Endogenous Testosterone Levels, Physical Performance, and Fall Risk in Older Men

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Background: Gonadal steroid levels decline with age in men. Whether low testosterone levels affect the development of common age-related disorders, including physical functioning and falling, is unclear.

Methods: This longitudinal, observational follow-up study sought to determine whether low testosterone levels are associated with physical performance and fall risk in older men. A total of 2987 community-based men aged 65 to 99 years were selected using a stratified random sampling scheme from a study cohort of 5993 volunteers. Bioavailable testosterone and estradiol levels and physical performance measures were determined from baseline. Incident falls were ascertained every 4 months during 4 years of follow-up. Generalized estimating equations were used to estimate risk ratios for the relation of sex steroids to falls.

Results: Fifty-six percent of the men reported at least 1 fall; many fell frequently. Lower bioavailable testosterone levels were associated with increased fall risk. Men with testosterone levels in the lowest quartile had a 40% higher fall risk than those in the highest quartile. The effect of low testosterone levels was most apparent in younger men (65-69 years) (relative risk, 1.8; 95% confidence interval, 1.2-2.7); testosterone level was not associated with falls in the oldest men (≥80 years). Lower testosterone concentrations were associated with reduced physical performance. However, the association between low testosterone levels and fall risk persisted despite adjustment for performance.

Conclusions: Falls were common among older men. Fall risk was higher in men with lower bioavailable testosterone levels. The effect of testosterone level was independent of poorer physical performance, suggesting that the effect of testosterone on fall risk may be mediated by other androgen actions.

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THE CONCENTRATIONS OF SEX steroids in serum decline with age in men, apparently as a result of complex alterations in reproductive physiologic characteristics. The importance of these changes remains controversial, but modifications in sex steroid levels have been postulated to underlie, in part, the occurrence of adverse events that accompany male aging. This hypothesis has received widespread attention, and the number of US men treated with testosterone has increased rapidly. Many elderly persons fall each year; repetitive falls are common, and the likelihood of falling increases quickly with advancing age. These falls account for numerous injuries and hospitalizations and a substantial health care burden. Sarcopenia and muscle weakness are common among older men and have been linked to the development of disability, particularly in the eighth and ninth decades of life, and the likelihood of falling is increased by the age-related development of sarcopenia, weakness, and impairments in physical performance. Testosterone is anabolic for muscle, and testosterone supplementation in older men results in increased strength. Thus, reductions in muscle mass, strength, and physical performance, and a resultant increase in fall risk, are prominent among the postulated effects of age-related declines in androgen levels. Despite the common perception that testosterone insufficiency is related to age-associated morbidity in men, the supporting epidemiologic evidence is limited and inconclusive. Some cross-sectional studies support the hypothesis that lower testosterone levels are linked to impaired physical functioning and fall history, but those findings are inconsistent. More important, no prospective data document this association. The Osteoporotic Fractures in Men (MrOS) Study is a co-
short study of men 65 years and older designed primarily to identify risk factors for falls and fractures. We report the associations among testosterone concentrations, physical performance, and fall risk during a mean follow-up of 4 years.

**STUDY METHODS**

Between March 1, 2000, and April 30, 2002, 5995 community-dwelling, ambulatory men 65 years and older were recruited for participation in the baseline examination of the prospective MrOS Study. The recruitment and characteristics of the population have been described elsewhere.23,24 Approximately 1000 participants were recruited at each of 6 academic medical centers: Oregon Health & Science University, Portland; Stanford University, Palo Alto, Calif; University of Alabama at Birmingham; University of California, San Diego; University of Minnesota, Minneapolis; and University of Pittsburgh, Pittsburgh, Pa. Recruitment efforts focused on community mailings from vehicle registration or voter registration lists, although community outreach activities were also used.23,26 The inclusion criteria were (1) age 65 years and older, (2) the ability to walk without assistance, (3) at least 1 native hip suitable for bone density measurements, (4) anticipated residence near a study site for the duration of follow-up, (5) the absence of a medical condition that would result in imminent death, and (6) the ability to understand and sign an informed consent form. The cohort was approximately 89% white.23 As of July 1, 2005, the cohort had 8.2% mortality and 1.1% voluntary termination. The institutional review board at each study center approved the study protocol, and written informed consent was obtained from all the participants.

**Sex Steroid Cohort**

Assays of sex steroids were performed using baseline serum samples from 2623 participants; results from these men form the basis of the present study. Men were selected from the general MrOS Study population using a stratified random sampling scheme so that the following characteristics were adequately represented: race, availability of an extensive set of skeletal imaging procedures (for analyses of the effects of sex steroids on fracture), and clinic site.27 The sampling target was 2643 participants, and sampling of 2623 (99%) was achieved. Measures of sex steroids were available in 2587 participants. As previously reported, men in whom sex steroids were measured were representative of the entire MrOS Study cohort on numerous characteristics (except for the inclusion, by intent, of a higher proportion of men of a minority race).2 Results from the 34 men being treated with androgens are excluded from these analyses.

At the baseline clinic visit, participants completed questionnaires and interviews regarding medical history, medication use, and lifestyle. Types of medications used regularly for the past month were coded during the clinic visit by trained staff. Information was recorded directly from prescription medications brought in by the participant. Medical history was assessed using self-reports on the questionnaire of several current and past illnesses, including stroke, hypertension, types of cancer, Parkinson disease, and myocardial infarction. General health status was assessed using a self-report of overall health relative to other men of the same age. Lifestyle factors, including smoking and alcohol consumption, history of falls in the past 12 months, and difficulties walking 2 to 3 city blocks or up 10 stairs, were also obtained from self-reports. Height was measured using a wall-mounted stadiometer, and weight was obtained using a balance beam scale. Total body lean and fat mass were assessed by means of dual-energy x-ray absorptiometry (Hologic 4500W; Hologic Inc, Waltham, Mass). Weight, lean mass, and fat mass each were divided by the square of height to provide the body mass index, lean mass index, and fat mass index, respectively.

**Physical Performance Measures**

Grip strength was assessed using a handheld dynamometer. Leg extension power, measured using the Nottingham power rig (University of Nottingham, Nottingham, England), correlates well with functional measures such as chair-rising speed, stair-climbing speed and power, and walking speed in elderly individuals.10,28 The narrow walk, used as an indirect measure of dynamic balance, involved walking a 6-m course while keeping each foot within a 20-cm-wide lane. A trial was considered successful if the participant had no more than 2 deviations from the lane. Time to complete 3 chair stands without using the arms to rise was used to assess lower extremity muscle capacity. Participants who could not complete the measures were classified as “unable.” The proportion unable was 2.3% for grip strength, 1.6% for leg power, 8.9% for narrow walk, and 2.8% for chair stands.

**Ascertainment of Falls**

At 4-month intervals, participants were queried by mailed questionnaire about the number of times they had fallen during the interval. Participants who fell in the previous 4 months were asked how many times (1, 2, 3, 4, or ≥5). The first questionnaire was mailed to enrolled participants on July 1, 2000. Participants who did not initially return a tri-annual questionnaire or who did not adequately complete the questionnaire were followed up with a telephone call. The present study includes fall reports from the first through the 15th (March 2005) tri-annual questionnaire cycles. A total of 2582 men (99.8%) completed at least 1 questionnaire; 90% returned 14 or more questionnaires. The mean number of questionnaires completed was 12 (corresponding to a mean of 4 years of follow-up), with a range of 1 to 15.

**LABORATORY ANALYSIS**

Morning blood samples were collected at the baseline clinic visit after an overnight fast; serum was prepared immediately, frozen at −20°C, and shipped on dry ice to a central facility, where it was stored at −70°C until assay. Assays were performed in duplicate, and all assays used stringent quality control.3 Total testosterone levels were determined using a solid-phase iodine 125 radioimmunoassay (Diagnostic Products Corp, Los Angeles, Calif); total estradiol levels using an ultrasensitive radioimmunoassay (Diagnostic Systems Laboratory Inc, Webster, Tex); sex hormone–binding globulin levels using an immunometric assay (Diagnostic Products Corp); and albumin levels using a Beckman LX 20 analyzer (Beckman-Coulter Instruments, Fullerton, Calif). For total testosterone level, the detectable range was 10 to 1600 ng/dL (0.3–55.5 nmol/L), and the coefficient of variation (CV), derived from repeated assays of a pooled serum sample, was 8.2%, with an intra-assay CV of 5.4%. For total estradiol level, the detectable range was 2.5 to 750 pg/mL (9-2752 pmol/L), the pooled serum sample CV was 13.3%, and the intra-assay CV was 8.3%. Estradiol values in 2 samples were decreased below the sensitivity level of the assay and were reported as half the lowest standard (ie, 1.25 pg/mL).
To evaluate whether the association between testosterone level and fall risk was affected by physical performance, we added variables for each physical performance measure sequentially to the final model. To control for a participant’s inability to perform the physical performance assessments, the statistical models included an indicator variable for participants who attempted but could not complete the performance measure or could not complete the performance measure owing to a physical limitation, and the corresponding physical performance variable was set to a value of zero. When physical performance measures were categorized into quartiles, the additional category representing “unable” was also included in the model.

RESULTS

STUDY POPULATION

The mean (SD) age of the participants was 73 (6) years (Table 1); 14% were 80 years or older. Most participants considered their health (compared with their peers) to be good to excellent. Variation in sex steroid concentrations was substantial, and increasing age was associated with lower bioavailable testosterone and estradiol concentrations. Increasing age was also associated with lower lean body mass (r = −0.21; P = .001), strength (grip strength: r = −0.40; leg power: r = −0.49; P < .001 for both), and physical performance (chair stand time: r = 0.23; narrow walk speed: r = −0.27; P ≤ .001 for both).

SEX STEROIDS, BODY MASS, AND PHYSICAL PERFORMANCE AT BASELINE

Men with higher levels of bioavailable testosterone had on average lower body weight, lower body mass index, and lower fat mass index, but lean body mass index did not vary by testosterone level (Table 1). Nevertheless, strength and physical performance were slightly better in men with higher levels of bioavailable testosterone (Table 1). Baseline levels of bioavailable estradiol were not associated with any measure of strength or physical performance.

FALL OUTCOMES

A total of 29,057 completed tri-annual questionnaires were returned by the 2587 participants who had available sex steroid measures. During the period of observation, 56% of the men reported at least 1 fall. Among men who fell, the rate of reported falls is shown in Figure 1. Those who reported at least 1 fall before baseline were at higher risk for falling during follow-up (RR, 2.63; 95% CI, 2.29–3.03; P < .001). In addition, falls occurred more commonly in older men (mean number of falls per year: 0.6 in men aged 65–69 years, 0.7 in men aged 70–79 years, and 1.0 in men ≥80 years), and older men fell more often (P < .001). More than 20% of those older than 80 years reporting falling 5 times or more compared with 10% of men aged 65 to 69 years.

The risk of falls was greater in men with reduced levels of strength or physical performance at baseline. Compared with men in the highest quartile of grip strength, men who could not perform the measure or who could
perform the measure but were in the lowest quartile were at approximately 40% greater risk for falling (multivariable RR, 1.4; 95% CI, 0.9-2.0; and multivariate RR, 1.7; 95% CI, 1.4-2.1, respectively). Fall risk was similarly increased with low leg power and with inability to complete narrow walk trials.

TESTOSTERONE LEVELS AND FALL RISK

With lower baseline bioavailable testosterone levels, there was a progressive increase in the risk of falls during follow-up (Table 2). Fall risk in men in the lowest quartile of baseline bioavailable testosterone concentration was more than 40% greater than that in men in the highest quartile, before and after adjustment for physical performance. To examine whether poorer health affected this association, we repeated the analysis after restricting the cohort to healthier men (self-reported good or excellent health, no history of either Parkinson disease or prostate cancer, no use of walking aids, and no self-report of mobility limitation). The association of testosterone level with fall risk was not materially different from that observed in the entire cohort, with the RR comparing the lowest to highest testosterone quartile being 1.47 (95% CI, 1.16-1.86) (Figure 2). The relative risk of falls for a 1-SD increase in bioavailable testosterone concentration is 0.89 (95% CI, 0.83-0.95; P<.001).

Men with lower levels of bioavailable testosterone were also at higher risk for multiple falls (≥2 per year) (bio-

Table 1. Baseline Characteristics of the Study Population and Differences by Quartiles of Bioavailable Testosterone Levels*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sample Cohort Overall (N = 2587)</th>
<th>1 (&lt;1.75 ng/dL)</th>
<th>2 (1.75-2.12 ng/dL)</th>
<th>3 (2.13-2.50 ng/dL)</th>
<th>4 (&gt;2.51 ng/dL)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>73.2 (5.7)</td>
<td>74.8</td>
<td>73.4</td>
<td>72.6</td>
<td>71.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Height, cm</td>
<td>173.9 (6.9)</td>
<td>173.7</td>
<td>174.2</td>
<td>174.2</td>
<td>173.6</td>
<td>.37</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>82.6 (13.4)</td>
<td>85.4</td>
<td>83.4</td>
<td>81.9</td>
<td>79.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI</td>
<td>27.3 (3.8)</td>
<td>28.2</td>
<td>27.4</td>
<td>27.0</td>
<td>26.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Lean BMI</td>
<td>18.7 (1.9)</td>
<td>18.8</td>
<td>18.8</td>
<td>18.7</td>
<td>18.6</td>
<td>.38</td>
</tr>
<tr>
<td>Fat BMI</td>
<td>7.0 (2.2)</td>
<td>7.9</td>
<td>7.1</td>
<td>6.8</td>
<td>6.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Alcohol consumption, drinks/wk</td>
<td>4.0 (6.6)</td>
<td>3.5</td>
<td>3.7</td>
<td>4.3</td>
<td>4.5</td>
<td>.02</td>
</tr>
<tr>
<td>Total testosterone, ng/dL</td>
<td>422.8 (157.9)</td>
<td>268.0</td>
<td>381.2</td>
<td>454.9</td>
<td>590.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total estradiol, pg/mL</td>
<td>173.8 (5.6)</td>
<td>15.4</td>
<td>17.4</td>
<td>18.6</td>
<td>19.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Bioavailable estradiol, pg/mL</td>
<td>12.1 (4.3)</td>
<td>10.4</td>
<td>11.9</td>
<td>12.7</td>
<td>13.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Average grip strength, kg</td>
<td>38.4 (8.0)</td>
<td>36.8</td>
<td>38.2</td>
<td>39.2</td>
<td>39.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Narrow walk best time, m/s</td>
<td>1.15 (0.27)</td>
<td>1.10</td>
<td>1.16</td>
<td>1.16</td>
<td>1.18</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Chair stand time, s</td>
<td>10.8 (3.1)</td>
<td>11.6</td>
<td>10.8</td>
<td>10.6</td>
<td>10.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Maximum leg power, W</td>
<td>210.7 (62.4)</td>
<td>199.0</td>
<td>213.0</td>
<td>214.3</td>
<td>217.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.02</td>
</tr>
<tr>
<td>White</td>
<td>76.6</td>
<td>75.9</td>
<td>77.2</td>
<td>78.8</td>
<td>74.4</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>9.0</td>
<td>11.3</td>
<td>7.1</td>
<td>6.6</td>
<td>11.0</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>7.0</td>
<td>7.1</td>
<td>8.5</td>
<td>7.7</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>4.8</td>
<td>3.9</td>
<td>4.3</td>
<td>4.7</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2.5</td>
<td>1.9</td>
<td>2.9</td>
<td>2.3</td>
<td>2.9</td>
<td></td>
</tr>
<tr>
<td>Very poor, poor, or fair health status, %</td>
<td>14.4</td>
<td>21.7</td>
<td>14.8</td>
<td>10.5</td>
<td>10.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>4.1</td>
<td>3.7</td>
<td>2.3</td>
<td>3.9</td>
<td>6.1</td>
<td>.002</td>
</tr>
<tr>
<td>Use of walking aids, %</td>
<td>3.6</td>
<td>6.4</td>
<td>3.4</td>
<td>2.6</td>
<td>1.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mobility limitation, %</td>
<td>14.6</td>
<td>23.3</td>
<td>13.8</td>
<td>11.1</td>
<td>10.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Unable to complete grip strength, %</td>
<td>2.3</td>
<td>2.3</td>
<td>2.4</td>
<td>2.1</td>
<td>2.4</td>
<td>.98</td>
</tr>
<tr>
<td>Unable to complete a narrow walk trial, %</td>
<td>8.9</td>
<td>13.3</td>
<td>8.7</td>
<td>7.4</td>
<td>6.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Unable to complete 5 chair stands, %</td>
<td>2.8</td>
<td>5.0</td>
<td>1.3</td>
<td>2.3</td>
<td>2.4</td>
<td>.001</td>
</tr>
<tr>
<td>Unable to complete power rig trials, %</td>
<td>1.6</td>
<td>2.6</td>
<td>1.8</td>
<td>1.1</td>
<td>1.1</td>
<td>.14</td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

*Data are given as mean (SD) unless otherwise indicated.
†The number of participants with complete data for bioavailable testosterone measures (testosterone, estradiol, and sex hormone-binding globulin) is 2486.

Statistical tests of continuous variables by quartile were conducted using analysis of variance. Categorical variables were tested by quartile using χ² tests.

Figure 1. The distribution of fall rates among men who fell during follow-up.
Table 2. Relation of Bioavailable Testosterone Levels and Fall Risk, With and Without Adjustment for Physical Performance

<table>
<thead>
<tr>
<th>Bioavailable Testosterone Level Quartile</th>
<th>Model 1* RR (95% CI)</th>
<th>P Value</th>
<th>Model 2† RR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (&lt; 1.75 ng/dL)</td>
<td>1.42 (1.19-1.70)</td>
<td>&lt;.001</td>
<td>1.40 (1.17-1.67)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2 (1.75-2.12 ng/dL)</td>
<td>1.27 (1.06-1.51)</td>
<td>.009</td>
<td>1.28 (1.07-1.52)</td>
<td>.006</td>
</tr>
<tr>
<td>3 (2.13-2.50 ng/dL)</td>
<td>1.26 (1.05-1.50)</td>
<td>.02</td>
<td>1.26 (1.06-1.50)</td>
<td>.01</td>
</tr>
<tr>
<td>4 (≥ 2.51 ng/dL)</td>
<td>1.00 NA</td>
<td></td>
<td>1.00 NA</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NA, not applicable; RR, risk ratio.

*SI conversion factor: To convert testosterone to nanomoles per liter, multiply by 0.0347.

† Additionally adjusted for grip strength, leg power, and ability to complete narrow walk trials.

Aging in men is accompanied by a reduction in circulating testosterone levels. We show that falls are common in older men and that men with low baseline testosterone levels are substantially more likely to fall than those with higher levels. Bioavailable testosterone concentration is associated with measures of physical performance, but the association of testosterone level to the risk of falling is apparent regardless of physical performance. Thus, the mechanisms by which testosterone level affects the propensity to fall may involve other pathways. Finally, the relationship between testosterone concentration and risk of falling tends to diminish with age.

In this cohort, falling was common, and it became more frequent as age increased. Lean mass and physical performance declined as age increased. Fall risk increased with lower grip strength and with measures of lower extremity weakness (use of walking aids, self-reported mobility limitations, and low leg power). In fact, low leg power or low grip strength was increasingly more predictive of fall risk as age advanced. These data supplement other studies in older men, in whom the development of sarcopenia and physical dysfunction was associated with increasing morbidity and disability. Androgen receptors are present in muscle, and androgens have pleiotropic effects on the physiologic characteristics of muscle. However, the importance of age-related declines in testosterone levels in the causation of changes in physical performance is controversial. In the present study, testosterone was not associated with lean mass. Men with the highest bioavailable testosterone levels tended to have slightly better physical performance measures than men with the lowest levels, but other studies in older men found that circulating testosterone levels have little or no association with similar measures. Although we hypothesized that lower testosterone levels might be linked to increased risk of falling via deficits in physical functioning, the relationship between testosterone levels and fall risk was not attenuated when measures of physical performance were included in the multivariate models. That the relationship between leg power and fall risk increased with age further suggests that the effects of testosterone on falls (most apparent in the younger men) may not be acting solely via effects on strength. There may be other androgen-dependent mechanisms that contribute to the causation of...
falling. For example, although vision was not associated with fall risk in the present cohort, other researchers have hypothesized that testosterone may affect visual performance or cognition\textsuperscript{45-46}.

The apparent independence of the effects of low testosterone levels and reduced physical performance on fall risk in this cohort raises questions about the potential utility of testosterone replacement in older men. Replacement doses of testosterone in hypogonadal men, and supraphysiologic doses in younger men, increase lean mass and strength.\textsuperscript{30} Skeletal muscle in older men retains its responsiveness to testosterone,\textsuperscript{15} and recently Page et al\textsuperscript{18} reported that older men with reduced testosterone levels treated with intramuscular testosterone experienced an increase in muscle mass and strength. These effects of testosterone therapy may reflect pharmacologic actions and a priori cannot be taken as evidence of a role of testosterone deficiency in the genesis of age-related declines in physical capacity. Nevertheless, the positive effects of testosterone treatment on physical function justify interest in the possible benefits of therapy in older men.

The effect of testosterone concentration on falls was strongest in the youngest men studied. In men aged 65 to 70 years, fall risk was substantially higher when levels of bioavailable testosterone were low, but the association between testosterone level and fall risk was much less apparent with increasing age, even after adjustment for multiple covariates. The reason for this interaction with age is unclear. Perhaps the waning effect of testosterone reflects a dominance of nonandrogen-dependent factors later in life or the emergence of relative androgen insensitivity in elderly individuals. The finding that relatively younger men are more affected by testosterone deficiency has potentially important implications for understanding the mechanisms of androgen effects and may affect the design of studies intended to examine the usefulness of testosterone replacement therapy in older men.

To our knowledge, this is the first study of the associations among endogenous sex steroid levels, physical performance, and incident fall risk in older men. It has major strengths, including the large community-based population, careful measurements, and almost complete follow-up for falls. The relatively long duration of observation and the large number of falls provide adequate power to confidently describe the relationships between testosterone level and fall risk. A primary strength of the MrOS Study is that it was specifically designed to investigate skeletal and nonskeletal risk factors for fracture in a diverse cohort of older men. Men in the MrOS Study cohort are geographically and racially diverse, generally healthy, and well educated. Distributions of total hip and femoral neck bone mineral density measured using dual-energy x-ray absorptiometry in the MrOS Study cohort and among men of similar ages in the Third National Health and Nutritional Examination Survey (NHANES III) are comparable, although the MrOS Study participants are slightly heavier and have mean bone mineral density that is 2\% to 8\% higher depending on age.\textsuperscript{25} Sex steroid levels in this cohort are similar to those in other cohorts.\textsuperscript{2} Thus, the results of this study are likely to be broadly applicable to similarly aged, generally healthy US men. Despite these advantages, there are also limitations. The MrOS Study is composed of volunteers who thus may be healthier than the general population of older men. On the other hand, there was wide variation in levels of physical performance and of fall rates, suggesting that the results are applicable to many men. Although we found no evidence of ethnic differences in the associations described herein, the MrOS Study is primarily composed of white men, and the results may not apply to those in other racial groups. Finally, the use of radioimmunoassay methods to measure sex steroid levels has recently been questioned.\textsuperscript{47-48} However, we used stringent quality control procedures, and measurements of the relatively high levels of testosterone in adult men (unlike those in women and children) are reliable using radioimmunoassay techniques.\textsuperscript{49} We found no association of estradiol to the outcomes considered herein, and the measurement of estradiol levels in men is more challenging using radioimmunoassays. Nevertheless, it is unlikely that a meaningful, independent effect of estradiol was undetected. Finally, although we adjusted for many covariates that may affect the interaction of testosterone and fall risk or physical performance, there may be others that we have not considered.

In summary, we show that older men fall frequently and that those with low levels of bioavailable testosterone are at substantially higher risk for falls. The association between lower testosterone levels and increased fall risk was undetected. Finally, although we adjusted for many covariates that may affect the interaction of testosterone and fall risk or physical performance, there may be others that we have not considered.

![Figure 3. Associations between leg power (quartiles) (A) and bioavailable testosterone levels (quartiles) (B) and fall risk according to age. A. Leg power risk ratios are adjusted for testosterone level, clinic site, participant race, age, history of falls, history of Parkinson disease, angina, arthritis, dizziness, cancer, and the use of central nervous system medications, use of walking aids, and mobility limitations and are compared with quartile 4 (highest) leg power. B. Bioavailable testosterone level risk ratios are adjusted for clinic site, age, participant race, history of falls, history of Parkinson disease, angina, arthritis, dizziness, cancer, and the use of central nervous system medications, use of walking aids, mobility limitations, and leg power and are compared with quartile 4 (highest) bioavailable testosterone levels. Error bars represent confidence intervals.](http://cme.jamanetwork.com/)
risk persisted after adjustment for measures of physical function and was strongest among relatively younger men. These findings strengthen the link between testosterone and the health of older men, suggesting that the effects of testosterone on fall risk may be via novel mechanisms and provide insight into how testosterone measurements might be useful for identifying men at higher risk for adverse events. Moreover, these results provide additional justification for trials of testosterone supplementation in older men and should aid in the design of those studies.

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