

# Bone mineral density in well-trained females with different hormonal profiles

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## Summary

**Objective:** The association between sex hormones and bone mineral density (BMD) has been studied in sedentary women, whereas only few studies have evaluated trained females. Therefore, the aim of this study was to assess the influence of sex hormones on BMD in well-trained females with different hormonal profiles: eumenorrheic females, oral contraceptive (OC) users and postmenopausal women. The secondary purpose was to determine if maximal oxygen consumption ( $\dot{V}O_{2max}$ ) or maximal back squat strength (1RM) could be good predictors of BMD in this population.

**Methods:** Sixty-eight eumenorrheic, forty-one monophasic-OC users and sixteen postmenopausal well-trained females participated in this study. A Dual-energy X-ray Absorptiometry scan (DXA), a basal blood sample and a maximal back squat and/or a maximal treadmill test were performed. In order to measure all volunteers under similar hormonal conditions (low sex hormone levels), all tests were carried out during the early follicular phase for the eumenorrheic females and in the withdrawal phase for the OC group.

**Results:** One way ANCOVA reported lower values of BMD in postmenopausal ( $1.13 \pm 0.07 \text{ g/cm}^2$ ) than in eumenorrheic ( $1.19 \pm 0.08 \text{ g/cm}^2$ ) ( $p=0.003$ ) and OC users ( $1.17 \pm 0.07 \text{ g/cm}^2$ ) ( $p=0.030$ ). Pearson's correlation showed a positive relationship between BMD and 1RM ( $p<0.001$ ), but not with  $\dot{V}O_{2max}$ .

**Conclusions:** Lower BMD has been reported in postmenopausal women compared to both, eumenorrheic females and OC users. BMD loss after menopause seems to be not fully compensated by exercise, but this could effectively mitigate it. Moreover, 1RM back squat reported a slight association to BMD. Hence, strength training may be the best choice to prevent BMD loss.

## Key words:

17 $\beta$ -estradiol. Progesterone. Oral contraception. Exercise. Postmenopause. Eumenorrheic.

## Densidad mineral ósea en mujeres entrenadas con diferente perfil hormonal

### Resumen

**Objetivo:** La asociación entre hormonas sexuales y densidad mineral ósea (DMO) ha sido bastante estudiada en mujeres sedentarias, pero no en mujeres entrenadas. Por tanto, el objetivo de este estudio fue analizar la influencia de las hormonas sexuales en la DMO de deportistas con diferentes perfiles hormonales: mujeres eumenorreicas, usuarias de la píldora anticonceptiva y mujeres postmenopáusicas. El segundo objetivo fue analizar si el consumo máximo de oxígeno ( $\dot{V}O_{2max}$ ) o la sentadilla trasera (1RM) serían buenos predictores de DMO en dicha población.

**Metodología:** Sesenta y seis mujeres eumenorreicas, cuarenta y una usuaria de píldora monofásica y dieciséis mujeres postmenopáusicas bien entrenadas participaron en el estudio. Una densitometría ósea (DXA), una analítica basal y una prueba de esfuerzo y/o de 1RM en sentadilla trasera fueron llevados a cabo. Con el objetivo de que todas las voluntarias fueran medidas bajo las mismas condiciones (bajos niveles de hormonas sexuales), todas las pruebas fueron realizadas en la fase folicular temprana para las mujeres eumenorreicas y en la fase no hormonal para las usuarias de píldora.

**Resultados:** ANCOVA de una vía mostró valores de DMO más bajos en mujeres postmenopáusicas ( $1,13 \pm 0,07 \text{ g/cm}^2$ ) comparado con las eumenorreicas ( $1,19 \pm 0,08 \text{ g/cm}^2$ ) ( $p=0,003$ ) y las usuarias de píldora ( $1,17 \pm 0,07 \text{ g/cm}^2$ ) ( $p=0,030$ ). La correlación de Pearson mostró una relación positiva entre DMO y sentadilla ( $p<0,001$ ), pero no mostró asociación con el  $\dot{V}O_{2max}$ .

**Conclusión:** Las mujeres postmenopáusicas presentan valores de DMO más bajo que las mujeres eumenorreicas y las usuarias de píldora. El descenso de DMO tras la menopausia parece no ser completamente compensado por la práctica de actividad física, aunque ésta puede atenuar ese descenso. Además, la sentadilla mostró una ligera asociación positiva con la DMO, por lo que el entrenamiento de fuerza podría ser la mejor opción para prevenir el descenso de DMO.

## Palabras clave:

17 $\beta$ -estradiol. Progesterona. Píldora anticonceptiva. Ejercicio. Postmenopausia. Eumenorreica.

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## Introduction

Osteoporosis is a skeletal disease represented by low bone mineral density (BMD) due to an imbalance between rates of bone formation and bone resorption. BMD homeostasis depends on two bone cells: osteoblasts (which stimulate bone formation) and osteoclasts (which stimulate bone resorption)<sup>1</sup>. Osteoclasts also produce a glycoprotein called sclerostin, which inhibits bone formation<sup>2-4</sup>. The activity of these two cells is affected by many factors such as pregnancies, tobacco, calcium intake, 17 $\beta$ -estradiol (E2) levels, age, oral contraceptive (OC) use and physical activity<sup>5</sup>.

Sex hormones, specifically E2, play a key role in bone growth. These sex hormones are essential for the maintenance of bone tissue, since E2 decrease osteoclasts formation and generation as well as stimulate their apoptosis<sup>6-9</sup>. In short, E2 suppress bone resorption and the production of sclerostin by inhibiting the osteoclasts activity. Moving on to the osteoblasts, in the last years some studies have proved the positive effect E2 has over these cells. It seems that these sex hormones stimulate osteoblasts activity, encouraging bone formation<sup>10-12</sup>. Although the role of the progesterone on BMD metabolism is still unclear<sup>13</sup>, it seems to have, together with E2, complementary bone action such as preserving peak bone mass and preventing pre- and perimenopausal bone loss<sup>14</sup>. Despite osteoporosis can also occur in young individuals, is most common in elderly population<sup>5</sup>, mainly due to the loss of the ovarian function and the decrease in sex hormones<sup>1</sup>. The drop in E2 produces an imbalance in bone formation and resorption, accelerating bone loss during the first years of the menopause<sup>15</sup>.

Furthermore, the use of OC pills has been widespread among females in the last few years, inducing a reduction of endogenous hormones production in this population. Depending on the dosages of exogenous sex hormones (ethinyl estradiol and progestin) presented in the contraceptive formulations, bone tissue metabolism might be affected<sup>16</sup>. Studies related to OC and BMD are still inconclusive possibly because of the differences in studies design, formulations and time of use of OC, different methods for measuring BMD and population characteristics<sup>16</sup>.

Exercise is advocated to be one of the best tools to increase bone mass and prevent its loss in elderly<sup>17,18</sup>. Physical and functional performance has been positive correlated with BMD as well as with the maximal oxygen consumption ( $\dot{V}O_{2max}$ ) and strength<sup>19-23</sup>, hence BMD may be associated with these two performance variables. Hence, it seems that increasing bone mass before the postmenopause it's a good way to prevent osteoporosis in elderly females<sup>24</sup>. In fact, an increase of 10% of bone tissue during the adulthood may reduce fracture risk in half in the future<sup>25</sup>.

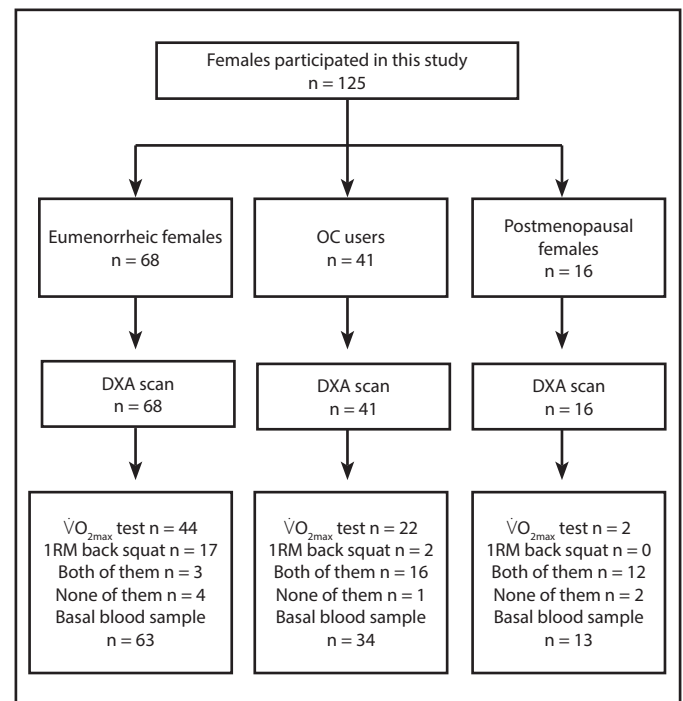
Taking into account all the data aforementioned, we hypothesized that, in active population, OC users may have lower values of BMD regarding eumenorrheic females whereas postmenopausal athletes might have similar values of BMD to eumenorrheic. Thus, the aim of this study was to analyse the influence of sex hormone concentration on BMD in female athletes, comparing three different hormonal profiles: eumenorrheic, monophasic OC users and postmenopausal female athletes. Furthermore, a secondary objective of the present study was to determine if  $\dot{V}O_{2max}$  and maximal squat strength are good predictors of BMD in this population.

## Material and method

### Participants

Sixty-eight eumenorrheic females (26-32 days cycles length), forty-one low dose monophasic OC users (4.13 $\pm$ 3.83 years intaking them) and sixteen postmenopausal females (at least one year without menstruation) participated in this study. Volunteers characteristics are shown in Table 1 and the flow chart for participation is shown in Figure 1. At the start of the data collection, all participants conducted a questionnaire gathering information about training status, health conditions, dietary supplements consumption and type of OC pills when appropriate. Brands and formulation of OC pills used were: Cecilia (n=3): ethinyl estradiol 0.03 mg and dienogest 2 mg; Drosure (n=2): ethinyl estradiol 0.03 mg and drospirenone 3 mg; Yasmin (n=9): ethinyl estradiol 0.03 mg and drospirenone 3 mg; Loette (n=4): ethinyl estradiol 0.02 mg and levonorgestrel 0.1 mg; Levobel (n=2): ethinyl estradiol 0.02 and levonorgestrel 0.1; Diane (n=4): ethinyl estradiol 0.035 mg and cyproterone 2 mg; Edelsin (n=1): ethinyl estradiol 0.035 and Norgestimate 0.25 mg; Drosbelallex (n=2): ethinyl estradiol 0.02 mg and Drospirenone 3 mg; Melodene (n=2): ethinyl estradiol 0.015 mg and gestodene 0.06 mg; Linelle (n=3): ethinyl estradiol 0.02 mg and levonorgestrel 0.1 mg; Stada (n=1): ethinyl estradiol 0.02 mg and drospirenone 3 mg; Sibilla (n=3): ethinyl estradiol 0.03 mg and dienogest 2 mg. Thereby, exogenous sex hormones concentration mean for the OC group was 0.03 $\pm$ 0.01 mg/day of ethinyl estradiol and 1.79 $\pm$ 1.28 mg/day of progestin. All of them were well-trained in endurance and/or in strength training (1.31 $\pm$ 0.41 hours per session, 3.9 $\pm$ 1.1 sessions per week with 7.65 $\pm$ 5.15 years of

Figure 1. Flow chart with the sample we had for each test.



OC: oral contraceptive; DXA: Dual-energy X-ray Absorptiometry scan;  $\dot{V}O_{2max}$ : maximal oxygen consumption; 1RM back squat: back squat maximal strength.