Testosterone secretion in elite adolescent swimmers does not modify bone mass acquisition: a 1-year follow-up study

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Objective: To investigate whether high plasma testosterone (T) levels affect areal bone mineral density (aBMD), bone geometry, and bone remodeling in young elite female swimmers (SW).
Design: Cross-sectional and 1-year follow-up study.
Setting: Pediatric endocrinology and gynecology units.
Participant(s): Twenty-five SW and 21 control subjects (CON) with breast stages IV or V (mean age 15.3 ± 1.3 y).
Intervention(s): None.
Main Outcome Measure(s): Clinical and biologic parameters, aBMD, and bone geometry.
Result(s): Two groups of SW were constituted on the basis of total T level. High T level SW (HSW; n = 15) presented higher T than SW with normal T (NSW; n = 10) and CON (0.63 ± 0.17; 0.36 ± 0.07, and 0.38 ± 0.14 ng/mL, respectively). The SHBG level (62.1 ± 18.7 vs. 43.3 ± 19.8 nmol/L) and the LH/FSH ratio (1.7 ± 1.1 vs. 0.9 ± 0.5) were higher, and menstrual disorders (60% vs. 23.8%) were more frequent in HSW than CON, and no difference was observed between the three groups for other sex hormones and insulin-like growth factor (IGF) 1 or IGF-binding protein 3. SW presented lower fat mass in the whole body and higher lean mass in the upper limbs only. aBMD was only modestly increased in the upper limbs in the SW groups, but no other bone-specific differences (aBMD, bone geometry, bone turnover markers) were demonstrated between SW and CON at baseline or for aBMD after 1 year in a subgroup of participants.
Conclusion(s): High plasma T levels have no detectable effect on bone mass and bone geometry in SW during the period of peak bone mass acquisition. (Fertil Steril® 2013;99:270–8. ©2013 by American Society for Reproductive Medicine.)
Key Words: High plasma testosterone levels, intensive training, swimmers, adolescent girls, PCOS-like, bone mass acquisition

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Our group recently reported a high prevalence of high total testosterone (T) levels associated with oligomenorrhea in young elite female swimmers (SW) compared with untrained adolescents (1). Other endocrine findings (high LH/FSH ratio and normal DHEAS and 17-OHP levels) suggested functional ovarian hyperandrogenism. Moreover, ultrasound confirmed a polycystic ovary (PCOS)–like syndrome in most of these swimmers (1).

In non–intensively trained adolescents, PCOS, which is characterized by hyperandrogenemia, chronic anovulation, and central adiposity, provides a unique natural model for the study of androgenic hormone influences on bone mass (2, 3). Androgens have direct stimulatory effects on bone cells through androgen receptors (4) or estrogen receptors (particularly ER-α) in osteoblasts (5) after their aromatization into estrogens (6). Various studies have attempted to demonstrate that the androgen overproduction and high serum estrogen levels usually observed in PCOS may counterbalance the deleterious effects of oligomenorrhea or amenorrhea on bone (7, 8). In these cases compared with other menstrual dysfunctions, bone status seems to be preserved (7–10). The question of additional bone mass gain due to the overproduction of plasma total T nevertheless remains controversial and may depend on menstrual disorder status (8). Moreover, other endocrine parameters modified in PCOS may also modulate bone cell activity. Insulin resistance and hyperinsulinemia may protect against bone mineral loss in women with PCOS (3, 9). Insulin directly stimulates osteoblastic activity and indirectly reduces the production of various proteins (SHBG and IGFBP) that increase free T and insulin-like growth factor (IGF) 1, which stimulate bone mass acquisition (3, 11).

Given the negative effect of menstrual disorders in highly trained girls (12), the hypothesis that high T levels can preserve bone health in elite adolescent swimmers during peak bone mass acquisition should be investigated (13). Although high T levels have been reported in other groups of endurance and power athletes (14, 15), the impact on bone mass has never been investigated in female athletes. The limited mechanical impact of swimming on bone provides a unique opportunity to evaluate the effects of the endocrine parameters, such as T overproduction, that are potentially modified by intensive training.

The aim of the present study was to determine whether high T levels affect areal bone mineral density (aBMD), bone geometry, bone remodeling or body composition in elite adolescent swimmers. Sex hormones, IGF-1 and IGF-binding protein (BP) 3 were investigated as potentially involved in bone metabolism. Last, in a subgroup of adolescents, the effect of high T levels on bone mass gain was evaluated 1 year later.

SUBJECTS AND METHODS

Subjects

The study protocol was reviewed and approved by the Regional Research Ethics Committee (CPP Sud-Mediterranee IV, Montpellier, France), and each child and her parents gave written informed consent before entering the study. A total of 46 postmenarcheal girls with ages ranging from 12 to 18.1 years (mean 15.5 $\pm$ 1.3), some of whom had been presented in an earlier study (1), were recruited for this case-control study. All of the participants presented breast stage IV or V (and pubic hair V). Moreover, as oligomenorrhea is common in adolescence, usually occurring immediately after the onset of menarche, only subjects with gynecologic age $>$18 months were included (16). Swimmers (SW) and control subjects (CON) were excluded if they used hormonal contraceptives or medications able to modify bone metabolism. Moreover, none presented obvious signs of acute or chronic illness known to affect bone health, and none reported a long period of immobilization or fracture within the past 12 months. All of the participants were white. SW were eligible if the training volume was $\geq$10 hours per week and if the intensive training history was $>$5 years. All the SW were recruited in high level clubs in and around Montpellier. Nonobese age- and ethnicity-matched CON were eligible if they performed only leisure physical activities for $<$4 hours per week and if they had no history of intensive training. They were recruited from secondary schools in the Montpellier district or among recreational swimmers.

Twenty-five SW with a mean training volume of 15.2 $\pm$ 4.4 hours per week were assigned to two subgroups according to their T levels: 15 composed the high T level SW group (HSW; T $\geq$0.5 ng/mL) and 10 composed the normal T level SW group (NSW; T $<$0.5 ng/mL). In adolescents, 0.5 ng/mL is the normal upper limit for T (17, 18). Twenty-one CON with a mean training volume of 1.8 $\pm$ 1.2 hours per week were included in this study.

Among the population initially evaluated, ten HSW, seven NSW, and eight CON were reassessed 1 year later. SW withdrew from the longitudinal study for the following reasons: reduced or ended training (n = 3), moved to another city for training (n = 2), and began hormonal contraceptive use (n = 2). For CON, the major reasons for withdrawing were the following: began hormonal contraceptive use (n = 8), wanted to end study participation (n = 3), and moved away (n = 2).

Methods

This study followed the same design described in detail in earlier publications (1, 19–21). Standing height was measured with a stadiometer to the nearest 0.1 cm. Weight was determined using a weight scale with a precision of 0.1 kg. Body mass index (BMI) was calculated as weight divided by the square of height (kg/m^2). Pubertal development was assessed by breast stages according to the Tanner classification (22) by an experienced pediatric endocrinologist. Skeletal age was determined with the Greulich and Pyle method (23). Height standard deviation score (height SDS) and weight standard deviation score (weight SDS) were calculated according to the French standard curves.

Medical and menstrual histories. Each subject responded to a medical questionnaire designed to assess general medical and menstrual history with questions regarding the age of menarche and the pattern of menses, including duration of the menstrual cycle, duration of menstrual bleeding, absence of menstruation, and painful menstruation. Secondary amenorrhea (absence of menstruation for $>$3 months in the postmenarche period and in the absence of pregnancy [16]) and oligomenorrhea (two or more menstrual cycles of $<$22 days or $>$41 days during the past year [24]) were defined as