

Effect of Testosterone Treatment on Body Composition and Muscle Strength in Men Over 65 Years of Age*

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ABSTRACT

As men age, serum testosterone concentrations decrease, the percentage of body mass that is fat increases, the percentage of lean body mass decreases, and muscle strength decreases. Because these changes are similar to those that occur in hypogonadal men, we hypothesized that increasing the serum testosterone concentration of men over 65 yr of age to that in young men would decrease their fat mass, increase their lean mass, and increase their muscle strength.

We randomized 108 men over 65 yr of age to wear either a testosterone patch or a placebo patch in a double blind study for 36 months. We measured body composition by dual energy x-ray absorptiometry and muscle strength by dynamometer before and during treatment. Ninety-six men completed the entire 36-month protocol.

Fat mass decreased (-3.0 ± 0.5 kg) in the testosterone-treated men during the 36 months of treatment, which was significantly different ($P = 0.001$) from the decrease (-0.7 ± 0.5 kg) in the placebo-treated

men. Lean mass increased (1.9 ± 0.3 kg) in the testosterone-treated men, which was significantly different ($P < 0.001$) from that (0.2 ± 0.2 kg) in the placebo-treated men. The decrease in fat mass in the testosterone-treated men was principally in the arms (-0.7 ± 0.1 kg; $P < 0.001$ compared to the placebo group) and legs (-1.1 ± 0.2 kg; $P < 0.001$), and the increase in lean mass was principally in the trunk (1.9 ± 0.3 kg; $P < 0.001$). The change in strength of knee extension and flexion at 60° and 180° angular velocity during treatment, however, was not significantly different between the two groups.

We conclude that increasing the serum testosterone concentrations of normal men over 65 yr of age to the midnormal range for young men decreased fat mass, principally in the arms and legs, and increased lean mass, principally in the trunk, but did not increase the strength of knee extension and flexion, as measured by dynamometer. (*J Clin Endocrinol Metab* 84: 2647–2653, 1999)

AS MEN AGE, their serum testosterone concentrations decrease. Cross-sectional studies show that at age 80 yr the total serum testosterone concentration is approximately 75%, and the free testosterone concentration is approximately 50% of that at age 20 yr (1, 2). A longitudinal study that followed a cohort of men for 15 yr also showed a decrease in serum testosterone concentration with age (3).

One possible consequence of this decrease in testosterone with increasing age is a change in body composition and a decrease in muscle strength. As men age, lean mass decreases, and fat mass increases (4). Similar changes occur in men whose serum testosterone is low because of pituitary or testicular disease; when they are treated with testosterone, lean mass increases, and fat mass decreases (5). Also as men age, their muscle strength decreases (6). In one study in hypogonadal men, testosterone treatment was associated with an increase in muscle strength (7).

Because of the similarities between the changes that occur when men age and those that occur when they become hypogonadal as the consequence of known pituitary or testic-

ular disease, we hypothesized that increasing the serum testosterone concentrations of elderly men to those found in young men would decrease their fat mass, increase their lean mass, and increase their muscle strength. We tested this hypothesis by selecting healthy men over 65 yr of age, assigning them randomly to receive either testosterone or placebo, and measuring body composition and muscle strength repeatedly during 3 yr of treatment.

Subjects and Methods

Subjects

We recruited men over 65 yr of age by mailings to alumni of the University of Pennsylvania and Temple University and by appeals via television and newspaper. From those who responded, we included men whose serum testosterone concentration was 1 SD or more below the mean for normal young men (<475 ng/dL). We excluded men who had diseases or were taking medications known to cause hypogonadism and men who had conditions that would affect muscle strength, such as a history of cerebrovascular accident. We also excluded men who had diseases that testosterone could exacerbate, such as prostate cancer and severe benign prostatic hypertrophy. One hundred and eight men met the criteria and enrolled after giving informed consent to a protocol approved by the University of Pennsylvania committee on studies involving humans.

Study design

Subjects were randomized to receive either testosterone or placebo in a double blind fashion. The subjects' treatment assignments were known only to the data manager, research pharmacist, and safety-monitoring

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board until the last subject completed the entire 36 months of the study. Testosterone was administered by a scrotal patch (Testoderm, Alza Corp., Palo Alto, CA); placebo patches were identical in appearance to the testosterone patches. Each subject was required to use a patch that delivers 6 mg/day initially, to wear it at all times except when bathing, to change the patch once a day, and to shave the scrotum once a week. The serum testosterone concentration was measured and reviewed in a blinded fashion every 3 months. The data manager directed that the dose be decreased to 4 mg/day if the serum testosterone concentration was more than 1000 ng/dL (34.7 nmol/L) and that the subject be reeducated in patch technique if the concentration was less than 250 ng/dL (8.7 nmol/L) above the pretreatment concentration. To maintain the blinding, the data manager directed in each case of change of dose that a subject in the placebo group be treated similarly.

Body composition

Body composition was determined by dual energy x-ray absorptiometry (8) using a DPX scanner (Lunar Corp., Madison, WI) with acquisition software versions 3.1–3.61 and body composition software version 1.3. Results included total mass, fat mass, and lean (fat-free) mass, each for total body, arms, legs, and trunk.

Muscle strength

Hand grip strength was measured by a Jaymar dynamometer (Salmon Preston, Boling Brook, IL). Subjects were coached orally to exert maximum effort during three trials, each separated by a 2-min rest. The maximum result was used for analysis.

The strength of knee extension and flexion was measured by Biodex dynamometer (Biodex Corporation, Shirley, NY). Before the measurements the subjects warmed up by using a stationary bicycle at low resistance for 5 min and then by two trials on the Biodex using submaximal effort and two trials using maximal effort. With the instrument set for 60° angular velocity, the subject was asked to extend the knee with maximal effort and then flex passively and repeat this maneuver twice after 15–20 s of rest. The procedure was repeated three times, with maximal effort flexing the knee and passive extension. The entire procedure was repeated with instrument set for 180° of angular velocity. The maximum value for extension and flexion at 60° and 180° of angular velocity was used for analysis.

Physical function

Physical function was assessed by walking and stair climbing. The time and the number of steps required for a subject to walk 25 ft at his usual pace was recorded. The time for the subject to climb 12 stairs was also recorded.

Questionnaires

Two questionnaires were used. One was the Medical Outcomes Study Short-Form-36 (MOS SF-36) (9), a generic health-related quality of life questionnaire that assesses eight areas, including physical functioning, role limitations because of health problems, bodily pain, social functioning, mental health, role limitations due to emotional problems, vitality, and general health perceptions. Each questionnaire was scored, and the raw scores were transformed to a 0–100 scale by computer. The

second questionnaire, designed for this study, consisted of eight questions, four about general sense of energy and four about sexual function. Scores were also 0–100. For each test, the four energy scores were averaged, and the four sexual function scores were averaged.

Statistical analyses

Analyses were performed using the intent to treat approach, so the last observation of each of the 12 men who did not complete the entire 36 months of treatment was carried forward to all subsequent time points. Within each group, the significance of the change from 0–36 months was tested using paired *t* test. Between groups, the principal test was the independent sample *t* test comparing the mean change from 0–36 months between the 2 treatment groups. We confirmed the results of this analysis using an analysis of covariance, comparing the final values adjusted for the pretreatment values, and by the Wilcoxon signed rank test. Because these 3 tests gave similar results, only the results of the comparisons of the differences are presented. Linear regression (10) was used to determine whether the effect of testosterone treatment depended on the pretreatment serum testosterone concentration.

Results

Of the 108 men who were randomized to receive either testosterone or placebo, 96 completed the entire 3 yr of the protocol. Of the 12 who discontinued, 1 (placebo group) was asked to because he was found to have a history of prostate cancer that he had concealed, 1 (testosterone group) developed prostate cancer, 2 died (both in the placebo group), and 8 (5 in the placebo group and 3 in the testosterone group) discontinued for personal reasons.

The mean serum testosterone concentration during the 36 months of the study did not change in the placebo-treated men. The mean serum testosterone concentration in the testosterone-treated group increased from 367 ± 79 ng/dL (\pm SD; 12.7 ± 2.7 nmol/L) before treatment to 625 ± 249 ng/dL (21.7 ± 8.6 nmol/L; $P < 0.001$) by the sixth month of treatment and remained at that level for the duration of the treatment period (11). The mean serum free testosterone concentration increased similarly. The effects of this treatment on bone mineral density and prostate and hematological parameters have been reported previously (11).

Body composition

The two groups of subjects had similar weight, body mass index, tissue mass, fat mass, and lean mass before treatment (Table 1). During the 36 months of treatment, the testosterone-treated subjects experienced a significant decrease in fat mass (-2.9 ± 0.5 kg) and an increase in lean mass (1.9 ± 0.3 kg), whereas the placebo-treated subjects did not experience a significant change in either (Table 1 and Fig. 1). The changes

TABLE 1. Parameters of body mass and composition in healthy, elderly men before and after 3 yr of testosterone or placebo treatment

Parameter	Placebo treatment			Testosterone treatment			<i>P</i>
	Pretreatment	36 months	Change	Pretreatment	36 months	Change	
Wt (kg)	81.9 \pm 11.2	82.1 \pm 11.4	0.4 \pm 3.8	82.6 \pm 9.3	82.4 \pm 9.7	-0.4 \pm 3.8	0.3
Body mass index	26.7 \pm 3.3	26.8 \pm 3.4	0.1 \pm 1.3	27.1 \pm 2.9	26.9 \pm 2.9	-0.1 \pm 1.4	0.4
Tissue mass (kg)	78.1 \pm 8.5	76.1 \pm 9.1	-0.9 \pm 3.6	79.0 \pm 8.8	77.7 \pm 9.1	-1.2 \pm 3.8	0.7
Fat mass (kg)	24.6 \pm 6.6	23.3 \pm 6.7	-0.7 \pm 3.1	24.3 \pm 6.7	21.0 \pm 6.7	-3.0 \pm 3.7	0.001
Lean mass (kg)	54.4 \pm 5.9	54.1 \pm 6.3	0.2 \pm 1.5	54.7 \pm 5.3	56.8 \pm 5.6	1.9 \pm 2.0	<0.001
IGF-I (ng/ml)	137 \pm 43	116 \pm 43	-21.7 \pm 22.5	126 \pm 43	118 \pm 44	-8 \pm 22	0.004

Values are the mean \pm SD for all 108 subjects in the study for all parameters. Change refers to the change from 0–36 months for each parameter in each treatment group. The *P* values are based on the independent sample *t* test comparing the mean change from 0–36 months between the two treatment groups.

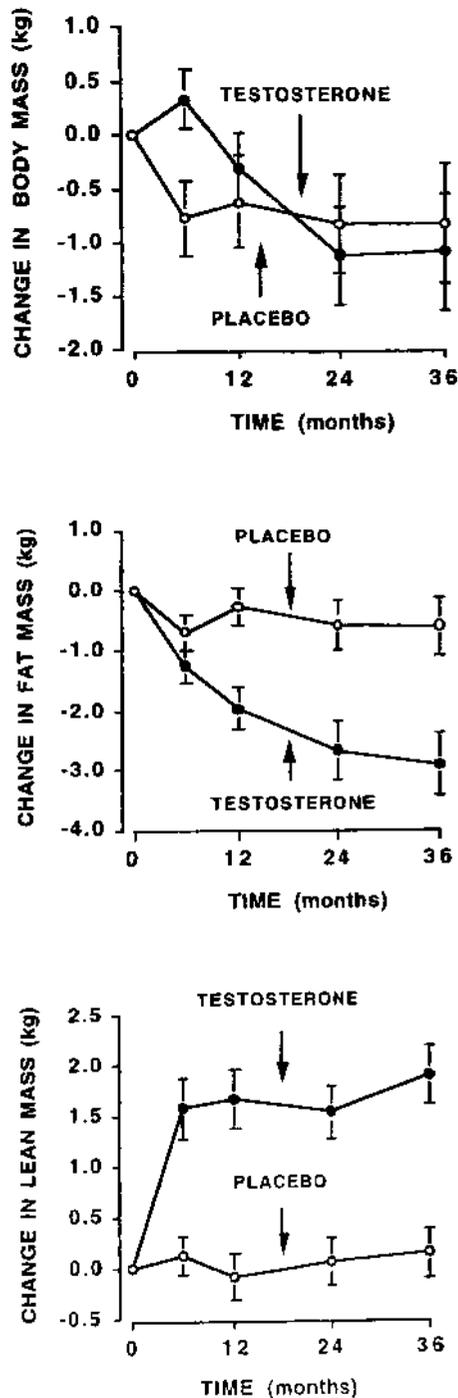


FIG. 1. Mean (\pm SE) change from baseline in total body mass, fat mass, and lean mass, as determined by dual energy x-ray absorptiometry, in 108 men over 65 yr of age who were treated with either testosterone or placebo (54 men each). The decrease in fat mass ($P < 0.005$) and the increase in lean mass ($P < 0.001$) in the testosterone-treated subjects were significantly different from those in the placebo-treated subjects at 36 months.

from 0–36 months differed significantly between the two groups for both fat mass ($P = 0.001$) and lean mass ($P < 0.001$). Linear regression analyses indicated that the effects of testosterone treatment on fat mass and lean mass varied inversely and significantly ($P < 0.02$) as a function of the

pretreatment serum testosterone concentration, but not as a function of the increment in serum testosterone concentration during treatment.

The decrease in fat mass in the testosterone-treated group during the 36 months of treatment was significant in the arms (-0.7 ± 0.1 kg; $P < 0.001$) and legs (-1.1 ± 0.2 kg; $P < 0.001$), but not in the trunk, whereas the increase in lean mass was significant in the trunk (1.7 ± 0.3 kg; $P < 0.001$), but not in the arms and legs (Fig. 2).

Serum insulin-like growth factor I concentrations fell significantly in both groups during the study, but significantly less ($P < 0.005$) in the testosterone-treated group (Table 1).

Muscle strength

The strength of knee extension at 60° and 180° of angular velocity was similar in both groups before treatment and decreased significantly ($P < 0.001$) in both groups during the course of 36 months of treatment, but the changes during treatment did not differ between the groups (Table 2). The strength of knee flexion at 60° and 180° of angular velocity did not differ between the two groups before or after treatment (Table 2). Hand grip strength did not differ between the two groups before or after treatment (Table 2).

Physical function

Changes in tests of physical function, including time to walk 25 ft, number of steps taken in walking 25 ft, and time to climb 12 stairs, did not differ between the 2 groups before or after treatment (Table 2).

Questionnaires

The perception of physical functioning, one of the eight parameters assessed by the MOS SF-36 questionnaire, decreased significantly ($P < 0.001$) in the placebo-treated group during the 36 months of treatment, but not in the testosterone-treated group. Perception of physical functioning in the testosterone-treated group was significantly greater ($P < 0.05$) in the testosterone-treated group than in the placebo-treated group at the end of the 36 months, when corrected for baseline values (Table 3 and Fig. 3). Linear regression analysis indicated that the effect of testosterone treatment on perception of physical functioning varied inversely and significantly ($P < 0.01$) as a function of the pretreatment serum testosterone concentration. The lower the pretreatment serum testosterone concentration, the greater the testosterone treatment effect on perception of physical function (Fig. 3). For a pretreatment serum testosterone concentration of 400 ng/dL, the effect of testosterone treatment was only $8.2 \pm 3.8\%$, but for a pretreatment serum testosterone concentration of 200 ng/dL, the effect of testosterone treatment was $30.2 \pm 8.3\%$ ($P < 0.005$).

There was no significant difference between the two treatment groups before or after 36 months of treatment in any other parameter in the MOS SF-36 questionnaire or in the energy or sexual function parameters of the study questionnaire (Table 3).

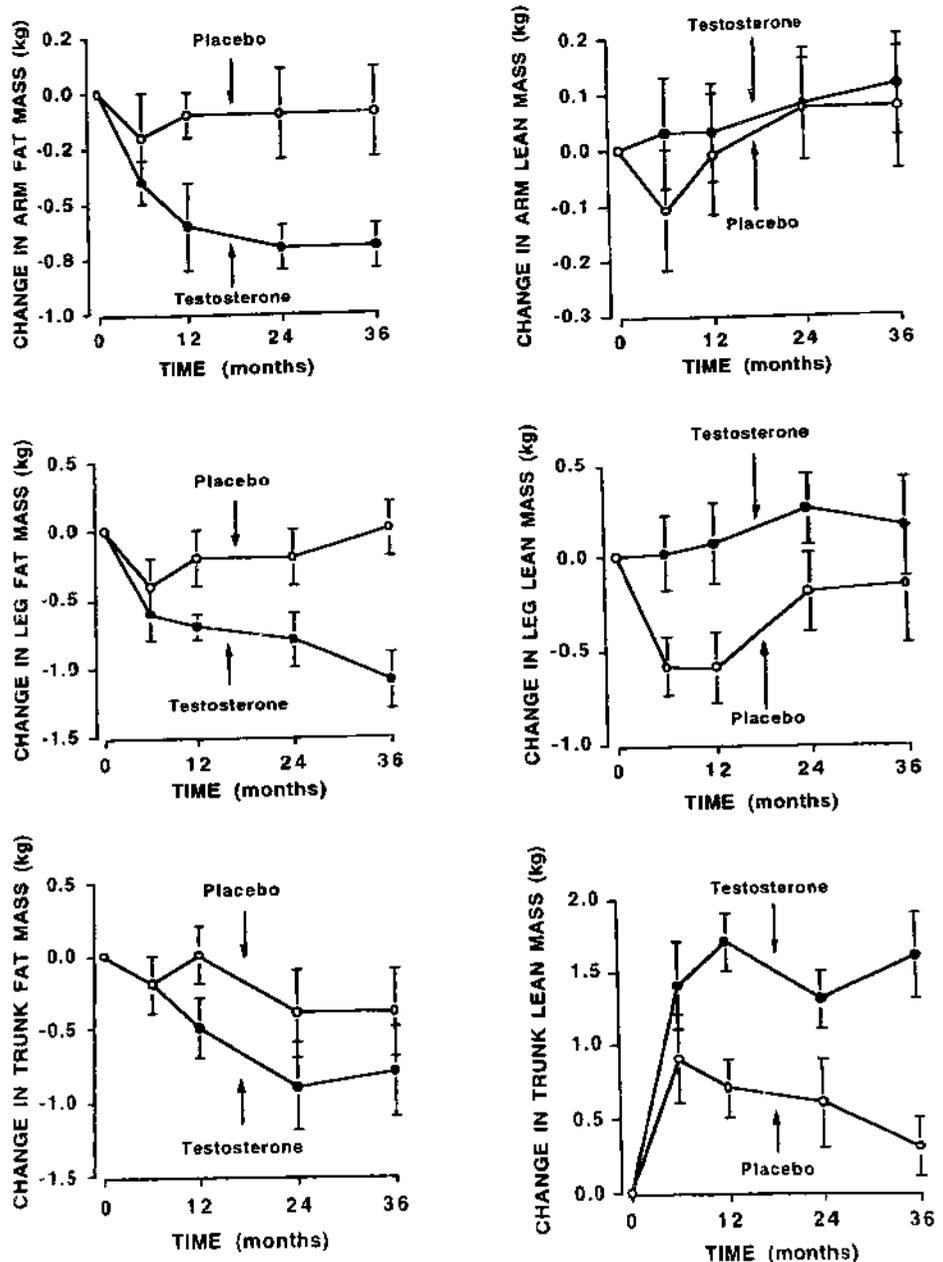


FIG. 2. Mean (\pm SE) change from baseline in the fat and lean mass of the arms, legs, and trunk, as determined by dual energy x-ray absorptiometry, of 108 men over 65 yr of age who were treated with either testosterone or placebo (54 men each). The decrease in fat mass in the arms ($P < 0.02$) and legs ($P < 0.001$) and the increase in lean mass of the trunk ($P < 0.001$) in the testosterone-treated subjects were significantly different from those in the placebo-treated subjects at 36 months. Other changes were not significantly different between the 2 groups.

Discussion

Increasing the serum testosterone concentration of healthy elderly men to that of young men increased their lean mass, especially of the trunk, and decreased their fat mass, especially of the arms and legs, but did not increase their strength of knee extension or flexion. Testosterone treatment also increased the subjects' self-perception of physical function, but not objective tests of physical function.

The overall effects of testosterone on body composition observed in this study are similar to the effects of testosterone on body composition in men who have frank hypogonadism due to known causes. In a study of 6 previously healthy men who were made severely hypogonadal by the administration of leuprolide, percent fat mass, as measured by dual energy x-ray absorptiometry, increased, and fat-free mass decreased

(12). In a study of 13 previously untreated hypogonadal men who were treated with 100 mg testosterone enanthate or cypionate once a week for 18 months, total body fat, as measured by quantitative computed tomography, decreased significantly (5). In another study, testosterone replacement was discontinued in 7 hypogonadal men for at least 12 weeks before they were tested. They were then treated with 100 mg testosterone enanthate once a week and tested again 10 weeks later. Testosterone treatment did not decrease the percent fat, but did increase the fat-free mass, as determined by underwater weighing (7). In a study of men who had acquired immunodeficiency syndrome wasting and had relatively low serum testosterone concentrations, transdermal testosterone treatment for 12 weeks decreased fat mass and increased lean mass (13). In another study of men with ac-

TABLE 2. Parameters of muscle strength and function in healthy, elderly men before and after 3 yr of testosterone or placebo treatment

Parameter	Placebo treatment			Testosterone treatment			<i>P</i>
	Pretreatment	36 months	Change	Pretreatment	36 months	Change	
Knee extension, 60°/s (ft lb)	98.2 ± 26.8	85.7 ± 25.2	-12.8 ± 17.6	99.5 ± 24.4	86.6 ± 23.9	-12.0 ± 13.5	0.9
Knee extension, 180°/s (ft lb)	65.1 ± 20.5	60.7 ± 20.6	-5.4 ± 14.0	63.2 ± 17.7	56.2 ± 16.4	-7.8 ± 12.5	0.4
Knee flexion, 60°/s (ft lb)	58.3 ± 17.3	54.2 ± 16.1	-4.9 ± 12.3	61.5 ± 15.9	55.5 ± 17.3	-5.9 ± 11.0	0.7
Knee flexion, 180°/s (ft lb)	46.3 ± 14.0	44.6 ± 12.1	-1.5 ± 9.7	49.5 ± 13.0	47.7 ± 12.1	-1.9 ± 9.2	0.8
Hand grip (ft lb)	39.1 ± 9.8	37.8 ± 9.4	-1.2 ± 6.3	40.0 ± 9.7	40.0 ± 9.9	-0.1 ± 7.1	0.4
Walking time (s)	6.7 ± 1.1	6.7 ± 1.0	0.1 ± 0.7	6.6 ± 1.0	6.4 ± 1.2	0.3 ± 1.1	0.4
No. of steps walked	11.7 ± 1.6	12.1 ± 1.4	0.4 ± 0.8	11.6 ± 1.6	11.8 ± 1.8	0.6 ± 1.3	0.4
Time to climb 15 stairs (s)	6.7 ± 2.4	6.8 ± 1.4	0.1 ± 2.0	6.5 ± 1.0	6.7 ± 2.0	0.6 ± 2.0	0.3

Values are the mean ± SD for all 108 subjects in the study for all parameters. Change refers to the change from 0–36 months for each parameter in each treatment group. The *P* values are based on the independent sample *t* test comparing the mean change from 0–36 months between treatment groups.

TABLE 3. Subjective parameters of well-being and function in healthy, elderly men before and after 3 yr of testosterone or placebo treatment

Parameter	Placebo treatment			Testosterone treatment			<i>P</i>
	Pretreatment	36 months	Change	Pretreatment	36 months	Change	
MOS SF-36 questionnaire							
Physical functioning	84.9 ± 15.2	77.4 ± 20.3	-8.0 ± 12.1	77.9 ± 20.1	83.4 ± 17.0	1.9 ± 17.3	0.01
Role limitations due to physical problems	90.0 ± 21.4	87.5 ± 22.9	-3.6 ± 31.0	91.1 ± 20.7	85.2 ± 23.1	-13.0 ± 25.1	0.2
Bodily pain	70.9 ± 18.9	72.0 ± 23.7	-2.2 ± 26.2	82.7 ± 16.9	77.3 ± 19.7	-5.6 ± 14.8	0.5
General health perceptions	80.2 ± 10.6	75.9 ± 15.3	-4.4 ± 14.0	78.1 ± 13.0	75.6 ± 15.4	-5.5 ± 14.6	0.8
Vitality	69.6 ± 12.8	64.9 ± 16.9	-5.6 ± 16.5	69.2 ± 16.1	64.3 ± 18.7	-9.4 ± 15.2	0.4
Social functioning	97.7 ± 5.8	92.5 ± 14.0	-5.0 ± 13.4	96.2 ± 8.2	91.7 ± 14.2	-5.9 ± 16.5	0.8
Role limitations due to emotional problems	91.7 ± 19.0	90.0 ± 21.3	-1.8 ± 22.4	89.4 ± 18.2	91.7 ± 17.8	2.6 ± 16.3	0.4
General mental health	85.2 ± 11.4	81.5 ± 12.6	-1.6 ± 9.9	84.1 ± 11.4	81.2 ± 13.9	-3.3 ± 11.2	0.5
Study questionnaire							
Energy	68.3 ± 15.8	63.4 ± 19.5	-4.1 ± 19.1	69.1 ± 16.3	65.5 ± 18.9	-3.1 ± 17.4	0.8
Sexual function	42.6 ± 16.9	40.4 ± 16.9	-2.0 ± 16.0	41.4 ± 19.5	45.8 ± 20.5	3.4 ± 19.6	0.2

All of the parameters are based on a scale of 0–100 in arbitrary units. Values are the mean ± SD. Change refers to the change from 0–36 months for each parameter in each treatment group. The *P* values are based on the independent sample *t* test comparing the mean change from 0–36 months between treatment groups.

quired immunodeficiency syndrome wasting and hypogonadism, treatment with 300 mg testosterone enanthate every 3 weeks for 6 months increased fat-free mass, but did not decrease fat mass (14). The overall effects of testosterone on body composition observed in this study are also similar to those seen in studies of older men treated with mildly pharmacological doses of testosterone (15–17).

Even though the reproducibility of regional body composition measurements by dual energy x-ray absorptiometry, especially of fat tissue, is less than that of total body composition (18), clear changes in regional body composition occurred in this study. The finding that testosterone decreased fat mass in the arms and legs suggests that its effect in those locations may have been on sc fat. This effect is similar to that observed in the 13 hypogonadal men, described above, in whom testosterone treatment clearly decreased sc fat, but only marginally decreased intraabdominal and visceral fat (5). The clinical significance of testosterone decreasing arm and leg fat is not at all clear. Although visceral fat has been associated with risk factors for cardiovascular disease and even clinical cardiovascular disease, sc fat of the arms and legs has not been so closely correlated. In a study of 58 obese men, visceral adipose tissue, as measured by computed tomography, was positively correlated with plasma glucose and insulin concentrations after an oral glucose load and was nega-

tively correlated with serum high density lipoprotein cholesterol concentration (19). Subcutaneous abdominal adipose tissue, however, was not independently correlated with these indexes of carbohydrate and lipoprotein metabolism, and femoral adipose tissue was not at all correlated. In a prospective study of 6718 men without a history of clinical coronary heart disease, 212 men developed coronary events during a subsequent mean observation period of 6.6 yr. Mean skinfold thickness at the time of initial examination in the men who eventually developed new coronary events was significantly greater than that in the men who did not develop coronary events at all 5 sites in the trunk, but in only 3 of 4 sites in the arm and in none of 4 sites in the thigh (20).

The finding that testosterone increased lean mass principally in the trunk is difficult to explain. The anatomical site of the increase, whether in the large muscles of the upper chest and back or other tissues, cannot be determined from these data.

The lack of an effect of testosterone on strength of knee extension does not support the principal hypothesis of the study and runs counter to conventional wisdom about the effect of testosterone. One possible explanation for the lack of an effect is that the pretreatment serum testosterone concentration was not sufficiently low, but this explanation seems unlikely, because linear regression analysis

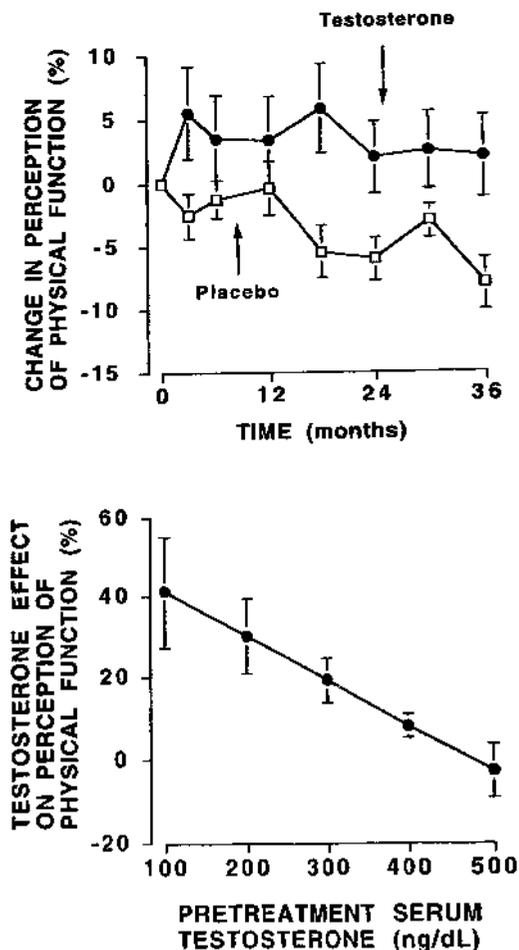


FIG. 3. *Upper panel*, Mean (\pm SE) change from baseline perception of physical function, as determined by the MOS SF-36 questionnaire, in 108 men over 65 yr of age who were treated with either testosterone or placebo (54 men each). The difference between the testosterone- and placebo-treated men at 36 months was significant ($P < 0.02$). *Lower panel*, The effect of testosterone treatment on percent change in perception of physical function during 36 months of testosterone treatment of men over 65 yr of age as a function of the pretreatment serum testosterone concentration. The lower the pretreatment serum testosterone concentration, the greater the effect of testosterone treatment on perception of physical function. The testosterone treatment effect was statistically significant overall at $P < 0.01$ and for testosterone concentrations of 100–300 ng/dL at $P < 0.005$. To convert testosterone values to nanomoles per L, multiply by 0.03467.

showed no relationship between the testosterone treatment effect on muscle strength and the pretreatment serum testosterone concentration. Another possible explanation is that the increase in the serum testosterone concentration during treatment was not sufficiently great, but this explanation seems unlikely, because the serum testosterone concentration increased by a mean of more than 250 ng/dL in the testosterone-treated subjects, so that their mean serum testosterone concentration was in the midnormal range for young men. Another possible explanation is that the tests of muscle strength employed were not the optimal tests to detect changes in muscle strength. In the study described above in seven frankly hypogonadal men in whom testosterone, administered in a non-

blinded fashion, increased muscle strength by 22%, muscle strength was assessed by a bench press instrument (7), whereas in the present study, strength was assessed by dynamometer. In three studies in which older men were treated with mildly pharmacological doses of testosterone, muscle strength increased in two (17, 21) but not in the third (15). In view of the lack of a significant increase in lean mass in the arms and legs in response to testosterone treatment in the elderly men in the present study, however, perhaps it is not surprising that there was no significant effect of testosterone on muscle strength.

Testosterone treatment did significantly increase the subjects' self-perception of their physical function, and it did so in inverse relationship to their pretreatment serum testosterone concentration. Testosterone did not, however, increase measured physical function. We cannot explain this discrepancy.

We conclude that raising the serum testosterone concentration of healthy elderly men to that of young men changed their body composition, in that it increased their lean mass and decreased their fat mass, principally in the arms and legs. The increase in serum testosterone concentration, however, did not increase the measured strength of knee extension or flexion. Body composition is now the second parameter in this study [bone mineral density of the spine was the first (11)], in which testosterone treatment of elderly men with low serum testosterone concentrations has been shown to be efficacious. Although prostate and hematological parameters were monitored, and no statistically significant changes occurred (11), the study was not designed to have sufficient statistical power to evaluate these effects, so we cannot draw definite conclusions about the risk of administering testosterone to men over 65 yr of age.

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