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Original Study

Sleep Duration and Disturbances Were Associated With Testosterone Level, Muscle Mass, and Muscle Strength—A Cross-Sectional Study in 1274 Older Men

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A B S T R A C T

Background: Testosterone level follows a circadian rhythm. However, whether sleep duration and disturbances can affect testosterone level, muscle mass, and strength remains unknown.
Objective: To examine the relationship of sleep duration and disturbances to testosterone level, muscle mass, muscle strength, and walking speed.
Participants and methods: We recruited 1274 community-dwelling men older than 65 years of age. Their early morning testosterone level was assayed by mass spectrometry. A sleep questionnaire was administered to enquire about their reported sleep duration, prolonged sleep latency (>0.5 hour), and subjective insomnia complaint. Muscle mass was measured by dual-energy x-ray absorptiometry. Testosterone level, muscle mass, handgrip strength, and walking speed were tested against sleep duration and disturbances.
Results: Testosterone increased with increasing sleep duration up to 9.9 hours, after which it decreased, giving rise to an inverted U-shaped relationship (P for quadratic trend <.05). A similar inverted U-shaped relationship occurred between sleep duration and muscle mass and function. Earlier go-to-bed time, despite being associated with a higher testosterone level ($P < .05$), was associated with weaker grip strength ($P < .05$). Earlier wake-up time was associated with higher muscle mass ($P < .05$) but neither grip strength nor walking speed. Neither prolonged sleep latency nor insomnia was associated with testosterone levels. However, prolonged sleep latency was associated with lower muscle mass ($P < .05$), weaker grip strength ($P < .05$), and slower walking speed ($P < .001$). Insomnia, on the other hand was associated with weaker grip strength ($P < .05$) and slower walking speed ($P < .001$) but not muscle mass.
Conclusions: Sleep duration and disturbances can affect testosterone level, muscle mass, and its function. Whether optimization of sleep can ameliorate age-associated decline in sex hormone and muscle performance warrants further studies.

Sleep time constitutes one-third of the life span in human beings. Though sleep appears to be a passive resting process, it adopts, on the contrary, an active restorative function in regulating the central nervous system[1] and other systems as well, including the endocrine system. Testosterone level follows a circadian rhythm, which troughs in late evening (8 PM) and starts to ascend during sleep and peaks in the morning (8 AM).[2,3] However, it has also been discovered that its elevation could be associated with sleeping rather than the timing of sleep. Testosterone rose even in day time sleep and remained low in the awakening night time.[4] Therefore, sleep might be one of the major determinants of testosterone production or secretion.

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Sleep disturbances are common in old age.[5,6] Moreover, older men who slept 6 to 8 hours or more had the highest level of testosterone.[7] On the other hand, testosterone is highly associated with muscle mass and muscle strength, which is an essential determinant of physical function in old age.[8–11] Therefore, it will be important to explore if sleep can affect testosterone level and muscle performance in older men. Furthermore, prolonged sleep latency, insomnia, and advance phase shift (earlier going to bed and waking up) also commonly occur in old age.[12] It is uncertain how these sleep disturbances, in addition to duration, can affect testosterone level, muscle mass, and muscle performance.

We, therefore, hypothesized that sleep could affect testosterone and attempted to examine whether sleep duration and sleep disturbances were associated with testosterone level, muscle mass, grip strength, and walking speed in a group of men older than 65 years of age.

Methods

Participants

The participants were recruited from the Osteoporotic Fractures in Men Hong Kong cohort, which forms part of the study of Osteoporotic Fractures in Men[13] together with participants from the US and Sweden. Two thousand community-dwelling men aged 65 years or older were recruited for a primary project examining the bone mineral density of older Chinese adults. Written informed consents were obtained. Only ethnical Chinese participants were recruited. We excluded those who (1) were unable to walk without assistance of another person; (2) had had a bilateral hip replacement because that would have affected the bone mineral density measurement; (3) were not competent to give informed consent; and (4) had medical conditions, in the judgment of the study physicians, which made it unlikely that they would survive the duration of the study (3 years). The sample was stratified so that approximately 33% were in each of the age groups: 65–69, 70–74, and 75 years and older. The study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong.

Sleep Questionnaire

The present sleep study was conducted during the second year follow-up of the parent osteoporosis study. Participants who turned up for the second year follow-up assessment of their bone mineral density were invited to participate. A sleep questionnaire[14,15] was administered to record the participants' go-to-bed time, wake-up time, self-report nocturnal sleep duration, prolonged sleep latency (more than 0.5 hours), and subjective insomnia complaint. Information of demographics and psychotropic medication usage were collected. Each participant was additionally tested by the Mini-Mental State Examination (MMSE)[16] and Geriatric Depression Scale[17] according to the original osteoporosis study protocol.[18]

Testosterone Assay

Fasting venous sampling from 8 AM to 9 AM hours was taken for assay of sex steroid hormones. Serum was stored at −80°C and then transported in dry ice (−78.5°C) by courier service to Quebec, Canada, for assay. A validated gas chromatography mass spectroscopy system[19,20] was used for analysis of sex steroids at the CHUL Medical Research Center, Quebec, Canada: testosterone (limit of detection, 0.05 ng/mL; intra-assay coefficient of variation (CV), 2.9%; inter-assay CV, 3.4%) and estradiol (E2) (limit of detection, 2.00 pg/mL; intra-assay CV, 1.5%; inter-assay CV, 2.7%). A 50% phenyl-methyl polysiloxane (DB-17HT) capillary column (30 m × 0.25 mm internal diameter; 0.15–1.0 mm film thickness) with helium as carrier gas was used. The analytes and the internal standard were detected using a HP5973 quadrupole mass spectrometer equipped with a chemical ionization source. Serum sex hormone binding globulin was measured using IRMA (Orion Diagnostics, Espoo, Finland; limit of detection 1.3 nmol/L, intra-assay CV, 3%; inter-assay CV, 7%). Free fractions of testosterone were calculated as described by Van den Beld et al,[8] taking the concentration of total testosterone (TT), total E2, and serum sex hormone binding globulin into account, and assuming a fixed albumin concentration of 43 g/L.

Muscle Mass Measurement

We measured body muscle mass by dual-energy x-ray absorptiometry (DXA) using a Hologic QDR 2000 densitometer (Hologic Delphi, software v 11.2; Hologic, Waltham, WA). In separating the appendicular muscle mass (ASM), a line of delineation was drawn between the head of the humerus and the glenoid fossa of the scapula to separate the upper limb from the trunk, and the leg consisted of the parts of the body between the inferior border of the ischial tuberosity to the most distal tip of the toes. Appendicular skeletal mass (ASM) was calculated by the summation of muscle mass measured in the 4 limbs, with the operator adjusting the cut lines of the limbs according to specific anatomical landmarks as described by Heymsfield et al.[21] The maximum coefficient of variation for muscle mass is 0.84%. Calibration with a Hologic body composition step phantom was performed at least 3 times per week. The participants were asked to stand upright without shoes and look straight ahead with standing heights measured by the Holtain Harpenden Stadiometer (Holtain Ltd, Crosswell, UK). Muscle mass was corrected for body size by dividing the ASM with the square of height[22,23] and was termed relative ASM.

Grip Strength and Walking Speed

Grip strength was measured using a dynamometer (JAMAR hand dynamometer 5030JI; Sammons Preston, Bolingbrook, IL) twice on each hand. The maximum of the 4 readings was used for analysis. The participant was instructed to walk in normal pace along a path of 6 m. It was repeated and the faster of the 2 speeds was taken for analysis.

Statistical Methods

Sleep duration were divided into 7 categories (<5 hours, 5–5.9 hours, 6–6.9 hours, 7–7.9 hours, 8–8.9 hours, 9–9.9 hours, and ≥10 hours). Testosterone level, namely TT, bio-available testosterone, and free testosterone, relative ASM, grip strength and walking speed, which were treated as dependent variables, were plotted against the 7 categories of sleep duration. Univariate analysis was undertaken to search for the trend of each dependent variable across the 7 categories of sleep duration, using P for trend method and P for quadratic method. Further multivariate analysis was then repeated with adjustment for age, body mass index, depression (GDS > 7), psychotropic drugs usage, and MMSE score. To search for the effect of sleep independent of testosterone on muscle mass and physical function, TT was added as a covariate into a multivariate model in analyzing the relationship of sleep duration to muscle mass, grip strength, and walking speed, respectively. In analyzing sleep-wake cycle shift, got-to-bed time and wake-up time were treated as continuous independent variables. Their associations with testosterone, muscle mass, and physical function were analyzed in the same manner as that of sleep duration. In addressing the effect of sleep disturbances on testosterone levels, muscle mass and physical