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Bone response to eccentric *versus* concentric cycling in adolescents with obesity

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Summary

Objectives: Because adolescents with obesity are susceptible to bone fragility during weight loss (WL), we evaluated the impact of eccentric (ECC) *versus* classical concentric (CON) training at the same oxygen consumption ($\dot{V}O_2$) on bone density, geometry and strength.

Methods: Thirty five adolescents were included into 2 training (CON and ECC cycling) and a control (CTR, without training) groups. Anthropometry, Dual-energy X-ray absorptiometry, hip structural analysis and quantitative bone ultrasound were assessed before and after the 12-week intervention.

Results: The trainings promoted significant improvements in body mass index, total fat (FM) and lean mass (LM), with better improvements for FM and LM in the ECC group ($p < 0.05$). Leg LM percentage increased only in the ECC group ($p < 0.05$). Total body bone mineral content and density increased in both training groups ($p < 0.001$) with significant time x group interactions only between ECC and CTR ($p < 0.05$). Buckling ratio at the intertrochanteric region and femoral shaft increased only in CTR and CON groups ($p < 0.05$). Speeds of sounds at the calcaneum increased only in ECC group ($p < 0.01$).

Conclusions: Bone fragility, from a compromised relationship between density, geometry and strength, might be prevented with the ECC modality.

Keywords: Childhood obesity; Bone mineral density; Bone strength; Eccentric training; Concentric training

1. Introduction

Pediatric obesity is a serious public health challenge [1]. Although excess body weight has traditionally been considered to have a positive effect on bones, this idea has become subject to debate [2–4]. Recent findings indicate that fat accumulation compromises bone mass and quality [5,6], particularly in adolescents with obesity, who show a high propensity to fracture [3,7,8]. Multidisciplinary weight loss (WL) interventions combining nutrition and physical activity are now considered as effective treatment strategies in adolescents with obesity, favoring a decreased body mass index (BMI) and fat mass (FM) [9]. However, WL would also generate a bone breakdown [4,5] related to decreased mechanical loading on the skeleton [5], decreased caloric intake [5] and alter the secretion of some key hormones and peptides involved in bone regulation [6,10]. Indeed, WL would decrease circulating estrogen and other sex hormones and increase sex hormone-binding globulin, which negatively influences bone osteoblastic and osteoclastic activity, directly or indirectly due to increased levels of cytokines (i.e. IL-1, IL-6 and tumor necrosis factor- α). Several other factors would also major bone resorption during WL, such as changes in bone modulating adipokines (leptin, adiponectine, insulin-like growth factor-1), the rise in the Ca-PTH axis and modifications in gut peptides that regulate both satiety and bone metabolism [5].

Such negative bone adaptations to WL reinforce the need to include physical activity in multidisciplinary programs, since it strengthens the bones [11], particularly during adolescence, when the bone's ability to adapt to mechanical loading is the greatest [12]. Based on the need to include physical interventions in WL programs, much research on physical activity has been conducted for the last 10–15 years to identify the best modality. While studies have shown the beneficial effects of interventions including moderate-intensity continuous training, high-intensity interval training, or concurrent-training on both FM and lean mass (LM) [13], their effectiveness on bone adaptations remains uncertain in adolescents with

obesity [14]. Longer interventions using higher exercise intensities and inducing a greater loss of FM and increase in LM would be associated with a trend of improved bone mass [14,15]. Recent studies supporting the mechanostat theory demonstrated that bone fragility might be prevented if LM is maintained [16,17]. LM, rather than FM, is the most important contributor to bone parameters [17]. Compared with aerobic training alone, combined aerobic and resistance training induces a greater gain in bone mineral content (BMC) during WL [18].

Recently, studies have focused on the use of eccentric (ECC) contraction modality, over the common concentric (CON) one, as an efficient and promising anti-obesity strategy for both adults and youths with obesity [19–21]. Muscles generate force by lengthening during ECC contractions or by shortening during CON contractions. For the same oxygen consumption ($\dot{V}O_2$), ECC cycling is characterized by a 3 to 4 times higher mechanical load (i.e. higher force applied on the skeleton) in comparison with CON cycling [20,22]. Our team recently demonstrated that ECC cycling training is two times more efficient than CON cycling training for decreasing whole-body FM and increasing LM in adolescents with obesity and induces greater strength gains and metabolic improvements than CON training performed at the same $\dot{V}O_2$ [20]. Based on the same population and considering the specific mechanical properties of ECC training (higher load developed in ECC for the same $\dot{V}O_2$), it seems relevant to better evaluate the impact of ECC cycling on bone adaptations. Therefore, the present study aimed to determine the impact of ECC cycling *versus* classical CON cycling performed at the same metabolic rate on bone density, geometry, and strength among adolescents with obesity.

2. Material and methods

2.1 Study participants

Thirty five adolescents (Tanner stages 3–4; 50% **females girls**) were included in this study. Patients met the following criteria: (1) 12–16 years old (**Tanner age 3-4**), (2) BMI > 90th

percentile according to the international cut-off points, (3) regular menstruations for females (4) no medication affecting energy metabolism and no regular tobacco or alcohol use; and (5) no contraindication to exercise. All the adolescents underwent a full medical examination. Informed consent was obtained from all individual participants included in the study and their parents. The trial has been conducted according to the Declaration of Helsinki principles, was approved by the relevant ethical committee (Comité de Protection des Personnes Est IV) and is registered with ClinicalTrials.gov (NCT02925572).

2.2 Study design and training program

The adolescents of the training groups were enrolled in a pediatric obesity center (Children Medical Centre for Adolescents with Obesity, La Bourboule, France). They were randomized using random size blocks to the 12-week CON or ECC cycling group. The training intervention was described in detail previously [20]. In brief, it consisted of a 12-week physical activity program with 36 total sessions (3 per week). The training consisted of three phases: i) Phase 1, a 2-week habituation period (i.e. progressive increase in exercise intensity and session time) to protect individuals from delayed-onset muscle soreness; ii) Phase 2 consisted of 40-minute ECC or CON cycling sessions at 50% $\dot{V}O_{2peak}$ for 5 weeks; and iii) Phase 3 consisted of 40-minute sessions with ECC or CON cycling at 70% $\dot{V}O_{2peak}$ for 5 weeks. ECC training was performed on ECC motor-driven ergometers (Cyclus2 Eccentric Recumbent; MSE Medical, France) and CON training on classical CON ergometers (Optibike Med 600; MSE Medical, France). A physical therapist and an exercise physiologist supervised all of the training sessions. The CTR group, which did not perform any physical training during 12 weeks, served as a control to distinguish the influence of growth on bone parameters. It was constituted, for ethical reasons of adolescents who were expecting their admission in the pediatric obesity center. All participants received the same dietary counseling (normo-caloric diet) throughout the 12-week period, without any guidelines for nutritional energy restriction [20].

Anthropometric, body composition, and bone assessments were measured before (T1) and after (T2) the 12-week intervention period.

Two types of bone analyses were conducted: i) dual-energy X-ray absorptiometry (DXA), which is considered as the reference method for assessing bone mineral density (BMD); and ii) quantitative bone ultrasound evaluation at the calcaneum, which was selected as a convenient estimate of bone in children because of the short examination time, easy implementation in routine activities, and absence of harmful effects. This focus on the calcaneum was conducted because of the potential differences between the 2 exercise modalities considering the mechanical constraint applied on the foot pedals and the pulls linked to muscular activity via the Achilles tendon.

2.3 Body composition and bone measurements by DXA

All subjects underwent DXA (Discovery A; Hologic Inc., Bedford, MA, USA) by a trained blinded technician for the assessment of body composition, 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 whole-body and standard body regions [20].

BMD (in g/cm^2) and BMC (in g) were determined at the total body less head (TBLH), lumbar spine (LS, L2-L4) and non-dominant hip. BMD measurements were converted to Z-scores. The TBS, which is related to bone microarchitecture and fracture risk, was calculated using TBS iNsight 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 (in cm^2 ; index of resistance to axial forces), BMD (g/cm^2),

endocortical diameter (in cm), average cortical thickness (in cm), width (in cm), cross-sectional moment of inertia (in cm⁴; estimate of resistance to bending forces in a cross-section), section modulus (Z, cm³; index of bending strength), and buckling ratio (BR; index of susceptibility to cortical buckling under compressive loads) [23]. Higher values are associated with greater predicted femoral strength for all HSA-derived parameters except BR, for which values over 10 are predictive of fracture risk [24].

2.4 Bone measurements by quantitative ultrasound

Broadband ultrasound attenuation (BUA) and speed of sound (SOS) values were measured at the calcaneum of the dominant limb in a circular region of interest using an Achilles Insight+ (Achilles Insight, GE, Lunar Corporation, Madison, WI, USA), a quantitative ultrasound (QUS) imaging device that quickly produces real-time images of the heel bone without transducer movement [25].

2.5 Statistical analysis

Statistical analyses were performed using Stata software (version 13; StataCorp, College Station, TX, USA). The tests were two-sided with a type I error set at 5%. Continuous data are expressed as mean \pm standard deviation according to statistical distribution. Normality was assessed using the Shapiro-Wilk test. Random-effects models for correlated data (bone parameters) were performed to measure time (T1 *versus* T2) and group (ECC, CON and CTR groups) effects and their interaction of time \times group considering intra- and inter-patient variability (subject as random effect). The normality of residuals from these models was studied using the Shapiro-Wilk test. When appropriate, a logarithmic transformation was proposed to achieve normality of the dependent outcome. The relationships between continuous parameters (i.e. variations in weight, LM, FM and bone parameters) were studied by estimating Pearson or Spearman correlation coefficients and applying Sidak's type I error correction due to multiple comparisons.

3. Results

Thirty-four adolescents completed the study, as one adolescent in the ECC group dropped out due to family reasons, resulting in $n = 11$ (6 females girls, 5 males boys) in the ECC group, $n = 12$ in the CON group (6 females girls, 6 males boys) and $n = 11$ in the CTR group (6 females girls, 5 males-boys). The mean patient age was 13.3 ± 1.2 years in the CON group, 13.6 ± 1.3 years in the ECC group and 13.7 ± 1.3 years in the CTR group ($p = 0.49$). The mechanical load were 3.7 times higher in the ECC group compared to the CON group (216.3 ± 70.2 W *versus* 59.2 ± 22.3 W for phase 1 ; 313.3 ± 94.9 W *versus* 82.5 ± 36.0 W for phase 2 $p < 0.001$).

3.1 Anthropometric, body composition and strength parameters

LM percentage and quadriceps strength increased only in the ECC group ($p < 0.05$). The anthropometric, body composition and functional parameters before *versus* after the training program were published elsewhere [20] and are summarized in **Table 1**. BMI decreased significantly at T1 *versus* T0 in both training groups ($p < 0.001$). Whole-body FM percentage decreased significantly at T1 *versus* T0 in both CON ($p < 0.05$) and ECC groups ($p < 0.01$), though to a larger extent in the ECC group (time \times group interaction between ECC and CON, $p = 0 < 0.05$). Whole-body LM percentage increased significantly at T1 *versus* T0 in both CON ($p < 0.05$) and ECC ($p < 0.01$) groups, with a greater increase in the ECC group (time \times group interaction, $p < 0.05$). BMI, whole-body FM and LM percentages were nor modified at T1 *versus* T0 in the CTR group ($p = 0.782$; $p = 0.837$ and $p = 0.925$ respectively). Leg ~~LM percentage and quadriceps strength increased only in the ECC group ($p < 0.05$). The anthropometric, body composition and functional parameters before *versus* after the training program were published elsewhere [20] and are summarized in **Table 1**.~~

3.2 Bone parameters

TBLH BMD and BMC increased significantly at T1 *versus* T0 in both CON and ECC groups ($p < 0.001$) but were not modified significantly in the CTR group ($p = 0.262$ and $p = 0.629$, respectively). The time x group interactions were significant between ECC and CTR ($p < 0.001$ for BMD and $p < 0.01$ for BMC). LS BMD also increased significantly at T1 *versus* T0 in both training groups ($p < 0.05$) whereas it was not modified in the CTR group ($p = 0.723$).

At the NN, BMD decreased at T1 *versus* T0 only in the CTR group ($p < 0.05$), with significant time x group interactions between CTR and CON ($p < 0.05$) and CTR and ECC ($p < 0.05$). ACT decreased only in the CTR group ($p < 0.05$), with a significant time x group interaction between CTR and ECC ($p < 0.05$). At the FS and IT, BR increased significantly in the CTR and in the CON groups ($p < 0.01$ and $p < 0.05$, respectively) whereas it was not modified in the ECC group ($p = 0.380$ and $p = 0.391$, respectively). The time x group interaction was significant between CTR and ECC at the IT ($p < 0.05$).

Bone parameters measured by DXA, including bone density and content, geometric and mechanical properties, are summarized in **Table 2**.

Concerning QUS at the calcaneum, SOS increased from $1581 \pm 52 \text{ s}^{-1}$ at T0 to $1601 \pm 50 \text{ m.s}^{-1}$ at T1 in the ECC group ($p < 0.01$), whereas it did not change significantly in the CON group ($1585 \pm 52 \text{ m.s}^{-1}$ at T0 *versus* $1590 \pm 52 \text{ m.s}^{-1}$ at T1, $p = 0.064$) and in the CTR group ($1568 \pm 44 \text{ m.s}^{-1}$ at T0 *versus* $1569 \pm 47 \text{ m.s}^{-1}$ at T1, $p = 0.948$). BUA was not modified significantly in the CON ($117 \pm 18.6 \text{ dB.MHz}^{-1}$ at T0 *versus* $113 \pm 12.4 \text{ dB.MHz}^{-1}$ at T1, $p = 0.639$), ECC ($122 \pm 20.7 \text{ dB.MHz}^{-1}$ at T0 *versus* $122 \pm 18.7 \text{ dB.MHz}^{-1}$ at T1, $p = 0.830$) and CTR ($123 \pm 12.6 \text{ dB.MHz}^{-1}$ at T0 *versus* $125 \pm 12.5 \text{ dB.MHz}^{-1}$ at T1, $p = 0.805$) groups.

Spearman correlation tests revealed no significant correlations between variations in weight, LM, FM, or bone parameters.

4. Discussion

Although ECC cycling has been recently shown to improve FM and LM to a greater extent than CON cycling performed at the same $\dot{V}O_2$ in adolescents with obesity, its effects on bone parameters remain unknown. Thus, the present study aimed to compare the bone density, geometry, and strength responses to ECC *versus* CON cycling training matched for $\dot{V}O_2$ in adolescents with obesity. Based on the TEXTOO trial, to our knowledge, the present analysis is the first to date to assess the effects of ECC cycling on bone parameters in adolescents with obesity. Our results show that a 12-week ECC cycling program is at least as efficient as classical CON cycling at improving BMC, BMD and several geometric and mechanical hip parameters measured by DXA in adolescents with obesity during a WL program and would prevent the increased BR (risk of fracture) that is usually observed after classical CON training.

Bone parameters measured at T0 in all groups are in line with those recently described by Chaplais et al., who reported using DXA lower quantitative bone health in adolescents with obesity *versus* maturation-matched lean adolescents [23]. This reinforces then the actual literature demonstrating that fat accumulation compromises bone quality [4,5]. The significant increases observed in the training groups for total body BMD and BMC demonstrate the adaptations of bone to physiological loads (being peak forces caused by muscles) and are concordant with those of previous interventional studies showing that physical activity can increase bone synthesis in children [26] and adolescents with obesity during WL programs, particularly if LM is maintained [16–18,22]. Thus, both training methods (ECC and CON) improved FM and LM and maintained sufficient loads to stimulate osteogenesis, which is of high importance since it has been demonstrated that skeletal adaptations may be compromised during growth relative to body mass and FM location [27,28]. The increased intensity of training during the different phases of the present protocol (Phase 1 to 3) may have prevented the accommodation of bone cells, which can be a limitation in some training programs including

only routine loading signals. Indeed, the prevention of the accommodation of bone cells is recognized as a fundamental rule that governs bone adaptations [11].

The osteogenic index of an exercise session, depending on its intensity, can be defined by the loads applied to the bone and calculated as magnitude of load (or stress) multiplied by the loading frequency [29]. Thus, as the mechanical load in the ECC group was 3–4 times higher than in the CON group [20], better improvements of BMD and BMC would have been expected in the ECC group. Nevertheless, time x group interactions were significant between ECC and CTR groups whereas they remain non significant between CON and CTR groups. Interestingly, SOS at the calcaneum, which has significantly been correlated with BMD in adults and adolescents [30,31], increased only in the ECC group. The high mechanical constraint applied on the foot pedals and the high pulls linked to muscular activity via the Achilles tendon during ECC modality would have induced a specific impact on bone mechanical properties measured at the calcaneum. QUS parameters have recently been recognized as added and complementary values to DXA assessments [32]. Thus, the results of the present study remain concordant with those of a previous trial suggesting that resistance training combined with aerobic training would induce greater bone improvements than aerobic training alone [18]. Nevertheless, despite the high load developed during ECC cycling, weight-bearing ECC exercise modalities (such as downhill running), which generate high impacts, may have a greater osteogenic potential. Indeed, a recent randomized trial performed in young rats compared a CON uphill running group with two ECC downhill running groups, one training at the same mechanic rate (same slope in both CON and ECC groups but lower $\dot{V}O_2$ in the ECC group) and one training at the same metabolic rate (same $\dot{V}O_2$ in both CON and ECC groups but higher slope in the ECC group), and a control group (without training), on femoral BMD (30). Although they also failed to show any significant difference between the ECC and CON modalities, the CON group showed a significant increase in BMD only on proximal femur, whereas the two ECC

groups showed significant improvements in total femoral BMD, with larger improvements (on both epiphysis and diaphysis) in the ECC group trained with the greater downhill slope [33].

However, while the fracture risk in adolescents who lose weight is of major concern [2,3,7], ECC training seems to prevent the increase in BR observed in the CTR and the CON training. Moreover, it would prevent the decreased ACT observed in the CTR group at the NN. The increases in BR have previously been observed in adolescents with obesity at the end of classical multidisciplinary interventions, with BR scores approaching the threshold of fracture prediction, particularly at the NN [23]. Our results are also in line with those of a previous trial performed in older adults with obesity, showing increased BR at the NN, IT, and FS in a diet-based WL group, while the increased BR was prevented in the diet plus exercise WL intervention, which included resistance exercises [34]. BR stabilization in the ECC group is of clinical importance since, with ACT, it is the parameter that is the most associated with the incidence of hip fractures independently of BMD [35]. The present results support that bone quality can be preserved with ECC training during WL programs in adolescents with obesity.

Although this study is the first to question the impact of ECC training on bone adaptation in adolescents, its results must be considered in light of some limitations. The first limitation is its relatively small sample size, as it was initially estimated based on body composition parameters that required 10–15 individuals per group [20]. Other methods such as peripheral quantitative computed tomography may have provided important information on bone size, geometry, and quality [36]. Nevertheless, despite its inability to distinguish trabecular and cortical bone and determine volumetric BMD [15], DXA remains the most common non-invasive technique for assessing pediatric bone health. The clinical assessment of bone geometry and microstructure using HSA can be helpful for monitoring weight management in adolescents with obesity [23], who are susceptible to postural, balance, motor disturbances and fractures [7]. It would have also been interesting to include a follow-up assessment to analyze

whether the observed changes are maintained over time after the training programs, which has not been possible for practical reasons. Furthermore, it would have been relevant to assess daily energy intake, in particular concerning dairy products, which consumption has recently been associated with beneficial changes in circulating levels of bone-related biochemical markers in adolescents with obesity following an exercise training [37]. It would have also been relevant to determine whether the trajectory of change in bone parameters was influenced by the different 3 phases of exercise intensity, which has not been possible in the present study for practical reasons.

ECC cycling training induces at least similar improvements in bone density and content and several geometric and mechanical hip parameters compared to CON cycling training performed at the same metabolic rate in adolescents with obesity but may prevent some alterations of bone resistance observed during WL interventions based on classical CON cycling training. Thus, the present results support the idea that bone fragility during WL, from a compromised relationship between density, geometry, and strength, might be prevented with an increased gradual intensity cycling training based on ECC modality. Thus, considering that ECC cycling training features greater adiposity reductions and additional beneficial effects on muscle mass, muscle strength, and metabolic risk parameters compared with CON cycling training [20], it would represent an optimal and appropriate training modality for patients with obesity to prolong WL while maintaining bone resistance. To improve future exercise prescriptions, larger interventional studies should investigate the impact of ECC and CON cycling programs on bone parameters using standardized experimental conditions of power output (same $\dot{V}O_2$ and mechanical power). The potential beneficial effect of ECC training performed with the same mechanical load but lower $\dot{V}O_2$ than CON training would be suitable for various chronic pathologies resulting in cardiac, respiratory, or muscular limitations to their exercise capacities. Moreover, whether other ECC training modalities such as weight bearing,

which can be obtained by descending stairs or walking downhill, would have greater effects on bone density, geometry, and strength, remains unknown.

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Table 1: Anthropometric, body composition and strength parameters before (T0) *versus* after (T1) the 12-week intervention for the control (CTR), the concentric (CON) and the eccentric (ECC) groups of adolescents with obesity (n = 34; mean \pm SD)

	CTR (n = 11)		CON (n = 12)		ECC (n = 11)	
	T1	T2	T1	T2	T1	T2
Weight (kg)	85.3 \pm 16	86.2 \pm 17	76.6 \pm 12	74 \pm 11 *	82.7 \pm 17	79 \pm 16 *
Height (cm)	165.8 \pm 7.2	166.9 \pm 6.8 *	159.6 \pm 7.7	161.5 \pm 7.5 *	163.4 \pm 7.2	164.5 \pm 7.6 *
BMI (kg.m ⁻²)	30.8 \pm 4.8	30.9 \pm 4.9	30.0 \pm 3.5	28.4 \pm 3.7 *†	30.8 \pm 4.9	29.0 \pm 4.5 *†
Whole body lean mass (kg)	52.1 \pm 9.2	53.2 \pm 9.2 *	50.3 \pm 8.7	49.3 \pm 8.5 *†	55.2 \pm 10.3	54.6 \pm 10.6 †
Whole body lean mass (%)	65.6 \pm 4.8	65.7 \pm 6.0	65.6 \pm 4.8	66.6 \pm 6.0 *†	67.2 \pm 4.8	69.7 \pm 6.3 *†#
Whole body fat (kg)	33.4 \pm 8.1	34.2 \pm 8.5 *	24.4 \pm 5.7	22.8 \pm 6.4 *†	25.5 \pm 8.3	22.1 \pm 8.2 *†
Whole body fat (%)	37.7 \pm 3.4	37.7 \pm 3.6	31.8 \pm 5.0	30.7 \pm 6.3 *†	30.3 \pm 5.1	27.5 \pm 6.6 *†#
Leg lean mass (kg)	18.4 \pm 3.0	18.9 \pm 3.1	18.4 \pm 3.8	17.8 \pm 3.9 *†	19.7 \pm 4.5	19.9 \pm 4.5 #
Leg lean mass (%)	43.3 \pm 4.7	41.5 \pm 3.3	61.5 \pm 5.8	60.7 \pm 7.1	64.5 \pm 5.5	66.4 \pm 6.5 *†#
Leg fat mass (kg)	14.3 \pm 3.2	14.3 \pm 3.2	10.8 \pm 3.3	10.8 \pm 3.6	10.2 \pm 3.7	9.3 \pm 3.5 *†#
Leg fat mass (%)	55.8 \pm 4.7	57.6 \pm 5.2	35.7 \pm 6.2	36.4 \pm 7.5	32.6 \pm 5.8	30.6 \pm 6.8 *†#
Isometric peak torque	155.8 \pm 35	160.0 \pm 32	150.3 \pm 29.7	156.3 \pm 31.1	147.1 \pm 33.9	181.5 \pm 17.8 *†#

BMI, body mass index ; T1, baseline ; T2, after the 12-week intervention. $\dot{V}O_2$, oxygen consumption. Intra-group interaction (time effect): *p <0.05. Time x group interactions : † p <0.05, significant difference with CTRL ; # p <0.05, significant difference with CON

Table 2: Bone parameters measured by DXA before *versus* after the 12-week intervention for the control (CTR), the concentric (CON) and the eccentric (ECC) groups of adolescents with obesity (n = 34; mean ± SD)

		CTR		CON		ECC	
		T1	T2	T1	T2	T1	T2
TBLH	BMD (g.cm ⁻²)	1.066 ± 0.75	1.079 ± 0.79	1.002 ± 0.102	1.067 ± 0.95 *	1.040 ± 0.1218	1.11 ± 0.12 **†
	BMC (g)	2132 ± 290	2146 ± 285	1920 ± 399	1982 ± 353 *	2052 ± 447	2159 ± 423 **†
Lumbar spine	BMD (g.cm ⁻²)	0.951 ± 0.139	0.955 ± 0.155	0.880 ± 0.130	0.902 ± 0.123 *	0.930 ± 0.130	0.960 ± 0.122 *
	TBS	1.28 ± 0.17	1.26 ± 0.16	1.27 ± 0.08	1.29 ± 0.09	1.30 ± 0.12	1.33 ± 0.12
	BMC (g)	51.23 ± 13.05	51.73 ± 11.39	44.80 ± 11.35	46.84 ± 11.01 *	52.61 ± 7.38	53.53 ± 10.20
Hip	BMD (g.cm ⁻²)	1.037 ± 0.123	1.009 ± 0.074	0.967 ± 0.124	0.962 ± 0.121	1.025 ± 0.174	1.025 ± 0.163
	BMC (g)	33.7 ± 5.6	33.4 ± 4.0	32.7 ± 6.9	32.2 ± 6.9	35.1 ± 8.4	34.8 ± 7.1
NN	BMD (g.cm ⁻²)	1.218 ± 0.141	1.166 ± 0.123 *	1.070 ± 0.191	1.066 ± 0.164 †	1.145 ± 0.212	1.151 ± 0.196 †
	ED (cm)	2.66 ± 0.32	2.72 ± 0.33	2.69 ± 0.34	2.78 ± 0.42	2.70 ± 0.25	2.74 ± 0.27
	ACT (cm)	0.24 ± 0.03	0.22 ± 0.03 *	0.21 ± 0.04	0.21 ± 0.03	0.22 ± 0.05	0.23 ± 0.04 †
	WIDTH (cm)	3.15 ± 0.32	3.14 ± 0.27	3.11 ± 0.36	3.19 ± 0.44	3.16 ± 0.24	3.18 ± 0.24
	CSA (cm ²)	3.66 ± 0.71	3.51 ± 0.28	3.18 ± 0.80	3.26 ± 0.80	3.44 ± 0.69	3.48 ± 0.59
	CSMI (cm ⁴)	2.93 ± 1.32	2.65 ± 0.64	2.47 ± 1.22	2.81 ± 1.81	2.70 ± 0.78	2.83 ± 0.72
	Z (cm ³)	1.76 ± 0.58	1.59 ± 0.30	1.47 ± 0.54	1.59 ± 0.69 †	1.63 ± 0.38	1.69 ± 0.35 †
	BR	6.85 ± 1.27	7.54 ± 1.85	8.03 ± 1.47	8.38 ± 1.51	7.60 ± 1.56	7.61 ± 1.68
IT	BMD (g.cm ⁻²)	1.100 ± 0.162	1.081 ± 0.090	1.031 ± 0.163	1.028 ± 0.154	1.130 ± 0.185	1.119 ± 0.204
	ED (cm)	4.59 ± 0.35	4.68 ± 0.33	4.25 ± 0.50	4.58 ± 0.78 *	4.48 ± 0.38	4.62 ± 0.40 *
	ACT (cm)	0.48 ± 0.04	0.46 ± 0.05 *	0.45 ± 0.08	0.45 ± 0.09	0.48 ± 0.09	0.47 ± 0.08
	WIDTH (cm)	5.56 ± 0.37	5.60 ± 0.32	5.14 ± 0.57	5.28 ± 0.86 *	5.44 ± 0.37	5.56 ± 0.31 *
	CSA (cm ²)	5.83 ± 0.53	5.80 ± 0.61	5.08 ± 1.12	5.38 ± 1.23	5.85 ± 1.02	5.91 ± 1.01
	CSMI (cm ⁴)	14.9 ± 2.96	15.3 ± 4.0	14.60 ± 4.74	14.02 ± 7.33	15.16 ± 4.02	15.78 ± 3.10
	Z (cm ³)	4.93 ± 0.75	4.93 ± 0.91	4.08 ± 1.34	4.44 ± 1.74	5.06 ± 1.09	5.18 ± 0.94
	BR	6.28 ± 0.67	6.88 ± 0.90*	6.33 ± 0.73	6.58 ± 0.92 *	6.56 ± 1.62	6.57 ± 1.45 †
FS	BMD (g.cm ⁻²)	1.507 ± 0.102	1.497 ± 0.107	1.542 ± 0.158	1.494 ± 0.200	1.573 ± 0.304	1.551 ± 0.269

ED (cm)	1.81 ± 0.24	1.89 ± 0.33	1.56 ± 0.25	1.74 ± 0.31 *	1.78 ± 0.56	1.89 ± 0.40 *
ACT (cm)	0.57 ± 0.06	0.56 ± 0.06	0.60 ± 0.08	0.57 ± 0.10	0.61 ± 0.16	0.59 ± 0.13
WIDTH (cm)	2.94 ± 0.19	2.99 ± 0.33	2.77 ± 0.23	2.89 ± 0.20 *	2.97 ± 0.26	3.07 ± 0.24 *
CSA (cm ²)	4.23 ± 0.40	4.27 ± 0.30	4.08 ± 0.55	4.12 ± 0.64	4.48 ± 0.84	4.53 ± 0.82
CSMI (cm ⁴)	3.49 ± 0.80	3.53 ± 0.63	2.99 ± 0.92	3.31 ± 0.87 *	3.65 ± 0.86	3.99 ± 0.88 *
Z (cm ³)	2.28 ± 0.35	2.34 ± 0.43	2.07 ± 0.48	2.18 ± 0.44 *	2.34 ± 0.45	2.48 ± 0.43 *
BR	2.74 ± 0.34	3.06 ± 0.29 *	2.39 ± 0.32	2.71 ± 0.51 *	2.76 ± 1.08	2.86 ± 0.82

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 interaction (time effect): *p <0.05. Time x group interaction : † p <0.05, significant difference with CTRL