

SHORT REVIEW

Effect of altered reproductive function and lowered testosterone levels on bone density in male endurance athletes

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The effect of intense physical activity on female reproductive hormones is well recognised¹⁻³ and there is evidence that menstrual disturbances associated with hypo-oestrogenism adversely affect bone density especially at the lumbar spine.^{4,5} Physical activity can also have a range of effects on male reproductive function depending upon the intensity and duration of the activity and the fitness of the individual.⁶ In particular, endurance training may be associated with reductions in circulating testosterone levels. Since testosterone has important anabolic roles, alterations in reproductive hormone profiles may have detrimental skeletal consequences similar to those seen in females with menstrual disturbances. The aim of this brief review is to present the limited literature on the relation between bone density and testosterone levels in male endurance athletes.

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Key terms: male endurance athletes; testosterone; bone density; reproductive function

An overview of male hypogonadal-pituitary-gonadal (HPG) axis regulation

The main functions of the testes are steroid biosynthesis and spermatogenesis. These are controlled by higher structures of the hypogonadal-pituitary-gonadal (HPG) axis operating under a negative feedback system, the major gonadal regulatory hormone being testosterone.⁷ Gonadotropin releasing hormone (GnRH), secreted in pulses by the hypothalamus, stimulates the pituitary gland to secrete the two gonadotropic hormones, luteinising hormone (LH) and follicle stimulating hormone (FSH). LH stimulates the testis to secrete testosterone, while FSH facilitates sperm production. Prolactin, a stress hormone produced in the pituitary gland, may also be involved in regulation of testicular sex steroid production.⁸

Metabolic roles of testosterone

Approximately 95% of circulating serum testosterone comes from production in the testis, with the remainder produced in the adrenal glands. Testosterone is found in plasma prima-

rily bound to proteins, mainly albumin and sex hormone binding globulin (SHBG), with a small portion (3%) circulating unbound and referred to as free testosterone.⁶ The biologically active form of testosterone is that bound to albumin and the small unbound or free portion.⁹ Half of the testosterone produced is cleared through the liver and the remainder is cleared through extrahepatic metabolism.

Testosterone serves as a circulating precursor for the formation of active metabolites, which in turn mediate many of the physiological phenomena that are involved in androgen action.¹⁰ One of these, dihydrotestosterone, has a more pronounced anabolic effect than testosterone.

Testosterone and its active metabolites have important reproductive functions, being responsible for the development and maintenance of secondary sex characteristics and for spermatogenesis. In addition, testosterone is a powerful anabolic hormone that stimulates tissue growth and development. Testosterone has important effects on bone mass, as demonstrated by the finding that hypogonadism in males is a risk factor for osteoporosis.¹¹⁻¹³ Testosterone may have direct effects on bone formation, given that androgen receptors have been identified on osteoblasts.¹⁴ It may also act indirectly through augmented nocturnal secretion of growth hormone and subsequently insulin-like growth factor 1 (IGF-1), particularly during puberty, and by increased muscular activity and stresses on the skeleton, promoting bone mass at local sites.

Effects of exercise on testosterone levels

Relatively short duration exercise bouts at maximum or near maximum intensity appear to increase serum testosterone levels,¹⁵⁻²⁰ with measurable changes evident within minutes. However, with prolonged acute submaximal exercise bouts of approximately two hours or longer,^{16,21} suppression of circulating testosterone is noted which may remain for several days.

There is controversy about the effects of chronic intense exercise on basal testosterone levels. Some cross sectional studies have found reductions of total testosterone and measures

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of biologically available testosterone levels^{15 22–26} in athletes compared with non-athletes, while others have reported no difference.^{27–32} Similar conflict is apparent in the findings of prospective studies. In these, previously sedentary males were placed on a strenuous exercise programme or conditioned athletes significantly increased their normal training volume. While some noted a reduction in testosterone levels,^{33–38} others observed no changes^{39–42} or an increase.^{43 44} These results suggest that some male athletes who train intensively may experience reductions in testosterone levels, although this is not a consistent phenomenon.

Discrepancies in the results of both cross sectional and prospective studies may be attributable to differences in subject characteristics in terms of age, race, and previous activity level, type of exercise programme, and measurement procedures, including sampling and analysing techniques. Since testosterone concentrations show fluctuations and a circadian pattern, the time of day when samples are obtained and the use of serial hormone determinations may influence study results. A further important point is that not all studies included assessment of free testosterone concentrations. These may be altered following exercise, despite non-significant changes in total testosterone.

Possible mechanisms for suppression of testosterone levels with long term exercise

Long term exercise associated suppression of serum testosterone may result from decreased production rates, decreased protein binding, or increased clearance.⁴⁵ Of these, the most likely mechanism is decreased testosterone production arising from either intrinsic failure of the testis to maintain adequate steroid biosynthesis, perhaps due to testicular microtrauma and temperature increase,⁴⁶ or from central dysfunction in the HPG axis. The latter is supported by reports of decreases in LH pulse amplitude¹⁷ and frequency³⁰ as well as changes in pituitary responses to hypothalamic stimulation by exogenous GnRH^{25 30} in male athletes. In addition, factors may interact with the HPG axis, including dietary intake^{38 47} and raised concentrations of stress related hormones.³¹

Skeletal effects of lowered testosterone levels in male athletes

There are few studies investigating the relation between testosterone levels and bone density in young male athletes. From a clinical perspective, it is important to clarify that although some male athletes do present with reduced testosterone levels, these concentrations are still within the normal range for adult men. Therefore detrimental effects on bone density may not be as dramatic as those described for females with athletic amenorrhoea.

Several studies have reported lower bone density in male runners than in non-runners or those running lesser distances.^{32 48 49} Male distance runners, averaging 92 km per week, were found to have 9.7% lower bone density at the lumbar spine than a group of non-runners.

No differences in bone density were found at the radial or tibial shafts.⁴⁹ Although hormonal status was not measured, the authors speculated that lowered testosterone levels may have played a part in explaining their results. Another study also reported negative correlations between running distance and lumbar spine, proximal femur, and total body bone density in male runners.⁴⁸ However, it was unable to show correlations between running distance and either serum total testosterone concentration or the free testosterone index (ratio between total testosterone and SHBG). The authors therefore suggested that the observed osteopenia—associated with increased running distance—was independent of male sex hormones.

MacDougall *et al*⁵² compared 22 sedentary males with 53 male runners, divided into five groups on the basis of their weekly running mileage. They showed that bone density of the trunk tended to be lower in those who ran more than 40 miles per week, while tibial bone density was greater in those who ran 15 to 20 miles per week and tended to be lower in those who ran further than this. Nevertheless, total testosterone concentrations were within the normal range for the runners and did not differ from the controls.

Male triathletes were found to have similar bone density at the spine as a group of sedentary males, whereas male rowers had significantly higher spinal bone density.²⁷ Although total serum testosterone levels of all groups fell within the normal range, triathletes had significantly lower levels than the controls. The authors claimed that the lower testosterone in the triathletes may have negated any positive skeletal effects arising from their higher levels of exercise. However, this cannot be stated conclusively without comparing the bone density of groups of triathletes with high and low testosterone levels. It is possible that some other factor common to triathlete training is affecting bone density independently of testosterone levels.

The results of these limited studies have failed to establish a relation between lowered circulating testosterone and osteopenia in male athletes. However, there are several methodological issues which should be considered. Only one study⁴⁸ included assessment of SHBG in addition to total serum testosterone to give an indication of the amount of free testosterone. Since the latter is the biologically active portion, levels of this fraction may be more relevant to skeletal health. Furthermore, none measured dihydrotestosterone, an active metabolite of testosterone which has a greater anabolic effect.¹⁰ Most studies employed single sampling procedures at differing times of the day, which may not necessarily provide a true representation of the hormonal levels. Radioimmunoassays were used to measure testosterone, and while these indicate the immunological activity of the hormone they do not necessarily reflect the biological activity. This depends not only on hormonal levels but also on receptor availability and sensitivity within the subject.⁷ It is possible that some male ath-

letes have reduced biological activity of testosterone despite normal circulating levels, and this may lead to bone loss.

Delayed puberty

Pubertal development, as assessed by age of menarche, appears to be delayed in female athletes.⁵⁰⁻⁵¹ It has been suggested that intense training in the premenarcheal years may contribute to this phenomenon.⁵² There is some evidence that females with a later menarcheal age have lower bone density.⁵³⁻⁵⁷ This may result from failure to maximise peak bone mass during the pubertal years. While there is no physiological index comparable to age of menarche in males, longitudinal data indicate that sporting participation has little effect on attained stature, the timing of peak height velocity, rate of statural growth, or sexual maturation in males.⁵⁸⁻⁵⁹ Whether these results necessarily apply to intense endurance exercise is less clear, as most studies do not focus on such extreme forms of exercise. Although males with delayed puberty have been found to show significant osteopenia,¹²⁻¹³ the pubertal delay in these reports is not attributed to sporting pursuits but is part of some other disease process or disorder. Research investigating the effects of intense training on pubertal progression, testosterone levels, and bone accrual in male athletes is warranted.

Summary

It is apparent that bone density in male athletes can be reduced without a concomitant decrease in testosterone, suggesting that bone density and testosterone concentrations in the normal range are not closely related in male athletes. Further research is necessary to monitor concurrent changes in bone density and testosterone over a period of time in exercising males. In any case, the effect of exercise on the male reproductive system does not appear as extreme as that which can occur in female athletes, and any impact on bone density is not nearly as evident.

These results imply that factors apart from testosterone concentrations must be responsible for the observed osteopenia in some male athletes. Many factors have the potential to adversely affect bone density, independently of alterations in reproductive function. These include low calcium intake, energy deficit, weight loss, psychological stress, and low body fat, all of which may be associated with intense endurance training. Future research investigating skeletal health in male athletes should include a thorough assessment of reproductive function in addition to these other factors.

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Commentary

Disturbances of normal menstrual function are known to occur following chronic, high intensity exercise in female athletes. The resultant low levels of sex steroids can result in bone loss, particularly from the lumbar spine. The lower bone density appears to be associated with a greater number of fractures, particularly stress fractures. Much less is known about the long term effects of intense exercise on reproductive function or bone density in male athletes. This review summarises the published reports on testosterone concentrations, bone density, and exercise in male athletes. The limited data suggest that bone density may be reduced, but that this is not always accompanied by lowered testosterone concentrations. There are, however, various technical problems with many of the studies and these are clearly highlighted. With the increasing participation in endurance sports, it is important to highlight any potential detrimental effects of the exercise. There is a need for larger, more thorough studies of the incidence of osteopenia in male athletes and the association with altered reproductive function and the incidence of fractures.

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