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# Bone Response to High-Intensity Interval Training versus Moderate-Intensity Continuous Training in Adolescents with Obesity

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## Keywords

Childhood obesity · Bone mineral density · Bone strength · High-intensity interval training · Moderate-intensity continuous training

## Abstract

**Introduction:** Since adolescents with obesity are prone to bone fragility during weight loss, the aim was to compare the impact of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) on bone density, geometry, and strength. **Methods:** Sixty-one adolescents were randomly assigned to 2 cycling trainings (HIIT and MICT) and a control (CTR, without training) group. Anthropometry, dual-energy X-ray absorptiometry with hip structural analysis and the trabecular bone score (TBS) were assessed before and after the 16-week intervention. **Results:** Body mass index (BMI) and fat mass (FM) percentage de-

creased at T1 versus T0 in both training groups ( $p < 0.001$  for HIIT,  $p = 0.01$  for MICT), though to a larger extent in HIIT ( $p < 0.05$ ). Total body bone mineral density (BMD) and bone mineral content (BMC) increased in both training groups ( $p < 0.001$ ), but to a greater extent in HIIT for BMC ( $p < 0.05$ ). Lumbar spine BMD and BMC increased in both training groups ( $p < 0.001$  for HIIT,  $p < 0.01$  for MICT), with a time  $\times$  group interaction between HIIT and CTR ( $p < 0.05$ ) only. TBS increased in both training groups ( $p < 0.01$  for HIIT,  $p < 0.05$  for MICT). Hip BMD and BMC increased in both HIIT ( $p < 0.001$  and  $p < 0.01$ ) and MICT ( $p < 0.01$  and  $p < 0.05$ ). At the narrow neck (NN), endocortical diameter, width ( $p < 0.01$ ), cross-sectional moment of inertia, and section modulus (Z) ( $p < 0.05$ ) increased only in the HIIT group, such as BMD and Z ( $p < 0.05$ ) at the intertrochanteric region (IT) and average cortical thickness ( $p < 0.001$ ) and width ( $p < 0.05$ ) at the femoral shaft. At the NN and IT, the buckling ratio decreased only in the HIIT group ( $p < 0.05$ ), predicting higher resistance to fracture.

**Conclusions:** In addition to inducing greater BMI and FM percentage decreases in comparison to MICT, HIIT improves multisite bone density, geometry, and strength, which heighten the justification for HIIT as part of weight loss interventions in adolescents with obesity.

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## Introduction

Pediatric obesity is a priority public health challenge [1]. Traditionally, excess body weight has been considered to have positive effects on the bone as it represents a mechanical load which can induce benefits for bone accrual [2–4]. This remains, however, subject to debate since recent findings suggest that excessive fat mass (FM) can compromise bone mass and quality [5, 6]. Indeed, FM can negatively influence bone tissue by nonmechanical mechanisms, including via hormones and cytokines [7]. A lack of sufficient physical activity and some nutritional deficits have also been found to alter bone density [8, 9]. Therefore, bone quality and structure are influenced by a balance of mechanical and inflammatory stimuli, nutrition, physical activity, and the hormonal milieu (particularly at puberty) [2]. It has now been well demonstrated that adolescents with obesity have suboptimal bone health compared to lean peers, which increases the likelihood of fractures during a crucial period of bone mineral acquisition [2, 3, 8, 10, 11].

Multidisciplinary weight loss interventions combining nutritional approaches and physical activity are the cornerstone of treatment strategies for adolescents with obesity in order to decrease body mass index (BMI) and FM [12] while preserving lean mass (LM) and improving fitness. However, weight loss can also lead to bone breakdown [2, 5] related to subsequent decreased mechanical loading on the skeleton [5], decreased caloric intake [5], and altered secretion of some key hormones and peptides involved in bone regulation [6, 13]. For example, weight loss decreases the circulating estrogen and increases the sex hormone-binding globulin, which negatively impacts bone osteoblastic and osteoclastic activity, directly or indirectly, related with the heightened levels of cytokines (i.e., IL-1, IL-6, and tumor necrosis factor- $\alpha$ ). Other drivers, such as changes in bone-modulating adipokines (leptin, adiponectin, and insulin-like growth factor-1), the rise in the Ca-PTH axis, and modifications in gut peptides that regulate both satiety and bone metabolism, also enhance bone resorption during weight loss [5]. Nevertheless, it is clear that physical activity can strengthen the

bone [14], particularly during adolescence, when the bone's ability to adapt to mechanical loading is the greatest [15].

Thus, for the last decade, research in the field of physical activity has attempted to identify the optimal exercise modalities to include in adolescents weight management interventions. For example, it has been shown that combined aerobic and resistance training induced a greater gain in bone mineral content (BMC) in comparison with aerobic training alone [16]. More recently, it has been demonstrated that eccentric cycling (which offers higher load for the same metabolic demand) is more effective in improving body composition than classical concentric cycling. In addition, eccentric cycling induced improvements in bone mineral density (BMD) and BMC while preventing some hip bone strength alterations usually observed during classical weight loss interventions [17]. More generally, it has been suggested that longer interventions with higher exercise intensities, inducing greater loss of FM and increase in LM would be associated with better improvements of bone mass [8, 17–20]. LM, rather than FM, has been suggested as the most important component of body composition for bone health [20].

Recent adult and adolescent obesity research focused on the use of high-intensity interval training (HIIT) over traditional moderate-intensity continuous training (MICT). HIIT is now recognized as an efficient and promising strategy for inclusion in weight management as it induces greater cardiometabolic improvements than MICT [21–24] while producing a lower rating of perceived exertion [25]. Moreover, acute HIIT has been shown to have beneficial effects on energy balance by both increasing energy expenditure and improving appetite control [26]. While our research group recently showed that HIIT is more efficient than MICT for decreasing FM percentage while maintaining LM in adolescents with obesity [27], its effects on bone adaptations in this population remains unexplored. Therefore, the present study aimed to determine the impact of HIIT versus MICT on bone density, geometry, and strength among adolescents with obesity.

## Materials and Methods

### *Study Participants*

Sixty-one adolescents were recruited (60% females) at the Pediatric Obesity Center (Centre Médical Infantile de Romagnat, France), at the time of their admission for weight management or at the time of joining a waiting-list control (CTR) group included adolescents waiting admission to the center. Full medical

examination was conducted by a pediatrician for all adolescents, during which adolescents and their parents were informed and given the study information sheets. All adolescents met the following inclusion criteria: (1) 12–16 years old (Tanner age 3–4 years); (2) BMI >95th percentile according to the international cutoff points; (3) regular menstruations for females; (4) no medication, no oral contraceptives, no hormone replacement therapy, and no supplemental calcium and/or iron during the last 12 months; (5) no regular tobacco or alcohol; (6) no contraindication to exercise; (7) self-reported physical activity <2 h per week (International Physical Activity Questionnaire); and (8) steady weight with no dietary intervention during the last 6 months. Complete information regarding the study was explained to the potential participants and their legal representative/s before their admission into the center, and informed consent was obtained during their medical screening visit. This study was conducted in accordance with the Helsinki declaration and received an ethical agreement from official authorities (CPP Sud Est VI: AU1178; Clinical Trial NCT02482220).

### Study Design

After the screening visit, adolescents in the training group were randomly allocated to either the MICT or the HIIT group for 16 weeks (permuted-block randomization conducted using a computer-generated random allocation) (Stata software, version 13, StataCorp, College Station, TX, USA). The intervention consisted of a 16-week residential multidisciplinary weight management program combining physical activity (4 sessions per week) and nutritional education (2 sessions per month). During the intervention, the adolescents were prescribed a normo-caloric diet (without energy restriction) based on their age and sex. Adolescents of the CTR group did not perform any physical training during the 16 weeks and served as CTRs to distinguish the influence of growth on bone parameters. Adolescents from the CTR group received the same nutritional counseling (normo-caloric diet) throughout the 16-week period. Anthropometry, body composition, and bone assessments were measured at baseline (T0) and after the 16-week period (T1), as described below.

### Training Program

Physical activities included leisure time activities (once per week), aquatic activities (once per week), and either MICT plus strength training (twice per week) or HIIT plus strength training (twice per week). The MICT group performed a 45-min ergometer bicycle exercise twice per week at 60% of their initial  $\dot{V}O_{2\text{peak}}$ . The HIIT group trained for 15 min twice per week on the same ergometer bicycle, alternating 30 s of intense exercise and 30 s of active recovery (free but compulsory pedaling). The intensity for the HIIT training progressively increased from 75% at baseline to 90%  $\dot{V}O_{2\text{peak}}$ . Regarding the strength training, exercises comprised bench press, pulley (lat, pull-down), leg-press, biceps curl, ankle extension machine (sitting), curl machine for triceps, abdominal machine, and trunk extensor machine. The adolescents had to perform 10 repetitions of each exercise interspersed by 1 min of rest, and to repeat this 3 times, with a rest period of 4 min between each round. The training intensity was individually set and progressively increased from 65% to 85% of 10 maximal repetitions at the end of the intervention. Save for the modality of training (MICT vs. HIIT), the adolescents received the same medical care throughout the residential stay.

### Anthropometric Measurements

Body weight and height were recorded to the nearest 0.1 kg and 0.5 cm, respectively, while wearing light clothes and bare-footed, using a digital scale (Seca, Les Mureaux, France) and a standard wall-mounted stadiometer (Seca, Les Mureaux, France). BMI was calculated as weight (kg) divided by height squared ( $\text{m}^2$ ), and was plotted on sex- and age-specific French reference growth curves for BMI percentile [27].

### Maximal Incremental Exercise Test

Each subject performed an incremental exercise test on a traditional concentric cyclo-ergometer (Ergoselect 100, Ergoline, MCG diagnostics, Germany). The saddle height was carefully adjusted to allow full revolution. After 3 minutes at a steady state, the initial power was set at 30 W for 3 min, followed by 15 W increments every minute until exhaustion (pedal cadence was kept constant at 60–70 revolutions per minute). The adolescents were strongly encouraged by the experimenters throughout the test to perform at maximal effort. The maximal exercise test was defined by at least 2 of the following criteria: heart rate >90% of the theoretical maximum heart rate ( $115 - 0.65 \times \text{age}$ ), respiratory exchange ratio ( $\text{RER} = \dot{V}CO_2 / \dot{V}O_2$ ) >1.1 or  $\dot{V}O_2$  plateau. Cardiac electrical activity was monitored continuously with heart rate telemetry (Mortara, Ultima series, Medisoft, MCG diagnostics, Germany) and combined with breath-by-breath gas exchange measurement (Ultima CardioO2, Medisoft, MCG diagnostics, Germany) to determine  $\dot{V}O_2$  and  $CO_2$  production ( $\dot{V}CO_2$ ).  $\dot{V}O_{2\text{peak}}$  was then defined as the average of the last 30 s of exercise before exhaustion at the maximal power output [27].

### Body Composition and Bone Measurements by DXA

All subjects underwent DXA (Discovery A; Hologic Inc., Bedford, MA, USA) in a fasted state. Standardized procedures were followed by a trained blinded technician for the assessment of body composition (FM and LM), bone densitometry assessment, trabecular bone score (TBS) and hip structural analysis (HSA) (QDR-4500A DXA; Hologic, Bedford, MA, USA). Body composition data were analyzed using the Hologic QDR Software for Windows version 12.6 to assess total LM and FM for the whole body [28].

According to the International Society for Clinical Densitometry recommendations for adolescents [29], BMD (in  $\text{g}/\text{cm}^2$ ) and BMC (in g) were determined at the total body less head (TBLH), lumbar spine (L2–L4), and nondominant hip. BMD measurements were converted to Z-scores. The TBS, which estimates fracture risk based on a determination of bone texture (an index correlated to bone microarchitecture) [30], was calculated using TBS iNsite software (Medimaps SA, France). The HSA was performed at the narrow neck (NN; narrowest part of the femoral neck), femoral shaft (FS; across the shaft 1.5 cm from the NN to the intersection of the neck and shaft axes), and the intertrochanteric region (IT; along the bisector of the angle of the axes of the NN and FS). The following parameters were obtained: cross-sectional area (CSA, in  $\text{cm}^2$ ; index of resistance to axial forces), BMD ( $\text{g}/\text{cm}^2$ ), endocortical diameter (in cm), average cortical thickness (ACT, in cm), width (in cm), cross-sectional moment of inertia (in  $\text{cm}^4$ ; estimate of resistance to bending forces in a cross-section), section modulus (Z,  $\text{cm}^3$ ; index of bending strength), and the buckling ratio (BR; index of susceptibility to cortical buckling under compressive loads) [28]. Higher values are associated with greater predicted femoral strength for all HSA-derived parameters, except the BR, for which values are predictive of inferior strength (BR values over 10 are highly predictive of fracture risk) [31].



**Table 1.** Anthropometric and body composition parameters before (T0) versus after (T1) the 16-week intervention for the control (CTR), the high-intensity interval training (HIIT), and the moderate-intensity continuous training (MICT) groups of adolescents with obesity ( $n = 49$ ; mean  $\pm$  standard deviation)

	CTR ( $n = 11$ )		HIIT ( $n = 19$ )		MICT ( $n = 19$ )	
	T0	T1	T0	T1	T0	T1
Height, cm	164.2 $\pm$ 5.6	165.2 $\pm$ 6.0*	160.4 $\pm$ 10.2	162.0 $\pm$ 10.0**	160.5 $\pm$ 8.0	161 $\pm$ 8.0**
Weight, kg	88.6 $\pm$ 14.7	90.1 $\pm$ 14.7	92.0 $\pm$ 18.5	84.9 $\pm$ 17.6***,###,†	90.7 $\pm$ 14.7	86.8 $\pm$ 13.3**,##
BMI, kg m <sup>-2</sup>	32.8 $\pm$ 5.1	32.9 $\pm$ 5.0	35.5 $\pm$ 4.6	32.1 $\pm$ 4.4***,###,†	35.3 $\pm$ 5.3	33.4 $\pm$ 5.0**,#
z-BMI	2.21 $\pm$ 0.4	2.16 $\pm$ 0.36	2.35 $\pm$ 0.3	2.10 $\pm$ 0.42***,##	2.32 $\pm$ 0.28	2.17 $\pm$ 0.32***,#
BMI percentile	97.9 $\pm$ 1.57	97.9 $\pm$ 1.58	98.6 $\pm$ 0.7	97.3 $\pm$ 2.0**,#	98.6 $\pm$ 0.7	97.9 $\pm$ 1.39**,#
Whole body LM, kg	54.3 $\pm$ 9.3	55.5 $\pm$ 9.5*	56.7 $\pm$ 11.8	54.0 $\pm$ 12.2***,###	54.0 $\pm$ 6.8	53.2 $\pm$ 6.6
Whole body fat, kg	33.4 $\pm$ 8.1	34.1 $\pm$ 8.5*	34.0 $\pm$ 8.2	29.1 $\pm$ 7.6***,###	34.8 $\pm$ 9.2	31.5 $\pm$ 7.6**,##
Whole body fat, %	37.7 $\pm$ 3.4	37.7 $\pm$ 3.6	36.9 $\pm$ 4.4	33.8 $\pm$ 3.6***,###,†	37.9 $\pm$ 4.3	35.9 $\pm$ 3.8**,#

BMI, body mass index; LM, lean mass; T0, baseline; T1, after the 16-week intervention. Intra-group interactions (time effects):  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ . Time  $\times$  group interactions. Significant difference with CTR: #  $p < 0.05$ ; ##  $p < 0.01$ ; ###  $p < 0.001$ . Significant difference between HIIT and MICT: †  $p < 0.05$

### Statistical Analysis

Statistical analyses were performed using Stata software (version 15, StataCorp, College Station, TX, USA). Continuous data were expressed as mean and standard deviation. The assumption of normality was assessed using the Shapiro-Wilk test. The comparisons between groups (CTR, HIIT, and MICT) at T0 were carried out using ANOVA or the Kruskal-Wallis test when the assumptions of ANOVA were not met. The homoscedasticity was studied using Bartlett's test of equality of variance. When appropriate (omnibus  $p$  value  $< 0.05$ ), a post hoc test was applied to consider multiple 2 by 2 comparisons. Tukey-Kramer's test and Dunn's test were used after ANOVA and the Kruskal-Wallis test, respectively. Then, to evaluate changes between T0 and T1, random-effects models (i.e., linear mixed models) for repeated data were performed. A participant was considered as a random effect in order to measure between and within-subject variability, whereas group (CTR without training, HIIT and MICT), time (T0 and T1), and group  $\times$  time interaction were fixed effects. The normality of residuals from these models was studied as aforementioned. When appropriate, a logarithmic transformation was applied to assess the normality of dependent variables. A Sidak's type I error correction was applied. The tests were 2-sided, with a type I error set at 5%.

## Results

From the initial 61 children enrolled ( $n = 25$  in each training group and  $n = 11$  in the CTR group), 49 completed the study, resulting in  $n = 19$  for MICT (12 females and 7 males),  $n = 19$  for HIIT (11 females and 8 males), and  $n = 11$  for CTR (6 females and 5 males). None of the drop-out subjects ( $n = 7$ ) were related to the intervention itself, but were due to family, disciplinary, or school-related reasons. Bone parameter data were incomplete for

$n = 5$  subjects. The mean patient age was  $13.0 \pm 0.8$  years in the MICT group,  $13.0 \pm 1.1$  years in the HIIT group, and  $13.2 \pm 1.0$  years in the CTR group ( $p = 0.56$ ).

### Anthropometry, Body Composition, and Strength Parameters

The anthropometric and body composition results are summarized in Table 1 (as previously reported [27]). While BMI and whole-body FM percentage were not modified in the CTR group ( $p = 0.983$  and  $p = 0.897$ , respectively), they decreased significantly at T1 versus T0 in both training groups ( $p < 0.001$  for HIIT,  $p = 0.01$  for MICT), though to a larger extent in the HIIT group (time  $\times$  group interactions between MICT and HIIT,  $p < 0.05$ ). Whole body LM decreased in the HIIT group ( $p < 0.001$ ), while it increased in the CTR group ( $p < 0.05$ ) (time  $\times$  group interactions between HIIT and CTR,  $p < 0.001$ ).

### Bone Parameters

Bone parameters measured by DXA, including multi-site BMC and BMD, and geometric and mechanical properties, are summarized in Table 2.

Total body: TBLH BMD and BMC increased at T1 versus T0 in both HIIT and MICT groups ( $p < 0.001$ ) but were not modified in the CTR group ( $p = 0.466$  and  $p = 0.956$ , respectively). TBLH BMC increased to a greater extent in the HIIT group than in the MICT group (time  $\times$  group interaction,  $p < 0.05$ ). The time  $\times$  group interactions were significant between HIIT and CTR for both BMD and BMC ( $p < 0.05$ ).

Lumbar region: Lumbar spine BMD and BMC increased at T1 versus T0 in both training groups ( $p < 0.001$

**Table 2.** Bone parameters measured by DXA before versus after the 16-week intervention for the control (CTR), the high-intensity interval training (HIIT), and the moderate-intensity continuous training (MICT) groups of adolescents with obesity ( $n = 49$ ; mean  $\pm$  standard deviation)

	CTR ( $n = 11$ )		HIIT ( $n = 19$ )		MICT ( $n = 19$ )	
	T0	T1	T0	T1	T0	T1
<b>TBLH</b>						
BMD, g.cm <sup>-2</sup>	1.066±0.080	1.079±0.79	1.021±0.111	1.064±0.119 <sup>***, #</sup>	1.058±0.090	1.090±0.092 <sup>***</sup>
BMC, g	2.132±290	2.135±283	1.916±387	2.018±393 <sup>***, #, †</sup>	1.960±362	2.026±336 <sup>***</sup>
<b>Lumbar spine</b>						
BMD, g.cm <sup>-2</sup>	0.941±0.150	0.946±0.137	0.903±0.200	0.938±0.189 <sup>***, #</sup>	0.955±0.137	0.974±0.124 <sup>**</sup>
TBS	1.28±0.17	1.26±0.16	1.22±0.11	1.27±0.12 <sup>**, ##</sup>	1.32±0.09	1.35±0.08 <sup>*, #</sup>
BMC, g	51.23±13.05	52.09±12.10	47.76±16.47	51.04±17.2 <sup>***, #</sup>	50.56±11.95	53.57±10.53 <sup>**</sup>
<b>Hip</b>						
BMD, g.cm <sup>-2</sup>	1.038±0.123	1.018±0.071	1.009±0.165	1.035±0.170 <sup>***, ##</sup>	0.982±0.106	0.997±0.107 <sup>*, #</sup>
BMC, g	37.3±10.8	33.4±4.0	33.2±5.4	37.4±5.2 <sup>**, #</sup>	32.3±5.2	34.3±5.1 <sup>**, #</sup>
<b>NN</b>						
BMD, g.cm <sup>-2</sup>	1.218±0.141	1.166±0.123 <sup>*</sup>	1.198±0.302	1.199±0.164 <sup>#</sup>	1.133±0.117	1.123±0.100
ED, cm	2.67±0.32	2.72±0.33	2.63±0.35	2.75±0.34 <sup>**, †</sup>	2.77±0.27	2.77±0.31
ACT, cm	0.24±0.03	0.23±0.03 <sup>*</sup>	0.24±0.03	0.24±0.03	0.22±0.02	0.22±0.02
Width, cm	3.15±0.33	3.13±0.23	3.11±0.34	3.22±0.31 <sup>**, †</sup>	3.21±0.27	3.20±0.29
CSA, cm <sup>2</sup>	3.66±0.71	3.51±0.28	3.59±0.49	3.63±0.49	3.47±0.49	3.41±0.40
CSMI, cm <sup>4</sup>	2.94±1.32	2.65±0.64	2.73±1.14	2.86±1.09 <sup>*, #</sup>	2.81±0.83	2.78±0.72
Z, cm <sup>3</sup>	1.77±0.58	1.58±0.30	1.61±0.52	1.66±0.54 <sup>*, #</sup>	1.64±0.35	1.61±0.29
BR	6.85±1.27	7.54±1.85	8.12±1.52	7.38±1.46 <sup>*, #</sup>	7.83±1.12	7.89±1.34
<b>IT</b>						
BMD, g.cm <sup>-2</sup>	1.100±0.062	1.081±0.090	1.143±0.074	1.161±0.082 <sup>*, #</sup>	1.107±0.129	1.112±0.131
ED, cm	4.60±0.35	4.69±0.37	4.40±0.83	4.40±0.57	4.47±0.60	4.51±0.66
ACT, cm	0.48±0.04	0.45±0.05 <sup>*</sup>	0.48±0.12	0.49±0.13 <sup>#</sup>	0.47±0.06	0.47±0.06
Width, cm	5.56±0.37	5.57±0.38	5.35±0.76	5.39±0.59	5.43±0.57	5.43±0.64
CSA, cm <sup>2</sup>	5.83±0.53	5.80±0.61	5.88±1.75	5.86±1.57	5.69±0.70	5.74±0.73
CSMI, cm <sup>4</sup>	14.99±2.96	15.09±4.1	13.97±5.86	14.10±6.38	15.25±5.22	15.40±5.11
Z, cm <sup>3</sup>	4.93±0.75	4.93±0.91	4.71±1.13	4.95±1.18 <sup>*</sup>	4.95±1.13	5.13±1.19
BR	6.28±0.67	6.88±0.90 <sup>**</sup>	6.47±1.76	6.21±1.74 <sup>*, #</sup>	6.42±1.19	6.39±1.11
<b>FS</b>						
BMD, g.cm <sup>-2</sup>	1.507±0.103	1.497±0.107	1.492±0.187	1.544±0.120 <sup>**, #</sup>	1.486±0.187	1.551±0.169 <sup>**, #</sup>
ED, cm	1.81±0.24	1.87±0.35	1.79±0.41	1.79±0.47	1.84±0.40	1.89±0.63
ACT, cm	0.57±0.06	0.56±0.06	0.55±0.11	0.61±0.11 <sup>***, ###</sup>	0.57±0.11	0.64±0.26
Width, cm	2.95±0.19	3.00±0.39	2.96±0.39	2.95±0.39 <sup>*</sup>	2.97±0.26	2.97±0.26
CSA, cm <sup>2</sup>	4.23±0.40	4.29±0.34	4.15±1.04	4.35±0.97 <sup>***, #</sup>	4.19±0.57	4.37±0.56 <sup>***</sup>
CSMI, cm <sup>4</sup>	3.49±0.80	3.53±0.6	3.51±1.45	3.78±1.47 <sup>*</sup>	3.43±0.95	3.57±1.07 <sup>*</sup>
Z, cm <sup>3</sup>	2.24±0.38	2.27±0.41	2.28±0.39	2.35±0.76	2.21±0.43	2.30±0.49
BR	2.74±0.34	3.92±0.44 <sup>*</sup>	2.85±0.62	2.59±0.63 <sup>***, ###</sup>	2.82±1.08	2.62±0.49 <sup>*, ##</sup>

ACT, average cortical thickness; BMC, bone mineral content; BMD, bone mineral density; BR, buckling ratio; CSA, cross-sectional area; CSMI, cross-sectional moment of inertia; ED, endocortical diameter; FS, femoral shaft; IT, intertrochanteric region; NN, narrow neck; TBLH, total body less head; TBS, trabecular bone score; Z, section modulus. Intra-group interactions (time effects): \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ . Time  $\times$  group interactions. Significant difference with CTR: #  $p < 0.05$ ; ##  $p < 0.01$ ; ###  $p < 0.001$ . Significant difference between HIIT and MICT: †  $p < 0.05$ .

for HIIT and  $p < 0.01$  for MICT), whereas they were not modified in the CTR group ( $p = 0.708$  and  $p = 0.448$ , respectively). The time  $\times$  group interactions were significant between HIIT and CTR ( $p < 0.05$ ). TBS increased at T1 versus T0 in both training groups ( $p < 0.01$  for HIIT and  $p < 0.05$  for MICT), whereas it was not modified in

the CTR group ( $p = 0.113$ ). The time  $\times$  group interactions were significant between HIIT and CTR ( $p < 0.01$ ) and MICT and CTR ( $p < 0.05$ ).

Hip region: Hip BMD and BMC increased significantly at T1 versus T0 in both HIIT ( $p < 0.001$  and  $p < 0.01$ , respectively) and MICT groups ( $p < 0.01$  and  $p < 0.05$ ,

respectively), whereas they were not modified in the CTR group ( $p = 0.315$  and  $p = 0.364$ , respectively). The time  $\times$  group interactions were significant between HIIT and CTR ( $p < 0.01$  and  $p < 0.05$ , respectively) and MICT and CTR ( $p < 0.05$ ).

#### *Hip Subregions*

At the NN, BMD decreased at T1 versus T0 only in the CTR group ( $p < 0.05$ ) (significant time  $\times$  group interaction between HIIT and CTR [ $p < 0.05$ ]). Endocortical diameter and width increased only in the HIIT group ( $p < 0.01$ ), with significant time  $\times$  group interactions between HIIT and MICT ( $p < 0.05$ ). CSMI and Z increased only in the HIIT group ( $p < 0.05$ ), with significant time  $\times$  group interactions between HIIT and CTR ( $p < 0.05$ ). The BR decreased only in the HIIT group ( $p < 0.05$ ), with a significant time  $\times$  group interaction between HIIT and CTR ( $p < 0.05$ ).

At the IT, BMD increased at T1 versus T0 only in the HIIT group ( $p < 0.05$ ), with a significant time  $\times$  group interaction between HIIT and CTR ( $p < 0.05$ ). ACT decreased only in the CTR group ( $p < 0.05$ ) (significant time  $\times$  group interaction between HIIT and CTR [ $p < 0.05$ ]). Z increased only in the HIIT group ( $p < 0.05$ ). The BR decreased in the HIIT group ( $p < 0.05$ ), whereas it increased in the CTR group ( $p < 0.01$ ) (significant time  $\times$  group interactions between HIIT and CTR [ $p < 0.05$ ]).

At the FS, BMD ( $p < 0.01$ ) and CSA ( $p < 0.001$ ) increased at T1 versus T0 in both training groups. For BMD, significant time  $\times$  group interactions were found between HIIT and CTR ( $p < 0.05$ ) and MICT and CTR ( $p < 0.05$ ). For CSA, a significant time  $\times$  group interaction was only found between HIIT and CTR ( $p < 0.05$ ). ACT increased at T1 versus T0 only in the HIIT group ( $p < 0.001$ ), with a significant time  $\times$  group interaction between HIIT and CTR ( $p < 0.001$ ). The BR decreased in the HIIT ( $p < 0.001$ ) and the MICT ( $p < 0.05$ ) groups, whereas it increased in the CTR group ( $p < 0.05$ ). Time  $\times$  group interactions were significant between HIIT and CTR ( $p < 0.001$ ) and MICT and CTR ( $p < 0.01$ ).

## **Discussion**

Multidisciplinary interventions based on HIIT training are effective in improving body fat, cardiorespiratory fitness, and cardiometabolic risk in adolescents with obesity [23, 24, 32, 33]. However, the effects of HIIT on bone parameters were largely unknown. The present study aimed to compare bone density, geometry, and strength

responses to HIIT versus MICT cycling training in adolescents with obesity. To our knowledge, the present study is the first to assess the effects of HIIT on bone parameters. Taken together, our results showed that a 16-week multidisciplinary weight loss program based on HIIT cycling training would improve multisite (whole body, lumbar, and hip) BMC and BMD and several geometric and strength (biomechanics) hip parameters measured by DXA, to a greater extent or at least similar, in comparison with MICT, while preventing the increased BR (risk of fracture) usually observed in adolescents with obesity.

Whole DXA bone parameters measured at baseline in both training and CTR groups are fully in line with previous studies in similar populations [17, 28], in particular with Chaplais et al. [28] who reported lower quantitative bone health (measured using DXA) in adolescents with obesity versus maturation-matched lean adolescents, supporting the literature demonstrating that fat accumulation compromises bone quality [2, 5, 7]. The significant multisite (whole-body, lumbar spine, and hip) BMC and BMD improvements after both HIIT and MICT showed that the training interventions induced bone adaptations to physiological loads (being peak forces caused by muscles), which is in line with previous interventional studies showing that exercise training can increase bone synthesis in children and adolescents with obesity during weight loss interventions [16, 17, 19, 20, 34, 35]. Thus, both training protocols improved BMI and FM (accompanied by a slight decrease in LM) and stimulated osteogenesis relative to body mass and FM location, which is vital during periods of growth [36, 37]. Moreover, both training protocols improved TBS, a predictor of trabecular bone microarchitecture between L1–L4 [38]. TBS is negatively correlated with BMI in adults [39–41] and in young adults [42], but may differ in older adults with obesity [43].

The greater improvements of whole-body BMC in the HIIT group in comparison with the MICT group may be due to the higher magnitude loading linked with the higher intensity of exercise sessions, inducing higher mechanical constraints and higher tendon pulls. Indeed, the osteogenic index of an exercise relies on its intensity and can be calculated as the magnitude of load (or stress) multiplied by the loading frequency [44]. This is in line with previous studies suggesting that resistance training or high loading exercise modalities are of particular importance for maintaining bone health in adolescents with obesity [16, 17]. Moreover, the progressive increase in intensity during the HIIT training protocol (75% at baseline to 90% VO<sub>2</sub>peak) would prevent the accommodation of

bone cells to mechanical load, which constitutes another common rule that governs bone adaptation [14]. The accommodation of bone cells has thus been recognized as the main limitation of some training programmes that include routine or monotonous loading signals, such as MICT.

Moreover, our results clearly demonstrate that HIIT reduces the risk of fracture, as shown by the decreases in the BR observed at the NN, the IT, and the FS after HIIT training, while by contrast, MICT seems to decrease the BR only at the FS. The increases in the BR observed in the CTR group have previously been observed in adolescents with obesity at the end of classical multidisciplinary interventions, with BR scores approaching the threshold of fracture prediction [28]. In a previous study carried out in adults with obesity, the increased BR at the NN, IT, and FS was reported after diet-based weight loss, whereas the addition of resistance exercises had a preventative effect [45]. While the fracture risk in adolescents who lose weight is of major concern [3, 4, 10], the present results thus support that bone quantity and quality can be improved with HIIT training during weight loss programs in adolescents with obesity. Moreover, HIIT would also increase ACT or prevent the reduction observed in the CTR group at the NN and the IT. These BR and ACT improvements following HIIT training are of clinical importance since these bone parameters are the 2 most strongly associated with the incidence of hip fractures independently of BMD [46]. As Z has also been significantly negatively correlated with the risk of fracture, the improvements in Z at the NN and the IT in the HIIT group also constitute additional arguments that strengthen the justification for HIIT when considering bone health [46].

Although this study is the first to investigate the impact of HIIT training on bone response in adolescents, results must be considered in light of some limitations. First, although the presence of a CTR group can be considered as a strength of the present analysis, the relatively small sample sizes have to be considered, as sample size was not initially estimated on bone parameters as a primary outcome. Second, the use of peripheral quantitative computed tomography would have provided additional information relative to bone size, geometry, and quality [47]. While DXA cannot distinguish cortical and trabecular bone and determine volumetric BMD [18], it remains nevertheless the most common noninvasive technique for the assessment of bone health in children and adolescents. The assessment of bone geometry and strength using HSA is useful in order to monitor weight management in adolescents with obesity, susceptible to postural,

balance, and motor deficits and fractures [10, 28]. Furthermore, it would have been relevant to include a follow-up assessment with the aim of exploring whether the observed changes were maintained or not over time following intervention, but this has not been possible for practical reasons. In addition, it would have been interesting to measure the consumption of dairy products, which has been associated with improvements in plasma levels of bone-related biochemical markers in adolescents with obesity following exercise training [48]. Moreover, metabolic (heart rate) or mechanical (speed and load) parameters were not recorded during the training sessions, which would have provided interesting additional information. Finally, our program was only composed of 2 specific sessions per week of HIIT or MICT (in order to match with the clinical possibilities of the medical center), and further studies with higher volumes of trainings should be conducted.

## Conclusion

To conclude, the present study showed that a 16-week multidisciplinary weight loss program based on HIIT cycling induced greater BMI and body composition improvements as well as increases in multisite (whole body, lumbar, and hip) BMC and BMD, and several geometric and strength hip parameters to a greater or similar extent as MICT while decreasing fracture risk. Taken together, all these results strengthen the justification for HIIT modalities as part of weight loss interventions in adolescents with obesity. They support the idea that during weight loss interventions, bone fragility, from a compromised relationship between density, geometry, and strength, might be improved with a progressive increased intensity of cycling training based on HIIT. Considering that HIIT would also induce greater cardiometabolic improvements than MICT [21–24, 27], regulate appetite control [26], and lower the rate of perceived exertion [25, 49] while offering a more enjoyable time efficient modality of practice [50], it would represent an optimal and appropriate training modality for adolescents with obesity to support weight loss while improving bone health.

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## Statement of Ethics

All of the adolescents and their parents provided written informed consent after being fully briefed and advised about the study procedures. This trial was approved by the relevant Ethical Committee (Comité de Protection des Personnes Sud Est VI, AU1178) and is registered with ClinicalTrials.gov (NCT02482220). It was conducted in compliance with the recommendations for good clinical practice and the Declaration of Helsinki.

## Conflict of Interest

The authors have no conflict of interests to declare.

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## Author Contributions

V.J. contributed to formal analysis, investigation, writing – original draft. C.T. contributed to investigation and data curation. O’M.G. contributed to writing – review and validation. L.M. contributed to investigation, methodology, writing – review, and validation. A.F. contributed to investigation, methodology, and data curation. M.M. contributed to investigation, methodology, and data curation. C.C. contributed to investigation. F.D. contributed to conceptualization, investigation, and methodology. Y.B. contributed to investigation and supervision. M.D. contributed to investigation and supervision. D.C. contributed to writing – review, validation, investigation, and methodology. B.P. contributed to data analysis. D.T. contributed to conceptualization, formal analysis, investigation, methodology, writing – review, and validation. All of the authors read and approved this work.

## Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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