
Abstract: OBJECTIVE: Androgen deficiency (AD) leads to bone loss and contributes to osteoporotic fractures in men. Although low bone mineral density (BMD) in AD men is improved by testosterone replacement, the responses vary between individuals but the determinants of this variability are not well defined. DESIGN AND METHODS: Retrospective review of dual energy X-ray absorptiometry (DEXA) of the lumbar spine and proximal femur in men with established AD requiring regular androgen replacement therapy (ART). After a DEXA scan all men were treated with testosterone implants (800 mg, approximately 6 month intervals). Patients were classified as having a congenital, childhood, or post-pubertal onset, as well as according to the adequacy of treatment prior to their first DEXA scan as untreated, partially treated or well treated. RESULTS: Men with AD requiring regular ART (n = 169, aged 46.3 +/- 1.1 years, range 22-84 years) underwent a DEXA scan prior to being treated with testosterone implants (800 mg, approximately 6 month intervals). In cross-sectional analysis at the time of the first DEXA scan untreated men (n = 24) had significantly reduced age-adjusted BMD at all four sites (L1-L4, femoral neck, Ward's triangle and trochanter). Well-treated men (n = 77) had significantly better age-adjusted BMD at all four sites compared with those who were partially treated (n = 66) or untreated (n = 24) with their age-adjusted BMD being normalized. In a longitudinal assessment of men (n = 60) who had two or more serial DEXA scans, at the second DEXA scan after a median of 3 years, men who were previously partially treated (n = 19) or untreated (n = 11) had proportionately greater improvements in BMD, significantly for Ward's triangle (P = 0.025) and the trochanter (P = 0.044) compared with men (n = 30) previously well treated. CONCLUSIONS: The present study demonstrates a positive relationship between adequacy of testosterone replacement and BMD in men with overt organic AD. Additionally, the BMD of well-treated AD men approximates that of age-matched non-AD controls. The greatest BMD gains are made by those who have been either untreated or partially treated, and optimal treatment over time (median 3 years) normalizes BMD to the level expected for healthy men of the same age.


Abstract: OBJECTIVE: The objective was to provide guidelines for the evaluation and treatment of androgen deficiency syndromes in adult men. PARTICIPANTS: The Task Force was composed of a chair, selected by the Clinical Guidelines Subcommittee of The Endocrine Society, five additional experts, a methodologist, and a professional writer. The Task Force received no corporate funding or remuneration. EVIDENCE: The Task Force used systematic reviews of available evidence to inform its key recommendations. The Task Force used consistent language and graphical descriptions of both the strength of recommendation and the quality of evidence, using the recommendations of the Grading of
Recommendations, Assessment, Development, and Evaluation group. CONSENSUS PROCESS: Consensus was guided by systematic reviews of evidence and discussions during three group meetings, several conference calls, and e-mail communications. The drafts prepared by the panelists with the help of a professional writer were reviewed successively by The Endocrine Society's Clinical Guidelines Subcommittee, Clinical Affairs Committee, and Council. The version approved by the Council was placed on The Endocrine Society's web site for comments by members. At each stage of review, the Task Force received written comments and incorporated needed changes. CONCLUSIONS: We recommend making a diagnosis of androgen deficiency only in men with consistent symptoms and signs and unequivocally low serum testosterone levels. We suggest the measurement of morning total testosterone level by a reliable assay as the initial diagnostic test. We recommend confirmation of the diagnosis by repeating the measurement of morning total testosterone and in some patients by measurement of free or bioavailable testosterone level, using accurate assays. We recommend testosterone therapy for symptomatic men with androgen deficiency, who have low testosterone levels, to induce and maintain secondary sex characteristics and to improve their sexual function, sense of well-being, muscle mass and strength, and bone mineral density. We recommend against starting testosterone therapy in patients with breast or prostate cancer, a palpable prostate nodule or induration or prostate-specific antigen greater than 3 ng/ml without further urological evaluation, erythrocytosis (hematocrit > 50%), hyperviscosity, untreated obstructive sleep apnea, severe lower urinary tract symptoms with International Prostate Symptom Score (IPSS) greater than 19, or class III or IV heart failure. When testosterone therapy is instituted, we suggest aiming at achieving testosterone levels during treatment in the mid-normal range with any of the approved formulations, chosen on the basis of the patient's preference, consideration of pharmacokinetics, treatment burden, and cost. Men receiving testosterone therapy should be monitored using a standardized plan.

Abstract: CONTEXT: Serum testosterone levels decline significantly with aging. Testosterone supplementation to older men might beneficially affect the aging processes. OBJECTIVE: To investigate the effect of testosterone supplementation on functional mobility, cognitive function, bone mineral density, body composition, plasma lipids, quality of life, and safety parameters in older men with low normal testosterone levels. DESIGN, SETTING, AND PARTICIPANTS: Double-blind, randomized, placebo-controlled trial of 237 healthy men between the ages of 60 and 80 years with a testosterone level lower than 13.7 nmol/L conducted from January 2004 to April 2005 at a university medical center in the Netherlands. INTERVENTION: Participants were randomly assigned to receive 80 mg of testosterone undecanoate or a matching placebo twice daily for 6 months. MAIN OUTCOME MEASURES: Functional mobility (Stanford Health Assessment Questionnaire, timed get up and go test, isometric handgrip strength, isometric leg extensor strength), cognitive function (8 different cognitive instruments), bone mineral density of the hip and lumbar spine (dual-energy x-ray absorptiometry scanning), body composition (total body dual-energy x-ray absorptiometry and abdominal ultrasound of fat mass), metabolic risk factors (fasting plasma lipids, glucose, and insulin), quality of life (Short-Form Health 36 Survey and the Questions on Life Satisfaction Modules), and safety parameters (serum prostate-specific antigen level, ultrasonographic prostate volume, International Prostate Symptom score, serum levels of creatinine, aspartate
aminotransferase, alanine aminotransferase, gamma-glutamyltransferase, hemoglobin, and hematocrit). RESULTS: A total of 207 men completed the study. During the study, lean body mass increased and fat mass decreased in the testosterone group compared with the placebo group but these factors were not accompanied by an increase of functional mobility or muscle strength. Cognitive function and bone mineral density did not change. Insulin sensitivity improved but high-density lipoprotein cholesterol decreased; by the end of the study, 47.8% in the testosterone group vs 35.5% in the placebo group had the metabolic syndrome (P = .07). Quality-of-life measures were no different except for one hormone-related quality-of-life measure that improved. No negative effects on prostate safety were detected. CONCLUSION: Testosterone supplementation during 6 months to older men with a low normal testosterone concentration did not affect functional status or cognition but increased lean body mass and had mixed metabolic effects. TRIAL REGISTRATION: isrctn.org Identifier: ISRCTN23688581.


Abstract: OBJECTIVE: To evaluate the effect of adding testosterone undecanoate 40 mg daily to estrogen therapy on bone markers, bone mineral density and body composition in oophorectomized women. METHODS: Fifty women, 45-60 years old, who had undergone a hysterectomy and bilateral salpingo-oophorectomy for benign disorders, were randomly assigned to oral treatment with testosterone undecanoate 40 mg plus estradiol valerate 2 mg daily or placebo plus estradiol valerate 2 mg daily. Twenty-four weeks later, cross-over was performed to the other treatment regimen. Forty-four women completed the study. Their serum concentrations of insulin-like growth factor (IGF)-I, IGF binding protein (IGFBP)-3, osteocalcin, carboxyterminal telopeptide aminoterminal (ICTP), of type I collagen propeptide of type I procollagen (PICP) and interleukin (IL)-1 receptor antagonist were measured at baseline and after 24 weeks of both treatments, as were also their body mass index (BMI) and blood pressure. Bone mineral density of the total body, spine and hip and total body fat, total lean body mass, trunk fat and trunk lean mass were determined by dual-energy X-ray absorptiometry measurements at baseline and after 24 weeks of both regimens. RESULTS: During treatment, the addition of testosterone counteracted the decrease in IGF-I and PICP seen with estrogen therapy alone. Osteocalcin and ICTP were significantly reduced to the same extent by both therapies. No change occurred in the IL-1 receptor antagonist. A significant increase was seen in total lean body mass with the estrogen/testosterone regimen, but the total fat mass, trunk lean or fat mass remained unchanged after 24 weeks of both treatments. No effect was detected on total, hip or spinal bone mineral density after treatment with estrogen alone or estrogen/testosterone. Likewise, BMI and blood pressure were unaffected. CONCLUSIONS: The addition of testosterone to oral estrogen might have positive effects on bone as suggested by the fact that it counteracted the decline in IGF-I and PICP levels. An anabolic effect on muscle was reflected by an increase in the total lean body mass. No adverse effects were noted on BMI, fat distribution or blood pressure during the 6-month treatment with oral testosterone undecanoate.


Abstract: Despite nearly a half-century of research on aging and sex steroids in men, answers to key questions that would allow us to confidently assess risk:benefit ratios for
androgen replacement in older men with the partial androgen deficiency of aging men (PADAM) syndrome remain uncertain. Although it is now reasonably clear that a significant percentage of otherwise healthy older men have decreases in testosterone and bioavailable testosterone to levels consistent with hypogonadism, the clinical implications of this change remain uncertain. Data suggest that low testosterone in older men is correlated to varying degrees with loss of lean body mass and muscle strength, and increased total and central body fat. Less certain, but suggestive, are data relating low testosterone levels to decreased bone density, loss of insulin sensitivity, and cognitive and affective deterioration, as well as reduced sexual function. Replacement of testosterone in older men has shown some positive effects on each of these variables, but findings have been inconsistent, perhaps because studies have employed different preparations and doses of androgens, treated for various durations, and defined their target populations in different ways. As important as beneficial effects is the potential for adverse effects, which may be greater in older men. Possible problems include sleep apnea, erythrocytosis, dyslipidemia with acceleration of atherosclerosis, and, of greatest concern, prostate cancer or hyperplasia. Studies to date have suggested that these outcomes are not major risks, but, in the absence of a large, randomized trial or trials, definitive information is not available. The US National Academies Institute of Medicine's recent report recommends that the National Institutes of Health support small efficacy trials aimed at treatment of androgen deficiency-related clinical conditions, but not a large, randomized trial to elucidate risk:benefit ratios. This recommendation, if adhered to, is likely to delay, rather than foster, progress in this important area.


Abstract: OBJECTIVE: During the past few years serious concern has been raised about the safety of combined estrogen/progestogen hormone therapy, in particular about its effects on the breast. Several observations suggest that androgens may counteract the proliferative effects of estrogen and progestogen in the mammary gland. Thus, we aimed to study the effects of testosterone addition on breast cell proliferation during postmenopausal estrogen/progestogen therapy. DESIGN: We conducted a 6-month prospective, randomized, double-blind, placebo-controlled study. A total of 99 postmenopausal women were given continuous combined estradiol 2 mg/norethisterone acetate 1 mg and were equally randomly assigned to receive additional treatment with either a testosterone patch releasing 300 microg/24 hours or a placebo patch. Breast cells were collected by fine needle aspiration biopsy at baseline and after 6 months, and the main outcome measure was the percentage of proliferating breast cells positively stained by the Ki-67/MIB-1 antibody. RESULTS: A total of 88 women, 47 receiving active treatment and 41 in the placebo group, completed the study. In the placebo group there was a more than fivefold increase (P<0.001) in total breast cell proliferation from baseline (median 1.1%) to 6 months (median 6.2%). During testosterone addition, no significant increase was recorded (1.6% vs 2.0%). The different effects of the two treatments were apparent in both epithelial and stromal cells. CONCLUSIONS: Addition of testosterone may counteract breast cell proliferation as induced by estrogen/progestogen therapy in postmenopausal women.

Abstract: OBJECTIVES: Ageing in men is associated with a gradual decline in serum testosterone levels and a concomitant loss of muscle mass, accumulation of central adiposity, impaired mobility and increased risk of bone fractures. Whether androgen treatment might be beneficial in these subjects is still under debate. We have carried out a systematic review of randomized controlled trials (RCTs) evaluating the effects of testosterone (T) administration to middle-aged and ageing men on body composition, muscle strength, bone density, markers of bone metabolism and serum lipid profile. DATA SOURCE: A comprehensive search of all published randomized clinical trials was performed using the MEDLINE, Cochrane Library, EMBASE and Current Contents databases. REVIEW METHODS: Guided by prespecified criteria, software-assisted data abstraction and quality assessed by two independent reviewers, 29 RCTs were found to be eligible. For each investigated variable, we reported the results of pooled estimates of testosterone treatment using the random effect model of meta-analysis. Heterogeneity, reproducibility and consistency of the findings across studies were explored using sensitivity and meta-regression analysis. RESULTS: Overall, 1,083 subjects were evaluated, 625 randomized to T, 427 to placebo and 31 to observation (control group). Weighted mean age was 64.5 years (range 49.9–77.6) and mean serum testosterone was 10.9 nmol/l (range 7.8–19). Testosterone treatment produced: (i) a reduction of 1.6 kg (CI: 2.5–0.6) of total body fat, corresponding to -6.2% (CI: 9.2–3.3) variation of initial body fat, (ii) an increase in fat free mass of 1.6 kg (CI: 0.6–2.6), corresponding to +2.7% (CI: 1.1–4.4) increase over baseline and (iii) no change in body weight. The effects of T on muscle strength were heterogeneous, showing a tendency towards improvement only at the leg/knee extension and handgrip of the dominant arm (pooled effect size=0.3 standard mean difference (SMD), CI: -0.0 to 0.6). Testosterone improved bone mineral density (BMD) at the lumbar spine by +3.7% (CI: 1.0–6.4%) compared to placebo, but not at the femoral neck, and produced a consistent reduction in bone resorption markers (pooled effect size = -0.6 SMD, CI: -0.017 to -0.003). Testosterone also reduced total cholesterol by 0.23 mmol/l (CI: -0.37 to -0.10), especially in men with lower baseline T concentrations, with no change in low density lipoprotein (LDL)-cholesterol. A significant reduction of high density lipoprotein (HDL)-cholesterol was found only in studies with higher mean T-values at baseline (-0.085 mmol/l, CI: -0.017 to -0.003). Sensitivity and meta-regression analysis revealed that the dose/type of T used, in particular the possibility of aromatization, explained the heterogeneity in findings observed on bone density and HDL-cholesterol among studies. CONCLUSION: The present analysis provides an estimate of the average treatment effects of testosterone therapy in middle-aged men. Our findings are sufficiently strong to justify further interventional studies focused on alternative targets of androgenic treatment carrying more stringent clinical implications, in particular the cardiovascular, metabolic and neurological systems.


Abstract: Increased longevity and population aging will increase the number of men with relative testosterone deficiency, as systemic levels of testosterone decrease by about 1% each year. Androgen deficiency should only be diagnosed in men with definite signs and symptoms, accompanied by low total testosterone levels measured in the morning by a reliable assay. Although clinical trials data are limited, current practice guidelines recommend testosterone replacement therapy for symptomatic men with low testosterone levels to improve bone mineral density, muscle mass and strength, sexual function, and quality of life. Testosterone replacement is not recommended for all older men with low
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Testosterone for Men

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Testosterone levels, and should be avoided in patients with prostate or breast cancer, hyperviscosity, erythrocytosis, untreated obstructive sleep apnea, or severe heart failure. The goal of all available testosterone treatment modalities (intramuscular injections, nongenital patch or gel, bioadhesive buccal and oral testosterone, and pellets) is to achieve serum testosterone levels in the mid-normal range during treatment. Cost varies widely among these preparations and may limit their use. Patients receiving testosterone replacement therapy should be re-evaluated 3 months after testosterone initiation and at least annually thereafter.


Abstract: It has generally been held that estrogen and testosterone are the major sex steroids regulating bone metabolism in women and men, respectively. However, the description of several "experiments of nature" led to a reconsideration of this notion. Thus, a male carrying homozygous mutations in the ER-alpha gene and two males with homozygous mutations in the aromatase gene had osteopenia, unfused epiphyses, and elevated indices of bone turnover. Though these findings indicated that estrogen plays a role in regulating the male skeleton, they left unresolved the issue of whether estrogen acted on the male skeleton mainly to enhance bone mass acquisition during growth and maturation, or whether it also acted to retard bone loss in aging individuals. To address this issue, several cross-sectional observational studies have related bone mineral density (BMD) to sex steroids in elderly men, and found that estrogen correlated better than testosterone with BMD. In addition, recent longitudinal studies from our group indicate that bioavailable estrogen correlated better than testosterone both with the gain in BMD in young men and with loss of BMD in elderly men. These observational studies do not, however, prove causality, which requires direct interventional studies. Thus, we eliminated endogenous testosterone and estrogen production in 59 elderly men (mean age 68 years), studied them first under conditions of physiologic testosterone and estrogen replacement, and then assessed the impact on bone turnover of withdrawing both testosterone and estrogen, withdrawing only testosterone, only estrogen, or continuing both. We found that estrogen played the major role in regulating bone resorption in these men, and that both estrogen and testosterone were important in maintaining bone formation. Collectively then, these findings indicate that estrogen plays a dominant role in regulating the male skeleton.


Abstract: In a population-based, cross-sectional study, we related age-associated changes in vBMD and in bone structural parameters to circulating bioavailable estradiol and testosterone levels in men. Associations between these bone mass/structural parameters and sex steroid levels were progressively stronger with age. Our previously postulated "threshold" for skeletal estrogen deficiency was most evident at cortical sites. INTRODUCTION: Serum sex steroids, particularly estrogen levels, are associated with bone mass in men, and previous work has suggested that there may be a "threshold" bioavailable estradiol (bio E(2)) level below which the male skeleton becomes estrogen deficient. However, previous studies addressing this issue have exclusively used DXA, which cannot separate trabecular from cortical bone or provide information on bone geometry or structure. MATERIALS AND METHODS: In an age-stratified population sample of 314 men (age, 22-91 years), we assessed volumetric BMD (vBMD) and bone
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geometry by QCT at the lumbar spine, femoral neck, distal radius, and distal tibia and related these to circulating bio E(2) and bio testosterone (T) levels. RESULTS: Compared with young men (age, 20-39 years), middle-aged men (age, 40-59 years) had significantly lower bio T (-26%, p < 0.001) and bio E(2) (-9%, p = 0.038) levels, and these decreases were even greater in the elderly men (age > or = 60 years, -60% and -38% for bio T and bio E(2), respectively, p < 0.001 for both). Reflecting their intact gonadal status, vBMD/structural parameters were not related to sex steroid levels in young men, whereas bio E(2) levels were associated consistently with vBMD and variably with bone geometric parameters in the elderly men; middle-aged men showed associations with bio E(2) and bio T at some sites. At all cortical sites, vBMD was associated with bio E(2) at low (<30 pM, R = 0.27-0.41, p < 0.05-0.001) but not high (> or =30 pM, R = -0.003 to 0.12, p = not significant) levels; no such differences were evident at trabecular sites. CONCLUSIONS: In men, bio E(2) is the most consistent predictor of vBMD and some bone geometric variables as assessed by QCT. We also extend our previous findings on a possible "threshold" for skeletal estrogen deficiency by showing that this is most evident for cortical sites.

Abstract: OBJECTIVE: The relation of hysterectomy and oophorectomy to change in bone mineral density (BMD) was examined in older women using and not using estrogen replacement therapy (ERT). METHODS: Women aged 60-80 years from the Rancho Bernardo Study attended clinic visits in 1988-1991 and 1992-1995 when hysterectomy and oophorectomy were ascertained, ERT use was validated and spine and hip BMD was assessed at both visits with DEXA. Women were either current ERT users or nonusers at both visits. RESULTS: Among these 447 women, average age was 71 (S.D.=9.0); average years postmenopause was 24.7 (S.D.=10.9). Overall, 122 had a hysterectomy with ovarian conservation and 91 had a hysterectomy with bilateral oophorectomy; 41% reported current ERT use for an average duration of 19.1 years (S.D.=10.8). Hysterectomized women were 2.3 times more likely to report ERT use than intact women (P<0.001). Comparisons adjusted for age, obesity, and age at menopause but not for ERT use showed hysterectomized women had less bone loss per year at the hip than intact women (P<0.001). However, this difference was explained by ERT; after adjustment for ERT, mean hip bone loss per year was -0.57% for intact women, -0.42% for hysterectomized women with ovarian conservation and -0.32% for bilaterally oophorectomized women (P's>0.10). There were no differences by hysterectomy or oophorectomy in bone loss at the spine or femoral neck. For all sites, women using ERT had higher BMD at both visits than nonusers (P's<0.001). Stratification by ERT showed that within users and nonusers, there were no differences in BMD or bone loss at any site by hysterectomy or oophorectomy. CONCLUSIONS: There are no long term effects of hysterectomy and bilateral oophorectomy on bone loss. Women who use ERT have better BMD than nonusers.

Abstract: CONTEXT: Hypopituitarism in women is characterized by profound androgen deficiency due to a loss of adrenal and/or ovarian function. The effects of testosterone replacement in this population have not been reported. OBJECTIVE: The objective of the study was to determine whether physiologic testosterone replacement improves bone
density, body composition, and/or neurobehavioral function in women with severe androgen deficiency secondary to hypopituitarism. DESIGN: This was a 12-month randomized, placebo-controlled study. SETTING: The study was conducted at a general clinical research center. STUDY PARTICIPANTS: Fifty-one women of reproductive age with androgen deficiency due to hypopituitarism participated. INTERVENTION: Physiologic testosterone administration using a patch that delivers 300 microg daily or placebo was administered. MAIN OUTCOME MEASURES: Bone density, fat-free mass, and fat mass were measured by dual x-ray absorptiometry. Thigh muscle and abdominal cross-sectional area were measured by computed tomography scan. Mood, sexual function, quality of life, and cognitive function were assessed using self-administered questionnaires. RESULTS: Mean free testosterone increased into the normal range during testosterone administration. Mean hip (P = 0.023) and radius (P = 0.007), but not posteroanterior spine, bone mineral density increased in the group receiving testosterone, compared with placebo, as did mean fat-free mass (P = 0.040) and thigh muscle area (P = 0.038), but there was no change in fat mass. Mood (P = 0.029) and sexual function (P = 0.044) improved, as did some aspects of quality of life, but not cognitive function. Testosterone at physiologic replacement levels was well tolerated, with few side effects. CONCLUSIONS: This is the first randomized, double-blind, placebo-controlled study to show a positive effect of testosterone on bone density, body composition, and neurobehavioral function in women with severe androgen deficiency due to hypopituitarism.

Abstract: Anorexia nervosa (AN) is complicated by severe bone loss, cognitive function deficits, and a high prevalence of major depression. We hypothesized that bone formation would increase and depressive symptoms and spatial cognition would improve with short-term physiological testosterone administration. We randomized 33 women with AN and relative testosterone deficiency to transdermal testosterone (Intrinsa, Procter and Gamble Pharmaceuticals, Cincinnati, OH), 150 mug, 300 mug, or placebo, for 3 wk. At baseline, free testosterone correlated with L4 bone density (r = 0.51, P < 0.001), body mass index (r = 0.39, P = 0.02), depressive symptoms (r = -0.44, P = 0.02), and spatial cognition (r = 0.45, P = 0.04). C-terminal propeptide of type 1 collagen levels were higher during testosterone administration than placebo (P = 0.03). The change in propeptide of type 1 collagen correlated with change in free testosterone over 3 wk (r = 0.50, P = 0.02). Osteocalcin and bone-specific alkaline phosphatase did not change. Depressed patients receiving testosterone improved from severely depressed to moderately depressed; the placebo group was unchanged (P = 0.02). Spatial cognition improved in the testosterone group, compared with placebo (P = 0.0015). Therefore, short-term low-dose testosterone may improve depressive symptoms and spatial cognition in women with AN. Low-dose testosterone may also prevent decreased bone formation in AN, but because testosterone did not affect all markers of bone formation studied, further data are needed.

Abstract: The aging process is accompanied by significant changes in body composition characterized by decreased fat free mass and increased and redistributed fat mass. Muscle loss results from the atrophy of muscle fibers and decreased synthesis of muscle proteins. Increased number of adipocytes and fat accumulation in non-adipose tissue leads to adiposity. These changes can impose functional limitations and increase morbidity. In men,
declining testosterone levels that occur with aging can be a contributing factor to these changes. Studies in hypogonadal men have shown that testosterone replacement is effective in increasing muscle mass and strength and decreasing fat mass. The molecular mechanisms of testosterone's influence on muscle and adipose are not fully elucidated. However, testosterone appears to stimulate IGF-1 expression directly and indirectly leading to increased muscle protein synthesis and growth. It may also counter the inhibitory effects of myostatin, cytokines, and glucocorticoids. The predominant effects of testosterone on fat mass are increased lipolysis and decreased adipogenesis. Current evidence suggests that testosterone replacement may be effective in reversing age-dependent body composition changes and associated morbidity. However, hypogonadism must be diagnosed carefully, and therapy should be monitored regularly in order to avoid the adverse effects associated with testosterone supplementation.

15. Ravaglia G, Forti P, Maioli F, et al. Body composition, sex steroids, IGF-1, and bone mineral status in aging men. J Gerontol A Biol Sci Med Sci. 2000;55:M516-21. Abstract: BACKGROUND: Bone loss in elderly men is associated with changes in body composition and reduced secretion of endogenous anabolizing hormones. The independent influences of body composition and endocrine factors on male bone metabolism, however, are unclear. METHODS: Bone mass density (BMD) (bone mass content [BMC, g]/projected bone area [BA, cm²]) at different skeletal sites, skeletal muscle, and body fat mass were measured by dual-energy X-ray absorptiometry in 129 men aged 20 to 95 years. Free testosterone, 17-beta-estradiol, dehydroepiandrosterone-sulfate, and insulin-like growth factor 1 (IGF-1) serum concentrations were measured. Because BMD may fail to control for differences in skeletal size, the associations of bone mass with body composition and hormones were studied by comparing BMD regression models incorporating age and knee height only with BMC regression models also incorporating BA. RESULTS: Skeletal muscle had close associations (p at least < .01) with BMD and BMC at almost all skeletal sites, but the strength of these associations was generally reduced in BMC with respect to BMD models. Weak associations (p < .05) were found in both models for fatness with femoral bone and for 17-beta-estradiol with total body and femoral bone. The association of 17-beta-estradiol with spinal bone was significant (p < .05) in the BMD but not in the BMC model. No association of BMC or BMD with androgens and IGF-1 reached significance. CONCLUSIONS: Skeletal muscle may be more important than fatness and anabolizing hormones in preserving bone mass in elderly men. In contrast to traditional belief, estrogens may be more important than androgens and IGF-1 in male bone metabolism.

16. Raynor MC, Carson CC, Pearson MD, Nix JW. Androgen deficiency in the aging male: a guide to diagnosis and testosterone replacement therapy. Can J Urol. 2007;14 Suppl 1:63-8. Abstract: A steady decline in androgen levels occurs in males as they age. Evidence suggests that this decline may be at least partially responsible for a variety of physical and mental changes associated with the aging process. For instance, abnormally low levels of androgens can lead to profound changes in bone density, body composition, as well as sexual and cognitive function. Testosterone replacement has been shown to produce improvements in many of these areas. However, this practice is not without risks, both proven and theoretic. Also, the diagnosis of androgen deficiency and the decision to treat is not always straightforward. The purpose of this article is to familiarize the clinician with issues associated with androgen deficiency in the aging male.
androgen deficiency as well as the risks and benefits of androgen replacement will be discussed. This should help clinicians better identify those patients in whom testosterone replacement therapy should be considered.


Abstract: There is evidence that estrogen decreases bone turnover in men as well as women. We therefore hypothesized that older men would show increased bone resorption in response to inhibition of the aromatase enzyme, which converts androgens to estrogen. Fifteen eugonadal men over 65 yr were treated for 9 weeks with 2.0 mg/day of anastrozole, an aromatase inhibitor. After 9 weeks of treatment, there were significant decreases in estradiol, estrone, and sex hormone-binding globulin levels by 29%, 73%, and 16%, respectively, and total testosterone increased significantly by 56%. Despite the limited decrease of estrogen and the increase in testosterone, C-telopeptide of type 1 collagen showed a progressive significant increase of 11%, 24%, and 33% (P for trend = 0.033) above baseline at 3, 6, and 9 weeks, respectively. N-telopeptide of type 1 collagen values were highly correlated with C-telopeptide of type 1 collagen, but the change in N-telopeptide of type 1 collagen was not statistically significant. Bone-specific alkaline phosphatase and N-terminal type I procollagen peptides showed significant decreases of 8% and 11% of baseline at 9 weeks. Osteocalcin decreased significantly by 30% at 18 weeks. We conclude that aromatase inhibition can reduce estrogen levels in older men, but this effect is limited, perhaps because of feedback stimulation of testosterone production, and that endogenous estrogen derived from aromatization of testosterone plays a role in bone metabolism of older men by limiting the rate of bone resorption.