention in any group.

328

329 **Metabolic Profile.** The lipid profile and glycemic parameters at baseline and after the 12-week  
330 intervention are listed in Table 3. Overall, plasma TG levels decreased after the intervention  
331 (time effect,  $p=0.02$ ,  $\eta^2 = 0.22$ ), without any group effect or group  $\times$  time interaction. Whatever

332 the training mode, TC, HDL-C, and LDL-C levels did not change. Glycemia, insulinemia,  
333 HbA1c, and HOMA-IR were not modified by the intervention.

334

335

## 336 **DISCUSSION**

337

338 The aim of this study was to compare the body composition and FatOx changes induced  
339 by a 12-week MICT, HIIT or HIIT + RT intervention in postmenopausal women with  
340 overweight or obesity. All three modalities improved body composition (body weight, FM  
341 loss), but HIIT (alone and with RT) led to a greater percentage of FM loss. Moreover,  
342 abdominal and visceral FM (%) were only reduced in the HIIT and HIIT + RT groups, and  
343 were significantly different from MICT. Our results also indicate that HIIT-induced total or  
344 (intra)-abdominal FM losses were not related to higher FatOx during moderate intensity  
345 exercise or during the 20min post-exercise period.

346

347 Physical activity is recommended in the framework of weight management programs to prevent  
348 weight gain, to induce weight loss, and to avoid weight regain after weight loss. Indeed,  
349 exercise on its own may generate significant weight and FM loss (10) with beneficial effects  
350 on health (11). Furthermore, (intra)-abdominal FM reduction is of interest due to FM  
351 association with CVD risks (34). The current international guidelines generally suggest  
352 endurance training as the best strategy for weight loss and FM reduction in both sexes. In the  
353 last position stand by the American College of Sports Medicine (ACSM) (11), moderate  
354 intensity physical activity (between 150 and 250 min.week<sup>-1</sup>) is recommended for preventing  
355 weight gain, and more exercise for providing significant weight loss. Recent evidence suggests  
356 that HIIT can be a time-efficient strategy to decrease whole-body and (intra)-abdominal FM in  
357 sedentary individuals with overweight/obesity (15, 35). In their meta-analysis, Wewege et al.



358 evaluated the effect of HIIT and MICT on weight and FM changes in individuals with  
359 overweight and obesity (35). Their found that both HIIT and MICT programs improved FM  
360 and waist circumference, even in the absence of body weight changes. They also showed that  
361 HIIT and MICT were similarly efficient, but that HIIT training required ~40% less time  
362 commitment. The meta-analysis by Maillard et al. (2018) focused on HIIT effects on whole-  
363 body and (intra)-abdominal FM loss in individuals with normal weight and with  
364 overweight/obesity. The authors confirmed that HIIT is a time-efficient strategy to decrease  
365 not only whole-body FM, but also abdominal and visceral FM (15). On the other hand, results  
366 were less convincing in postmenopausal women. Indeed, only three studies have evaluated the  
367 effects of HIIT on body composition in this population (16, 36, 37), and only one showed a  
368 positive effect of HIIT on total and (intra)-abdominal FM loss (16). To our knowledge, no  
369 study is available on the effects of HIIT + RT on body composition in postmenopausal women.

370

371 Our results indicate that MICT, HIIT and HIIT + RT programs (3 sessions.week<sup>-1</sup>, 12 weeks)  
372 decrease body weight, waist and hip circumferences and whole-body FM in postmenopausal  
373 women with overweight/obesity. This confirms the conclusions of the two previously  
374 mentioned meta-analyses. However, when expressed as delta change values (post-pre/pre ×  
375 100), our study showed that in post-menopausal women, FM losses were significantly higher  
376 in the HIIT and HIIT + RT (-3.1 kg and -4.4 kg, respectively) than in the MICT group (-0.1  
377 kg). ~~Conversely, the meta-analysis by Wewege et al. found that HIIT and MICT were similarly~~  
378 ~~effective (35).~~ Compared with the three studies on postmenopausal women and HIIT-induced  
379 body composition changes, our results are similar to those of the ~~meta-analysis~~ study performed  
380 by Maillard et al. (16), but in contradiction with those reported by Mandrup et al. (36) and  
381 Steckling et al. (37) who did not detect any HIIT effect on total FM. These discrepancies could  
382 be explained by the different exercise modalities (14). Indeed, we used the same HIIT protocol

383 as Maillard et al. (16) (*i.e.*, 60 x 8s at 80-90% of PHR, 12s active recovery), whereas Mandrup  
384 et al. and Steckling et al. used three blocks of varying intervals with multiple periods of  
385 maximum performance for 1h (36), and 4x 4 min 90%HRmax + 3 min active recovery 70  
386 HRmax (37), respectively. Furthermore, in the study by Mandrup et al. (36), women did not  
387 have obesity, and it is well known that HIIT-induced FM loss is more effective in individuals  
388 with obesity (15). Finally, Mandrup et al. and Steckling et al. did not evaluate dietary intakes  
389 and/or physical activity levels during their interventions. A spontaneous increase of energy  
390 intake or a decrease in total energy expenditure could explain the absence of effect on FM in  
391 these works. In our study, the levels of physical activity and total energy intake remained  
392 unchanged, strengthening our conclusion that HIIT is an efficient strategy to lose body weight  
393 and FM in postmenopausal women with overweight/obesity.

394 At baseline the plasma values were within the normal ranges, and this may explain why training  
395 did not modify the lipid profile and glucose homeostasis. Although our participants did not  
396 have hypertriglyceridemia (defined as a TG concentration higher than 150 mg.dL<sup>-1</sup> or 1.7  
397 mmol.L<sup>-1</sup>) and higher risk of cardiovascular disease (38), we observed a decrease of TG levels  
398 over time, but without difference between groups.

399 Our results also demonstrate that only HIIT and HIIT + RT significantly decreased (intra)-  
400 abdominal FM (*i.e.*, subcutaneous FM from the abdomen and visceral FM). It is worth noting  
401 that despite exercising almost half the time compared with the MICT group (20min *vs.* 40min),  
402 women in the HIIT group lost 7.4% of total abdominal FM and 3.2% of visceral FM.  
403 Conversely, no change was observed in the MICT group, and the total abdominal FM loss in  
404 the HIIT + RT group was not higher than in the HIIT group, despite the longer exercise time  
405 (40min). These results confirm the meta-analysis by Maillard et al. (15) showing that HIIT  
406 significantly reduces abdominal ( $p = 0.007$ ) and visceral ( $p = 0.018$ ) FM, with no difference  
407 between men and women.

408

409 The mechanisms underlying HIIT-induced total and (intra)-abdominal FM loss are still not  
410 completely elucidated, but might partly be explained by significant higher lipolysis during  
411 exercise and greater post-exercise total and abdominal fat oxidation (15). These adaptations are  
412 probably facilitated by the higher excess post-exercise oxygen consumption observed after  
413 exercises performed above 75%  $VO_{2max}$  (39). Indeed, lipid oxidation decreases above 40–  
414 50%  $VO_{2max}$ , but higher intensities still induce significant lipolysis from  $\beta$ -adrenergic receptors  
415 stimulation. Thus, HIIT can increase plasma FFA levels during exercise and then promote  
416 greater fat oxidation during the recovery period. This adaptation could explain why people who  
417 are engaged in regular vigorous physical activities are less fat than those who never take part  
418 in such activities (32). After an acute session of HIIT, MICT or High-Intensity Resistance  
419 Training (HIRT) performed by recreationally active women, Wingfield et al. (40) demonstrated  
420 lower RER in the HIIT than the MICT and HIRT groups (30min and 60min of recovery),  
421 confirming the higher post-exercise fat oxidation in HIIT.

422 It is now recognized that higher amount of visceral/abdominal fat is lost in HIIT compared with  
423 MICT programs (15). As the content of  $\beta$ -adrenergic receptors is higher in intra-abdominal  
424 than in subcutaneous adipose tissue (41), the higher HIIT-induced sympathetic nervous system  
425 stimulation could explain the larger reliance on visceral FM. Moreover, visceral adipose tissue  
426 is characterized by smaller adipocytes, greater lipolytic activity, and lower responses to the  
427 antilipolytic effects of insulin compared with subcutaneous depots (42). Lastly, subcutaneous  
428 or (intra)-abdominal FM losses may also be facilitated by HIIT-induced PGC1- $\alpha$  transcription  
429 stimulation. Shirvany and Arabzadeh (43) recently proposed that the increase of PGC1- $\alpha$   
430 expression in muscle tissue may induce endocrine effects on adipose tissue and adipokines,  
431 leading to higher fat oxidation. Altogether, this may explain why HIIT promotes greater  
432 abdominal and visceral FM losses compared with the traditional MICT.

433

434 We also made the hypothesis that HIIT, compared with MICT, might increase fat oxidation at  
435 rest and during free-living physical activities (walking, cycling, gardening...) by altering  
436 metabolic flexibility. To test this hypothesis, we determined fat oxidation before and after the  
437 training period at rest and during a moderate-intensity exercise (40min at 50% of PPO) and  
438 during the 20min recovery time. None of the training modes altered RMR ( $\text{kcal}\cdot\text{day}^{-1}$ ) and  
439 substrate oxidation at rest. As expected, FatOx levels were significantly increased, but without  
440 any difference among the three groups. The mean FatOx change measured after training (~  
441 +32%) was similar to what reported by other studies using the same amount of activity (12  
442 weeks/3 times per week). For example, Talanian et al. (44) showed an increase of 36% in  
443 whole-body fat oxidation during a 1 hour-cycling performed at 60%  $\text{VO}_{2\text{peak}}$  after a HIIT  
444 program (two weeks, 7 sessions including 10 x 4min at 90%  $\text{VO}_{2\text{peak}}$  with 2min recovery) in  
445 young sedentary women with overweight or obesity. Our study, which was the first to compare  
446 FatOx in postmenopausal women with overweight/obesity at rest, during moderate intensity  
447 physical activity and during the recovery period after three different training programs, did not  
448 find a greater impact of HIIT on metabolic flexibility and no correlation appeared between  
449 FatOx and total or (intra)-abdominal FM loss. Thus, the hypothesis of a greater FatOx after  
450 HIIT programs was not verified in postmenopausal women and cannot explain the larger  
451 adipose tissue reduction.

452 Our study also examined the effects of HIIT combined with RT on body composition  
453 in postmenopausal women. An increase of muscle mass after HIIT + RT program might  
454 enhance RMR and therefore, the 24h EE. The 24h EE increase could favor in turn body FM  
455 loss because a part of the EE is provided through lipid oxidation. The recent meta-analysis by  
456 Sabag et al. (45) shows that HIIT + RT leads to similar muscle mass gain (hypertrophy) as RT  
457 alone. Furthermore, concurrent HIIT and RT does not negatively affect muscle mass gain.

458 However, these results should be considered with caution because this meta-analysis concerned  
459 263 young participants (18-34 years) among whom only 33 were inactive or untrained. Thus,  
460 these conclusions are probably more adapted to young athletes than to individuals with  
461 overweight/obesity.

462 In our study, loss of total and of (intra)-abdominal FM was not significantly different in the  
463 HIIT and HIIT + RT groups. In fact the lack of muscle mass gain (kg) in the HIIT + RT group  
464 could explain this finding. Indeed, the duration or volume and/or intensity of the RT protocols  
465 in our study could have been insufficient to induce a significant increase of muscle mass. It is  
466 not possible to compare our results with the literature because this is the first study dealing  
467 with HIIT + RT effects on body composition in postmenopausal women. However, three  
468 studies on endurance training + RT have been performed. For example, Martin et al. (46) did  
469 not find any effect of HIIT or combined training (aerobic + resistance exercises) on total body  
470 fat (%) and muscle mass index ( $\text{kg}\cdot\text{m}^{-2}$ ) in postmenopausal women after a 12-week  
471 intervention. Davidson et al. found greater total, abdominal and visceral FM losses following  
472 a 6-month MICT + RT program (30min walking at 65-70%  $\text{VO}_2\text{max}$  + 9 resistance exercises,  
473 3 d·wk<sup>-1</sup>) compared with MICT or RT alone in older adults with obesity (42). These  
474 adaptations were associated with significant skeletal muscle gain, which may confirm the  
475 potential link between muscle mass gain and FM loss after RT. Finally, Nunes et al. (47)  
476 demonstrated a decrease of whole-body FM (-0.3%) after a 12-week MICT + RT program (60  
477 min of walking at 70% of PHR and resistance exercises at 70% of one repetition maximum; 3  
478 d·wk<sup>-1</sup>) in postmenopausal women. However, they did give any information on FFM and  
479 muscle mass changes. Additional studies using different RT modalities (duration, volume,  
480 intensity) are probably needed to determine whether RT alone or together with HIIT might  
481 promote muscle mass gain in postmenopausal women, leading to significant FM loss.

482

483 One of the limitations of this study concerns the groups tested. Indeed, it is difficult to conclude  
484 about a potential effect of HIIT + RT without knowing whether the RT intervention alone could  
485 induce positive adaptations. Thus, to determine whether the RT intervention can favor muscle  
486 adaptations, it would have been interesting to add also a RT group. We decided to have the  
487 same session duration for the MICT and HIIT + RT programs since a lack of time has been  
488 cited as a barrier for overweight/obese people. This limited the amount of RT work and this  
489 might not have been enough to induce muscle mass gain, especially in women. Furthermore,  
490 we can also hypothesize that the HIIT + RT combination may alter muscle adaptations by  
491 inducing molecular pathway interferences between training modalities. Indeed, it has been  
492 suggested that endurance training performed before RT negatively affects RT adaptations  
493 through inhibition of the AKT-mTOR pathway activation by AMPK (25). Finally, a last group,  
494 MICT+ RT, might induce different adaptations but appeared to us less attractive due to the  
495 duration of the session ( $\geq 1$  hour).

496

497 In conclusion a 12-week cycling MICT or HIIT  $\pm$  RT program (3 sessions.week<sup>-1</sup>) can  
498 be proposed to non-dieting postmenopausal women with overweight/obesity to decrease  
499 weight and whole-body FM. HIIT programs seems more successful in reducing (intra)-  
500 abdominal FM than the traditional moderate continuous training. As the level of subcutaneous  
501 abdominal and visceral FM is correlated with the CVD risk, this study confirms that HIIT is an  
502 effective and time-efficient modality to reduce such risk in this population. HIIT + RT did not  
503 potentiate this effect, but improved body composition by increasing the percentage of FFM,  
504 including muscle mass. HIIT-induced greater total and (intra)-abdominal FM loss is not related  
505 to changes in metabolic flexibility at rest, during moderate intensity exercise, or during the  
506 recovery period. Additional studies are needed to better understand the underlying mechanisms

507 of HIIT-induced FM loss and to determine whether the concomitant muscle mass gain induced  
508 by RT potentiates these adaptations.

509

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513 sessions and their help in data collection.

514

### 515 **Conflict of interest**

516 The results of this study are presented clearly, honestly, and without fabrication, falsification,  
517 or inappropriate data manipulation. The results of the present study do not constitute  
518 endorsement by the American College of Sports Medicine.

519

### 520 **Competing interests**

521 The authors declare that they have no competing interests.

522

### 523 **Authors' contributions**

524 MD was the PhD student on the MATISSE study and designed and supervised the different  
525 training modalities. She met all participants, collected and analyzed all heart rate monitoring  
526 data during training, supervised training sessions, collected and analyzed the data obtained for  
527 RMR and during the prolonged exercise (FAT oxidation measurements), carried out the  
528 anthropometric measurements and wrote the first and subsequent drafts of the paper. MR was  
529 a co-investigator, and assisted with the study design. CM, PB and MD, physicians, assisted  
530 with the study design, and oversaw the medical aspects of the study. AB and FM were sport  
531 instructors, supervised training sessions with MD, and helped collecting data for RMR and

532 during the prolonged exercise (FAT oxidation measurements). NB conceived the study idea,  
533 was responsible for the overall study design, and for monitoring data collection. BP was  
534 responsible for all statistical analyses. All authors read and approved the final manuscript.

535

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540 publication.

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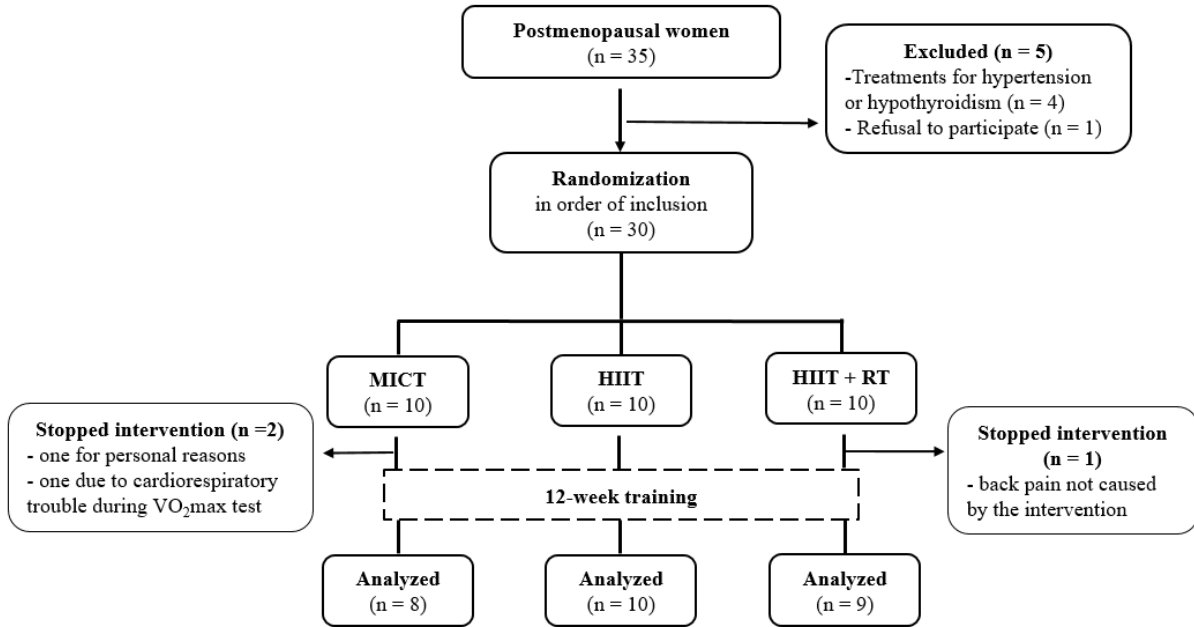
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676 **Figure Legends**

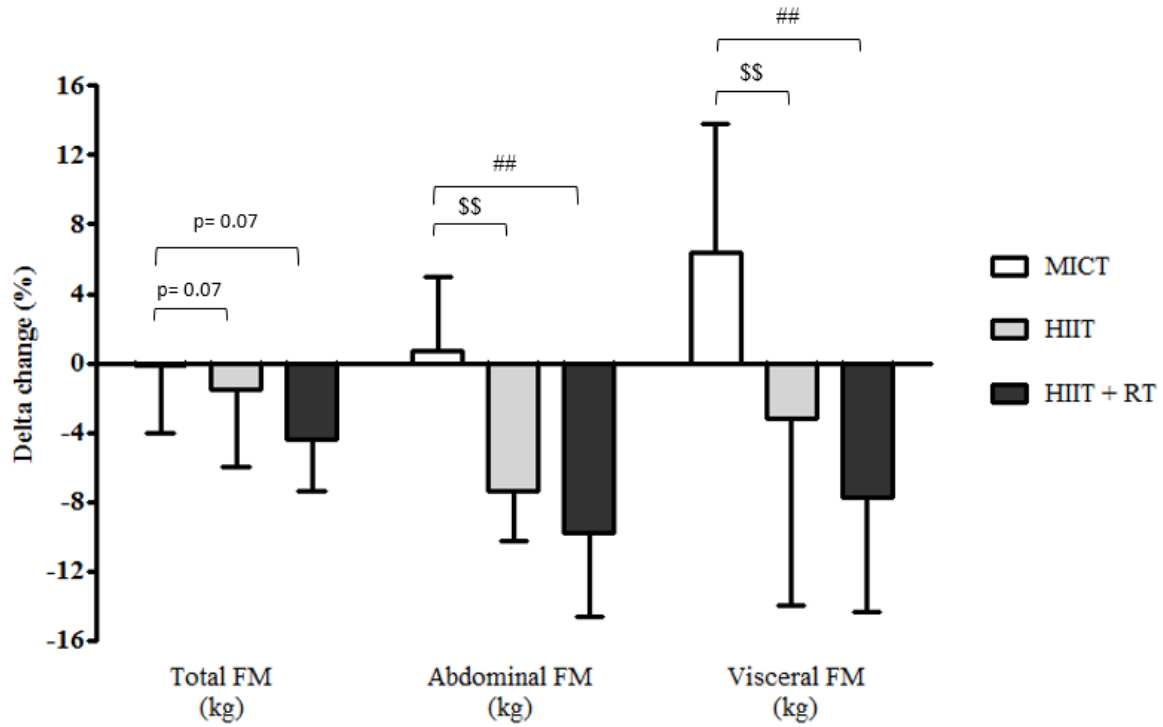
677 **Figure 1:** Flowchart of participants' recruitment.

678 HIIT: high-intensity interval training; MICT: moderate-intensity continuous training; HIIT +  
679 RT: high-intensity interval training + resistance training.



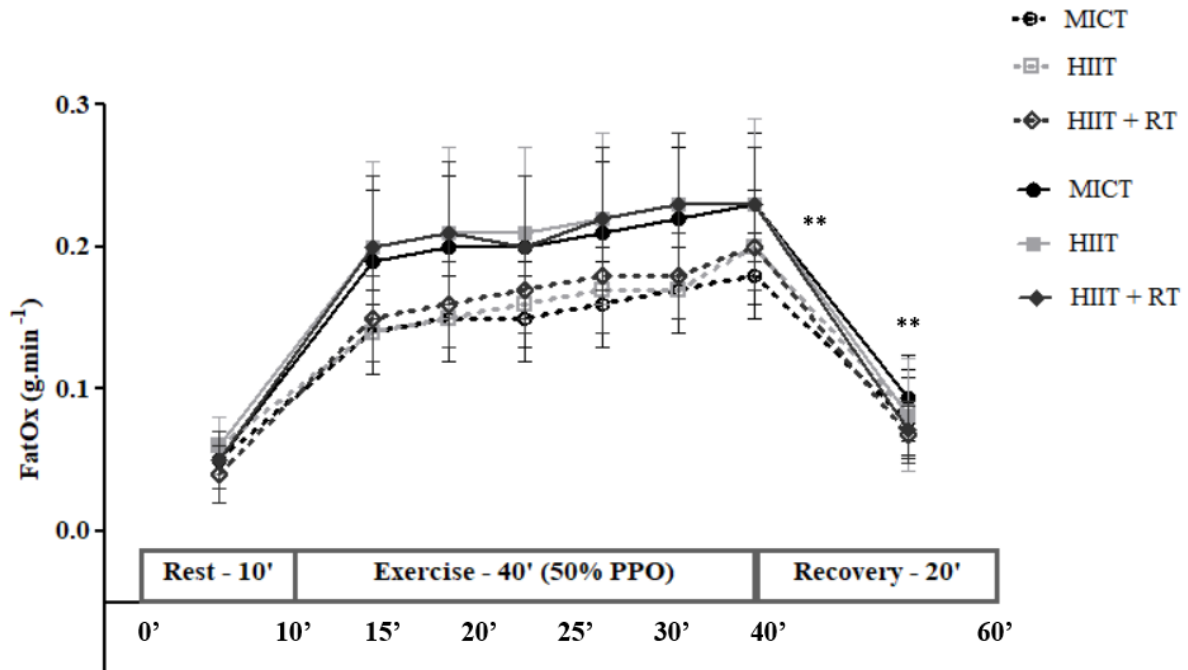
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682 **Figure 2:** Body composition changes (based on dual-energy X-ray absorptiometry imaging)  
 683 between baseline and the end of the 12-week training program in the MICT (n = 8), HIIT (n =  
 684 10) and HIIT + RT (n = 9) groups. Data are the mean  $\pm$  SD. MICT: moderate-intensity  
 685 continuous training; HIIT: high-intensity interval training; HIIT + RT: high-intensity interval  
 686 training + resistance training; FM: fat mass; delta change (%) = [(12 weeks – baseline/baseline)  
 687  $\times$  100].  
 688 #:  $p \leq 0.01$ : HIIT + RT vs. MICT group; \$:  $p \leq 0.01$ : HIIT vs. MICT group.



689  
 690

691 **Figure 3:** Fat oxidation (FatOx, g.min<sup>-1</sup>) at rest, during exercise (50% of PPO) and during the  
 692 20min recovery in the MICT (n = 8), HIIT (n = 10) and HIIT + RT (n = 9) groups at baseline  
 693 and after the 12-week intervention. Data are the mean ± SD. The values at rest correspond to  
 694 the mean of the last 5 minutes. The values during the recovery period correspond to the mean  
 695 of the 20min post-exercise period. Six values are presented for the cycling exercise period (at  
 696 15, 20, 25, 30, 35 and 40min of exercise).  
 697 \*\*\*: time effect (pre- vs post-intervention), p ≤0.005.  
 698 MICT: moderate-intensity continuous training; HIIT: high-intensity interval training; HIIT +  
 699 RT: high-intensity interval training + resistance training.



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	MICT		HIIT		HIIT +RT		ANOVA ( <i>p</i> )		
	Pre	Post	Pre	Post	Pre	Post	<i>G</i>	<i>T</i>	<i>G × T</i>
<b>BMI (kg.m<sup>2</sup>)</b>	31.2 ± 3.0	30.9 ± 2.8	31.5 ± 4.3	31.1 ± 4.4	31.4 ± 4.0	31.1 ± 3.7	0.99 0.00	<b>0.02</b> <b>0.21</b>	0.98 0.00
<b>Waist circumference (cm)</b>	100.8 ± 5.4	99.2 ± 6.0	100.9 ± 9.3	97.1 ± 8.8	101.4 ± 10.0	98.8 ± 10.8	0.91 0.00	<b>0.01</b> <b>0.44</b>	0.44 0.09
<b>Hip circumference (cm)</b>	109.7 ± 6.6	107.2 ± 7.3	110.1 ± 9.1	107.8 ± 7.6	106.3 ± 9.6	104.3 ± 8.1	0.58 0.04	<b>0.001</b> <b>0.44</b>	0.97 0.09
<b>Body weight (kg)</b>	80.5 ± 7.1	79.7 ± 7.3	81.6 ± 12.7	80.8 ± 12.9	75.6 ± 8.9	74.9 ± 8.0	0.41 0.07	<b>0.02</b> <b>0.21</b>	0.95 0.00
<b>Total FM (kg)</b>	30.7 ± 5.3	30.7 ± 5.4	27.7 ± 10.7	27.1 ± 10.6	28.1 ± 1.9	26.8 ± 1.8	0.50 0.06	<b>0.002</b> <b>0.34</b>	0.06 0.21
<b>Total FM (%)</b>	37.9 ± 4.0	38.3 ± 4.4	33.7 ± 11.6	33.4 ± 11.5	36.9 ± 3.8	<b>35.5 ± 3.8**</b>	0.66 0.03	<b>0.02</b> <b>0.20</b>	<b>0.03</b> <b>0.25</b>
<b>Total FFM (kg)</b>	49.8 ± 3.7	49.1 ± 4.0	45.1 ± 15.6	44.9 ± 15.5	47.6 ± 4.2	48.1 ± 3.6	0.41 0.07	0.88 0.00	0.19 0.13
<b>Total FFM (%)</b>	62.1 ± 4.0	61.7 ± 4.4	56.3 ± 19.3	56.7 ± 19.3	64.1 ± 3.8	<b>64.5 ± 3.9**</b>	0.67 0.03	<b>0.02</b> <b>0.20</b>	<b>0.03</b> <b>0.25</b>
<b>Muscle mass (kg)</b>	47.7 ± 3.6	47.1 ± 3.9	43.3 ± 14.9	43.1 ± 14.9	45.7 ± 4.0	46.1 ± 3.3	0.44 0.07	0.79 0.00	0.29 0.10



<b>Muscle mass (%)</b>	59.5 ± 3.9	59.2 ± 4.2	54.0 ± 18.5	54.3 ± 18.6	60.7 ± 3.8	<b>62.0 ± 3.9**</b>	0.61 0.04	<b>0.02</b> <b>0.19</b>	<b>0.03</b> <b>0.25</b>
<b>Total abdominal FM (kg)</b>	7.6 ± 1.7	7.6 ± 1.7	7.4 ± 1.9	<b>6.9 ± 1.9**</b>	7.2 ± 1.7	<b>6.5 ± 1.7**</b>	0.67 0.03	≤ 10 <sup>-8</sup> <b>0.73</b>	≤ 10 <sup>-4</sup> <b>0.48</b>
<b>Visceral FM (kg)</b>	4.2 ± 1.7	4.4 ± 1.8	4.5 ± 1.1	4.3 ± 1.0	3.1 ± 1.4	<b>2.9 ± 1.4#£</b>	0.08 0.19	0.48 0.02	<b>0.02</b> <b>0.27</b>
<b>VO<sub>2</sub>max (mL.min<sup>-1</sup>.kg<sup>-1</sup>)</b>	25.3 ± 2.8	28.5 ± 2.9	30.5 ± 6.9	35.6 ± 6.4	31.5 ± 4.1	35.0 ± 4.1	<b>0.04</b> <b>0.24</b>	≤ 10 <sup>-7</sup> <b>0.71</b>	0.25 0.11
<b>PPO (Watts)</b>	85 ± 9	102 ± 12	96 ± 23	122 ± 21	104 ± 13	120 ± 14	<b>0.04</b> <b>0.24</b>	≤ 10 <sup>-7</sup> <b>0.71</b>	0.34 0.09
<b>PPO (Watts.kg<sup>-1</sup>)</b>	1.1 ± 0.1	1.3 ± 0.2	1.2 ± 0.4	1.4 ± 0.7	1.4 ± 0.2	1.6 ± 0.2	0.1 0.18	≤ 10 <sup>-7</sup> <b>0.76</b>	0.30 0.10

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703 **Table 1: Anthropometric measurements, body composition and aerobic fitness in the MICT, HIIT and HIIT + RT groups at baseline**  
704 **(pre) and at the end (post) of the training programs.**

705 Values are the mean ± SD.

706 G: group effect; T: time effect; G×T: group × time interaction.

707 BMI: body mass index; FM: fat mass; FFM: free-fat mass; Muscle mass = FFM – Bone Mineral Content from DXA; PPO: peak power output.

708 \*\*: p ≤ 0.005 (pre vs. post in the same group); #: p ≤ 0.05 (HIIT + RT vs. MICT); £: p ≤ 0.05 (HIIT + RT vs. HIIT).

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	MICT		HIIT		HIIT +RT		ANOVA ( <i>p</i> )		
	Pre	Post	Pre	Post	Pre	Post	<i>G</i>	$\eta^2$ <i>T</i>	<i>G</i> × <i>T</i>
<b>REST</b>									
<b>RMR</b> (kcal.day <sup>-1</sup> )	1403 ± 259	1430 ± 259	1615 ± 206	1514 ± 230	1426 ± 317	1392 ± 317	0.23 0.11	0.56 0.01	0.68 0.03
<b>FatOx</b> (g.min <sup>-1</sup> )	0.05 ± 0.02	0.05 ± 0.02	0.06 ± 0.02	0.06 ± 0.02	0.04 ± 0.02	0.05 ± 0.01	0.23 0.12	0.47 0.02	0.98 0.00
<b>FatOx</b> (%)	48.5 ± 17.5	50.3 ± 15.0	48.0 ± 14.5	53.7 ± 12.8	44.2 ± 15.5	48.8 ± 8.5	0.67 0.03	0.26 0.05	0.90 0.00
<b>CHOOx</b> (g.min <sup>-1</sup> )	0.14 ± 0.04	0.14 ± 0.03	0.16 ± 0.05	0.13 ± 0.04	0.16 ± 0.06	0.14 ± 0.05	0.73 0.02	0.16 0.08	0.95 0.05
<b>CHOOx</b> (%)	51.5 ± 17.5	49.7 ± 15.0	52.0 ± 14.5	46.3 ± 12.8	55.9 ± 15.5	51.3 ± 8.5	0.67 0.03	0.26 <b>0.05</b>	0.90 0.00
<b>EE</b> (kcal.min <sup>-1</sup> )	0.97 ± 0.18	0.99 ± 0.17	1.12 ± 0.14	1.05 ± 0.16	0.99 ± 0.22	0.97 ± 0.22	0.23 0.11	0.56 0.01	0.69 0.03
<b>EXERCISE</b>									
<b>FatOx</b> (g.min <sup>-1</sup> )	0.17 ± 0.03	0.21 ± 0.05	0.16 ± 0.03	0.22 ± 0.06	0.18 ± 0.03	0.22 ± 0.05	0.68 0.03	≤ <b>10<sup>-5</sup></b> <b>0.48</b>	0.81 0.02
<b>FatOx</b> (%)	41.9 ± 5.7	51.8 ± 10.8	39.8 ± 5.5	50.7 ± 11.1	40.6 ± 5.2	53.6 ± 10.9	0.72 0.03	≤ <b>10<sup>-4</sup></b> <b>0.44</b>	0.89 0.01
<b>CHOOx</b> (g.min <sup>-1</sup> )	0.60 ± 0.7	0.52 ± 0.12	0.67 ± 0.18	0.57 ± 0.15	0.72 ± 0.18	0.52 ± 0.17	0.46	<b>0.006</b>	0.46

							0.06	<b>0.27</b>	0.06
<b>CHOOx (%)</b>	58.1 ± 5.7	48.2 ± 10.8	60.2 ± 5.5	49.3 ± 11.1	59.4 ± 5.2	46.3 ± 10.9	0.72 0.03	≤ <b>10<sup>-4</sup></b> <b>0.44</b>	0.89 0.01
<b>EE (kcal.min<sup>-1</sup>)</b>	3.7 ± 0.3	3.9 ± 0.4	4.0 ± 0.8	4.0 ± 0.7	4.3 ± 0.9	4.0 ± 0.6	0.45 0.06	0.63 0.00	0.29 0.10
<b>RECOVERY</b>									
<b>FatOx (g.min<sup>-1</sup>)</b>	0.08 ± 0.03	0.09 ± 0.03	0.08 ± 0.03	0.08 ± 0.04	0.07 ± 0.02	0.07 ± 0.02	0.69 0.03	≤ <b>10<sup>-5</sup></b> <b>0.48</b>	0.81 0.02
<b>FatOx (%)</b>	52.5 ± 10.8	57.2 ± 12.1	52.6 ± 10.8	55.9 ± 11.0	47.6 ± 12.3	53.9 ± 10.0	0.72 0.03	≤ <b>10<sup>-4</sup></b> <b>0.44</b>	0.89 0.01
<b>CHOOx (g.min<sup>-1</sup>)</b>	0.20 ± 0.05	0.21 ± 0.10	0.18 ± 0.04	0.18 ± 0.09	0.21 ± 0.06	0.17 ± 0.06	0.47 0.06	<b>0.006</b> <b>0.27</b>	0.45 0.06
<b>CHOOx (%)</b>	47.5 ± 10.8	42.8 ± 12.1	47.4 ± 10.8	44.1 ± 11.0	52.4 ± 12.3	46.0 ± 10.0	0.72 0.03	≤ <b>10<sup>-4</sup></b> <b>0.44</b>	0.89 0.01
<b>EE (kcal.min<sup>-1</sup>)</b>	1.5 ± 0.3	1.6 ± 0.4	1.4 ± 0.3	1.4 ± 0.6	1.4 ± 0.3	1.3 ± 0.3	0.45 0.06	0.63 0.01	0.29 0.10

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713 **Table 2: Substrate utilization and energy expenditure at rest, during moderate intensity continuous exercise (50% of PPO) and during**  
714 **the 20min recovery time in the MICT, HIIT, and HIIT + RT groups at baseline (pre) and after (post) the training programs.**

715 Values are the mean ± SD.

716 G: group effect; T: time effect; G×T: group × time interaction.

717 RMR: resting metabolic rate; EE: energy expenditure; FatOx: fat oxidation; CHOOx: carbohydrate oxidation.

	MICT		HIIT		HIIT + RT		ANOVA ( <i>p</i> )		
	Pre	Post	Pre	Post	Pre	Post	<i>G</i>	$\eta^2$ <i>T</i>	<i>G</i> × <i>T</i>
<b>Glycemia</b> (mmol.L <sup>-1</sup> )	1.2 ± 0.7	1.2 ± 0.4	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.6	1.2 ± 0.7	0.19 0.13	0.47 0.02	0.74 0.03
<b>Insulinemia</b> (μU.L <sup>-1</sup> )	11.2 ± 3.	9.1 ± 3.3	12.9 ± 14.8	12.5 ± 13.0	11.5 ± 3.3	11.7 ± 4.4	0.82 0.02	0.27 0.05	0.79 0.03
<b>HbA1c</b> (%)	5.6 ± 0.5	5.5 ± 0.4	6.1 ± 0.9	6.0 ± 0.7	5.8 ± 0.2	5.7 ± 0.2	0.19 0.13	0.52 0.02	0.50 0.06
<b>HOMA-IR</b>	3.0 ± 1.2	2.2 ± 0.8	3.9 ± 4.7	3.8 ± 4.4	2.8 ± 0.8	3.0 ± 1.4	0.64 0.04	0.39 0.03	0.42 0.07
<b>Total Cholesterol</b> (mmol.L <sup>-1</sup> )	6.3 ± 1.3	6.3 ± 1.3	5.6 ± 1.1	5.4 ± 1.2	6.2 ± 1.0	6.2 ± 1.0	0.27 0.10	0.43 0.03	0.86 0.01
<b>HDL-C</b> (mmol.L <sup>-1</sup> )	1.7 ± 0.4	1.6 ± 0.1	1.7 ± 0.9	1.7 ± 0.5	1.7 ± 0.5	1.7 ± 0.4	0.82 0.01	0.77 0.00	0.69 0.03
<b>LDL-C</b> (mmol.L <sup>-1</sup> )	3.5 ± 1.6	3.6 ± 1.4	3.3 ± 0.8	3.4 ± 0.8	3.9 ± 1.0	3.9 ± 0.8	0.40 0.08	0.83 0.00	0.79 0.02
<b>TG</b> (mmol.L <sup>-1</sup> )	1.4 ± 1.1	1.1 ± 0.5	1.2 ± 0.7	0.9 ± 0.4	1.2 ± 0.5	1.2 ± 0.6	0.43 0.07	<b>0.02</b> <b>0.22</b>	0.41 0.07

720 **Table 3: Glycemic control and lipid profile in the MICT, HIIT and HIIT + RT groups at baseline (pre) and after (post) the training**  
721 **programs.**

722 Values are the mean  $\pm$  SD.

723 G: group effect; T: time effect; G $\times$ T: group  $\times$  time interaction.

724 HDL: High Density Lipoproteins, LDL: Low Density Lipoproteins, C, cholesterol; TG: Triglycerides.

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