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Original Study

Low Testosterone Levels, Depressive Symptoms, and Falls in Older Men: A Cross-Sectional Study

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A B S T R A C T

Objectives: While several studies have cited a potential association between testosterone deficiency and risk of falls among community-dwelling older men, evidence for such an association is conflicting. Depressive symptoms, which occasionally accompany testosterone deficiency but which are often neglected as associated symptoms, may actually provoke falls independent of or jointly with testosterone deficiency. We examined the association between testosterone levels, depressive symptoms, and falls, and assessed the joint effect of testosterone levels and depressive symptoms on falls among older men.
Design, Setting, and Participants: Data for this cross-sectional study were obtained from 869 men aged over 60 years who participated in health check-ups conducted in 2010 from 2 Japanese municipalities. Salivary testosterone (sT) levels were measured using an enzyme-linked immunosorbent assay, and depressive symptoms were assessed via the short form of the Center for Epidemiologic Studies Depression Scale.
Main outcome measures: Self-reported "any fall" over the 1-month period.
Results: Among the total of 482 participants analyzed (median age, 70 years), 10.8% reported any fall. On comparison between 90th percentile sT levels and lower levels, our logistic regression model with restricted cubic splines showed that lower sT levels were associated with an increased likelihood of suffering any fall after adjustment for sociodemographic characteristics, comorbidities, and mobility function. For example, 5th percentile sT was associated with any fall [adjusted odds ratio (OR), 4.23; 95% confidence interval (CI), 1.66–10.8]. Depressive symptoms were also strongly associated with any fall [adjusted OR, 3.49 (95% CI, 1.52–8.04)]. We noted no apparent interaction of sT and depressive symptoms with falls ($P = .079$), suggesting that the joint effect of testosterone deficiency and depressive symptoms on falls was multiplicative. Indeed, compared with a combination of 90th percentile sT values and no depressive symptoms, adjusted OR for any fall in a combination involving 5th percentile sT and depressive symptoms was 14.8-fold (95% CI, 3.76–58.0).
Conclusions: Our findings indicated that both relatively low testosterone levels and presence of depressive symptoms were independently associated with falls among older men. Causality of these associations should be confirmed in future prospective studies.

Falls are a serious public health problem, with one-third of community-dwelling individuals aged over 65 years falling at least once annually[1] and with 5% to 10% of falls resulting in fracture, head injury, or other serious injuries.[2] While falls in older individuals are multifactorial, age-related decline in lower extremity strength or

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mobility function are recognized as important contributors.[3–5] Separately, age-related decline in testosterone levels in men is a growing concern, with approximately 30% of men aged 40–79 years showing testosterone deficiency.[6] However, while previous studies have suggested that low testosterone levels are associated with reduced extremity strength or mobility function in older men,[7,8] relatively few have examined the association between low testosterone levels and falls, with conflicting results despite the ostensibly plausible biological connections.

One concern with these previous studies examining the relationship between testosterone deficiency and falls is their lack of consideration for presence of depressive symptoms.[9–11] Testosterone-deficient individuals are likely to have concurrent depressive symptoms,[12] and depressive symptoms are also associated with falls.[4] One study found no association between testosterone levels and incident falls after adjustment for confounders including depressive symptoms,[13] suggesting the potential importance of examining the effects of testosterone deficiency on falls independent of depressive symptoms. In addition, if both testosterone deficiency and depressive symptoms are proven to be associated with falls, whether or not men with *both* testosterone deficiency and depressive symptoms are more likely to suffer falls than those with either condition alone would also be of clinical relevance, as these individuals are likely to be seen by physicians specialized in treating testosterone deficiency.[14,15]

Here, to examine whether or not testosterone deficiency and depressive symptoms are independently associated with falls in community-dwelling older men, we analyzed data from the Locomotive Syndrome and Health Outcome in Aizu Cohort Study (LOHAS). We further evaluated how the strength of the association between the composite of testosterone deficiency and depressive symptoms and falls is larger or smaller than the product of the strength of the association between testosterone deficiency and falls and that between depressive symptoms and falls.

Methods

Our cross-sectional study was approved by the Research Ethics Committee of Fukushima Medical University School of Medicine. The LOHAS is a population-based study conducted starting in 2008 involving residents aged 40–80 years who participated in annual health check-ups among 2 communities (Tadami and Minamiaizu Towns) in Fukushima Prefecture, Japan. Eligibility criteria for this study were "aged over 60 years" and "participated in the health check-up conducted in 2010." No exclusion criteria were set. All participants provided written informed consent. Details of the design of the LOHAS have been reported previously.[16]

Measurement of Salivary Testosterone

Salivary concentration of testosterone (sT) was the main exposure, measured using an enzyme-linked immunosorbent assay (ELISA) on the RE52631 system (IBL International GmbH, Hamburg, Germany) and expressed in pg/mL (to convert to picomoles per liter, multiply by 3.47). sT reflects the level of free testosterone in plasma. Saliva was collected in the morning, at least 30 minutes after breakfast. Participants rinsed their mouth gently with water and were asked to avoid brushing their teeth. All participants collected whole saliva by directly spitting into polypropylene tubes through a polypropylene straw-tube. If a participant had little saliva, he was instructed to chew gum prepared specially for saliva collection. The supernatants of saliva obtained after centrifugation (3000 × g, 10 minutes) were kept at −80°C for further analysis. sT was measured in the laboratory of Teikyo University (Tokyo, Japan). For men aged 20–40 years, median sT is 139.4 pg/mL (10th to 90th percentile, 43.8–288.0 pg/mL). The intra- and interassay coefficients of variance were 3.9%–8.8% and 6.7%–8.0%, respectively. Slight cross-reactions with other natural steroids in the human body and their profiles were as follows: dihydrotestosterone, 2.5%; androstenedione, 0.85%; and others, <0.1%.[17]

Depressive Symptoms

Depressive symptoms were considered as secondary exposures in light of their usefulness in predicting fall risk according to the literature and their potentially close association with testosterone deficiency.[4,12] Depressive symptoms were assessed using the 10-item version of the Center for Epidemiological Studies Depression Screening Index (CES-D). The cutoff score for depressive symptoms was set as a score of 10 or greater, as was recommended in the literature.[18] Although data on physician-diagnosed depression was unavailable in the LOHAS study, we assumed its use would considerably underestimate the true proportion of depression, as previous studies have shown that depression is underdiagnosed more often by Japanese physicians than those in other countries due to stigma related to psychiatric disorders within Japanese society.[19,20]

Clinical Outcomes

We examined "any fall over a 1-month period" as the clinical outcome based on participants' answers to the question, "Over the past year, have you fallen down?" to establish fall history. Participants who responded, "Yes," were then asked the follow-up question, "How many times have you fallen down over the past month?" with responses of "zero," "once," "twice," or "three or more times" allowed. Those who reported at least "once" were considered to have had "any fall" over the previous month. Regarding our decision to examine falls over the previous month instead of the previous year, we believed that reverse-causality would be more unavoidable if we were to use fall over the past year rather than the past month in investigating relationship with present sT level, and a systematic review has suggested that recalling fall experience at a 1-year interval might underestimate true fall incidence compared to recalling incidence at a 1-month interval.[21]

Measurement of Potential Confounding Variables

Potential confounding variables examined in the present study were sociodemographic characteristics including age, exercise habit, and living alone, as well as the presence of cerebrovascular disease and the presence of incontinence, all obtained via self-reported questionnaire; body mass index and blood pressure, as measured by local nurse practitioners; hypertension, defined as systolic blood pressure ≥140 mm Hg and diastolic blood pressure ≥90 mm Hg or by individuals reporting attending a physician for treatment; diabetes, defined as having glycosylated hemoglobin values ≥6.1%, as described by the Japanese Diabetes Society [equivalent to ≥6.5% described in National Glycohemoglobin Standardization Program values[22]] or by individuals reporting attending a physician for treatment; and timed up and go (TUG) test. Individuals were considered to engage in exercise if they answered "yes" to the question concerning whether or not they had participated in moderate physical activity (making the individual breathe somewhat harder than normal and including situations such as carrying light loads, bicycling at a regular pace, or doubles tennis) in the previous 7 days. Individuals were considered to have incontinence if they answered "once a week or more" to the question of whether or not they leaked urine because they could not defer the sudden urge to urinate. The TUG test, in which individuals are timed when rising from a chair, walking 3 m, and turning to return to sit on the chair, is considered to be a reflection of function in